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Neurobiology of the structure of personality: Dopamine, facilitation of incentive motivation, and extraversion

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Abstract: Extraversion has two central characteristics: (1) *interpersonal engagement,* which consists of affiliation (enjoying and valuing close interpersonal bonds, being warm and affectionate) and agency (being socially dominant, enjoying leadership roles, being assertive, being exhibitionistic, and having a sense of potency in accomplishing goals) and (2) *impulsivity,* which emerges from the interaction of extraversion and a second, independent trait (constraint). Agency is a more general motivational disposition that includes dominance, ambition, mastery, efficacy, and achievement. Positive affect (a combination of positive feelings and motivation) is closely associated with extraversion. Extraversion is accordingly based on *positive incentive motivation.*

Parallels between extraversion (particularly its agency component) and a mammalian behavioral approach system based on positive incentive motivation implicate a neuroanatomical network and modulatory neurotransmitters in the processing of incentive motivation. A corticolimbic-striatal-thalamic network (1) integrates the salient incentive context in the medial orbital cortex, amygdala, and hippocampus; (2) encodes the intensity of incentive stimuli in a motive circuit composed of the nucleus accumbens, ventral pallidum, and ventral tegmental area dopamine projection system; and (3) creates an incentive motivational state that can be transmitted to the motor system.

Individual differences in the functioning of this network arise from functional variation in the ventral tegmental area dopamine projections, which are directly involved in coding the intensity of incentive motivation. The animal evidence suggests that there are three neurodevelopmental sources of individual differences in dopamine: genetic, "experience-expectant," and "experience-dependent." Individual differences in dopamine promote variation in the heterosynaptic plasticity that enhances the connection between incentive context and incentive motivation and behavior.

Our psychobiological threshold model explains the effects of individual differences in dopamine transmission on behavior, and their relation to personality traits is discussed.

Keywords: behavioral sensitization; dopamine; extraversion; heterosynaptic plasticity; incentive motivation; neurobiology; personality

1. Introduction

Twenty-five years ago, Gray (1973) revolutionized thinking about the nature of personality traits. He argued that they reflect motivational systems that evolved to increase adaptation to classes of stimuli associated with positive and negative reinforcement. Individual differences in personality thereby reflect variation in the sensitivity to such stimuli, and overall personality represents the relative strength of sensitivities to various stimulus classes. For example, impulsive people can be described as more sensitive to reward than to punishment, approaching rewarding situations even when punishers make restraint more appropriate. Sensitivity ultimately means reactivity of the neurobiology associated with a motivational system. Gray (1973; 1992) accordingly outlined neurobehavioral models of several traits and others have extended Gray's work (e.g., Cloninger et al. 1993; Netter et al. 1996; Zuckerman 1991b). Nevertheless, a comprehensive neurobehavioral model of a personality trait has yet to be proposed. Such a model must specify at least five points: (1) the behavioral and emotional characteristics of a trait, particularly those that are central to its definition, (2) the motivation inferred to underlie those central characteristics, (3) the network of brain structures that integrates the motivation, (4) the neurobiological variables that account for individual differences in the functioning of the network, and (5) the sources of those individual differences. This target article specifies all five points in a model of one personality trait – extraversion – and evaluates the human evidence related to the model.

In developing the model, we followed the strategy outlined in Figure 1. Personality psychology was used to define

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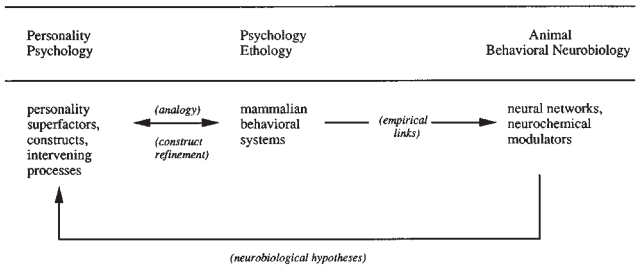


Figure 1. A modeling strategy for deriving neurobiological hypotheses about higher-order traits of personality. See text for details.

the behavioral, emotional, and motivational characteristics of extraversion. Next, we identified a mammalian behavior pattern with corresponding characteristics, as described in the psychological and ethological literatures. Once an analogous motivation was identified, animal neurobiological research provided empirical links to its neural organization and neurochemical modulation. These hypotheses were then extended to humans and subjected to empirical tests.

2. Extraversion: Central characteristics and underlying motivation

Extraversion is a higher-order trait that is derived from a set of correlated lower-order traits. The lower-order traits are measures of behavioral and emotional characteristics – such as social dominance, positive emotional feelings, sociability, achievement, and motor activity – that together comprise a more general behavior pattern referred to as extraversion. No common understanding of the neurobehavioral process underlying extraversion exists. Trait psychologists have emphasized different subsets of lower-order characteristics depending on their concept of extraversion. Watson and Clark (1997) summarized the literature on these characteristics; we have integrated their analysis into Table 1, although our conceptual conclusions differ from theirs. The characteristics are listed across the top row of Table 1, and an "x" indicates which characteristics were cited by the specific psychologist listed in the left column.

Variation in emphasis on the characteristics of extraversion has resulted in the use of terms other than *extraversion* for the higher-order trait (e.g., Costa & McCrae 1992; Eysenck & Eysenck 1985; Gray 1973; 1987), including *social activity* or *sociability* (Buss & Plomin 1984; Guilford et al. 1976; Zuckerman 1994a; Zuckerman et al. 1988; 1991), *surgency* (Goldberg 1990), *novelty seeking* (Cloninger et al. 1991; 1993), and *positive emotionality* (Tellegen 1985; Tellegen & Waller 1997). Despite this terminological variation, a higher-order trait resembling extraversion is identified in virtually every taxonomy of personality (Buss & Plomin 1984; Cattell et al. 1980; Cloninger et al. 1993; Comrey 1970; Costa & McCrae 1985; 1992; Digman 1990; Eysenck & Eysenck 1975; 1985; Goldberg 1981; Guilford & Zimmerman 1949; Jackson 1984; Tellegen & Waller 1996; Zuckerman et al. 1991), and in many psychometric tests of psychopathology (Gough 1987; Hathaway & McKinley 1943). Because of the long history of the term *extraversion*, first introduced by Jung (1921) to describe variation in orientation toward the world, and because the term already has recognized meaning to trait psychologists, we adopt it here.

Two of the characteristics in Table 1 are most frequently cited as central to extraversion, though they are differentially weighted by trait psychologists: interpersonal engagement and impulsivity. We analyze these two characteristics for the purpose of defining the type of motivation underlying extraversion, which we propose is incentive motivation. Extraversion must be clarified in this way as a prelude to identifying an analogous motivation and its neurobiology in animals.

2.1. The interpersonal engagement characteristic of extraversion

Every trait psychologist except Guilford and Cloninger has identified interpersonal engagement as one of the central characteristics of extraversion. Even Guilford identified a higher-order trait termed *social activity* (composed of sociability, ascendance-dominance, and activity-energy), but he believed that extraverted behavior was more closely related to the distinct, higher-order trait of impulsivity (rhathymia); see Guilford and Zimmerman 1949. As shown in Table 1, interpersonal engagement is not a unitary characteristic, but rather has two components. One component, *sociability* or *affiliation*, reflects enjoying and valuing close interpersonal bonds and being warm and affectionate; the other component, *agency*, reflects social dominance and the enjoyment of leadership roles, assertiveness, exhibitionism, and a subjective sense of potency in accomplishing goals. These two components are represented, respectively, in lower-order traits of extraversion, such as warmth-gregariousness versus assertiveness (Costa & McCrae 1992), social closeness versus social potency (Tellegen & Waller 1997), sociability versus ascendance-dominance (in social activity; Guilford & Zimmerman 1949), warmth (in agreeableness) versus assertion (insurgency; Goldberg & Rosolack 1994), warmhearted-socially enmeshed versus dominant-ascendant (Cattell et al. 1980), and sociability versus ambition (in surgency; Hogan 1983). These two components are also consistent with the two major traits identified in the theory of interpersonal behavior: warm-agreeable



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Table 1. *Characteristics of extraversion included in the theories or multidimensional personality questionnaires of trait psychologists*

	Characteristics of Extraversion[a]					
	Interpersonal Engagement					
Author[b]	Sociability/ Affiliation	Agency	Activation	Impulsivity-Sensation Seeking	Positive Emotions	Optimism
Buss & Plomin	X					
Cattell et al.	X	X		X	X	X
Cloninger et al.		X	X	X		
Costa & McCrae	X	X	X		X	X
Eysenck & Eysenck						
Early	X		X	X	X	
Later	X	X	X	?	X	
Goldberg & Rosolack	X	X	X		X	X
Guilford & Zimmerman				X		
Hogan	X	X				
Jackson	X	X		X		
Jung	X		X	X		
Tellegen	X	X	X		X	X
Zuckerman	X					

[a]Sociability/Affiliation: agreeableness, affiliation, social recognition, gregariousness, warmth, social closeness; Agency: surgency, assertion, endurance, persistence, achievement, social dominance, exhibitionism, ascendancy, ambitious; Activation: lively, talkativeness, energy level, activity level, active; Impulsivity-Sensation Seeking: impulsivity, sensation seeking, excitement seeking, novelty seeking, bold, risk taking, unreliable, unorderly, adventurous, thrill and adventure seeking, monotony avoidance, boredom susceptibility; Positive Emotions: positive emotions, positive affect, elated, enthusiastic, exuberant, cheerful, merry, jovial; Optimism: optimistic.
[b]Buss & Plomin (1984); Cattell et al. (1980); Cloninger et al. (1991, 1993); Costa & McCrae (1985, 1992); Eysenck early (Eysenck & Eysenck 1975); Eysenck later (Eysenck & Eysenck 1985); Goldberg & Rosolack (1994); Guilford & Zimmerman (1949); Hogan (1983); Jackson (1984); Jung (1921); Tellegen (1982, 1985; Tellegen & Waller, 1997); Zuckerman (1994); Zuckerman et al. (1988, 1991).

versus assured-dominant (Wiggins 1991; Wiggins et al. 1988). These traits form the two major orthogonal dimensions in Figure 2, and they are accompanied by two additional dimensions identified by Wiggins that further characterize interpersonal behavior (gregarious-extraverted versus aloof; arrogant versus unassuming). Within this multidimensional structure (referred to as a circumplex), all interpersonal behavior can be represented as a combination of the two major traits.

Several trait psychologists have proposed that affiliation and agency extend beyond interpersonal behavior and represent distinct dispositions that emerge as two separate lower-order traits of extraversion (Hogan 1983; Tellegen & Waller 1997). Although affiliation is clearly interpersonal in nature, agency represents a more general disposition encompassing dominance, ambition, mastery, efficacy, and achievement. The nature of this disposition is reflected in trait terms such as agency (Wiggins 1991; Wiggins et al. 1988), social dominance (Cattell et al. 1980; Costa & McCrae 1992; Guilford & Zimmerman 1949; Tellegen 1982), ambition (Watson & Clark 1996), surgency (Goldberg & Rosolack 1994; Hogan 1983), achievement (Tellegen & Waller 1997), and ascendancy (Cattell et al. 1980; Guilford & Zimmerman 1949). Thus, agency is a disposition that is manifest in a range of achievement-related as well as interpersonal contexts.

Church and Burke (1994) supported a two-component structure of extraversion by demonstrating that the lower-order traits of extraversion measured by Costa and McCrae's (1992) questionnaire factored into agency (assertiveness, activity) and affiliation (warmth, positive emotions, agreeableness). Furthermore, when general affiliation and agency traits were derived in joint factor analyses of several multidimensional personality questionnaires (Cattell et al. 1980; Jackson 1984; Tellegen 1982), the lower-order trait of achievement loaded strongly (0.71) on agency but weakly (−0.08) on affiliation, whereas lower-order traits related to affiliation showed a strong reverse pattern (Tellegen & Waller 1997).

Several studies found a similar pattern in joint factor analyses of multidimensional personality questionnaires (Church 1994; Costa & McCrae 1989; Tellegen & Waller 1997); two general traits were identified in each case as affiliation and agency. This made it possible to plot the loadings of lower-order traits from several studies in relation to the general agency and affiliation traits (see Appendix A). When trait loadings are plotted from different studies, the interrelations among traits will be only approximations in a quantitative sense, but the pattern with respect to the general affiliation and agency traits is instructive. For purposes of comparison, the lower-order traits are plotted within the interpersonal trait structure of Wiggins in Figure 2. Lower-order traits of achievement, persistence, social dominance, and activity all load much more strongly on agency than on affiliation, whereas traits of sociability and agreeableness show a reverse pattern. Lower-order traits of well being and positive emotions are associated with both agency and affiliation approximately equally.

2.2. Clarifying the motivational nature of extraversion

Results described so far raise the possibility that the lower-order traits associated with the agency factor (i.e., social dominance, achievement, endurance, efficacy, activity, en-

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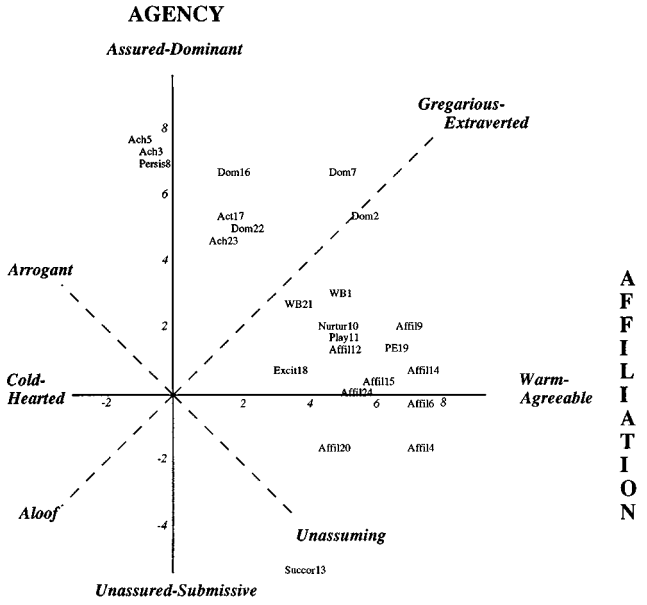


Figure 2. A structure of interpersonal behavior composed of four adjective-labeled dimensions, with the two predominant orthogonal dimensions labeled Agency and Affiliation. The figure illustrates that the interpersonal engagement characteristic of extraversion is composed of two different dispositions of affiliation and agency. Within the structure, lower-order traits representing either agency or affiliation components of extraversion are plotted according to their loadings on general Agency and Affiliation traits derived in several studies. See Appendix A for the identity of the abbreviations of trait measures (shown with numbers), the questionnaires to which the abbreviations correspond, and the studies providing the trait loadings.

ergy) represent different manifestations of a single underlying process. All of these traits suggest a form of behavior that is activated or motivated to achieve goals, including both social (e.g., social dominance) and work-related (e.g., achievement) goals. Several trait psychologists include activation as either a specific component of extraversion or one that is moderately correlated with it (see Table 1), as reflected in the traits of activity (Buss & Plomin 1984; Costa & McCrae 1992; Eysenck & Eysenck 1985; Zuckerman et al. 1991), energy and talkativeness (Goldberg & Rosolack 1994), and liveliness (Eysenck & Eysenck 1985).

It would be incorrect to assume that the activation accompanying extraversion is only a nonspecific form of arousal (although such arousal may be a part of extraversion; Fowles 1980). Tellegen and associates argue convincingly that the type of activation linked with extraversion is positive affect, wherein affect refers to a joint experience of emotional feelings and motivation (Tellegen 1985; Tellegen et al. 1988; Tellegen & Waller 1997). Tellegen's (1982) higher-order trait of extraversion includes the lower-order trait of well being, which reflects the extent to which an individual generally feels positive affect. Positive affect has also been associated with extraversion in studies by Costa and McCrae (1980; 1984), who later included it as a lower-order trait of extraversion in their personality questionnaire (Costa & McCrae 1985; 1992). Positive affect is also incorporated in extraversion in the questionnaires of Cattell et al. (1980) and Goldberg and Rosolack (1994), and is part of Eysenck and Eysenck's (1975) early description of extraversion (cheerful, optimistic, and enthusiastic). When various measures of positive affect were factor analyzed jointly with several multidimensional personality questionnaires (Watson & Clark 1997), positive affect loaded as highly and specifically on a general extraversion trait as traits of social activity (Guilford & Zimmerman 1949), surgency (Goldberg & Rosolack 1994), and extraversion (Eysenck & Eysenck 1985). This is consistent with reports of strong, specific correlations between measures of positive affect and extraversion (e.g., 0.66 with Eysenck's extraversion and 0.61 with Goldberg's surgency trait; Watson & Clark 1997). Moreover, Watson and Clark (1997) have shown in two independent samples that, consistent with previous studies (Hogan 1983; Wiggins 1979; 1982; Wiggins et al. 1988), independent measures of positive affect correlate more strongly with both agency and affiliation components of extraversion (both 0.42) than agency and affiliation correlate with each other (0.14).

In contrast to an individual's typical level of positive affect, which represents *trait* measurement, it is also possible to measure current level of self-reported mood, which represents *state* measurement. Watson and Tellegen's (1985) integration of the literature on the structure of state mood indicates that it is composed of two orthogonal affective dimensions, positive and negative affects. In agreement with the results on trait-positive affect, the subjective experience of state positive affect is a combination of positive emotional feelings and motivation, which is reflected by the adjectives most strongly associated with a state of high positive affect (e.g., elated, enthusiastic, excited, peppy, strong, energetic, active). This suggests that both trait- and state-positive affects reflect the same motivation, which facilitates pleasurable engagement with the environment (Watson & Tellegen 1985). Indeed, the mean level of state-positive affect, based on 90 days of current mood ratings, is specifically and significantly correlated with trait measures of positive affect (0.65–0.67, Watson & Clark 1997; Zevon & Tellegen 1982) and is moderately related to extraversion itself (0.20–0.50; Costa & McCrae 1980; 1984; Emmons & Diener 1985; 1986; Tellegen 1985; Warr et al. 1983; Watson & Clark 1984; 1997).

Our interpretation of this pattern of evidence is that extraversion is closely associated with strong positive affect, which in turn reflects an underlying motivational system. This interpretation is grounded in Gray's (1973; 1987; 1992) proposal that higher-order traits of personality are based on underlying motivational systems, with extraversion arising from what Gray (1973; 1992) and Fowles (1980; 1987) call the *behavioral activation or approach system.* The latter is a motivational system activated by signals of reward. Extraversion can accordingly be interpreted as sensitivity to signals of reward, as supported by the work of Newman and colleagues (Newman 1987; Newman et al. 1985; Wallace & Newman 1990) and Ball and Zuckerman (1990). In the animal neurobehavioral literature, signals of reward are called *positive incentive stimuli,* and the motivation activated by those stimuli is called *positive incentive motivation.* Therefore, our concept of extraversion is based on incentive motivation rather than on a nonspecific behavioral activation system.

Incentive motivational theory is meant to explain how goal-directed behavior is elicited and guided by incentive stimuli (or their central representations) in interaction with central drive states (Bindra 1978; Panksepp 1986a;

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Toates 1986). Although incentive motivation may be either positive or aversive, only the former is relevant to extraversion. Robinson and Berridge (1993) suggest that positive incentive motivation involves three distinct processes that typically co-occur. First, engagement with unconditioned positive incentive stimuli activates the neural substrates for pleasure, which normally serves as a trigger for the following two processes. Second, through classical associative learning, the experience of pleasure is associated with the neutral stimulus context (e.g., objects, acts, events, places) in which pleasure occurred. The previously neutral stimuli thereby become conditioned incentive stimuli, which upon reoccurring have the capacity to elicit anticipatory pleasure and incentive motivation. Because of the predominance of symbolic (conditioned) processes in guiding human behavior in the absence of unconditioned stimuli, conditioned incentives are particularly important elicitors of a positive incentive motivational disposition (Fowles 1987; Gray 1973).

The third process encodes incentive stimuli (or their central representation) for their intensity or salience, thereby attributing a motivational value to the stimuli. In this way, the incentive motivational influence on emotional and behavioral responses is scaled. Subsequent exposure to the incentive stimuli (or activation of their central representation) elicits an incentive motivational state that facilitates and guides approach behavior to a goal. In humans, incentive motivational states are associated with strong positive affect characterized by feelings of desire, wanting, excitement, enthusiasm, energy, potency, and self-efficacy. These feelings are distinct from, but typically co-occur with, feelings of pleasure and liking (MacLean 1986; Robinson & Berridge 1993; Watson & Tellegen 1985). We propose that variation in this process of encoding incentive salience is the basis of individual differences in the frequency and intensity of incentive motivation and, by extension, is the main source of individual differences in extraversion.

2.3. The impulsivity characteristic of extraversion

The association of impulsivity with extraversion remains an unresolved issue. Impulsivity comprises a heterogeneous cluster of lower-order traits that includes terms such as *impulsivity, sensation seeking, risk taking, novelty seeking, boldness, adventuresomeness, boredom susceptibility, unreliability,* and *unorderliness.* On the basis of Jung's concept of extraversion, Eysenck and Eysenck (1975) included impulsivity in their measure of extraversion, only to remove much of it later because evidence indicated that impulsivity and extraversion were separate traits (Guilford 1975; 1977; Rocklin & Revelle 1981). Currently, most trait models of personality also separate impulsivity and extraversion into distinct traits (Costa & McCrae 1985; 1992; Goldberg & Rosolack 1994; Tellegen 1982; 1985; Tellegen & Waller 1997; Zuckerman 1994a; Zuckerman et al. 1991).

However, several trait psychologists continue to associate impulsivity and extraversion. Gray (1973; 1987; 1992) proposed that impulsivity represents the interaction of the higher-order traits of extraversion, neuroticism and psychoticism. Eysenck (Eysenck 1981; Eysenck & Eysenck 1985) defined nine lower-order traits of extraversion that include sensation seeking, venturesomeness, carefreeness, and liveliness, whereas impulsivity itself is included in the higher-order trait of psychoticism. Similarly, Cloninger's personality questionnaire replaces extraversion with a higher-order trait of novelty seeking, which, according to several lines of evidence, is aligned much more closely with impulsivity and sensation seeking than with extraversion (Cloninger et al. 1991; 1993; Heath et al. 1994; Stallings et al. 1996; Waller et al. 1991; Zuckerman et al. 1991; Zuckerman, personal communication).

This issue is complex, because the content of the measures of impulsivity is heterogeneous, ranging from purely motor and cognitive impulsivity to novelty and sensation seeking, boldness, thrill and adventure seeking, and risk-taking. Not all of these measures are highly interrelated, nor are they consistent in their correlation with extraversion (see below). Furthermore, some measures of impulsivity lack affective content (e.g., conscientiousness, Costa & McCrae 1992; Goldberg & Rosolack 1994, and constraint, Tellegen & Waller 1997), and these measures in particular are not, or are only weakly, related to extraversion. In contrast, other measures of impulsivity have positive affective content (e.g., novelty seeking, Cloninger et al. 1993, several sensation seeking measures, Zuckerman 1994a, and venturesomeness, boldness, and risk-taking measures in several questionnaires). To illustrate this point (Fig. 3), we plotted the trait loadings derived in 11 studies (see Appendix B) in which two or more multidimensional personality questionnaires were jointly factor analyzed in order to derive general, higher-order traits of personality. All studies identified a higher-order trait of impulsivity that lacks affective content, which in Figure 3 is labeled *constraint* following Tellegen (1982; 1985; Tellegen & Waller 1997), who introduced the term to emphasize its independence from affective traits such as extraversion and neuroticism. All studies also found constraint to be orthogonal to a general, higher-order extraversion trait.

Figure 3 shows a continuous distribution of traits within the two intersecting orthogonal dimensions of extraversion and constraint. Nevertheless, three relatively homogeneous clusterings of traits can be delineated on the basis of the position and content of traits, relative to extraversion and constraint. First, lower-order traits associated with extraversion (i.e., sociability, dominance, achievement, positive emotions, activity, energy) or extraversion itself cluster at the high end of the extraversion dimension without substantial association with constraint. A tight clustering of most traits to extraversion is evident, although several lower-order traits of extraversion are "pulled" toward the high end of constraint in a few studies, which may be due to differences in definitions of trait content or in measurement. Second, various traits of impulsivity that do not incorporate strong positive affect (e.g., conscientiousness) cluster tightly around the high end of the constraint dimension without substantial association with extraversion; Eysenck's psychoticism trait and various aggression measures are located at the low end of constraint and show little association with extraversion. The anchoring of the two extreme ends of constraint by conscientiousness and psychoticism also was observed by Zuckerman (1991). Third, all but one trait measure of impulsivity that incorporates positive affect (i.e., sensation seeking, novelty seeking, risk-taking) are located within the dashed lines in Figure 3 and are moderately associated with both extraversion and constraint.

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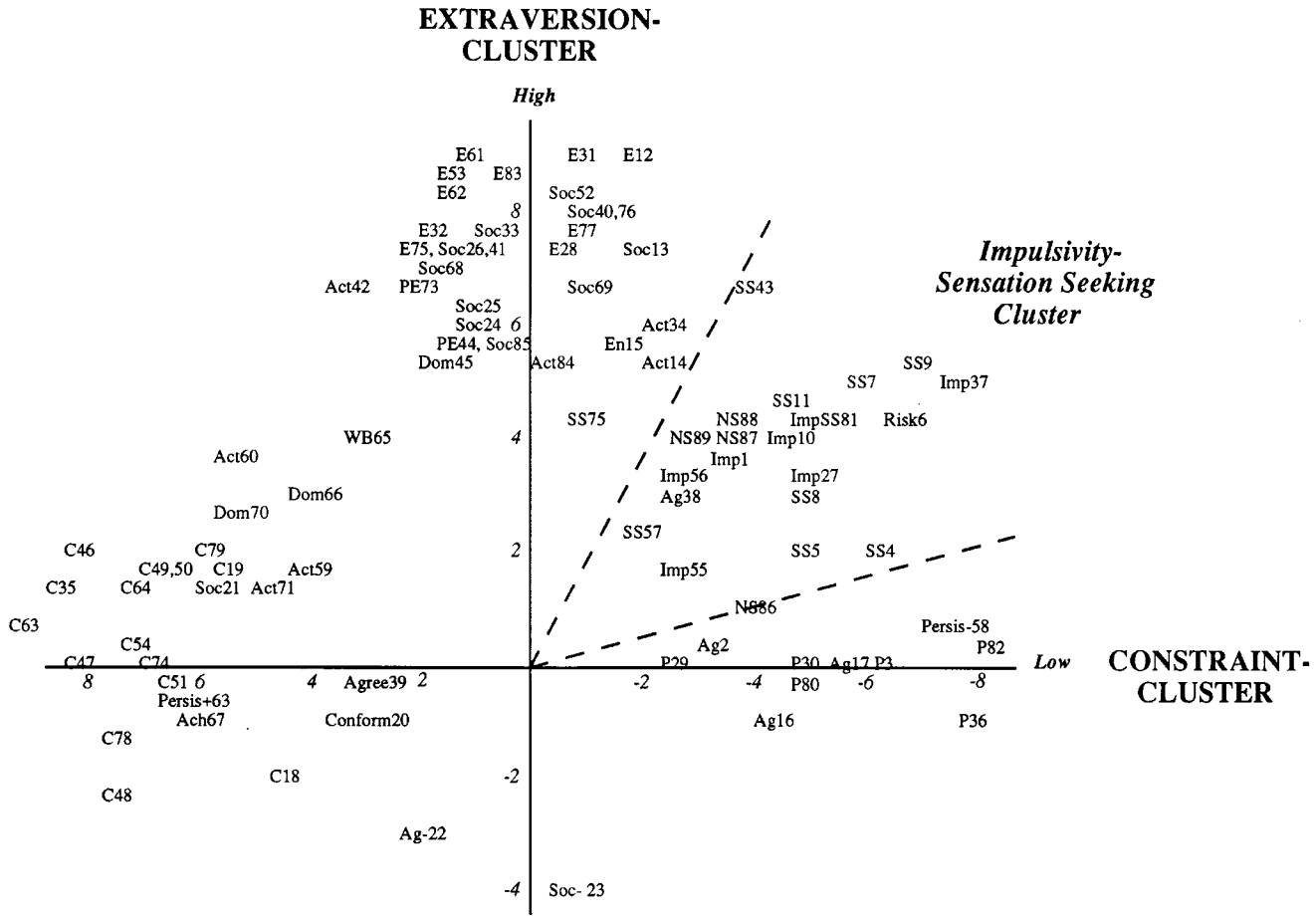


Figure 3. A plotting of loadings of personality traits derived from 11 studies in which more than one multidimensional personality questionnaire was jointly factor analyzed as a means of deriving general traits of personality. All of these studies defined a general nonaffective impulsivity trait, referred to as constraint (horizontal dimension in the figure), that was separate from the general extraversion trait (vertical dimension in the figure). The figure illustrates three clusterings of traits: an extraversion cluster at the high end of the extraversion dimension; conscientiousness and psychoticism-aggression clusters at the high and low ends of the constraint dimension, respectively; and an impulsivity-sensation seeking cluster within the dashed lines. The figure illustrates that extraversion and *nona*ffective constraint dimensions are generally identified and found to be orthogonal and that impulsivity-sensation seeking traits associated with strong positive affect arise as a joint function of the interaction of extraversion and constraint. See Appendix B for the identity of the trait measure abbreviations with numbers, the questionnaires to which the abbreviations correspond, and the studies providing the trait loadings.

2.4. Lines of causal neurobiological influence in the structure of personality

Although the clustering of traits in Figure 3 is instructive with respect to the structure of personality, Gray's (1973; 1987; 1992) challenge concerning where the lines of causal influence lie within that structure remains cogent. Both Cloninger (1986; 1987; Cloninger et al. 1991) and Zuckerman (1991) have argued that a major line of neurobiological influence lies with the cluster of impulsivity and sensation seeking traits rather than along the extraversion dimension. Similarly, Gray (1973; 1987; 1992) proposed that impulsivity rather than extraversion is associated with a line of causal influence. His impulsivity trait would lie with the impulsivity cluster in Figure 3 if (1) neuroticism (defined as an overall amplifier of emotion) is aligned with the constraint dimension in Figure 3, (2) high psychoticism is positioned at the low end of the constraint dimension (as occurs in Fig. 3), and (3) extraversion is interpreted as the relative sensitivity to signals of reward versus punishment.

At the level of behavior, we also suggest that impulsivity arises from an interaction of traits, but specifically between extraversion and constraint as in Figure 3. We differ from others in our interpretation of the nature of this interaction. Extraversion, when interpreted as reflecting incentive motivation, consists of positive affect and action-readiness; therefore, high levels of extraversion can be associated with action-proneness that shades toward impulsivity under conditions of strong positive affect. This behavioral disposition interacts with constraint. For us, constraint lacks ties to a specific motivational system, which is supported by the traits that cluster around the constraint dimension in Figure 3. We suggest that constraint functions as a threshold variable that modulates stimulus elicitation of motor behavior, both positive and negative affects, and cognition, all of which may be associated with serotonin functioning (Depue 1995; 1996; Depue & Spoont 1986; Depue & Zald 1993) as was also proposed by others (Panksepp 1982; Soubrie 1986; Spoont 1992; Zuckerman 1991b). This formulation is consistent with findings that low constraint is as-

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sociated with both reduced serotonin functioning and with a generalized motor-cognitive-affective impulsivity, but not preferentially with any specific motivational system (Coccaro & Siever 1991; Depue 1995; 1996; Depue & Spoont 1986; Spoont 1992). Gray's (1973; 1987; 1992) theoretical treatment of neuroticism as a general amplifier of reactivity to both signals of reward and punishment, hence influencing the magnitude of both impulsivity and anxiety, is more consistent with our concept of constraint. Similarly, Eysenck and Eysenck's (1985) psychoticism trait and Zuckerman's (1989; 1991) impulsivity trait overlap our concept, whereas Cloninger's personality model does not include a trait analogous to constraint.

We are nevertheless in basic disagreement with the positions of Gray, Cloninger, and Zuckerman concerning the lines of causal neurobiological influence, which we propose lie along the two orthogonal dimensions of extraversion and constraint rather than along an impulsivity diagonal resulting from their interaction. The main reason for our disagreement is that we believe the impulsivity–sensation seeking traits in Figure 3 represent *emergent* traits that result from the interaction of extraversion, constraint, and possibly harm-avoidance in the case of sensation seeking (Depue 1995; 1996). If extraversion and constraint have coherent neurobiological influences, such an emergent trait would be expected to have heterogeneous neurobiological sources of influence. Accordingly, research attempting to detect a neurobiological variable strongly and specifically associated with that trait would likely produce weak and inconsistent results. For instance, in Gray's (1973; 1992) model, impulsivity emerges from two levels of complex interactions between the higher-order traits of extraversion and neuroticism. First, extraversion represents the interaction of the relative strength of sensitivities to two distinct classes of stimulus: signals of reward (more the extravert) and punishment (more the introvert). The model is affectively bipolar, with high and low extremes of extraversion being associated with different predominant affective states: positive or negative. Sensitivities to these two stimulus classes undoubtedly have distinct neurobiological foundations. Second, the intrinsically interactive trait of extraversion interacts with neuroticism, entailing the further influence of at least one more neurobiological variable, to form the emergent trait of impulsivity. At the level of behavior, it is plausible that impulsivity represents the interaction of several higher-order traits, even if those traits are based on distinct motivations. However, at the level of neurobiology we doubt that coherent lines of causal influence are associated with traits of such complexity.

We propose that causal neurobiological influence can be identified most clearly by dissecting higher-order traits into more homogeneous components (if they are initially heterogeneous). In the case of affective higher-order traits, more homogeneous components would reflect single motivational systems, which naturally are affectively unipolar. Positive incentive motivation, for instance, is associated with a unipolar dimension of positive affect that ranges from strong presence to complete absence at the extremes (Tellegen & Waller 1997; Watson & Tellegen 1985). We accordingly prefer to dissect extraversion into separate components of agency and affiliation because they are more likely to be associated with separable motivations and neurobiological influences (e.g., Di Chiara et al. 1992). Our model of extraversion, which focuses on the agency component, is based on a single neurobiological network that integrates incentive motivation. Consequently, we assume that individual differences in the neurobiology of the agency component of extraversion are *not* linked causally to the neurobiology associated with other higher-order traits. Theoretical arguments far exceed data in the debate over where to place the lines of causal influence within the relational structure of personality. Nevertheless, we believe that our theoretical position is important, because it directs the search in the animal literature to the neurobiological foundations of incentive motivation and ultimately of extraversion itself.

3. Analogous structure of personality traits and behavioral systems

As indicated in Figure 1, we wish to draw an analogy between extraversion and a mammalian behavioral system in order to derive their neurobiological basis. The analogy is illustrated in Figure 4 by framing both extraversion and the behavioral system in the same structure.

3.1. Personality trait structure

Higher-order personality traits can be modeled in the hierarchical structure shown in Figure 4A for extraversion. This structure illustrates the interrelations among the characteristics and underlying processes of extraversion discussed above. In the figure, each lower-order trait is associated with extraversion, because each trait reflects the influence of the same underlying processes (i.e., energy, incentive motivation, positive affect, cognition). Some of the lower-order traits, such as positive affect and activation, represent underlying processes directly, whereas others reflect their influence as manifested in different environmental contexts (e.g., competitive: social potency; long-term goal acquisition: achievement; and social: affiliation). We attribute to extraversion a central mechanism that provides a facilitatory modulation of all underlying processes. This modulatory influence binds the processes together and scales their intensity, leading to varying degrees of facilitation of behavioral approach. The final specific forms of behavior associated with different contexts (e.g., social, achievement-related) are manifested in the lower-order traits and are presumably mediated by specific behavioral systems (see below).

3.2. Behavioral system structure

From an evolutionary biology perspective, behavioral systems may be understood as behavior patterns that evolved to adapt to stimuli critical for survival and species preservation (Gray 1973; MacLean 1986; Panksepp 1986a; Schneirla 1959). Linkage of behavioral systems to critical stimulus conditions suggests that their neurobiology is integrated with brain networks responsible for both the recognition of stimulus significance and the activation of effector systems (e.g., locomotor, facial, vocal, autonomic, hormonal). Collectively, this group of interrelated brain functions is referred to as *emotion* (LeDoux 1987; 1996). Thus, behavioral systems are fundamentally emotional systems. This distinction is important because the word *emotion,* derived from the latin verb *emovere* (to move, to push), not only implies

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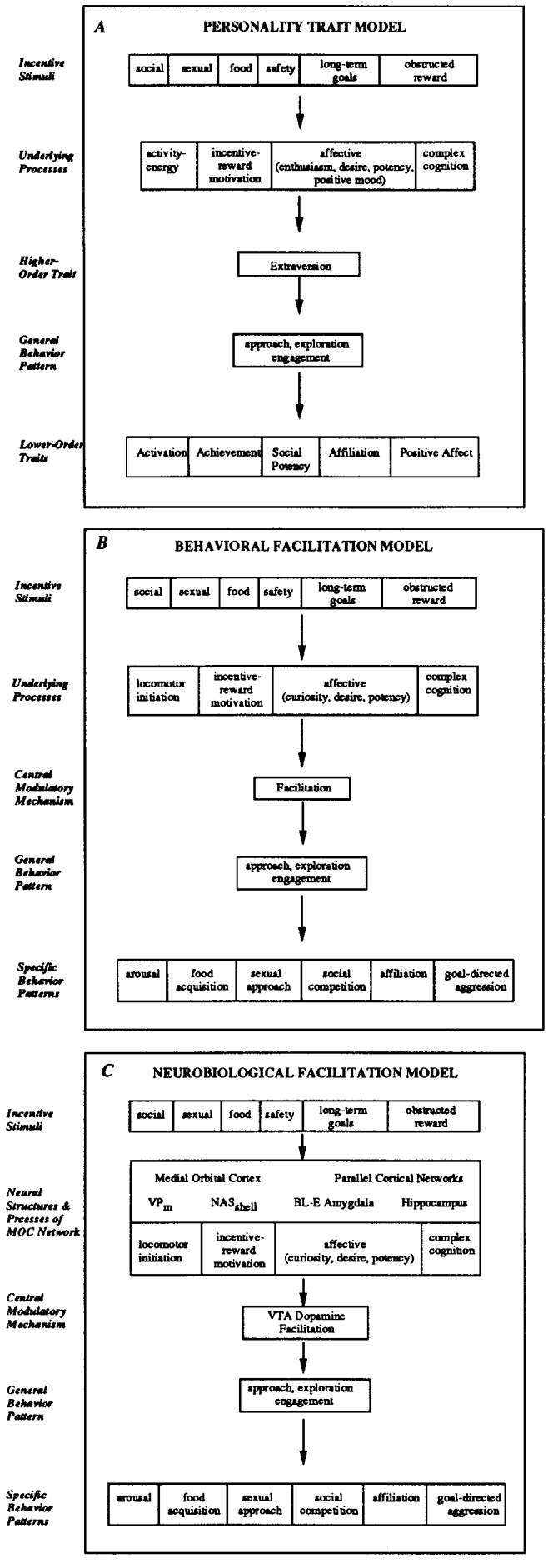


Figure 4. Path diagrams that represent three structural models: extraversion (A), behavioral facilitation (B), and neurobiological facilitation (C). In (A) and (B), extraversion and facilitation are proposed to correspond in that both are associated with a central modulatory mechanism that facilitates the general behavior pattern of approach and, subsequently, lower-order traits or specific behavior patterns, respectively. In (C), the neurobiological foundation of the facilitation mechanism is illustrated as the broadly projecting VTA dopamine neurons, which facilitate approach behavior and, subsequently, specific behavior patterns. Also in (C), the neurobiological structures that serve as regions of integration for the underlying processes illustrated in (A), (B), and (C) are defined. Furthermore, the existence of separable, parallel cortical networks that integrate complex cognitive processes that would guide incentive motivated behavior through the environment are indicated in part C. VTA = ventral tegmental area; VP_m = ventromedial subterritory of the ventral pallidum; NAS_{shell} = shell subterritory of the nucleus accumbens, a part of the ventral striatum; BL-E Amygdala = basolateral complex and extended amygdala. See the text for details on the functional interactions among the various levels of the path diagrams.

activation of behavior, but also a motivational state and emotional experience that is concordant with the reinforcement properties of critical stimuli (Gray 1973; Rolls 1986).

Behavioral systems vary along a dimension of increasing generality (Blackburn et al. 1989; Gray 1973; MacLean 1986; McNaughton 1989; Panksepp 1986a). At lower levels of the dimension, specific interoceptive and exteroceptive stimuli related to primary biological aims elicit behavior and emotions that are relatively specific to those conditions (e.g., sexual, social, food). At the highest level of the dimension, there are a limited number of general behavioral systems that are more flexible and have fewer immediate objectives and more variable topographies (Blackburn et al. 1989; MacLean 1986; McNaughton 1989). These systems are activated by broad classes of stimulus (Depue, in press a; Gray 1973; Rolls 1986) and regulate general emotional-behavioral dispositions, such as desire-approach or anxiety-inhibition, that modulate goal-directed activity. It is the relatively small number of general systems that directly influences the structure of mammalian behavior at higher-order levels of organization, because, like extraversion, their modulatory effects on behavior derive from frequent activation by broad stimulus classes.

There is one general behavioral system that is based on underlying processes and behaviors that correspond to extraversion. This system is activated by, and serves to bring an animal in contact with unconditioned and conditioned positive incentive stimuli (Beninger 1983; Depue, in press a; Gray 1973; Hebb 1949; Koob et al. 1993; Panksepp 1986a; Schneirla 1959; Stewart et al. 1984). As outlined by Gray (1973), incentive stimulus conditions also include signals of safety that may lead to termination of aversive stimuli (as in active avoidance of punishment) and signals of frustrative nonreward, where affective aggression may lead to removal of obstacles to reward. This system is consistently described in all animals across phylogeny (Hebb 1949; Schneirla 1959), but has been defined at two conceptual levels: (1) behavioral, as a search (MacLean 1986), foraging (Panksepp 1986a), and approach system (Gray 1973; Schneirla 1959); and (2) underlying process, as an incentive (Beninger 1983), expectancy (Panksepp 1986a), preparatory (Blackburn et al. 1989), and activation system (Fowles 1987; Gray 1973). We define this system as *behavioral approach based on incentive motivation.*

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To illustrate the correspondence with extraversion, we structured the behavioral system hierachically in Figure 4B. In the figure, approach behavior (the output) is jointly supported by several underlying processes (i.e., locomotor initiation, incentive motivation, positive affect, cognitive) that direct behavior to a rewarding goal. As in the structure of extraversion, a higher-order central mechanism is proposed that underlies the joint activation of these supporting processes. For reasons that will become clear in discussion of neurobiology below, this mechanism is termed *facilitation*, which corresponds to the modulatory mechanism embodied in extraversion in Figure 4A.

3.3. Conclusion

We propose that a common neurobiology exists at higher-order levels of personality and behavior (extraversion and facilitation in Fig. 4). Animal research demonstrates that behavioral facilitation is associated with the functional properties of the ventral tegmental area (VTA) dopamine (DA) projection system. Just as extraversion and facilitation emerge as higher-order constructs that incorporate a modulatory mechanism that operates across lower-order traits and supporting processes, the VTA DA projection system also might be considered a higher-order modulator of a neurobiological network that integrates behavioral functions associated with extraversion. If correct, the general form of this three-part parallelism suggests that the higher-order relational structure of personality may be associated with a few, not many, neuromodulator systems that have sufficiently widespread brain distributions to modulate the variety of supporting processes associated with higher-order traits.

In the following discussion, we define the neurobiology of behavioral facilitation. This neurobiology is extended to the essence of personality – individual differences – by assessing the role of DA in various personality traits, as well as in three neurodevelopmental processes that represent fundamental sources of individual differences in general. The effects of individual differences in DA functioning on behavioral facilitation are then organized within a psychobiological threshold model, which yields implications for conceptualizing individual differences in extraversion. We conclude by discussing other variables to be considered in a multifactorial neurobehavioral model of extraversion.

4. A neurobiological framework for behavioral facilitation

We suggest that both behavioral facilitation and extraversion are closely associated with incentive motivation. Therefore, DA's role in incentive motivation is critical to the proposal that the VTA DA projection system underlies both constructs. In this section, we review the relevant animal literature, and then place behavioral facilitation within a broader neuroanatomical network devoted to incentive modulation of goal-directed behavior.

4.1. A general functional role for VTA DA ascending projections

Because VTA and substantia nigra DA ascending projections innervate between 20 and 30 structures, it is unlikely that DA mediates any specific behavioral functions (Le Moal & Simon 1991; Oades & Halliday 1987). Instead, the functional effects of DA are largely dependent on the type of process integrated within terminal structures and their associated networks. Behavioral deficits resulting from DA inactivation can be reinstated, not just by DA agonists (Kelley & Stinus 1985), but also by changes in the internal environment (e.g., hunger) and by stress or strong emotional stimuli (Koob et al. 1993; Le Moal & Simon 1991; Oades 1985; Taghzouti et al. 1986). Additionally, selective DA lesions in various projection areas create behavioral deficits that are similar to deficits produced by electrolytic lesions of those same areas (Le Moal & Simon 1991; Louilot et al. 1987). Thus, behavioral processes seem intact but latent in the absence of DA.

Independent of brain region, DA has the general function of facilitating neural processes subserving goal-directed behavior (Bozarth 1987; Depue, in press a; Deutch et al. 1993; Fibiger & Phillips 1987; Le Moal & Simon 1991; Louilot et al. 1987; Oades 1985; Oades & Halliday 1987; Robbins & Everitt 1992). DA agonists or antagonists in the VTA or nucleus accumbens (NAS), which is a major terminal area of VTA DA projections, in rats and monkeys facilitate or markedly impair, respectively, locomotor activity to novelty and food; exploratory, aggressive, social, and sexual behaviors; the number of attempted behavioral strategies; acquisition and maintenance of approach and active avoidance behavior; response reversal; spontaneous alternation; food-hoarding; and maternal nursing behavior. These deficits are not motor per se because diurnal locomotor patterns remain unchanged, and animals can perform tasks normally once they are moved or pushed by the experimenter to do so (Oades 1985). These deficits are evident neither in nonvolitional motor behavior, such as escape, nor in consummatory behavior (Blackburn et al. 1989; Le Moal & Simon 1991). It is precisely incentive motivation that is lost, so that volitional behavior elicited by incentive stimuli cannot be initiated or facilitated (Beninger 1983; Bozarth 1987; Everitt & Robbins 1992; Koob et al. 1993; Le Moal & Simon 1991). We emphasize that DA *mediation* of incentive motivation is not proposed here; rather, DA is seen as providing a strong *modulatory* influence – facilitation – on incentive motivation. Put generally, incentive motivation is neurobiologically organized in regions of integration, whereas DA serves to neuromodulate those regions (Le Moal & Simon 1991; Mesulam 1990).

4.2. DA and incentive motivation

DA agonists injected in the NAS reduce, while both DA D_1 and D_2 antagonists increase, the threshold for electrical intracranial self-stimulation reward, a response model of incentive motivation (Bozarth 1987; Everitt & Robbins 1992; Fibiger & Phillips 1987; Knapp & Kornetsky 1994; Koob et al. 1993; Le Moal & Simon 1991; Mogenson et al. 1993). Increased DA metabolism during intracranial self-stimulation in the VTA is confined to structures of the ventral striatum, especially the NAS (Fibiger & Phillips 1987), and studies using both self-administration of electrical stimulation and of stimulant drugs revealed a converging activation of VTA mesolimbic DA pathways (Porrino 1987). Furthermore, dose-dependent DA D_1, D_2, and D_3 receptor activation in the VTA–NAS pathway facilitates the acute rewarding effects of stimulants, and the NAS is a particularly strong site for intracranial self-administration of DA and DA agonists (Hoebel et al. 1983; Le Moal & Simon 1991; Pich et al. 1997). D_1 and D_2 agonists injected in the NAS also modu-

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late behavioral responses to conditioned incentive stimuli in a dose-dependent fashion (Cador et al. 1991; Robbins et al. 1989; Wolterink et al. 1989). Conversely, decreases in DA metabolism induced by uncontrollable stress are associated with marked and long-lasting reductions in self-stimulation in the NAS and dorsal VTA, suggesting reduced incentive motivation (Anisman et al. 1993; Zacharko & Anisman 1991). Additionally, DA lesions (using 6-OHDA, with terminal field ablations of 95% or more) in the NAS or VTA create a reduction in motivation to work for reward, extinction-like responding, and long-lasting reductions in self-administration of stimulants (Caine & Koob 1993; Fibiger & Phillips 1987; Koob 1992; Koob et al. 1993; Phillips & Fibiger 1978; Pich et al. 1997; Robledo et al. 1992), whereas lesions of other DA terminal fields affect stimulant self-administration very little, if at all (Roberts & Zito 1987).

The initiation phase of locomotor activity is closely tied to incentive motivational input to the motor system. DA D_1 and D_2 agonists, particularly when injected in the NAS compared with the dorsal striatum, facilitate the initiation, speed, and vigor of locomotion (Clarke & White 1987; Fishman et al. 1983; Le Moal & Simon 1991; Oades 1985) and markedly increase the frequency and duration of spontaneous exploratory activity (Fink & Smith 1980). In inbred mouse strains, both the quantity of spontaneous exploratory locomotion and amphetamine-induced locomotion are both positively related to the number of VTA DA neurons, as well as to the relative density of innervation of DA terminals and to DA content in the NAS; accordingly, these behavioral effects may be related to the proportionately greater synthesis and release of DA in high DA neuron strains (Fink & Reiss 1981; Oades 1985; Sved et al. 1984; 1985). In contrast, VTA DA projections to the amygdala and olfactory tubercle do not significantly influence initiation of locomotor activity or stimulant self-administration, although projections to the ventral pallidum can be moderately facilitative (Oades 1985; Oades et al. 1986; Pich et al. 1997).

In single-unit recording studies, VTA DA neurons are activated preferentially by appetitive incentive stimuli, whereas responses to signals of punishment occur in only a few cells (Mirenowicz & Schultz 1996; Schultz et al. 1995b; 1997). DA cells, the majority of which are located in the VTA, respond vigorously to, and in proportion to the magnitude of, both conditioned and unconditioned incentive stimuli, and in anticipation of reward (Bowman et al. 1996; Henriksen & Giacchino 1993; Houk et al. 1995; Koob et al. 1993; Le Moal & Simon 1991; Mark et al. 1991; Mitchell & Gratton 1992; Mirenowicz & Schultz 1996; Nishino et al. 1987; Pfaus et al. 1990; Schultz et al. 1993; 1995b; 1997; Weiss et al. 1992).

VTA DA neuron responses to incentive stimuli may play a role in facilitating the association between stimuli that predict reward and behavioral responses that obtain reward (Schultz et al. 1997). The optimal stimuli for activating DA neurons are phasically occurring unpredicted food and liquid rewards, whereas fully predicted stimuli are ineffective (Schultz et al. 1995b). As an experiment progresses, DA neurons show increased activity in the presence of neutral stimuli that consistently predict reward, and a concurrent decrease in activity to the unconditioned rewards, until DA responding has transferred completely to the conditioned incentive stimuli (Schultz et al. 1995b; 1997). The same process is observed when control of behavioral responding is transferred to earlier occurring stimuli that are predictive of the primary incentive stimulus (Schultz et al. 1997). Thus, "DA discharge ratchets backward in time, in a sequence of familiar events, so as to respond to earlier and earlier predictors of reinforcement" (Houk et al. 1995, p. 250). However, DA activity is not necessary to the development of associations between stimuli per se, even associations involving reward (Beninger 1983; Everitt & Robbins 1992; Le Moal & Simon 1991). Instead, DA activity is critical to the control of appetitive behavior by conditioned incentive stimuli – specifically, to link stimuli predicting reward to the response-facilitation mechanism in the NAS (Beninger 1983; LeMoal & Simon 1991; Schultz et al. 1997).

4.3. Neuroanatomical integration of incentive information

The critical role of the VTA-NAS DA pathway in the facilitation of incentive motivation suggests that the NAS is a site of integration of incentive information. The caudomedial shell region of the NAS (NAS_{shell}) is a major point of convergence of motivational information from many limbic structures (Heimer et al. 1993; Kalivas et al. 1993; Wright et al. 1996). Particularly high rates of intracranial self-stimulation and energy use (2-deoxyglucose uptake) during self-stimulation are found mainly in the NAS_{shell} (Deutch et al. 1993). Although NAS cells decrease firing during periods of focused attention and consummatory events, they increase firing to primary and conditioned signals of reward and novelty, and during intervals when reward is expected and during engagement in rewarding social and aggressive activity (Apicella et al. 1991; Henriksen & Giacchino 1993; Le Moal & Simon 1991; Schultz et al. 1992; 1995a). In contrast, pharmacologic impairment of NAS_{shell} functioning leads to an extinction-like response on established reinforcement schedules, long-lasting decreases in the self-administration of reinforcing drugs, and reduced effort in working for drug reward (Lyness et al. 1979; Lyness & Smith 1992; Roberts et al. 1980).

Responses of NAS neurons to conditioned incentives are due to afferent excitatory stimulation arising from several sources: (1) the basolateral complex of the amygdala (i.e., the basal, accessory basal, and lateral nuclei; Kalivas et al. 1993; Wright et al. 1996), (2) regions comprising the extended amygdala (Everitt & Robbins 1992; Mogenson et al. 1993; Nishijo et al. 1988; Pert et al. 1992), (3) the hippocampus (Everitt & Robbins 1992; Gaffan 1992), and (4) the prefrontal medial orbital cortex (Thorpe et al. 1983; Watanabe 1990). All of these structures are strongly interconnected (Kalivas et al. 1993), but, as discussed below, each provides different, specific information about the salient incentive context to the NAS.

4.3.1. The basolateral complex of the amygdala. The basolateral amygdala of the rat (Wright et al. 1996) and monkey (Heimer et al. 1993) provides massive, topographically organized, compartmentally bounded innervation of the NAS_{shell}. With simultaneous stimulation of both the amygdala and VTA (Boldry et al. 1991; Willins et al. 1992), NAS stimulation more readily produces initiation of forward locomotion (Deutch et al. 1993) and exploratory activity to novelty (Kelley et al. 1989). In both monkeys and humans, the basolateral amygdala plays a critical role in classical stimulus-reinforcement conditioning (Aggleton 1992; Bechara et al. 1995; Cahill & McGaugh 1990; Everitt & Robbins 1992; Gaffan 1992; LeDoux 1996a; LeDoux et al. 1990;

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Selden et al. 1991). Bilateral basolateral amygdala lesions specifically impair the association of discrete stimuli with reinforcement, whereas the motivational efficacy of food rewards or of DA injections in the NAS remains intact (Aggleton 1992; Everitt & Robbins 1992; Gaffan 1992). This indicates that the basolateral amygdala performs stimulus-reinforcement associative functions, whereas DA release in the NAS modulates an incentive motivational influence. Nevertheless, lesions of either the basolateral amygdala or NAS impair responding for reward, suggesting that these two structures are serially connected (Everitt & Robbins 1992; Mogenson et al. 1993).

4.3.2. Regions comprising the extended amygdala. Basolateral and olfactory amygdala complexes send massive projections to a group of structures collectively referred to as the extended amygdala, which represents a macrostructure that is characterized by two divisions, central and medial (Heimer et al. 1993; Martin et al. 1991). Stretching from the central and medial nuclei of the amygdala, the central and medial divisions merge specifically with the caudomedial region of the NAS_{shell}. Many intrinsic connections occur along these divisions, particularly the central division (Heimer et al. 1993), suggesting that high-level integration occurs within the extended amygdala (Koob & LeMoal 1997; LeDoux 1996a). Although the manner in which behavioral functions are organized within the extended amygdala is not understood, these structures appear to integrate information related to reinforcement, stimulus-reward associations, and motivation (Koob et al. 1993). Pharmacologic and lesion manipulations of all central extended amygdala structures modify incentive motivation to work for rewards and initiation of locomotor activity as a means of obtaining rewards (Heimer et al. 1993; Kalivas et al. 1993; Koob 1992; Koob et al. 1993). Most structures of the extended amygdala can transmit this motivationally relevant information to some or all hypothalamic and brainstem structures related to emotional expression (Heimer et al. 1993), leading Holstege (1991; 1992) to consider the extended amygdala as a third or emotional motor system.

4.3.3. The hippocampus. The hippocampus topographically innervates the NAS_{shell} (Groenewegen et al. 1991), but lesions of the fimbria-fornix or ventral hippocampus do not impair the association of discrete stimuli with reinforcement (Bechara et al. 1995; Gaffan 1992). Instead, hippocampal, but not basolateral amygdala, lesions disrupt Pavlovian associations formed between the spatial and contextual interrelations of environmental stimuli and reinforcement (Annett et al. 1989; Selden et al. 1991; Sutherland & McDonald 1990). On the other hand, NAS lesions can produce behavioral deficits closely related to those following impairment of hippocampal functions (Annett et al. 1989). Thus, doubly dissociable limbic-striatal functions (amygdala-NAS versus hippocampal-NAS) may correspond to the compartmentalization of the NAS (Everitt & Robbins 1992; Gaffan 1992; LeDoux 1992; 1996).

4.3.4. The prefrontal medial orbital area. The orbital frontal cortex, particularly Brodmann's posterior medial orbital prefrontal cortical area 13 (MOC 13), integrates the most complex level of associations of reinforcement with both stimuli and responses (Rolls 1986; Thorpe et al. 1983). MOC 13 has strong connectivity with regions that process all sensory modalities of contemporaneous and stored information, as well as topographically organized efferents that densely innervate the NAS_{shell} (Deutch et al. 1993; Goldman-Rakic 1987; Kalivas et al. 1993). Through its dense reciprocal connections with the basolateral, central, and extended amygdala regions, MOC 13 has access to emotional and reinforcement associations of contemporaneous and recalled sensory events (Goldman-Rakic 1987; Porrino et al. 1981). MOC 13 forms higher-level conditional representations of sensory events by associating them with existing or newly developing response-reinforcement contingencies; more simply, MOC 13 may abstract an integrated structure of appetitive and aversive behavioral contingencies from the environment (Thorpe et al. 1983). When behavioral responses evoke unexpected reinforcement outcomes, MOC 13, in collaboration with the basolateral amygdala (Everitt & Robbins 1992) and hippocampus (Gray et al. 1991), encodes the new contingencies that are relevant to the modification of response programs (Thorpe et al. 1983). MOC 13 may be capable of holding such representations of behavioral-reinforcement contin-

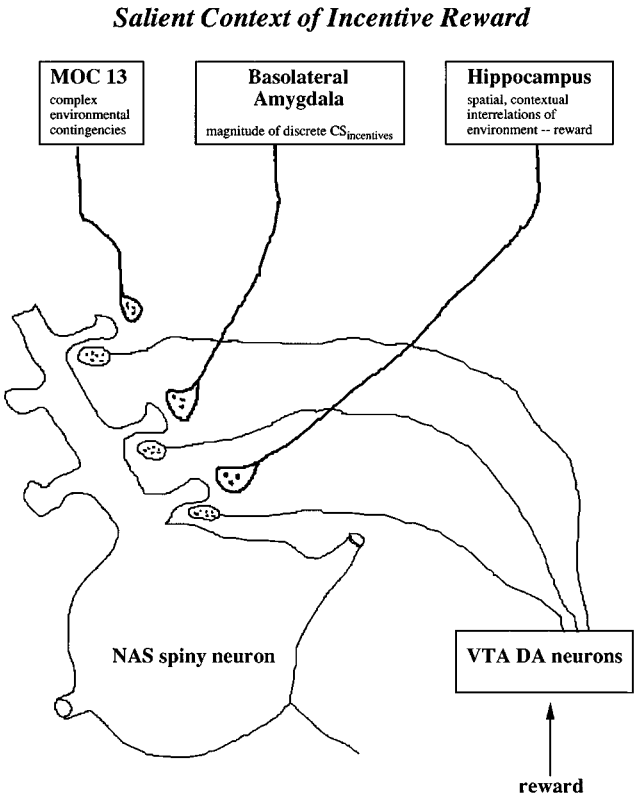


Figure 5. Interdigitation of cortical (medial orbital prefrontal) and limbic (basolateral amygdala, hippocampus) sources of the salient context of reward with VTA DA projections on the dendritic shafts of an NAS medium-spiny neuron. Synaptic contacts with NAS neurons of the more active cortical and limbic efferents are strengthened by dopamine, a process referred to as heterosynaptic plasticity. In this way, dopamine is thought to strengthen the connections between inputs of the salient incentive context and incentive processes integrated in the NAS_{shell}. MOC 13 = medial orbital prefrontal cortex, Brodmann's area 13; VTA = ventral tegmental area; DA = dopamine; NAS_{shell} = shell subterritory of the nucleus accumbens, a part of the ventral striatum; VP_m = ventromedial subterritory of the ventral pallidum; MD = mediodorsal nucleus of the thalamus. See text for details.

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gencies in working memory as motor strategies are selected over time (Goldman-Rakic 1987; Scalaidhe et al. 1997). This capacity would allow a comparison of the valence and magnitude of outcome expectancies associated with several possible response strategies, followed by an updating of contingencies as circumstances unfold during the temporal duration of the selected response strategy (Houk et al. 1995).

4.3.5. Convergence of the sources of afferent excitatory stimulation on the NAS_{shell}. The above discussion is integrated in Figure 5, where the information transferred by MOC 13, the basolateral amygdala, and the hippocampus to the NAS_{shell} represents the salient context of incentive stimuli (Houk et al. 1995; Pierce et al. 1996a; 1996b; Schultz et al. 1995b; 1997). Context includes distinctive attributes of incentive stimuli (e.g., modality, size, color, scent, texture, etc.) as well as their immediate sensory surroundings (e.g., position, location of targets of action, etc.), both of which are integrated with respect to internal drive states, desirability of action, and intended actions in the near future. Contextual information arrives from these areas via 5,000 to 20,000 glutamatergic efferents that interdigitate on the heads of dendritic spines of single medium-spiny neurons in the NAS_{shell} (Gronewegen et al. 1990; Groves et al. 1995; Houk et al. 1995; Kalivas et al. 1995; Schultz et al. 1995b; Takagishi & Chiba 1991; Wickens & Kotter 1995). Most of these efferents are excitatory to NAS function and are reciprocated (Kalivas et al. 1993; Pierce et al. 1996a). Between 4,500 and 8,000 VTA DA efferents synapsing on spinal shafts of single NAS neurons interdigitate with the contextual glutamatergic inputs (Groves et al. 1995; Grace 1991; Meredith et al. 1993; Schultz et al. 1995b). As discussed in more detail in section 5.3.1, neuroanatomical association between cortical and limbic glutamate and VTA DA efferents on NAS dendrites allows DA to facilitate the synaptic strength of the glutamatergic inputs to the NAS. This DA facilitation would promote the activation of incentive motivation by, and approach behavior toward, the most salient context (Houk et al. 1995; Kalivas 1995; Pierce et al. 1996a; 1996b; Schultz et al. 1995b; 1997; Toshibiko et al. 1994; Wickens & Kotter 1995).

4.4. Generation of an incentive motivational state within a motive circuit

Kalivas et al. (1993) proposed that incentive context and reinforcement associations, which are integrated in the amygdala and MOC, are translated into an incentive motivational state within a motive circuit (Kalivas et al. 1993). The circuit includes the NAS_{shell}, ventromedial subterritory of the ventral pallidum (VP_m), and VTA DA ascending projections (see the lower half of Fig. 6). All three regions are strongly, reciprocally, and preferentially connected with each other, as compared with other subregions of the striatum and pallidum (Deutch et al. 1993; Heimer et al. 1993). Functionally, these regions are interdependent in that the rewarding self-administration of electrical stimulation and stimulant drugs, as well as the initiation of locomotor activity, can be elicited from all three regions (Kalivas et al. 1993; Klitenick et al. 1992; Koob et al. 1993). Additionally, impairment of any one of these regions blocks the initiation of locomotor activity normally elicited by stimulation of either of the two remaining regions (Austin & Kalivas 1991; Kalivas et al. 1993).

One major function of the integration of information in the NAS_{shell} is to encode the motivational intensity or salience of incentive stimuli (Kalivas et al. 1993). The NAS_{shell} can transmit this code back to the extended amygdala as a means of influencing extended amygdala output to brainstem autonomic and somatomotor regions (Heimer et al. 1993) and to the VP_m for further integration. Because the VP_m can transmit the information back to the VTA (Zahm 1989), the NAS_{shell}–VP_m–VTA loop can be closed, setting up a reverberatory capacity within the circuit that permits temporal maintenance of an incentive motivational state (Kalivas et al. 1993). With a reverberatory mode engaged, the intensity of an incentive motivational state could be modulated, in accord with variation in reward value of stimuli encountered, via afferent feedback to the motive circuit from the MOC, amygdala regions, and hippocampus.

The current motivational code established in the motive circuit can be transmitted from VP_m to MOC 13 via the mediodorsal nucleus of the thalamus (Deutch et al. 1993; Groenewegern 1988; Kalivas et al. 1993). Presumably, this code is merged with the most current representation of behavioral-reinforcement contingencies held in working memory by MOC 13, perhaps invoking a reintegration that reflects a change in motivational state (Houk et al. 1995). MOC 13 then may transmit the updated contingency structure back to the motive circuit via efferents to the NAS_{shell} and VTA (Deutch et al. 1993; Groenewegen et al. 1990; 1991; Kalivas et al. 1993). The result would be a continual iterative updating, not only of incentive motivational intensity as integrated in the motive circuit, but also of reinforcement priorities and behavioral outcome expectations as constructed in MOC 13.

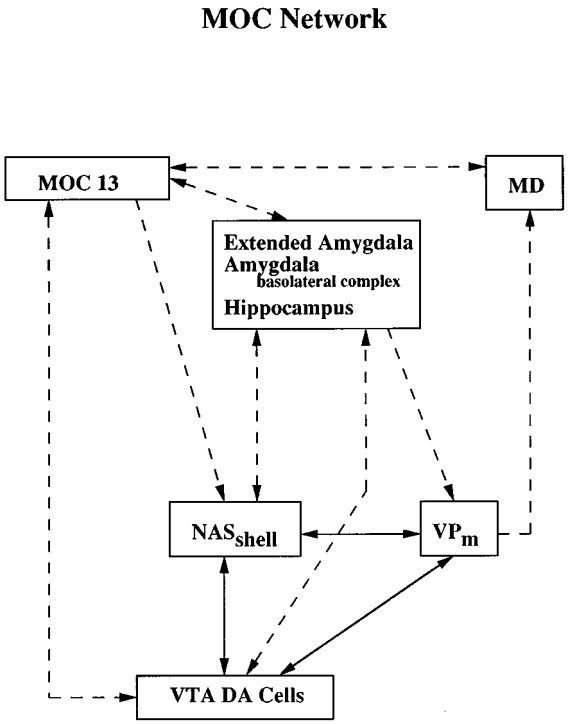


Figure 6. A schematic illustration of a medial orbital prefrontal cortical network that integrates and regulates incentive-motivational modulation of goal-directed behavior. Solid lines at the bottom of the figure indicate connections within a central motive circuit of the network. See text for details. MOC 13 = medial orbital prefrontal cortex, Brodmann's area 13; VTA = ventral tegmental area; DA = dopamine; NAS = nucleus accumbens, a part of the ventral striatum.

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4.5. Neural organization of incentive-facilitated behavior in a medial orbital network

Although the motive circuit encodes the intensity of incentive motivation, a broader network of distributed neural structures is implicated in the modulatory influence of incentive motivation on appetitive behavior. Extending the ideas of others (Deutch et al. 1993; Groenewegen et al. 1990; 1991; Heimer et al. 1993; Kalivas et al. 1993), we propose an MOC network as illustrated in Figure 6. In keeping with the structure of other network models (Alexander et al. 1990; Goldman-Rakic 1987; Groenewegen et al. 1990; 1991; Mesulam 1990), the origin and termination site of this network lies within the prefrontal cortex, specifically MOC 13. Connections between all components of the network are topographically organized (Groenewegen et al. 1990; 1991), indicating that the basal ganglia-thalamocortical circuits of the ventral forebrain are congruent with the structure of more dorsally located cortical circuits outlined by Alexander et al. (1990).

The MOC network incorporates three basic components: (1) a motive circuit that integrates, maintains, and updates information to form an intensity encoded incentive motivational state, (2) the VTA DA projection system that facilitates neural integration, which occurs in the motive circuit, as well as within network interactions more generally, and (3) MOC 13 that performs higher-order regulation of network processes, which is consistent with similar proposals regarding the rat ventral prefrontal cortex (Deutch et al. 1993; Kalivas et al. 1993; Thorpe et al. 1983; Watanabe 1990). Only MOC 13 has the requisite features to exert such high level regulation, including cellular properties that can maintain a current reinforcement expectation in working memory while it is updated within the network; and extensive patterns of connectivity with other MOC network structures, with cortical and subcortical structures that integrate contemporaneous and stored information within and across all sensory modalities and with brainstem somatomotor regions (Scalaidhe et al. 1997). Moreover, because a portion of ventral prefrontal efferents appear to be highly collateralized (Beckstead 1979a), the MOC may provide a coordinated modulation of network regions. For example, the MOC could vary the level of facilitation of motor, autonomic, and neurohormonal components of appetitive behavior according to contextual circumstances (Rolls 1986; Thorpe et al. 1983).

Topographically organized efferents from the MOC to the NAS_{shell} (which overlap amygdala input to the shell; Beckstead 1979a; 1979b; Oades & Halliday 1987) and VTA create fine-point modulation of the VTA–NAS DA pathway (Deutch et al. 1993; Groenewegen et al. 1990; 1991; Kalivas et al. 1993; Takagishi & Chiba 1991). These efferents use excitatory amino acids (such as glutamate) that have excitatory effects on both NAS_{shell} and VTA neurons (Deutch et al. 1993; Grace 1991; Imperato et al. 1990; Kalivas et al. 1989; Youngren et al. 1993). In addition to direct MOC-NAS_{shell} efferents that exert a modulatory influence on DA release in the NAS_{shell} (Grace 1991; Le Moal & Simon 1991), MOC-VTA efferents increase the activity of VTA DA cells that project to the NAS_{shell}, central and basolateral amygdala, and VP_m (Groenewegen et al. 1990; 1991). MOC input strongly regulates burst firing of VTA DA cells, which is associated with a doubling of DA release per action potential in the NAS (Gonon 1988; Johnson et al. 1992; Suaud-Chagny et al. 1992). Incentive stimuli also elicit increased DA release in the NAS_{shell} (Deutch et al. 1993), and because DA release in the NAS_{shell} gates motivational information arriving from the amygdala and hippocampus (Mogenson et al. 1993), MOC regulation of VTA–NAS_{shell} DA projections may have a significant indirect impact on the transfer of motivational information to the VP_m and hence around the entire motive circuit.

In addition to regulating the intensity and temporal maintenance parameters of the motive circuit, MOC 13 could influence whether the incentive motivational state is eventually transmitted to the voluntary motor system. The MOC network likely interacts with a parallel motor network that is involved in translating motivational state to motor areas (Joel & Weiner 1994). Deutch et al. (1993) concluded that such a motor network is associated with the core region of the NAS (NAS_{core}), and is involved in attaching the motivational codes of the shell region to voluntary motor activity. Hence, the NAS_{core} may represent the interface between motivation and voluntary movement. The threshold for eliciting DA utilization is lower for MOC network structures than for structures associated with the NAS_{core} (Deutch et al. 1993). Thus, as suggested by others (Deutch et al. 1993; LeMoal & Simon 1991), behavioral responses to incentive stimuli may be facilitated by DA in a graded manner as follows. First, DA facilitates the generation of an incentive motivational state in the NAS_{shell}, which is associated with behavioral outcome expectations in the MOC network. Next, if reward acquisition is expected, DA facilitates attachment of an incentive motivational intensity code to motor acts and initiation of locomotor activity via the NAS_{core} network. Finally, DA facilitates sensory-motor integration in the dorsal striatopallidal system to provide coordinated motor responses that lead to reward.

4.6. Conclusions on the neural organization of behavioral facilitation

Figure 4C illustrates that VTA DA projections to structures of the MOC network provide the neural substrate for extraversion and behavioral facilitation, as diagrammed in Figures 4A and 4B, respectively. The VTA is a site of massive convergence of motivational information from many limbic and MOC network structures, including the MOC and NAS_{shell} (Oades & Halliday 1987). Both the NAS and MOC provide a converging point-to-point activation of VTA DA neurons, which, in turn, project widely to facilitate processes integrated within MOC network structures (Kalivas et al. 1993; Oades & Halliday 1987; Phillipson & Griffiths 1985).

As outlined in Figure 4C, behavioral facilitation involves various patterns of VTA DA innervation. First, reciprocal innervation between VTA DA neurons and the NAS_{shell} (Phillipson & Griffiths 1985) facilitates incentive motivation and, in collaboration with the NAS_{core}, initiation of locomotion, as reviewed above. Second, VTA DA efferents to the VP_m, which modulate VP cell firing rates (Napier 1992), may facilitate the initiation of appetitive motor activity (Klitenick et al. 1992), as well as the back projection of information via VP_m–VTA efferents, thus promoting temporal maintenance of an incentive motivational state within the motive circuit.

Third, there is dense VTA DA innervation of the basolateral and central amygdaloid nuclei (Oades & Halliday 1987), both of which innervate the NAS_{shell} (Kelley et al. 1982). DA effects in the amygdala are complex due to the different functions of the various amygdala nuclei and other routes by which the amygdala can influence the NAS (e.g.,

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via efferents to the MOC and VTA), and to the influence of the amygdala itself on DA transmission in the NAS (Aggleton 1992; Kalivas et al. 1993). Kalivas et al. (1993) proposed that VTA DA efferents to the amygdala facilitate the flow of motivational information from the amygdala to the NAS_{shell}, VP, and the VTA itself. VTA DA projections to the central and medial nuclei of the amygdala may be particularly relevant to facilitation of emotional expression because these nuclei serve as important output centers of the amygdala to brainstem and hypothalamic areas involved in activation of vocal, gross motor, facial, hormonal, and autonomic components of emotional behavior (Aggleton 1992; Depue & Spoont 1986; Kalivas et al. 1993; Pert et al. 1992; Spoont 1992).

Finally, incentive motivation in humans is associated with both positive emotional feelings such as elation and euphoria and motivational feelings of desire, wanting, craving, potency, and self-efficacy. Robinson and Berridge (1993) argued that motivational feelings are related most directly to the process of attributing incentive salience to stimuli, as discussed above. Both sets of subjective experiences may be facilitated by VTA DA projections to the NAS_{shell} and amygdala in order to generate a broader and more enduring state that encourages engagement with the environment. In humans, DA-activating psychostimulant drugs induce both sets of feelings (Koob et al. 1993; Stewart et al. 1984). Additionally, neuroimaging studies of cocaine addicts found that, during acute administration, the intensity of a subject's subjective euphoria increased in a dose-dependent manner in proportion to cocaine binding to the DA uptake transporter (and hence DA levels) in the striatum (Volkow et al. 1997). Moreover, cocaine-induced activity in the NAS was linked equally strongly (if not more strongly) to motivational feelings of desire, wanting, and craving, as to the emotional experience of euphoric rush (Breitner et al. 1997).

The emotional and motivational feelings associated with DA facilitation of incentive motivation raises the possibility that abnormal DA transmission underlies certain forms of affective disorders (Willner & Scheel-Kruger 1991; Wise & Bozarth 1987). We have considered both qualitative and quantitative alterations in DA-induced behavioral facilitation as both causal and moderating factors in bipolar, unipolar, and seasonal affective conditions (Depue 1995; Depue et al. 1987; Depue & Iacono 1989; Depue & Zald 1993). Space does not permit adequate treatment of this literature; hence, readers are referred to these references.

4.7. DA reactivity to aversive stimuli

Although the role of MOC network structures in positive incentive motivation and behavioral facilitation has been our focus, these structures do not function exclusively in a hedonically pleasurable context, just as incentive motivation itself may be appetitive or aversive. The basolateral and extended amygdala are involved in associative processes related to negative reinforcement and punishment, as well as the expression of negative emotions of fear or anxiety and of aversive behaviors such as defensive or affective aggression (Aggleton 1992; LeDoux 1992; 1996; LeDoux et al. 1990). Specific MOC 13 neurons respond to aversive and nonrewarding stimuli (Thorpe et al. 1983), whereas the hippocampus may play a role in conveying information concerning unexpected and aversive behavioral outcomes to the NAS (Gray et al. 1991). Additionally, stressors or their conditioned cues that are not uncontrollable and enduring can enhance behaviors typically associated with incentive motivation, such as novelty- and stimulant-induced locomotor activity, self-administration of stimulants, the reinstatement of stimulant self-administration after extinction, and VTA-NAS DA transmission itself (Abercrombie et al. 1989; Anisman et al. 1993; Herman et al. 1982; Mantz et al. 1989; Piazza & Le Moal 1996; Roth et al. 1988; Young et al. 1993). The capacity of both stressors and incentive stimuli to enhance NAS DA activity may be due to one or more of the following factors.

4.7.1. Anatomical heterogeneity. Anatomical heterogeneity within the VTA and NAS raises the possibility that they may integrate several distinct behavioral functions, not simply those associated with positive incentive motivation. For example, the NAS is composed of three major areas (shell, core, and rostral pole) that have different patterns of histochemistry, cytoarchitecture, and extrastriatal connectivity (Wright et al. 1996; Zahm & Heimer 1993). The NAS_{shell} alone has different zones (Wright & Groenewegen 1995); projects to the VTA, substantia nigra, and periacqueductal gray (Berendse et al. 1992); and can be divided into at least three subterritories that may have different functional affiliations (Wright et al. 1996): rostral, ventral caudomedial (which has been the focus of our discussion), and dorsal caudomedial, also referred to as the "septal" pole or "cone" (Deutch et al. 1993; Heimer et al. 1993; Zahm & Brog 1992). Similarly, VTA cell groups are heterogeneous in structure, projection targets, and stimulus reactivity (Deutch et al. 1993; Oades & Halliday, 1987). Although most VTA DA neurons respond preferentially to unconditioned and conditioned incentive stimuli, those responding to unconditioned and conditioned aversive stimuli and anxiogenic agents appear to be localized more in the caudal midline aspects of the VTA, project mainly to the ventromedial prefrontal cortex (infralimbic cortex in the rat) rather than the NAS or other cortical areas (e.g., cingulate, piriform, and entorhinal), and specifically innervate the deep layers of infralimbic cortex (Anisman et al. 1993; Bannon et al. 1983; Deutch & Roth 1990; Deutch et al. 1991; 1993; Roth et al. 1988; Young et al. 1993; Zacharko & Anisman 1991). Furthermore, the threshold for stress-induced DA reactivity is not homogeneous across or within structures: It is lowest of all regions in the infralimbic cortex, whereas in the NAS it is lowest in the cone region, followed by other areas of the shell, and finally by the core (Deutch & Cameron 1992). Because most VTA DA neurons projecting to NAS regions do not appear to be directly responsive to aversive stimuli (Mirenowicz & Schultz 1996), the increased DA utilization in the NAS may result from at least two sources. First, VTA DA innervation of efferents from infralimbic regions to the NAS, and perhaps from the amygdala to the NAS, may trans-synaptically regulate NAS DA release (Barbieto et al. 1990; Lindefors 1993). Second, neurons in infralimbic, limbic, and autonomic regions that register aversive stimuli may activate specific DA neurons at the level of the VTA, which then enhance DA transmission in selected NAS terminal fields.

Anatomical and connectional heterogeneity in brain regions may be associated with integrative activities of separate parallel-but-interacting circuits (Joel & Weiner 1994). For instance, basolateral amygdala subregions project to specific compartments of the NAS_{shell} and NAS_{core}, suggesting that these subregions differentially influence particular NAS outputs subserving separate functions (Wright et al. 1996). Wright et al. (1996) suggested that the acces-

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sory basal amygdala nuclei project via the NAS_{core}, substantia nigra (pars reticulata), and medial thalamus to the prelimbic cortex, whose projections reach autonomic centers in brainstem and spinal cord. Similarly, the infralimbic cortex and the cone of the NAS_{shell} have dense reciprocal connections with areas linked to autonomic functions (Brog et al. 1993; Deutch & Cameron 1992; Goldman-Rakic 1987; Thorpe et al. 1983; Zahm & Brog 1992) and have the lowest thresholds for stress-induced DA release from distinct VTA DA afferents (Deutch et al. 1993). Anxiogenic agents activate, whereas anxiolytics prevent, stressor-induced increases in DA synthesis and utilization in the infralimbic cortex but not the NAS (Anisman et al. 1993; Knorr et al. 1989; Roth et al. 1988). These various findings suggest that DA may facilitate the integration of autonomic arousal within a VTA DA-infralimbic-NAS_{cone} circuit informed by basolateral amygdala input. Such a circuit may operate in parallel to, but interact with (Deutch et al. 1993; Joel & Weiner 1994), other corticostriatal circuits, such as the MOC 13 network. In this way, alterations of DA transmission in the NAS induced by different stimulus contexts (e.g., stressful versus rewarding) may arise from activation of separable but overlapping neurobiological networks.

4.7.2. Goal-directed behavior. Goal-directed behavior is often required to adapt to stressors, such as in incentive-motivated avoidance (approach to the reward of safety) or affective aggression aimed at removing an object blocking acquisition of reward (Anisman et al. 1993; Depue & Iacono 1989; Gray 1973). Moreover, mesocortical DA appears to facilitate higher-order cognitive processes that guide behavior through both rewarding and aversive environments (Luciana et al. 1992; in press; Luciana & Collins 1997). Thus, joint activation of VTA-NAS DA and VTA-prefrontal DA projections could be required in many circumstances associated with stress.

When no successful adaptive behavior is possible, as in uncontrollable stress, the resulting behavioral sequence of preparation for, then withdrawal from, goal-directed action has been associated with a pattern of NAS DA transmission that is distinguishable from that elicited by psychostimulants (Cabib & Puglisi-Allegra 1996). Although results may vary across brain regions, inbred strains, and types of stressor (Anisman et al. 1993), stress-induced extracellular DA in the NAS follows a time-dependent biphasic pattern of a short-lasting increase that typically endures fewer than 5 days of repeated stress (Cabib & Puglisi-Allegra 1994; 1996; Imperato et al. 1993; Rouge-Pont et al. 1993), followed by a subsequent decrease to subbasal levels that lasts as long as the stressful circumstances persist (Cabib & Puglisi-Allegra 1994; Pothos et al. 1995; Rossetti et al. 1993). Approximately 20 minutes after termination of the stressor, DA release returns to levels found during the initial exposure to the stressor, indicating that the decrease in DA release is inhibited actively when responding is not adaptive (Anisman et al. 1993).

4.7.3. VTA-NAS DA projections and heterosynaptic plasticity. VTA-NAS DA projections may have an overarching role of facilitating heterosynaptic plasticity, thereby strengthening the connections of all salient incentive stimuli, both positive and negative, in the NAS (Bindra 1978; Horvitz et al. 1997; Puglisi-Allegra & Cabib 1990; Robinson & Berridge 1993). When integrated with the discussion in section 4.7.1 above, this possibility is consistent with our proposal: DA facilitation of connections of positive and aversive stimulus contexts in the NAS may occur within separable VTA-NAS circuitries that are associated with different motivational-behavioral patterns.

4.7.4. Stress-induced enhancement of NAS DA and positive affect. Finally, stress-induced enhancement of NAS DA transmission may facilitate a positive emotional state to diminish the aversive effects of stress, thereby serving a protective function under prolonged stressful conditions (Anisman et al. 1993; Piazza & Le Moal 1996; Sapolsky 1992).

5. Neurodevelopmental sources of individual differences in DA functioning

There are three basic challenges to deriving a neurobiological model of a personality trait: (1) to define the network of neural structures associated with the trait, which has been the focus of our discussion thus far; (2) to explain how individual differences occur within the functioning of that network; and (3) to identify the sources of individual differences. With respect to emotional traits of personality, the network integrates information provided by broad classes of stimulus, such as incentives, and generates a motivational state and behavioral response pattern. We propose that individual differences in a neurobiological variable that broadly influences the functional properties of a network, such as the VTA DA projection system, contribute strongly to variation in sensitivity to a specific class of stimuli and, hence, to stable behavioral propensities. This possibility lies at the foundation of a neurobiological model of extraversion (Gray 1973; 1992). Animal research demonstrates that individual differences in DA functioning do contribute significantly to variation in incentive-motivated behavior (Cabib & Puglisi-Allegra 1996; Le Moal & Simon, 1991; Piazza & Le Moal 1996; Phillips 1997; Puglisi-Allegra & Cabib 1997; Robinson 1988). Because individual differences emerge through dynamic developmental processes (Collins & Depue 1992), our discussion of the animal work on individual differences in DA functioning is organized around three neurodevelopmental sources of input to the brain (Greenough & Black 1992).

5.1. Genotype-driven processes

Genotype-driven processes operate most extensively prenatally and influence the basic structure and function of neuron populations (Greenough & Black 1992). Much evidence relating DA to behavioral expression relies on the use of inbred strains, which provide a well-defined and stable genotype for analysis (Crabbe et al. 1994; Plomin et al. 1991). One problem with this strategy is that behavioral differences between strains of disparate origins could reflect many genetic and neurochemical differences between strains, and cosegregation of traits could be due to the occurrence of genetic differences at the same or different loci (Phillips 1997; Robinson 1988). These complexities are increased with behavioral traits, which tend to be polygenic in nature (Bouchard 1994; Plomin 1990), because behavioral contrasts between strains may reflect disparate components of polygenic complexes (Phillips 1997). For instance, C57BL/6 (C57) and DBA2 (DBA) mice are among the most studied inbred strains in the behavioral pharmacology of DA, and they differ in several parameters of the DA system that relate directly to be-

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havioral differences (Puglisi-Allegra & Cabib 1997). These strains also exhibit several qualitatively different behavior patterns that rely on separate DA networks (e.g., mesoaccumbens versus nigrostriatal) and on different modes of inheritance. Therefore, we discuss behavioral differences that rely on the VTA-NAS DA pathway in an effort to focus on genetic influences on DA facilitation of incentive motivation.

An example of a genotype-driven process is variation in the number of DA neurons produced during prenatal development. Inbred mouse strains with variation in the number of neurons in the VTA DA cell group show marked differences in behaviors dependent on DA transmission in the VTA-NAS pathway, including levels of spontaneous exploratory activity and DA agonist-induced locomotor activity (Fink & Reis 1981; Oades 1985; Ross et al. 1976; Segal & Kuczenski 1987; Shuster et al. 1977; Sved et al. 1984; 1985). That this increased behavioral facilitation in high versus low DA neuron strains is due to DA transmission is suggested by their greater density of DA terminals in target fields, greater synthesis and release of DA, greater DA agonist-induced inhibition of prolactin secretion, and, important in terms of incentive motivation, increased DA content in the NAS.

There is a similar relation between behavior and DA transmission in C57 and DBA inbred mouse strains (Cabib & Puglisi-Allegra 1996; Phillips 1997; Puglisi-Allegra & Cabib 1997). C57 mice show greater novelty-induced locomotor activity than DBA mice (Anisman & Cygan 1975; Anisman et al. 1975; Wenger 1979), which is particularly relevant because novelty-induced locomotion is strongly modulated by the number of DA neurons in the VTA region (Fink & Reis 1981) and by natural and stimulant-induced variation in DA transmission (Fink & Smith 1980; Joyce et al. 1983; Kelley et al. 1975; Koob et al. 1981). Moreover, novel conditions have been found to enhance DA transmission in the NAS (Piazza et al. 1991b). Not surprisingly then, C57 mice exhibit a shift to the left of the dose-effect curve of amphetamine on locomotor activity relative to DBA mice (Cabib 1993; Phillips et al. 1994; Stevens et al. 1986; Zocchi et al. 1996). C57 mice also are characterized by a greater propensity to acquire self-administration of psychostimulants than the DBA strain, suggesting an enhanced incentive motivational effect in C57 mice (Belknap & O'Toole 1991; Belknap et al. 1993; Carney et al. 1991; Crabbe et al. 1994).

The increased effects of psychostimulants in C57 mice are associated with several indicators of enhanced DA transmission in the VTA-NAS pathway. Enhanced amphetamine-induced locomotor effects in C57 mice were accompanied by greater release of DA in the NAS compared with DBA mice (Zocchi et al. 1996). Variation in NAS DA release may be the result of strain-dependent differences in DA D_2, but not D_1, receptor densities. Increased density of D_2 autoreceptors located on VTA neurons, and lower D_2 postsynaptic receptors in the NAS, were observed in DBA relative to C57 mice (Erwin et al. 1993; Kanes et al. 1993; Ng et al. 1994; Puglisi-Allegra & Cabib 1997; Puglisi-Allegra et al. 1994). Activation of D_2 autoreceptors inhibits impulse flow, synthesis, and release rates of DA neurons (White & Wang 1984), and D_2 autoreceptors have higher affinity relative to postsynatic DA receptors for DA and DA agonists (Bannon et al. 1980; Skirboll et al. 1978). Therefore, low-dose DA agonists activate D_2 autoreceptors, thereby inhibiting DA transmission, and decrease the behavioral facilitation that accompanies postsynaptic DA activation (Depue et al. 1994). As would be predicted from DBA's higher D_2 autoreceptor:D_2 postsynaptic receptor density ratio, data from DBA compared with C57 mice have suggested reduced DA synthesis that is largely independent of DA release (Cabib & Puglisi-Allegra 1991; Kuczenski & Segal 1989; Zetterstrom et al. 1988; Zocchi et al. 1996), greater inhibitory effects of low-dose DA agonists on mesoaccumbens DA metabolism and on locomotor activity (Cabib & Puglisi-Allegra 1991; Zocchi et al. 1996), and weaker effects of higher DA-agonist doses on locomotor activation. Finally, the DA differences between these strains may relate to the finding that DBA mice are more vulnerable to loss of incentive motivation (anhedonia) induced by uncontrollable shock, as indexed by a marked and persistent reduction of intracranial self-stimulation in the NAS and anteromedial prefrontal cortex (Zacharko et al. 1987; 1990).

A similar pattern of associations between behavioral and DA indicators was demonstrated in two inbred rat strains, Lewis and Fisher 344. Lewis rats exhibited increased novelty-induced (Camp et al. 1994) and stimulant-induced (Camp et al. 1994; George & Goldberg 1988; George et al. 1991) locomotor activity, a greater propensity to acquire self-administration of a variety of psychostimulants as well as a conditioned place preference to cocaine and morphine (George 1990; Suzuki et al. 1988; Suzuki et al. 1988; 1992), and a shift to the left in the dose-effect curve of methamphetamine on locomotor activity (Camp et al. 1994). No Lewis-Fischer strain-dependent differences in basal DA concentrations in the NAS (Camp et al. 1994) or in D_1 or D_2 receptor binding or function (George et al. 1991; Luedtke et al. 1992) were identified. Compared with Fisher rats, Lewis rats did show larger and more prolonged elevations of extracellular concentrations of DA in the NAS in response to acute systemic injection of DA agonists (Camp et al. 1994; Chen et al. 1991); however, conflicting results were found in studies in which absolute rather than baseline-corrected DA elevation values were used (Strecker et al. 1993; Terwilliger et al. 1991). Additionally, there is evidence indicating higher rates of DA synthesis and postsynaptic D_1 receptor activation in Lewis rats than in Fisher rats (Beitner-Johnson et al. 1991; 1992).

Thus, several inbred mouse and rat strains exhibit consistent relations between greater VTA DA neuron number and/or heightened DA transmission in the VTA-NAS DA pathway and enhanced incentive-motivated behavior patterns, such as novelty- and stimulant-induced locomotor activity and an increased propensity to acquire self-administration of stimulants. This suggests that influences from genetic variation in VTA–NAS DA projections are expressed in terms of significant individual differences in the threshold to elicit incentive motivation.

5.2. Experience-expectant processes

Experience-expectant processes involve widespread cortical synapse overproduction during sensitive periods in brain development (Greenough & Black 1992; Rakic et al. 1986). Following overproduction, excess cortical synapses are "pruned back" in response to environmental stimulation. The basic implication of experience-expectant processes for the development of individual differences is that the degree of stimulation-rich environment will be encoded in the number of functional synaptic connections within

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neural pathways. Moreover, during expectant periods, individual differences in both genotype-driven processes (e.g., VTA DA neuron number) and environmental experience (e.g., time spent exploring novel environments) would be expected to collaborate. Therefore, the outcomes of such periods might establish different trajectories in the functional development of the VTA DA system across individuals, and thus partially specify eventual trait levels of behavioral facilitation. It is unknown whether experience-expectant processes are a significant source of individual differences in DA transmission, although the effects of drug-induced DA activation on behavior during periods of rapid developmental change can be persistent (Feigenbaum & Yanai 1984; Middaugh & Zemp 1985; Spear & Brake 1983; Spear et al. 1980). An initial task is to identify sensitive periods in the postnatal development of the VTA DA system – for example, as marked behaviorally around 1 year of age in humans by a relatively abrupt increase in locomotor exploration of novel environments.

5.3. Experience-dependent processes

Experience-dependent processes encode experience unique to the individual through interactions of neurotransmitter systems that modulate dendritic outgrowth, synaptogenesis, and synaptic regression (Chen et al. 1997; Colman et al. 1997; Magee & Johnston 1997; Mattson 1988). Through these mechanisms, neurotransmitter activity may regulate synaptic connectivity within the distributed structures of a particular neural network (Uno & Ozawa 1991). For example, the activity of VTA DA neurons may influence synaptic relations within pathways of the MOC network. Indeed, VTA DA release in terminal regions facilitates dendritic branching in the NAS, hippocampus, and neocortex in rats (Lindefors 1993; Shankaranarayana-Rao et al. 1993). Because most DA synaptogenesis occurs postnatally and continues into adulthood (Le Moal & Simon 1991), experience-dependent effects may be an important ontogenetic mechanism in the formation, and even stability, of individual differences in DA system reactivity. In that sense, experience-dependent processes are central to understanding personality as a dynamic developmental construct that involves the collaboration of genetic and environmental influences across the lifespan.

Behavioral sensitization is a form of experience-dependent heterosynaptic plasticity that involves DA neurotransmission in both the NAS and VTA (Browman et al. 1996; Groves & Thompson 1970; Kalivas 1995; Koob & Le Moal 1997; Robinson & Becker 1986; Robinson & Berridge 1993; Robinson et al. 1988; Stewart 1992). It is produced by intermittent noncontingent administration of a variety of psychostimulants or stressors and is demonstrated by a progressive and enduring enhancement of behavior elicited by a noncontingent psychostimulant test challenge administered days to weeks after the initial exposure phase (Badiani et al. 1995a; 1995b; 1995c; Kalivas 1995; Kalivas & Stewart 1991; Prasad et al. 1995; Robinson & Becker 1986; Sorg et al. 1994; Stewart 1992). Behavioral sensitization also can be induced through repeated *self*-administration of cocaine (Hooks et al. 1994), may be expressed by use of natural incentives (Mitchell & Gratton 1992; Mitchell & Stewart 1990), and, when accompanied by repeated administration of stress or psychostimulants, can enhance the acquisition of amphetamine and cocaine self-administration (Horger et al. 1990; 1992; Piazza & Le Moal 1996; Piazza et al. 1989; 1990; Woolverton et al. 1984). Therefore, it is likely that enhanced incentive motivation is central to behavioral sensitization (Koob & Le Moal 1997; Robinson & Berridge 1993). We focus on behavioral sensitization because it serves as a starting point for understanding experience-dependent variation in DA facilitation of incentive motivation within the MOC network and, theoretically, in the development of extraversion trait levels.

Behavioral sensitization encompasses two temporally and spatially distinct occurrences of heterosynaptic plasticity. The *development* of behavioral sensitization involves an early sequence of molecular and cellular events within the VTA region, whereas its enduring *expression* is associated with subsequent changes in the release of and postsynaptic response to neurotransmitters in the NAS (Kalivas 1995; Kalivas & Stewart 1991; Miserendino & Nestler 1995; Paulson & Robinson 1991; Robinson & Becker 1986; Robinson et al. 1988; Self et al. 1994). Although sensitization can develop in a context-independent manner as a nonassociative process (Anagnostaras & Robinson 1996; Castaneda et al. 1988; Henry & White 1991; Vezina & Stewart 1990), the expression of behavioral sensitization is largely context-specific (Anagnostaras & Robinson 1996; Bell & Kalivas 1996; Stewart 1992). That is, the behavioral expression of an existing sensitized neural substrate is dependent on the similarity of the context extant during the development of sensitization and the context of the subsequent test challenge environment. Anagnostaras and Robinson (1996) argued persuasively that context acts more as an occasion-setter for behavior than as an excitatory or inhibitory conditioned stimulus, and thereby determines whether sensitization is expressed at any particular time or place. As occasion-setter, context modulates (facilitates or inhibits) the pharmacologic elicitation of a sensitized unconditioned response. Thus, expression of a sensitized behavioral response appears to involve the interaction of converging efferents representing salient context and sensitized neural processes (Post et al. 1992; Wolf et al. 1995).

5.3.1. Heterosynaptic plasticity in the NAS and VTA. Although enhancing NAS DA transmission is not sufficient to establish behavioral sensitization, its expression is temporally associated with a psychostimulant-, mu-opioid-, or stress-induced enduring increase in DA release, particularly in the NAS_{shell} (Castaneda et al. 1988; Kalivas 1995; Kalivas & Duffy 1990, 1993a; Kalivas & Stewart 1991; Paulson & Robinson 1991; Pierce & Kalivas 1995; Robinson 1993; Robinson & Becker 1986; Robinson & Camp 1990; Sorg et al. 1994), where D_1 rather than D_2 receptors appear to mediate these effects (Henry & White 1991; Kalivas 1995; Kalivas & Stewart 1991; Martin-Iverson & Burger 1995; Miserendino & Nestler 1995; Nestler & Aghajanian 1997; Pierce & Kalivas 1995). A glutamate-DA interaction is an important dynamic in the expression of behavioral sensitization in the NAS. Glutamate increases the release of DA in the NAS (Kalivas 1995; Kalivas & Stewart 1991), and motor activity elicited by injection of either DA or glutamate agonists into the NAS is diminished by coadministration of antagonists to the other neurotransmitter (Bell & Kalivas 1996; Kalivas 1995; Karler et al. 1991; 1994; Pierce et al. 1995; 1996a; 1996b). NAS neurons also show enhanced responsiveness to glutamate in sensitized states that may be related to glutamate receptor adaptations observed in the NAS (Lu et al. 1997; Nestler & Aghajanian 1997; Pierce et al. 1996a; Zhang et al. 1997). Lesions of the glu-

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tamatergic efferents from prefrontal cortex, amygdala, and hippocampus (representing contextual inputs, see Fig. 5) to the NAS prevent a sensitized behavioral response (Dahlin et al. 1994; Kalivas 1995; Kalivas & Stewart 1991; Pert et al. 1992; Yoshikawa et al. 1991), suggesting that these efferents serve as contextual occasion-setters.

The manner in which DA facilitates heterosynaptic plasticity in interaction with glutamate in the NAS was recently modeled. The effect of DA release on dendritic spines of NAS neurons is proposed to be dependent on the strength of glutamate-induced activity of the NAS neuron arising from cortical and limbic contextual inputs (Houk et al. 1995; Wickens & Kotter 1995). As shown at the top of Figure 7, these inputs vary naturally in strength as a function of their relation to the salient incentive context. In the middle of the figure, DA release causes long-term depression of weakly afferented, low-activity NAS neurons, whereas it simultaneously facilitates strongly afferented, high-activity NAS neurons, which are in the minority during an episode of environmental stimulation (Chiodo & Berger 1986; Graybiel et al. 1994; Houk et al. 1995; Schultz et al. 1995b; Wickens & Kotter 1995). Thus, the effect of DA release on NAS neurons is to increase the contrast gradient between weak and strong glutamatergic inputs in relation to the salient incentive context. With repeated strong glutamatergic and DA efferent input to NAS neurons (bottom of Fig. 7), DA release increases this contrast gradient via induction of long-term potentiation (Begg et al. 1993; Wickens & Kotter 1995). Because the learning capabilities of the isolated striatum are limited, in this way DA plays an important role in selective strengthening of glutamatergic efferents to the NAS, thereby enhancing the association of salient contexts (conveyed by corticolimbic efferents) with previously successful responses (Schultz et al. 1997).

Heterosynaptic plasticity in the development of behavioral sensitization occurs in part through the interaction of DA and glutamate in the VTA region. Although increased firing of VTA DA neurons in itself is not a prerequisite for the development of behavioral sensitization, enhanced VTA somatodendritic DA release onto D_1 (but not D_2) receptors is a common factor in such development (Kalivas 1995; Kalivas & Duffy 1993b; Kalivas & Stewart 1991; Pierce et al. 1996b). D_1 receptors are not expressed on VTA neurons (Mansour et al. 1992), but are found in large quantity in the ventral midbrain, mainly on terminals of forebrain efferents to VTA cells. Thus, VTA somatodendritic DA release appears to activate glutamate release via D_1 receptors located on glutamatergic forebrain efferents to VTA neurons (Carlezon et al. 1997; Criswell et al. 1990; Kalivas 1995; Kalivas & Alesdatter 1993; Kalivas & Duffy 1995; Kalivas & Stewart 1991; Karler et al. 1989; Nestler & Aghajanian 1997; Pierce et al. 1996a; 1996b; Zhang et al. 1997).

A proposed sequence of events that induces heterosynaptic plasticity in the VTA and NAS has been outlined (Kalivas 1995; Koob & Le Moal 1997; Nestler & Aghajanian 1997; Piazza & Le Moal 1996; Pierce et al. 1996a; Sorg et al. 1997). Repeated administration of psychostimulants or stress produces increased VTA somatodendritic DA release, which results in D_1-mediated enhanced glutamatergic release from prefrontal, amygdala, hippocampal, and other forebrain efferents to VTA DA neurons. Stimulation of glutamate receptors on VTA DA soma and/or dendrites further increases somatodendritic DA release (Kalivas 1995; Nestler & Aghajanian 1997), which, reciprocally,

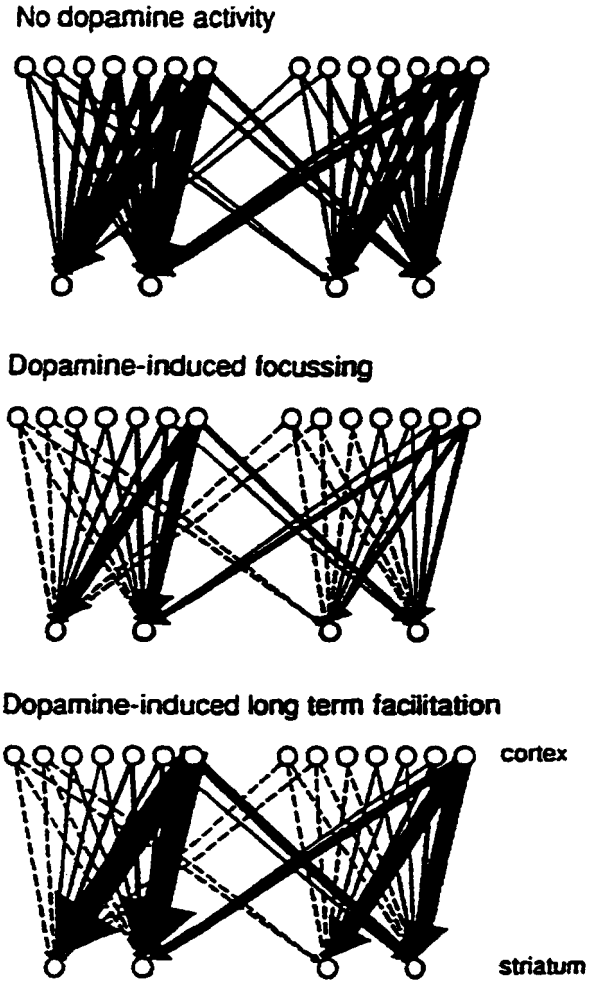


Figure 7. Progressive, differential effects of dopamine release on weak (depressing) and strong (facilitating) cortical and limbic inputs to nucleus accumbens (NAS) spiny neurons. In the bottom of the figure, the salient inputs to the NAS have been enduringly strengthened by dopamine release via a process thought to be similar to long-term potentiation. (From Schultz et al. 1995b.)

strengthens the heterosynaptic connections between glutamate efferents conveying contextual information and VTA DA neurons (Johnston 1997; Kalivas 1995; Murphy & Glanzman 1997; Nestler & Aghajanian 1997). Prefrontal glutamatergic efferents to VTA DA neurons may be particularly influential in this sequence. Although prefrontal glutamatergic efferents to the NAS can influence NAS DA release directly, the primary pathway for prefrontal regulation of NAS DA release is via projections directly to the VTA (Taber et al. 1995). Sensitization-induced strengthening of prefrontal regulation of VTA DA neurons could enhance NAS DA release, and hence the expression of behavioral sensitization, in two ways: (1) by inhibition of VTA DA neurons projecting to prefrontal areas, which in turn would disinhibit prefrontal-NAS glutamate efferents that enhance DA release in the NAS (Sorg et al. 1997), and (2) by direct activation of VTA DA neurons projecting to the NAS; when prefrontal input to these neurons is particularly strong, glutamate-mediated burst firing of VTA DA neurons may occur, which is associated with markedly enhanced DA release in the NAS (Gonon 1988; Johnson et al. 1992; Suaud-Chagny et al. 1992).

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5.3.2. Individual differences in DA functioning and behavioral sensitization. A preponderance of studies suggest a strong relation between individual differences in novelty-induced locomotion, other DA-modulated behaviors, and behavioral sensitization, although variation of results exists as a function of type of behavior (e.g., mesoaccumbens-mediated versus nigrostriatally mediated motor patterns), sensitization criteria (e.g., increased locomotor activity versus a hyperactivity-stereotypy multiphasic pattern), dose level, and subject population (e.g., outbred versus inbred strains) (Deminiere et al. 1989; Hooks et al. 1991a; 1992c; Piazza & Le Moal 1996; Piazza et al. 1989; Robinson 1988). In these studies, subjects (typically rats) are selected on the basis of degree of locomotor reactivity to a novel environment, where high and low responders are defined by a median split in locomotor scores. Across a wide range of doses, high responders exceed low responders in the rate of responding and in the amount of drug administered during the acquisition of psychostimulant self-administration (Piazza & Le Moal 1996; Piazza et al. 1989; 1991a), and in levels of intra-VTA self-stimulation (Eisler et al. 1994). These differences appear to be influenced by genetic variation (Ambrosio et al. 1995; Elmer et al. 1995) and by the number of DA neurons in the VTA region (Fink & Reis 1981). In many studies, pretreatment novelty-induced locomotion is positively correlated across animals with locomotor reactivity to psychostimulants administered systemically (Deroche et al. 1993; Exner & Clark 1993; Hooks et al. 1991a; 1991b; 1992a; 1992b; 1992c; Piazza et al. 1989; 1991a) or into the NAS or VTA (Hooks et al. 1993; Hooks & Kalivas 1994; Piazza & Le Moal 1996).

Behavioral differences between high and low responders are related to variation in DA transmission. A direct relation exists between DA utilization in the NAS and level of spontaneous exploratory activity to novelty (Ahlenius et al. 1987; Barnes et al. 1987; Brose et al. 1987). Additionally, extracellular concentration and release of DA in the NAS is greater and more prolonged in high than in low responders in both basal levels (Bradberry et al. 1991; Hooks et al. 1992a; Piazza et al. 1991b), and levels induced by novelty (Piazza et al. 1991b), stimulants (Bradberry et al. 1991; Hooks et al. 1991b; 1992a), and stressors (Rouge-Pont et al. 1993). The correlations across animals between novelty-induced locomotor scores and basal and stress-induced NAS DA concentrations appear to be substantial (0.54, 0.86, respectively; Rouge-Pont et al. 1993). Sensitivity to the postsynaptic effects of DA also appears to be increased in high versus low responders, the former showing an enhanced locomotor response to intra-NAS infusion of DA, as well as a combination of a 20% increase in D_1, but a 50% decrease in D_2, receptor binding (Hooks et al. 1994). Furthermore, lower DA concentrations in prefrontal cortex were found in high rather than low responders, correlating -0.56 ($p < 0.01$) with locomotor scores across animals (Piazza et al. 1991b). The importance of this last finding is that DA levels in the prefrontal cortex are reduced in behaviorally sensitized rats (Kalivas 1995; Sorg et al. 1997) and are inversely related to basal and stress-induced concentrations of DA in the NAS, as well as to locomotor reactivity to, and propensity to self-administration of, psychostimulants (Deutch et al. 1990; Louilot et al. 1989; Schenk et al. 1991; Simon & Le Moal 1988; Vezina et al. 1991). Finally, novelty-induced locomotion is positively correlated with basal and stress- and novelty-induced corticosterone secretion, which in turn is related to the amount of drug administered during the acquisition of self-administration of amphetamine and cocaine (Goeders & Guerin 1994; Piazza & Le Moal 1996; Piazza et al. 1991a). Functionally, corticosterone enhances firing of VTA DA neurons projecting to the NAS, sensitivity of D_1 and D_2 receptors, DA release in the NAS, and DA release to stressors (Piazza et al. 1991a; Piazza & Le Moal 1996).

In the study by Piazza et al. (1989), high responders acquired self-administration of amphetamine, whereas low responders did not, which may reflect the latter group's reduced DA transmission and, hence, lower incentive motivation during opportunities for psychostimulant reward. However, when low responders were provided DA enhancement via sensitization to amphetamine, subsequent acquisition of self-administration of amphetamine was equivalent to high responders. Similarly, when a high dose of amphetamine was employed, Hooks et al. (1992c) observed robust sensitization in low responders who had failed to sensitize at lower doses. Thus, individual differences in DA functioning, even if influenced by fixed characteristics in DA systems, may be modifiable by strong experiences acting through experience-dependent processes.

The role of DA in both behavioral sensitization and individual differences in novelty-induced locomotion leads to the prediction that high locomotor responders will more readily sensitize to DA-active psychostimulants. At low to moderate doses of stimulants, a correlation between pretreatment novelty-induced locomotion and degree of subsequent sensitization was observed in several studies (Hooks et al. 1991a; 1992b; 1992c; Piazza et al. 1989; 1990). In some cases the relation was substantial (0.84; Hooks et al. 1992c) and may be influenced by genetic variation in DA concentrations in the NAS (Cabib 1993; Camp et al. 1994; Fink & Reis 1981). On the basis of this relation, we propose that the capacity of the VTA-NAS DA pathway for experience-dependent plasticity, indexed by behavioral sensitization, is modulated by stable individual differences in DA transmission in the VTA-NAS pathway, indexed by novelty-induced locomotion. If true, this hypothesis implies that individual differences in VTA-NAS DA pathway transmission modulate the strength of afferent connections carrying the salient incentive context to NAS neurons and, hence, the extent to which that context facilitates approach behavior.

Concordant with this proposal, the inbred strain of C57 mice, which shows enhanced DA transmission, developed robust behavioral sensitization when repeated amphetamine treatments occurred in the same environment in which the test challenge of amphetamine was administered. In other words, strong context-dependent behavioral sensitization was exhibited (Cabib 1993). The inbred strain of DBA mice, which shows lower DA transmission, failed to exhibit significant context-dependent sensitization. When saline was administered in the same drug-paired environment, C57 but not DBA mice exhibited hyperactivity, indicating that the occasion-setting context exerted a much stronger facilitating effect on the locomotor activity of C57 mice even in the absence of stimulant drugs. In contrast, when amphetamine administration was *not* paired with the test environment (context-independent sensitization), the two strains showed comparable sensitization 6 to 7 days after withdrawal from amphetamine pretreatment (Robinson 1988). Thus, the generally enhanced DA transmission of

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C57 mice appears to interact with the plastic process of strengthening the facilitatory influence of salient context on sensitized responding, not with the basic development of behavioral sensitization. Similar findings favoring context-dependent sensitization in a selected line of rats with enhanced responses to novelty have been reported (Ahmed et al. 1993).

5.4. Conclusion

The regulation of neuroarchitecture by DA may be one avenue for collaboration among genotype-driven, experience-expectant, and experience-dependent processes (Collins & Depue 1992). As an illustration, individual differences in the number of VTA DA neurons represent an outcome of genotype-driven processes. This variable markedly influences the sensitivity to incentive stimuli and DA agonists and, thereby, can be thought of as a temperament trait underlying behavioral facilitation and extraversion (Depue, in press a; in press b). If the number of DA neurons is relatively large, an individual will possess the structural capacity to release high levels of DA at terminal sites of VTA projections during experience-expectant sensitive periods. Such an individual would be predisposed to stabilize a large number of synaptic contacts within MOC network structures. Although an enhanced functional outcome in high-DA neuron individuals would not occur if environmental experience were reward-impoverished, findings in animal behavior genetics suggest that an individual with a rich genetic endowment of DA neurons actively explores the environment in search of rewarding stimulation (Fink & Reis 1981; Sved et al. 1984; 1985). Thus, the likely (but not inevitable) outcome of the sensitive period would be a strong functional capacity in the VTA DA system to facilitate responses to incentive stimuli.

It is likely that experience-dependent processes would maintain this capacity because an enduring predisposition to engage incentive stimuli established during experience-expectant development would entail frequent activation of synapses in the terminal fields of VTA DA projections. The notion that early experience has prolonged effects on VTA DA functional properties is supported by findings that uncontrollable prenatal stress produced permanent alterations in NAS and prefrontal DA transmission in adulthood (Deminiere et al. 1992; Fride & Weinstock 1988). Similarly, persistent changes in DA metabolism and behavior have been observed with the administration of psychostimulants during periods of rapid developmental change (Feigenbaum & Yanai 1984; Middaugh & Zemp 1985; Spear & Brake 1983; Spear et al. 1980).

Thus, early experiential processes may lay the foundation for trends in positive incentive motivated behavior by moderating the strength of later experience-dependent processes involving the functional capacities of the VTA DA projection system (Collins & Depue 1992). For example, stable individual differences in VTA DA transmission appear to affect the expression of behavioral sensitization by modifying the strength of synaptic connections of contextual efferents in the NAS. Therefore, across the lifespan, extensive synaptic arborization within MOC network circuitry of an individual with high VTA DA transmission would consistently enhance responsivity to incentive stimuli, which would be manifested in a high, stable level of behavioral facilitation. This provides one means of understanding the high interindividual stability of psychometric measures of extraversion over as many as 20 years (Costa & McRae 1994; McGue et al. 1993).

6. A psychobiological model of the effects of individual differences in DA functioning on incentive-facilitated behavior

Individual differences in DA transmission are associated with variation in encoding the salience of positive incentive contexts and, in turn, with the capacity of those contexts to elicit or set the occasion for rewarding goal-directed behavior. We now more specifically model the influence of individual differences in DA transmission on the facilitation of behavioral responding and discuss the implications of the model for extraversion.

6.1. A psychobiological threshold model of behavioral facilitation

Models of DA-induced behavioral facilitation often employ a minimum threshold that represents a central nervous system weighting of the external and internal factors that contribute to response facilitation (Stricker & Zigmond 1986; White 1986). The threshold is weighted most strongly by the joint function of two main variables: magnitude of incentive stimulation and level of DA postsynaptic receptor activation (Blackburn et al. 1989; Cools 1980; Mogenson et al. 1993; Oades 1985; Scatton et al. 1988; White 1986). The relation between these two variables is represented in Figure 8 as a trade-off function (Grill & Coons 1976; White 1986), where pairs of values (of incentive magnitude and DA activation) specify a diagonal representing the minimum threshold value for response facilitation. Because the two input variables are interactive, independent variation in

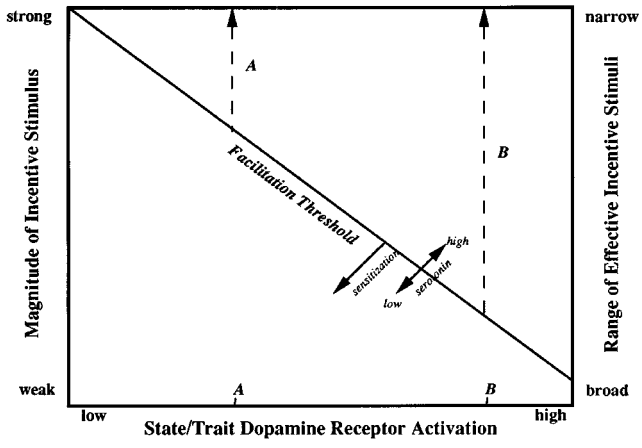


Figure 8. A minimum threshold for behavioral facilitation is illustrated as a trade-off function between incentive stimulus magnitude (left vertical axis) and dopamine postsynaptic receptor activation (horizontal axis). Range of effective (facilitating) incentive stimuli is illustrated on the right vertical axis as a function of level of dopamine activation. Two hypothetical individuals with low and high trait dopamine postsynaptic receptor activation (demarcated on the horizontal axis as A and B, respectively) are shown to have narrow (A) and broad (B) ranges of effective incentive stimuli, respectively. Threshold effects due to serotonin modulation and sensitization of dopamine transmission are illustrated as well.

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either one not only modifies the probability of response facilitation, but it also simultaneously modifies the value of the other variable that is required to reach a minimum threshold for facilitation.

The main determinant of facilitatory efficacy of incentive stimuli is the magnitude of reward. Response facilitation in sated animals is strongly related to sucrose or saccharine concentration in water and food (Grill & Coons 1976; Stellar et al. 1979), to the numeric quantity and quality of reward (Koob 1992; Koob et al. 1993; Nishino et al. 1987; Schultz 1986), and to the level of enhancement (versus degradation) of conditioned incentive stimuli (Schultz 1986). Other stimulus-reward variables that influence DA neuronal activity are less well researched, but the availability of reward and effort required to obtain it are important factors (Nishino et al. 1987; Schultz 1986; Tombaugh et al. 1982). The magnitude of both unconditioned and conditioned incentive stimuli is strongly associated with the quantity of DA release in the NAS and with a graded increase in the frequency and duration of VTA DA neuronal activity, an activity that is well correlated with behavioral effort and velocity (Nishino et al. 1987). Thus, magnitude of incentive reward is stongly related to the induced level of DA transmission and to the probability of response facilitation (Blackburn et al. 1989; Nishino et al. 1987; Schultz 1986; Schultz et al. 1995b; White 1986).

The findings reviewed above show that state changes in DA transmission in the VTA-NAS_{shell} pathway activation influence the threshold for response facilitation. State alterations in DA transmission also modify the salience and response-facilitatory effectiveness of incentive stimuli. Increased DA transmission markedly enhances responding to conditioned reinforcers (Beninger 1983; Blackburn et al. 1989; Robbins 1975; Robbins et al. 1983), an effect that is due selectively to a dose-dependent DA release in the NAS (Le Moal & Simon 1991). Conversely, acute administration of DA receptor antagonists reduces the facilitatory effectiveness of conditioned incentive stimuli at doses that do not decrease subsequent consummatory motor patterns (Blackburn et al. 1989; Koob et al. 1993; Le Moal & Simon 1991), suggesting that facilitation under such conditions is achieved by only strong incentive stimuli.

As discussed in section 5, the threshold of response facilitation is associated with genetic variation that affects stable levels of VTA DA transmission, as well as with induced long-term or permanent changes, particularly those involving DA release in the NAS, that alter previous threshold values. Sensitization-induced increased NAS DA release was associated with enhancement of the salience of incentive stimuli and of locomotor activity to subsequent DA agonist challenge. Figure 8 illustrates a sensitization effect as a reduction in the threshold for response facilitation across the entire range of effective incentive stimuli, as suggested by Robinson (1988; Robinson & Berridge 1993).

6.2. Implications for extraversion

This model allows behavioral predictions that have implications for conceptualizing extraversion. A trait dimension of VTA DA postsynaptic receptor activation is represented on the horizontal axis of Figure 8, where two individuals with divergent trait levels are demarcated: A (low trait level) and B (high trait level). First, for any given incentive stimulus, the degree of state DA response will, on average, be larger in individual B than in individual A. This is the neurobiological equivalent of what Gray (1973) refers to as individual differences in sensitivity to signals of incentive reward and is our hypothetical basis of variation in behavioral facilitation and extraversion. Because degree of state DA activity affects the salience of incentive stimuli, the subjective emotional and motivational experiences that are naturally elicited by incentive stimuli and are part of extraversion – elation-euphoria, desire, incentive motivation, sense of potency or self-efficacy – will also be more enhanced in individual B than in individual A (Koob 1992; Koob et al. 1993; Stewart et al. 1984).

Second, the difference between individuals A and B in magnitude of subjective experience may contribute to variation in the contemporaneous encoding of a stimulus' incentive intensity or salience. In this regard, DA modulation of the encoding of incentive salience may represent one form of state-dependent learning. Furthermore, variation in contemporaneous salience encoding may affect the incentive salience encoded during subsequent memory consolidation (Robinson & Berridge 1993). Accordingly, individuals A and B may develop differences in their long-term encoding of incentive stimuli, due primarily to consistent differences in the intensity of positive affective representations of these stimuli (Mishkin 1982). Differences in stored affective representations of stimuli could have marked effects on behavior, because central representations may be retrieved via prefrontal cortical projections as a means of motivating behavior when explicit goal cues are not present in the immediate environment (Goldman-Rakic 1987; 1995). Thus, individuals A and B may develop differences in their capacity to facilitate behavior by central incentive representations of abstract or temporally delayed goals, such as, for example, a college degree 4 years hence. Put differently, individuals A and B may differ in activation and sustainment of achievement motivation by central representations of delayed rewards, which represents one lower-order trait defining extraversion (see Table 1).

Third, trait differences in DA transmission may have marked effects on the range of effective (i.e., facilitating) incentive stimuli. This is illustrated in Figure 8, where the right vertical axis represents the range of effective incentive stimuli. Increasing trait levels of DA postsynaptic receptor activation (horizontal axis) are associated with an increasing efficacy of weaker incentive stimuli and, thus, with an increasing range of effective stimuli. In Figure 8, individuals A and B are shown to have a narrow (A) versus broad (B) range of effective incentive stimuli, respectively.

Fourth, the broader range of effective incentives for individual B suggests that, on average, individual B will experience more frequent elicitation of approach behavior and more pervasive positive emotional and motivational feelings associated with extraversion. This means that the probability, at any point in time, of being in a DA-facilitated state for individual B is higher, on average, than for individual A. Therefore, when incentive stimuli are encountered, their subjectively evaluated salience will show a stronger positive bias for individual B than for individual A. Thus, extraversion trait differences reflecting variation in DA transmission may proactively influence the salience evaluation of incentive stimuli and may not be restricted to reactive motivational and motoric processes of behavioral facilitation (Bindra 1978; Robinson & Berridge 1993).

Fifth, trait differences in both incentive encoding and

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range of effective incentive stimuli may interact to produce individual variation in the dynamics of behavioral engagement with the environment. The positive relation between state DA transmission and incentive stimulus efficacy suggests that, as an initial incentive stimulus enhances DA release in the NAS, the facilitatory efficacy of subsequently encountered incentive stimuli may be increased proportional to the degree of the initial DA enhancement. Under conditions of strong DA enhancement, perhaps even previously subthreshold incentives may come to facilitate behavior for a period of time. This dynamic process of gradually rising incentive motivation might affect the degree of facilitation of behavior throughout the temporal course of the behavioral engagement (degree of effort, vigor, and vigilance, all of which are affected by DA transmission in the motive circuit; Kalivas et al. 1993), and hence the aggregate incentive salience encoded for the eventual goal. This may relate to the positive relation between DA transmission and resistance to extinction (Le Moal & Simon 1991). In our example, individual A is predicted to exhibit reduced effort and less resistance to extinction relative to individual B in situations in which reward is relatively weak, intermittent, or based on delayed gratification. As the latter "obstacles" to reward increase, individual A is predicted to show reduced perseverance or earlier extinction of reward acquisition behavior (i.e., less enduring behavioral facilitation) than individual B due to less DA reactivity to the incentive stimuli. Perhaps the failure of low novelty-induced locomotion groups to acquire self-administration of amphetamine represents the interactive effects of the above factors (Piazza et al. 1989).

Sixth, variation in DA facilitation is associated with behavioral flexibility when changes in motor, affective, and cognitive response patterns are required by environmental circumstances (Oades 1985). DA lesions (6-OHDA) of the VTA, dorsolateral prefrontal cortex (Brozoski et al. 1979), and NAS (Louilot et al. 1987) reduce or completely abolish spontaneous alternation, reversal, resistance to extinction, and the number of cognitive strategies used in response to environmental modifications (Cools 1980; Le Moal & Simon 1991; Oades 1985), whereas DA agonists produce the opposite effects. When DA transmission is very low, a problem in exceeding the facilitation threshold of any response may occur. At abnormally high DA transmission levels, an extremely high rate of facilitated switching between response alternatives may occur (as perhaps in mania; Depue & Iacono 1989), which can evolve into a low variety of responses (e.g., stereotypy) as if the currently initiated response is locked on and other response alternatives cannot enter the circuit (Oades 1985; Spoont 1992). Thus, returning to our example, compared with individual A, individual B is predicted to manifest more flexibility in changing motor, affective, and cognitive response strategies, and thus more flexible (or facilitated) adaptation to environmental contingencies as they fluctuate over time.

7. Individual differences in DA functioning and personality

There is a paucity of work on individual differences in DA functioning in normal humans, so the validity of our model of extraversion cannot be fully evaluated at present. Individual differences in VTA DA neuron number have been observed in humans (Oades & Halliday 1987), but whether such variation produces individual differences in behavioral facilitation is unknown. However, two points are relevant. First, there is a high degree of axon collateralization near terminal sites of DA neurons, such that single DA neurons can establish 500,000 to 1,000,000 synaptic contacts within spatially restricted striatal areas (Grace 1991; Groves et al. 1995). Second, each medium spiny striatal neuron receives 4,500 to 8,000 DA terminals (Grace 1991). Thus, individual differences in human VTA DA cell number could produce a remarkable variation in synaptic contacts within a particular DA terminal region, as well as significant behavioral effects as demonstrated in animal work.

Several personality theorists have suggested that the VTA DA projection system may be associated with human personality traits, but there is a lack of clarity as to which traits are thought to be of greatest relevance (Cloninger et al. 1993; Gray 1987a; 1992; Netter et al. 1996; Netter & Rammsayer 1991; Rammsayer et al. 1993; Zuckerman 1991b). Zuckerman (1991b) suggested that "Dopamine seems to mediate a general behavioral approach system that might be identified with extraversion or sensation seeking, but it could also involve impulsivity or other p[sychoticism] type tendencies" (p. 186). Although most theorists posit a relation of DA to behavioral approach and extraverted-like behavior, Gray, Cloninger et al., Netter et al., and Zuckerman have aligned DA's predominant association not directly with extraversion, but rather with aggression and/or the cluster of impulsivity-sensation seeking traits illustrated in Figure 3.

Empirically, the situation is not much clearer, probably because the number of relevant studies is small and the neurobiological methodologies are relatively crude. No significant differences were found between normal introverts and extraverts in urinary levels of DA or of a major DA metabolite in response to two DA antagonists (Rammsayer et al. 1993). However, the relation of urinary level to central estimates of DA functioning is questionable (Depue & Iacono 1989). Additionally, no significant relation of DA agonist- or antagonist-induced prolactin decreases or increases, respectively, were associated with aggression or the Zuckerman sensation seeking scales of disinhibition, experience seeking, and boredom susceptibility (Netter et al. 1996).

DA pharmacologic manipulations in relation to both extraversion and sensation seeking scales indicated that the relation of DA activity to reaction time performance is an inverted U-shaped function (Netter & Rammsayer 1991; Rammsayer et al. 1993). Subjects high on these traits showed impaired or improved task performance depending on whether a DA agonist or antagonist, respectively, was applied; the reverse pattern was found in subjects low in these traits. Zuckerman (1984) suggested a similar relationship between catecholamine (including DA) activity and sensation seeking, sociability, and anxiety. Our interpretation is that a positive correlation exists between three variables: DA functioning, extraversion and sensation-seeking trait levels, and position on the inverted U-shaped performance curve. Thus, DA agonism worsens the performance of high DA-high trait subjects by "pushing" them into the upper, descending limb of the performance curve where performance is deteriorating, but improves the performance of low DA-low trait subjects by "pushing" them up the ascending limb of the curve where performance is improving. DA antagonists would have the opposite effects on high and

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low personality trait subjects, as was found in the above studies.

Recent work raises the possibility that genetic variation in the DA D_4 receptor is a source of individual differences in behaviors relevant to extraversion, including addiction to DA agonists (Comings et al. 1991) and novelty- and reward-seeking (Benjamin et al. 1996; Ebstein et al. 1996). Even here, however, results are not completely clear: Although certain genotypes were related to extraversion, positive emotions, excitement seeking, and novelty seeking, the same genotypes were not related to the impulsivity subscale of Cloninger's Novelty Seeking Scale (Benjamin et al. 1996), suggesting a stronger relation with extraversion than impulsivity per se. Additionally, on the basis of Cloninger et al.'s (1987) prediction that early onset alcoholics are high on novelty seeking, and thus should have greater DA reactivity to alcohol (a DA agonist), Heinz et al. (1996) assessed DA agonist-induced growth hormone responses in detoxified, early onset alcoholics, but found no significant association with Cloninger's Novelty Seeking Scale.

We assessed the association of individual differences in DA D_2 reactivity and extraversion (Depue et al. 1994), as measured by Tellegen's Multidimensional Personality Questionnaire (Tellegen & Waller 1997). Two indices of DA response – inhibition of prolactin secretion and activation of spontaneous eye blinking – served as a within-study replication of a DA-extraversion association because they are innervated by separate DA projection systems. Several prolactin and blink indices of D_2 receptor effects were strongly, significantly, and specifically related to extraversion (e.g., $r = 0.75$, $p < 0.003$), but not to two other personality factors (i.e., constraint and negative emotionality [neuroticism]; Depue et al. 1994). Additionally, the degree of D_2 agonist-activated blink and prolactin values were strongly and significantly related to each other as well as to extraversion, indicating that the effects of D_2 activation are similar and are similarly related to extraversion, across two variables that are influenced by separate DA systems. These findings were replicated using the same methods on a larger sample. The relation of extraversion to D_2 agonist-induced prolactin values was 0.60 ($p < 0.01$), but was not significantly different from zero for other factors (e.g., constraint [$r = 0.05$], the impulsivity subscale of constraint [$r = 0.11$], and negative emotionality [$r = 0.08$] [$p > 0.25$ for all factors]; Depue 1995; 1996). In a separate analysis, D_2 agonist-induced prolactin was not correlated significantly with Zuckerman's Sensation Seeking Scales of Disinhibition ($r = -0.10$) and Boredom Susceptibility ($r = -0.12$), nor with Tellegen's Aggression Factor ($r = -0.02$) or the Buss-Durkee Hostility Inventory ($r = -0.22$). These nonsignificant associations also were found by others (Netter et al. 1996). However, D_2 agonist-induced prolactin was significantly but moderately correlated with Eysenck's impulsivity scales associated with strong positive affect (venturesomeness, $r = 0.40$; risk taking, $r = 0.33$, $p < 0.05$ for both factors).

Overall, this set of findings of (1) a high significant relation between DA indicators and extraversion, (2) near-zero correlations of DA indicators with constraint, aggression, and sensation seeking scales lacking strong positive affect, but (3) a moderate correlation with impulsivity scales incorporating positive affect supports (1) our placement of a DA dimension directly in line with the extraversion dimension and (2) an indirect DA influence on impulsivity traits incorporating positive affect (see Fig. 3). Of interest is that prolactin, reflecting the action of DA in the hypothalamus, was strongly related to extraversion, whose behaviors reflect the function of VTA DA cells. DA cell groups, including those in the VTA and hypothalamus, manifest a common genetic influence on cell number that is reflected in their functional properties. For instance, DA agonist effects are correlated across prolactin secretion, exploratory behavior, and locomotor activity in inbred strains of mice that differ in both VTA and hypothalamic DA cell number (Fink & Reis 1981; Oades 1985; Sved et al. 1984; 1985). Therefore, it is possible that the high heritability of extraversion (Bouchard 1994; Tellegen et al. 1988) is related to genetic influences on DA cell groups and that unmeasured genetic variance in our subjects contributed substantially to the observed correlations between extraversion and drug response indices controlled by separate DA projection systems. In any case, the consistently strong and specific DA-extraversion associations found in our studies indicate that the emotional-motivational functions of DA derived from animal research may hold for humans as well.

8. Concluding remarks

We have proposed an analogy between behavioral facilitation and extraversion based on the functioning of the VTA DA projection system. Models of personality traits based on only one neurotransmitter are clearly too simplistic and will require the addition of other modifying factors (Ashby 1996). In our model, DA facilitation is only one, albeit predominant, contributor to extraversion. Individual differences of psychobiological origin in lower-order traits that comprise inventory measures of extraversion may be less dependent on DA functioning (e.g., affiliation) and, accordingly, will represent error variance in predicting extraversion from DA functioning alone. Furthermore, there are neuromodulators of DA function whose receptors are expressed by VTA neurons, including cholecystokinin, opiates, substance P, and neurotensin (Deutch et al. 1987; 1993; Kalivas & Abhold 1987; Kalivas et al. 1993).

State or trait variation in the functional properties of biological variables that influence the functioning of MOC network structures could influence DA neurotransmission in the NAS_{shell}. For example, genetic variation in retinoic acid and retinoid receptors modifies the expression of D_1 and D_2 receptors preferentially in the ventral striatum and influences incentive-related locomotor and cocaine responsivity (Kreczel et al. 1998). Additionally, DA functioning in the amygdala and ventral prefrontal cortex modulates DA utilization in the NAS, as well as the sensitivity to self-administration of DA agonists (Le Moal & Simon 1991; Piazza et al. 1991b). State (due, for instance, to a history of stressors) and trait differences in the secretion of, or sensitivity to, glucocorticoids significantly modulate DA functioning in the VTA and NAS and influence incentive-facilitated behaviors (Piazza & Le Moal 1996), such as the amount of stimulants self-administered and the magnitude of behavioral sensitization (but see Badiani et al. 1995c). Furthermore, both neurotensin and substance P, which influence DA neurotransmission in the NAS (Kalivas et al. 1993) and basal and psychostimulant-induced locomotor activity, differ in the VTA and NAS of high and low locomotor responders to novelty (Hooks et al. 1994; Kalivas et al. 1995).

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Functional levels of neurotransmitters that provide a strong, relatively tonic inhibitory influence on DA are particularly significant modifying factors because of their persistent effects on the threshold of behavioral facilitation. Serotonin is such a factor. It is an inhibitory modulator of a host of DA-facilitated behaviors, including the reinforcing properties of psychostimulants, novelty-induced locomotor activity, acquisition of self-administration of cocaine, and DA utilization in the NAS (Depue & Spoont 1986; Herve et al. 1981; Kelland & Chiodo 1996; Loh & Roberts 1990; Lucki 1992; Piazza et al. 1991b; Ritz et al. 1987; Spoont 1992). Moreover, low trait levels of serotonin activity in animals and humans result in exaggerated expression of, or reduced threshold for, a broad range of DA-facilitated behaviors (Coccaro & Siever 1991; Depue & Spoont 1986; Spoont 1992). This modulatory influence arises in large part from the dense dorsal raphe efferents to the VTA and NAS_{shell}, connections that are known to modulate DA activity (Deutch et al. 1993; Kalivas et al. 1993; Schultz 1986). A proposed serotonin influence on the threshold of behavioral facilitation is illustrated in Figure 8. For similar reasons, functional levels of g-aminobutyric acid (GABA) activity also may influence the threshold of behavioral facilitation. Because of its structural similarity to GABA, baclofen may have a GABA-mimetic action as an inhibitor of substance P, a neuromodulator that has excitatory effects on VTA DA neurons (Kalivas et al. 1993; Le Moal & Simon 1991). Baclofen withdrawal is associated with supersensitivity of postsynaptic receptors of the mesolimbic DA system and with extreme facilitation of behavior (i.e., mania; Depue & Iacono 1989).

Finally, the mitochondrial enzyme monoamine oxidase (MAO) is responsible for presynaptic degradation of biogenic amines and, therefore, modifies DA functioning, particularly human MAO-B that has DA as its major substrate (Mitra et al. 1994). MAO activity is stable over time and is under genetic control (Haier et al. 1980). Pharmacologic inhibition of MAO in bipolar affective disorder is associated with the onset of extremely facilitated affective behavior (i.e., mania), which is often interpreted as being due to increased DA neurotransmission (Depue & Iacono 1989). From a trait perspective, reduced MAO activity levels in the general population are associated with an increased probability of impulsivity, sensation seeking behavior, and affective lability (Haier et al. 1980; Zuckerman 1991b). Thus, in the general population, MAO-B activity appears to be inversely related to the magnitude of DA-induced facilitation of behavior. Although studies of the relation of extraversion and MAO (often unspecified as to type) have been inconsistent (Zuckerman 1991b), we found MAO-B activity to be inversely related to Tellegen's measure of extraversion ($-0.50, p < 0.01$) in the general population, suggesting that DA functioning and MAO-B activity interact to influence levels of extraversion (Depue 1995; 1996).

Despite the complexity inherent in the neurobiology of personality, there is good reason to start with one neurotransmitter, explore the details of its relation to personality traits, and gradually build complexity by adding additional factors. This is particularly true when biogenic amines (DA, serotonin, norepinephrine) are involved. Amines are phylogenetically old and modulate brain structures associated with behavioral processes relevant to personality, including emotions, motivation, motor propensity, and cognition (Luciana & Collins 1997; Luciana et al. 1992; in press). Moreover, none of the amines appear to play primarily a mediating role in the central nervous system, as we have seen for DA. Rather, each may have a specific modulatory role in influencing neural processes (Depue, in press a; Depue et al. 1994; Depue & Spoont 1986; Le Moal & Simon 1991; Mesulam 1990; Oades 1985; Spoont 1992). This fact, together with their broad distribution patterns in the brain (Oades 1985; Oades & Halliday 1987; Tork 1990), indicates that variation in a single amine can have widespread effects on behavior and on the functioning of multifocal neural networks (Mesulam 1990). Animal research on the behavioral effects of both DA and serotonin clearly supports this. Thus, variation in the biogenic amines may provide a powerful predictor of human behavioral variation, as has been demonstrated robustly for serotonin functioning (Coccaro & Siever 1991; Depue & Spoont 1986; Spoont 1992). Therefore, single amine models of behavior may serve as important building blocks for more complex models of personality traits. If so, the suggestion of LeMoal and Simon (1991), put forth in their extensive review of DA and behavior, is an appropriate closing to our discussion: "we predict that individual differences in adaptation will be in the near future an important field of research and that investigations on the dopaminergic network will provide insights on these psychological typologies" (p. 185).

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APPENDIX A: PERSONALITY QUESTIONNAIRE TRAITS[a] THAT CORRESPOND TO THE NUMBERED TRAIT ABBREVIATIONS ILLUSTRATED IN FIGURE 2

Study	Numbered Trait Abbreviation (in numerical order)	Corresponding Personality Questionnaire Trait[b]
Tellegen & Waller 1997		
	WB1	Tellegen Multidimensional Personality Questionnaire, Well Being
	Dom2	Tellegen Multidimensional Personality Questionnaire, Social Potency
	Ach3	Tellegen Multidimensional Personality Questionnaire, Achievement
	Affil4	Tellegen Multidimensional Personality Questionnaire, Social Closeness
	Ach5	Personality Research Form, Achievement
	Affil6	Personality Research Form, Affiliation
	Dom7	Personality Research Form, Dominance
	Persis8	Personality Research Form, Endurance
	Affil9	Personality Research Form, Exhibition
	Nurtur10	Personality Research Form, Nurturance
	Play11	Personality Research Form, Play
	Affil12	Personality Research Form, Social Recognition
	Succor13	Personality Research Form, Succorance
Church 1994		
	Affil14	Costa & McCrae NEO, E1-Warmth
	Affil15	Costa & McCrae NEO, E2-Gregariousness
	Dom16	Costa & McCrae NEO, E3-Assertiveness
	Act17	Costa & McCrae NEO, E4-Activity
	Excit18	Costa & McCrae NEO, E5-Excitement Seeking
	PE19	Costa & McCrae NEO, E6-Positive Emotions
	Affil20	Costa & McCrae NEO, Agreeableness
	WB21	Tellegen Multidimensional Personality Questionnaire, Well Being
	Dom22	Tellegen Multidimensional Personality Questionnaire, Social Potency
	Ach23	Tellegen Multidimensional Personality Questionnaire, Achievement
	Affil24	Tellegen Multidimensional Personality Questionnaire, Social Closeness

[a]References for the trait measures may be found in the study that used them.
[b]NEO = neuroticism-extraversion-openness.

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APPENDIX B: PERSONALITY QUESTIONNAIRE TRAITS[a] USED IN 11 STUDIES THAT CORRESPOND TO THE NUMBERED TRAIT ABBREVIATIONS ILLUSTRATED IN FIGURE 5

Study	Numbered Trait Abbreviation[b] (in numerical order)	Corresponding Personality Questionnaire Trait [c]
Zuckerman et al. 1989		
	Imp1	Buss-Plomin EASI, Inhibitory Control
	Ag2	Buss-Plomin EASI Anger
	P3	Eysenck Personality Questionnaire, Psychoticism
	SS4	Sensation Seeking Scales, Boredom Susceptibility
	SS5	Sensation Seeking Scales, Experience Seeking
	Risk6	Jackson Personality Inventory, Risk Taking
	SS7	Buss-Plomin, EASI Sensation Seeking
	SS8	Sensation Seeking Scales, Disinhibition
	SS9	Karolinska Scale of Personality, Monotony Avoidance
	Imp10	Karolinska Scale of Personality, Impulsivity
	SS11	Sensation Seeking Scales, Thrill-Adventure Seeking
	E12	Eysenck Personality Questionnaire, Extraversion
	Soc13	California Personality Inventory, Sociability
	Act14	Buss-Plomin EASI Activity
	En15	Jackson Personality Inventory, Energy Level
	Ag16	Buss-Durkee Hostility Inventory
	Ag17	Personality Research Form, Aggression
	C18	Strelau Temperament Inventory, Restraint
	C19	Jackson Personality Inventory, Responsibility
	Conform20	Jackson Personality Inventory, Conformity
	Soc21	California Personality Inventory, Socialization
	Ag-22	Karolinska Scale Personality, Inhibition of Aggression
	Soc-23	Karolinska Scale of Personality, Detachment
	Sco24	Buss-Plomin EASI, Sociability
	Soc25	Jackson Personality Inventory, Social Participation
	Soc26	Personality Research Form, Affiliation
	Imp27	Buss-Plomin EASI, Decision Time
Goldberg & Rosolack 1994		
	E28	Eysenck Personality Questionnaire, Extraversion (with factors I and III)
	P29	Esysenck Personality Questionnaire, Psychoticism (with factors I and III)
	P30	Eysenck Personality Questionnaire, Psychoticism (with factors I and II)
Zuckerman et al. 1993 (four factor solution with entire scales)	E31	Costa & McCrae NEO Extraversion
	E32	Eysenck Personality Questionnaire, Extraversion
	Soc33	Zuckerman-Kuhlman Personality Questionnaire, Sociability
	Act34	Zuckerman-Kuhlman Personality Questionnaire, Activity
	C35	Costa & McCrae NEO, Conscientiousness
	P36	Eysenck Personality Questionnaire, Psychoticism
	Imp37	Zuckerman-Kuhlman Personality Questionnaire, Impulsive Sensation Seeking
	Ag38	Zuckerman-Kuhlman Personality Questionnaire, Aggression
	Agree39	Costa & McCrae NEO, Agreeableness
Zuckerman et al. 1993 (five factor solution with primary scales included)	Soc40	Costa & McCrae NEO, E2 - Gregariousness
	Soc41	Costa & McCrae NEO, E1 - Warmth
	Act42	Costa & McCrae NEO, E4 - Activity
	SS43	Costa & McCrae NEO, E5 - Excitement Seeking
	PE44	Costa & McCrae NEO, E6 - Positive Emotions
	Dom45	Costa & McCrae NEO, E3 - Assertiveness
	C46	Costa & McCrae NEO, C4 - Achievement
	C47	Costa & McCrae NEO, C5 - Self-Discipline
	C48	Costa & McCrae NEO, C6 - Deliberation
	C49	Costa & McCrae NEO, C3 - Dutiful

(*continued*)

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APPENDIX B: (*Continued*)

Study	Numbered Trait Abbreviation[b] (in numerical order)	Corresponding Personality Questionnaire Trait [c]
	C50	Costa & McCrae NEO, C1 - Competence
	C51	Costa & McCrae NEO, C2 - Order
Angleitner & Ostendorf 1994[d]		
	Soc52	Buss-Plomin EASI III, Sociability I
	E53	Costa & McCrae NEO, Extraversion
	C54	Costa & McCrae NEO, Conscientiousness
	Imp55	Buss-Plomin EASI III, Non Inhibition Control
	Imp56	Buss-Plomin EASI III, Short Decision Time
	SS57	Buss-Plomin EASI III, Sensation Seeking
	Persis-58	Buss-Plomin EASI III, Non Persistence
	Act 59	Buss-Plomin EASI III, Activity - Tempo
	Act60	Buss-Plomin EASI III, Activity - Vigor
Panter et al. 1994		
	E61	Goldberg Surgency
	E62	Costa & McCrae NEO, Extraversion
	C63	Goldberg Conscientiousness
	C64	Costa & McCrae NEO, Conscientiousness
Church 1994		
	WB65	Tellegen Multidimension Personality Questionnaire, Well-Being
	Dom66	Tellegen Multidimensional Personality Questionnaire, Social Potency
	Soc68	Costa & McCrae NEO, E1 - Warmth
	Soc69	Costa & McCrae NEO, E2 - Gregariousness
	Dom70	Costa & McCrae NEO, E3 - Assertiveness
	Act71	Costa & McCrae NEO, E4 - Activity
	SS72	Costa & McCrae NEO, E5 - Excitement Seeking
	PE73	Costa & McCrae NEO, E6 - Positive Emotions
	C74	Costa & McCrae NEO, Conscientiousness
Tellegen & Waller 1997		
	E75	Tellegen Mulitidimen. Personality Questionnaire, Positive Emotionality
	Soc76	California Personality Inventory, Personal Orientation
	E77	Eysenck Personality Questionnaire, Extraversion
	C78	Tellegen Multidimensional Personality Questionnaire, Constraint
	C79	California Personality Inventory, Rigidity
	P80	Eysenck Personality Questionnaire, Psychoticism
Zuckerman 1996		
	ImpSS81	Zuckerman-Kuhlman Personality Questionnaire, ImpSS
	P82	Eysenck Personality Questionnaire, Psychoticism
	E83	Eysenck Personality Questionnaire, Extraversion
	Act84	Zuckerman-Kuhlman Personality Questionnaire, Activity
	Soc85	Zuckerman-Kuhlman Personality Questionnaire, Sociability
Waller et al. 1991 (interscale correlations, not factor loadings)	NS86	Cloninger Tridimensional Personality Questionnaire, Novelty Seeking [average of NS subscale correlations X Tellegen MPQ Well-Being (best E estimate) & Control (best Constraint estimate)]
Stallings et al. 1996 (interscale correlations, not factor loadings)	NS87	Cloninger Tridimensional Personality Questionnaire, Novelty Seeking (NS correlated x EPQ E & P)
	NS88	Cloninger Tridimensional Personality Questionnaire, Novelty Seeking (NS correlated x EPQ E & KSP Impulsivity)
	NS89	Cloninger Tridimensional Personality Questionnaire, Novelty Seeking (NS correlated x EPQ E & KSP Monotany Avoidance

[a]References for the trait measures may be found in the study that used them.
[b]A "minus" sign appearing after letters but before the number indicates the inverse of the abbreviated descriptor (e.g., Soc-23 is detachment, the inverse of sociability).
[c]EASI = energy-activity-sociability-impulsivity; Sensation Seeking Scales = of Zuckerman; NEO = neuroticism-extraversion-openness; MPQ = Multidimensional Personality Questionnaire; KSP = Karolinska Scale of Personality.
[d]Only established questionnaires used.

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The integration of motivation

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Abstract: We propose that a control system will address the causal dynamics of the neural network that Depue & Collins regard as underlying extraversion. We briefly describe a control system approach and articulate the notion of integration. The integration of goals and regards is achieved by subcortical assessment of reward in the nucleus accumbens and VTA (ventral tegmental area) transmission of this information largely by dopaminergic systems and representation of reward in the MOC (medial orbital cortex). Thus reward information is collected, integrated, and evaluated in the MOC. Such control decisions rely on constraining processes, a functional property of the MOC mediated largely by serotonergic neurons.

If we regard the brain as a hierarchy of control systems, key issues arise regarding how these systems work together to optimize the internal (e.g., endocrine) and external (e.g., motor) manifestations of extraversion.

Control systems. In the simplest case, each control system contains perception, action, and motivational mechanism. Perception mechanisms represent relevant situations (e.g., low blood glucose concentrations) to the control system. Action mechanisms include internal (e.g., mobilization of glycogen) and external (e.g., foraging) activities undertaken by the control system. While a very simple open-loop control system may merely connect specific perceptions with specific actions (in a reflex type of control), most subsystems also include a set point that represents a desired situation or goal. The system computes an error signal from the difference between the desired and the perceived situations and selects actions that reduce the error signal. Thus a control system determines goals and incentive levels, prescribes actions, assesses error and correction, measures progress, and ascertains whether goals have been attained.

Integration. We concur with Depue & Collins (D&C) that multiple neuroanatomical regions and transmitter systems are involved in the control of extraversion. We also share their view that there are multiple incentives (e.g., food, attachment, sex, and safety) that depend on many control systems. These control systems vary according to the type of incentive and which components of the perception-action hierarchy are involved. Nonetheless, to ensure appropriate internal (e.g., endocrine) and behavioral outputs these multiple control systems must function together; they must be integrated. In this context, integration involves the resolution of conflicting action tendencies (e.g., approach vs. avoid). Integration also involves generating courses of action that use available resources to satisfy the systems goals as completely as possible and take into account all the separate constraints the different control subsystems impose on action. Thus integration mechanisms include the comparison and prioritization of control systems, combination of control systems, and the constraint of one system by others. We agree with D&C's suggestion that specific, specialized control systems (e.g., those involved in thirst or hunger) function relatively autonomously. Typically they are not interactive with other systems, although the threat of predation or other danger may suppress their function. Such systems are likely to involve primarily phylogenetically ancient neuroanatomical structures and neurotransmitters. At a higher, less specific level, control systems are more likely to interact – facilitating and constraining each other. Such systems are likely to include multiple cortical and subcortical components and to rely on diverse, interacting neuromodulators.

Subsystems must be able to generate information such as reward potential and the resources needed to meet the specified goal and they must assess current progress toward that end. Subsystems must be able to use information about the status of other subsystems and to constrain their output accordingly. The system would not need to function linearly and sequentially – causes of behavior could arise from alterations anywhere in the system. Control systems supporting extraversion would be continuously operating, unceasingly evaluating and maintaining goals. As D&C indicate, the available human and animal data implicate the MOC as playing a primary role in such a control system.

Our Figure 1 presents an idealized control system framework for extraversion. A *goal signal* is information describing perceivable properties of a desired state and a *reward signal* is information describing the satisfaction of, or progress toward, a goal. A *constraint signal* is information sent from one area to another which reduces that area's options and/or activation level, and a *constraining process* evaluates and selects one possible activation pattern and reduces others. Goal and reward processes would be mediated by dopamine, and selection and constraining processes by serotonin. We can tentatively identify VTA and NAS (nucleus accumbens)

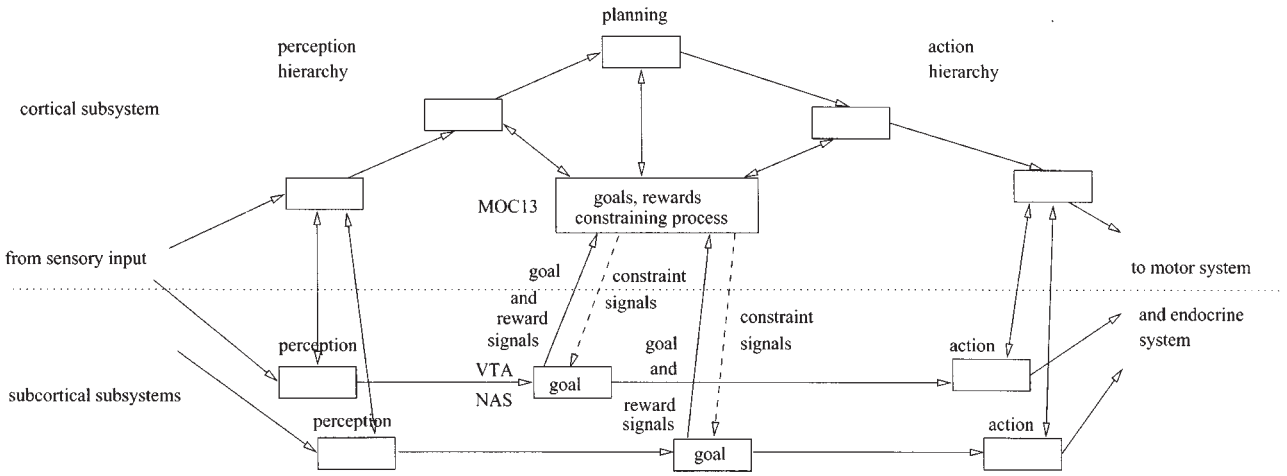


Figure 1 (Bond & Raleigh). Two-level system framework consisting of cortical and subcortical subsystems.

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with the setting of goals and the assessment of reward in the subcortical subsystem. The extended amygdala may be involved as an intermediate integration process for goal and reward signals.

Extraversion. Depue & Collins suggest that individual differences in dopaminergic function underlie individual differences in extraversion. A control system would suggest that individual differences in dopaminergic function may achieve this end by altering the rate at which the system processes information. This might be tested by examining the effects of dopaminergic agonists on the latency of behavioral manifestations of extraversion (e.g., approach). Differences between highly extraverted and less extraverted individuals should disappear with this treatment. Less extraverted subjects should be more responsive to this pharmacological intervention. According to the control system approach, individuals with diminished serotonergic function in the MOC should be less able to develop integrated and constrained actions and so less likely to engage in extraverted patterns of behavior. This could also be tested by localized application of serotonergic agonists to the MOC. Again, the expectation would be that more extraverted individuals will be less sensitive to such treatments.

Of genes, environment, and destiny

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Abstract: The target article approaches individual differences in terms of phenotypic differences developing through the interaction between a specific genetic make up and environmental variables. This interaction is proposed to be cooperative and oriented toward a progressive stabilisation of the trait. However, experimental data from animal studies indicate that environmental pressure promotes dramatic changes in phenotypic expression in mature organisms. Indeed, environmental constraint not only promotes the phenotypic expression of facilitated VTA-NAS DA transmission in genotype-resistant individuals; it also inhibits its expression in genetically prone individuals. This is in line with negative genotype-environment correlation revealed by behavior genetics.

Depue & Collins's (D&C's) attempt to develop a neurobiological view of the personality trait extraversion is certainly stimulating for basic research on psychobiology. One of the most interesting and suggestive aspects of this work is the one dedicated to the development of individual differences. D&C suggest a homology between the extraversion and the behavioral facilitation system based on a common neurobiological substratum (essentially the ventral tegmental area (VTA)-nucleus accumbens (NAS)-dopamine (DA) system). This allows the problem of individual differences to be approached in terms of phenotypic differences developing through the interaction between a specific genetic make-up and environmental variables.

The interaction between genotype and environment that supports the development of the "behavioral facilitation" phenotype is proposed to be cooperative and oriented toward a progressive stabilisation of the trait. Thus, at earlier stages of development a genetically facilitated VTA-NAS DA transmission (essentially owing to a high number of mesencephalic DA neurons) would increase individual chances of collecting experiences from stimulation-rich environments which in turn increase the number of functional synapses in neural pathways (experience-expectant processes). The first hypothesis has yet to be supported by experimental data from animal models. However, it suggests a way to develop animal models of active genotype-environment correlation: individuals select or create environments that are correlated with their genetic propensities (Plomin 1994).

Later in life, a "behavioral facilitation" phenotype characterised by enhanced VTA-NAS DA transmission will lead some individuals to be more susceptible to the incentive salience of rewarding stimuli, increasing the probability as well as the frequency of synaptic activation in the terminal fields of VTA DA projections. This experience will in turn strengthen the functional capacity of VTA DA projections, thus stabilising the "trends" established in the course of early development into traits. D&C also propose an animal model for experience-dependent processes based on heterosynaptic plasticity, psychostimulant-induced behavioral sensitisation. Behavioral sensitisation has already enjoyed a long and successful career as animal model of psychoses (Lyon 1991; Robinson 1988) and drug abuse (Robinson & Berridge 1993). This success has produced a wealth of data about the neurobiological bases of the phenomenon (reported by D&C) but little understanding of its psychobiological meaning.

Moreover, it should be pointed out that as a model of a process promoting stability in personality traits, behavioral sensitisation lacks the structural validity that supports its use as a model for drug abuse and, partly, for psychotic syndromes. Indeed, drug abuse is developed through drug taking and symptoms of amphetamine-induced psychoses in humans are almost indistinguishable from those induced by the endogenous pathology. One possible way to overcome this limitation is to find nonpharmacological factors, that is, environmental conditions capable of promoting behavioral sensitisation. Until now, experimental data offer a single example of such conditions. Indeed, behavioral sensitisation to psychomotor stimulant drugs can be observed following chronic or repeated stress experiences (see Puglisi-Allegra & Cabib 1997).

Nevertheless, data obtained in inbred strains of mice as well as from genetic studies fail to support the idea of a cooperative interaction between genetically related VTA-NAS DA transmission and stress. Thus, as repeatedly stated by D&C, mice of the inbred strain C57BL/6, when compared with DBA/2, represent a good model of behavioral facilitation phenotype promoted by facilitated VTA-NAS DA transmission. Moreover, C57BL/6 mice are characterised by a lower number of D2 DA autoreceptors within the VTA in comparison with mice of the DBA/2 strain. This difference, as thoroughly discussed in the D&C target article, is in agreement with the different behavioral phenotypes expressed by the two strains (see target article, sect. 5.1). A classic genetic analysis as well as an analysis of quantitative trait loci in recombinant inbred strains indicated that mesoaccumbens DA autoreceptor density is a polygenic trait controlled by a major genotype stress interaction that involves genes controlling regulatory factors related to stress response (such as CRH- and steroid-related products) and neural or synaptic plasticity (such as rate-limiting factors for protein synthesis, potassium channel proteins, glutamate, and gangliosides) (Cabib et al. 1997). These observations support a major role for variability in VTA D2 DA receptors in phenotypic variability related to the functional capacity of VTA DA projections.

Stress, however, reduces VTA DA receptors in DBA/2 mice and increases them in C57BL/6 mice (Cabib et al. 1998). Moreover, stressed DBA/2 mice show enhanced locomotor response to amphetamine challenge (Badiani et al. 1992; Cabib et al. 1995; Cabib & Bonaventura 1997), reduced sensitivity to behavioral inhibition promoted by acute stress experiences (Cabib & Puglisi-Allegra 1996; Cabib et al. 1995; Puglisi-Allegra et al. 1990), and spontaneous stereotyping (Cabib & Bonaventura 1997). All these responses can be considered indexes of facilitated DA transmission (Badiani et al. 1992; Cabib & Bonaventura 1997; Cabib & Puglisi-Allegra 1996; Cabib et al. 1995; Puglisi-Allegra et al. 1990). In contrast, stressed mice of the C57BL/6 strain show no changes (Cabib & Bonaventura 1997) or reduced (Badiani et al. 1992) locomotor response to amphetamine, enhanced sensitivity to behavioral inhibition promoted by acute stress experiences (Cabib & Puglisi-Allegra 1996; Puglisi-Allegra et al., 1990) and no sign of spontaneous stereotypes (Cabib & Bonaventura 1997).

Thus, experimental data from animal studies suggest that environmental pressure may promote dramatic changes in phenotypic expression in mature organisms. Indeed, environmental constraint not only promotes the phenotypic expression of facilitated VTA-NAS DA transmission in genotype-resistant individuals; it

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also inhibits its expression in genetically prone individuals. These conclusions cannot be criticized for being based on the effects of extreme, hence pathogenic, environmental conditions. Indeed, long-term exposure to large doses of addictive substances required for inducing behavioral sensitisation is pathogenic too.

Finally, the qualitative plasticity of phenotypes suggested by the experimental data is not surprising because development is a lifelong phenomenon defined by the ability of the organism to reorganise and *change* in the face of a changing environment (Schneirla 1966); and genetic studies, as already discussed, indicate the existence of negative genotype-environment correlation (Plomin 1994).

Does extraversion predict positive incentive motivation?

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www/academic/ps/corr.htm

Abstract: I focus on a number of issues arising from Depue & Collins's target article that require further consideration: (1) data that fail to confirm extraversion effects in positive incentive experiments; (2) the role of personality factors, other than extraversion, in dopamine agonism on positive mood states; (3) the role of extraversion in nonspecific arousal, indicating that extraversion may not be an homogeneous trait; and (4) the problem of identifying neurobiologically important traits from existing structural models of personality. I applaud the heuristic value of the model presented and suggest ways in which aspects of the model may be used to identify the personality traits associated with positive incentive motivation.

Depue & Collins (D&C) provide an elegant synthesis of structural personality models and a wide range of brain data relating to dopamine functions; but inevitably, given the present state of knowledge, their conclusions concerning the role of extraversion in positive incentive motivation are speculative, and not altogether consistent with the limited data that is currently available.

Experimental studies of personality and reinforcement. Does extraversion actually predict positive incentive motivation? D&C's model shares many features with Gray's (1970) reinforcement theory of personality. It, therefore, seems sensible to evaluate their model in the light of work that has already explored the empirical links between personality and incentive motivation. A large body of this research was conducted at the Institute of Psychiatry, under the direction of Professor Jeffrey Gray (for a summary of these data, see Pickering et al. 1997). In this research programme, a broad range of personality traits was sampled, and a variety of behavioural measures (e.g., classical, instrumental, and procedural learning; and modulation of the eyeblink startle reflex by emotion) were used, in both positive and negative incentive motivation contexts.

In common with other studies (e.g., Zinbarg & Mohlman 1988), our results are informative but sobering, revealing a diversity of findings: few studies support the claim that variation in reactivity to cues of positive emotional valence are strongly related to extraversion (or impulsivity, in the case of Gray's theory). In contrast, associations between variation in reactivity to secondary aversive cues and anxiety have proved relatively easy to confirm. However, like other investigators (e.g., Zinbarg & Revelle 1989), we have found numerous significant associations between positive incentive motivation and personality, indicating that incentive motivation and personality are indeed related, albeit seemingly in a highly complex manner.

Given the importance attached to dopamine in positive incentive motivation by D&C as well as many other researchers, we have also investigated the effects of d-amphetamine on mood (Corr & Kumari 1998). We observed an inverted-U interaction with psychoticism, not extraversion: low psychoticism individuals had improved positive mood, while individuals high in psychoticism had impaired positive mood under amphetamine (relative to placebo, in a double-blind design). (Given the similar effects of amphetamine and psychoticism on latent inhibition, our findings are not unexpected; Gray et al. 1991.)

Thus, previous research seems to show that: (1) extraversion is not preferentially related to positive incentive motivation; and (2) dopamine effects in mood are not mediated by extraversion.

Yet, as discussed in the target article, extraversion and positive emotion are related, even when positive emotion is experimentally induced (e.g., Rusting & Larsen 1997). One plausible explanation of these data is that positive incentive motivation and positive emotion are only weakly related, perhaps because incentive motivation usually entails active approach behaviour, which may engender different emotional drive states (and be related to personality traits other than extraversion) to the emotional states experienced upon consummation of an appetitive act. (Perhaps only the latter emotions are more related to extraversion?)

Extraversion and nonspecific arousal. Given D&C's conjecture that extraversion is a homogeneous trait linked to a single motivation system, it follows that extraversion should not be related to other neurobiological processes. However, the one consistent finding in experimental studies of extraversion is its mediating role in nonspecific arousal, across a range of performance measures (Eysenck & Eysenck 1985). For example, we have found extraversion $\times$ arousal interactive effects on procedural learning and critical flicker/fusion, when arousal is manipulated by either caffeine (Corr et al. 1995) or haloperidol (Corr & Kumari 1997). It is significant that, in our study, haloperidol, a potent dopamine antagonist, interacted with extraversion in a manner consistent with Eysenck's (1967) nonspecific arousal hypothesis – an interpretation in terms of reduced positive incentive motivation seemed much less tenable.

Given that extraversion is associated with both nonspecific arousal and positive emotion, then are we not compelled to conclude that extraversion is a heterogeneous, emergent trait that does not fulfill D&C's criterion for homogenous, single motivational system traits?

It would be premature to interpret these or comparable data as providing strong evidence against important hypotheses of D&C's model; but such data serve to illustrate the complexity of personality effects and the practical problem of devising sensitive experimental tests of positive incentive motivation.

Personality structure. The case for extraversion, made upon theoretical analysis of existing personality structures is, prima facie, appealing, but nevertheless highly conjectural. First, multivariate statistical procedures cannot determine the true underlying nature of traits: their vice is shared variance (communality) at the surface level of description. This surface structure is constrained by such factors as selection of items, response biases, and gene-environment interactions. Numerous structural models of personality exist, and we do not, at present, have adequate criteria for determining which model corresponds best to lines of neurobiological influence.

Next, D&C point to the need to separate secondary (heterogeneous) traits from primary (homogeneous) traits. But how is the admirable aim achieved? By fiat, D&C assert that Gray's impulsivity factor is a secondary (heterogeneous) trait, emerging from the interaction of extraversion (E) and neuroticism (N) (does Gray's theory not claim that E and N emerge from the interaction of impulsivity and anxiety? See Gray 1970). In any event, such arguments have little scientific appeal, because we simply do not know which traits are heterogeneous and which are homogenous: theoretical considerations alone cannot answer this question. We must turn to experiment; but we have already seen that experiment does not support the contention that extraversion is a homogeneous trait.

Where should we look for traits of positive incentive motivation? D&C's discussion of the separate processes involved in incentive motivation is highly valuable. If sensitive behavioural measures of distinct motivational processes (e.g., stimulus salience, response organization/execution, etc.) could be developed, then item analysis techniques could be used to construct scales that map

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directly upon these separate processes. There have already been a number of notable attempts to design personality scales that directly measure motivational systems (e.g., Carver & White 1994); these scales are often relatively successful in predicting positive incentive motivation (e.g., Zinbarg & Mohlman 1998). This strategy may be more profitable than relying upon arbitrary criteria to choose between existing (surface) trait descriptions of personality.

In summary, I applaud the conceptual rigour of Depue & Collins's model, which has considerable heuristic appeal. To be sure, many problems remain to be addressed, but this is the normal business of science, to which Depue & Collins have made an admirable contribution.

Dopaminergic influences beyond extraversion

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Abstract: Studies of human performance indicate that extraverts show enhanced motivation in relation to reward signals, but not in relation to safety signals under defensive conditions. When it occurs under defensive conditions, enhanced motivation may be related to neuroticism. While extraverts show some attentional skills consistent with frontal dopaminergic facilitation, other frontal capacities may be related to conscientiousness. These findings suggest that dopaminergic influences on response and attentional processes may contribute to additional personality dimensions such as neuroticism and conscientiousness.

Depue & Collin's (D&C's) target article relates psychometrically defined personality processes to underlying neurophysiological mechanisms, using recent models of incentive motivation as a mediating link. This strategy is reasonable, but the paper neglects a level of analysis that provides additional support and suggestions for extending the model. The discussion would benefit from considering experiments on human extraversion, particularly those dealing with the proposed motivational and response processes. In this commentary, we discuss experiments on performance measures of motivational and response processes in humans, and consider possible dopaminergic contributions to other dimensions beyond extraversion.

A number of studies suggest a relation between extraversion and positive incentive motivation. For example, Newman and his colleagues have found extraverts to show more passive avoidance errors (Newman et al. 1985) and faster circle tracing (Wallace & Newman 1990) than introverts in contexts involving potential reward. We have found extraverts to show enhanced response facilitation elicited by a pretarget cue under rewarding conditions (Reed & Derryberry 1995), as well as enhanced attention to the location of a potentially rewarding target (Derryberry & Reed 1994a). The combination of a reward-related attentional bias and response facilitation fits well with the type of model proposed by D&C.

The underlying motivational processes, however, and their relation to extraversion remain unclear. For example, some of the positive incentive effects are strongest in neurotic extraverts rather than pure extraverts (e.g., Derryberry & Reed 1994a; Wallace & Newman 1990). This may reflect the influence of a single causal mechanism that runs diagonally to extraversion and neuroticism (Gray 1987b), or a separate neuroticism-related mechanism that interacts with extraversion (Wallace et al. 1991). A role for neuroticism is also suggested by the enhanced response facilitation found in more introverted individuals, such as the facilitated startle reactions (Corr et al. 1995) and faster circle tracing (Wallace et al. 1991) evident in anxious subjects under stressful conditions. Also relevant in this regard are the connections between the ventral tegmental area and the fear-related circuitry within the central amygdala and frontal cortex. Such connections are likely to underlie the stress-related dopaminergic reactivity discussed in the target article (sect. 4.7). These findings make it difficult to relate dopamine solely to positive incentive motivation and extraversion. Instead, they suggest an additional influence on defensive motivation and traits related to neuroticism.

A possible solution to this problem can be found in D&C's model of incentive motivation. Following Gray (1987b), the model suggests that the facilitative mechanism is activated not only by signals of reward, but also by safety signals in order to facilitate active avoidance under defensive conditions (sect. 3.2). This makes good sense in that behavior and attention directed in relation to sources of safety and relief are crucial to coping with threat. However, it predicts that extraverts will show a motivational pattern of facilitated approach and active avoidance, and this does not appear to be the case. Questionnaire studies indicate that approach and active avoidance tendencies are negatively correlated, with only the former related to extraversion (Wilson et al. 1990). In reaction time studies, extraverts show response facilitation under appetitive conditions involving reward for fast responses, but not when fast responses would allow the avoidance of punishment (Reed & Derryberry 1995). In studies assessing attention to signals of reward and safety, extraverts show an attentional bias favoring rewarding cues, but not safety cues. It is individuals high in trait anxiety who favor safety signals (Derryberry & Reed, in preparation). This again suggests that defensive forms of incentive motivation, perhaps facilitated by dopamine, may be more closely related to anxiety/neuroticism than extraversion.

Another intriguing issue involves dopaminergic influences upon frontal executive functions. D&C approach such functions in their discussion of behavioral flexibility (sect. 6.2), but more specific influences on attention, working memory, and inhibitory control might also be predicted. Generally consistent with such predictions, Matthews (1997) has found extraverts to show enhanced verbal working memory and divided attention, skills that are adaptive in high information flow environments. It is important to note that these frontal capacities involve multiple component skills, and it seems likely that some of them are independent of extraversion. For example, one childhood temperament model has identified general factors related to positive affectivity, negative affectivity, and effortful control. This last factor, which is assumed to depend on frontal attentional systems, seems most closely related to adult factors such as conscientiousness and constraint (Ahadi & Rothbart 1994). Diamond et al. (1997) have cataloged a range of working memory and response inhibition tasks which appear to depend on frontal dopamine functions. A battery of tasks similar to those used by Diamond has been found to relate to parents' reports of the child's effortful control (Carlson 1997).

Depue & Collins have provided a most detailed and useful perspective on extraversion. Their approach is particularly valuable in its capacity to integrate subcortical motivational and cortical representational processes within a developmental framework. They adopt a reasonable strategy of beginning with a single transmitter system, while acknowledging that the converging influences from other transmitter systems may also contribute to extraversion. Given the comments above, our impression is that a complementary strategy will be useful in considering dopaminergic modulation. Rather than contributing to a single personality dimension, these modulatory processes may diverge to influence multiple dimensions.

Computations in extraversion

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Abstract: We make two suggestions with regard to Depue & Collins's (D&C's) target article. First, regarding the functioning of MOC13, we pro-

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vide data indicating that, contrary to D&C's apparent position, this structure is not necessary for instrumental conditioning. Second, we suggest that D&C's approach would be advanced by reference to formal computational theory, in particular the work of Grossberg. We suggest that an integration of Grossberg's and D&C's models can provide a more complete account of extraversion.

Depue & Collins's (D&C's) target article makes a substantial contribution to relating neurobiology and personality research. They have provided a detailed and convincing development of the notion that the incentive motivation system underpins individual differences in extraversion. D&C propose that incentive motivation information is encoded and integrated in a circuit involving Brodmann's posterior medial orbital prefrontal cortical area 13 (MOC13).

The link between neuroanatomy and extraversion is interesting, but the putative roles of the specific structures could be challenged. In particular, we would like to question the role of orbitofrontal cortex (MOC13). D&C claim that "MOC13 forms higher-level conditional representations of sensory events by associating them with existing or newly-developing response-reinforcement contingencies" (sect. 4.3.4). This implies that MOC13 is implicated in instrumental conditioning. Although the electrophysiological data provided by Thorpe et al. (1983) indicate that neurons are responsive to information about the reward or punishment associated with a stimulus, this does not imply that MOC13 is crucial for instrumental conditioning. Indeed, Thorpe et al. state that OFC represents whether particular stimuli continue to be associated with reinforcement, and it allows behaviour to be modified when it is no longer appropriate. In line with this, OFC lesions in monkeys and humans do not impair instrumental conditioning; they impair the ability to modify responses to stimuli that are no longer reinforced (e.g., Dias et al. 1996; Rolls et al. 1994).

D&C's detailed description of the neuroanatomy of incentive motivation is extremely interesting. They provide a valuable account of the circuitry involved in incentive motivation processes, from the encoding of incentive stimuli to the production of an incentive motivational state that triggers behaviour. However, we believe that their approach would be advanced by considering formal computational theory, such as the work of Armony et al. (1995), and in particular, Grossberg (e.g., Grossberg & Levine 1987). One problem with D&C's focus on the neuroanatomy is that it fails to account for crucial aspects of incentive motivation; for example, the dissociation between instrumental learning and relearning, and the "persistence problem." In contrast, a computational approach such as Grossberg's adaptive resonance theory (ART) of classical and instrumental conditioning can.

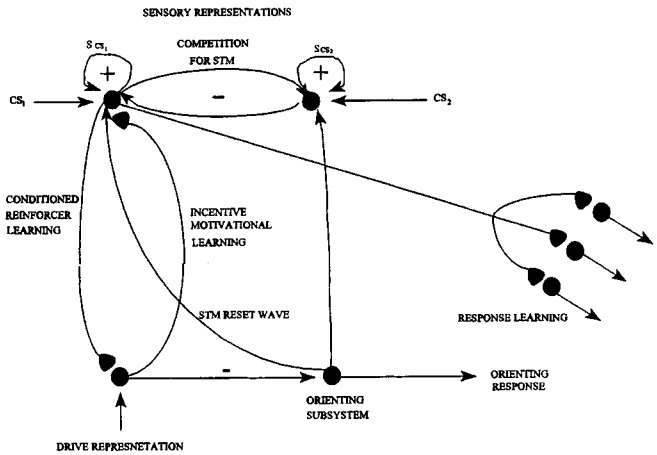


Figure 1 (Fine & Blair). Grossberg's schematic conditioning circuit: conditioned stimuli (CS) activate sensory representations (S_{CSi}), which compete amongst themselves for limited short-term memory activation and storage. The activated S_{CSi} signals elicit conditionable signals to drive representations and motor command representations. Mismatches between learned expectations and drive input representations trigger the orienting subsystem, resetting STM activations of sensory representations. Adapted from Grossberg & Levine (1987; p. 5019).

D&C's account appears to predict an association between instrumental learning and relearning. In contrast, Grossberg's ART circuit predicts the observed dissociation. In Grossberg's model there are interactions between attentional and orienting subsystems (see Fig. 1). Incentive motivational learning is achieved by interactions between drive and sensory cue representations. Relearning occurs when mismatches between reinforcements and learned expectations of reinforcements activate the orienting subsystem, which resets the activation levels of the sensory representations. As D&C describe, the role of MOC13 in detecting unexpected reinforcements could suggest that this region is the neural locus of an orienting subsystem. This integration of Grossberg's and D&C's models makes possible an explanation of the specific relearning deficit seen in subjects with damage to MOC13.

Second, D&C's account cannot explain the persistence problem, also known as the "turkey-love fiasco," namely, how incentive motivation and appropriate behaviour are maintained during the parallel processing of several motivationally incompatible conditioned stimuli. To illustrate, "during an otherwise uneventful turkey dinner with one's lover, suppose that one alternately looks at lover and turkey, where lover is associated with sexual responses . . . and turkey is associated with eating responses. Why do we not come away from dinner wanting to eat our lover and have sex with turkeys?" (Grossberg & Levine 1987, pp. 5019–20). D&C argue that MOC13 is involved in updating reinforcement priorities but this is not sufficient to explain how, for example, the turkey-love fiasco could be resolved. In Grossberg's model, a sensory cue with incentive motivational properties can quickly augment attention to itself via self-generated incentive motivational feedback signals. In this way, erroneous conditioning from a CS to the wrong CR when more than one CS is present cannot occur. The sensory feedback signals occur independent of the orienting subsystem. If this subsystem is mediated by MOC13, then blocking, unblocking, and latent inhibition, for example, should all occur in MOC13 lesioned animals.

Thus, Grossberg's model could be usefully integrated with the anatomical claims made by D&C. Moreover, as detailed by D&C, the evidence that dopamine acts as a facilitator of incentive motivation is strong. It could be suggested that the nucleus accumbens shell, ventral pallidum, and ventral tegmental area are implicated in the incentive motivational learning pathways shown in Figure 1. Indeed, Grossberg (1982) speculates that dopamine is the neurotransmitter that subserves the gated dipoles in these pathways. As described by D&C, dopamine antagonists would reduce conditioned incentive motivation-governed behaviour but it would not affect unconditioned consummatory behaviour and information about stimulus-reinforcement associations (represented by the conditioned reinforcer learning pathway).

Variation in sensitivity to different classes of stimuli across individuals, as suggested by Gray (1973), could be represented as differing responsiveness of drive representations. For example, an individual highly responsive to positive social cues might be one whose drive representations for those cues have a low threshold for activation. This will manifest itself behaviourally as extraversion. In other words, Gray's suggestion that individual differences in extraversion follow from variation in sensitivity to different classes of stimuli can be fully realised at both the cognitive and neuroanatomical levels by an integration of Grossberg's and D&C's models. This also raises the question of whether there are individual differences in sensitivity to more specific classes of stimuli than just reward and punishment. For example, according to Blair's violence inhibition model, psychopaths suffer from a specific insensitivity to distress cues (e.g., Blair 1995); it seems more than plausible that there could be a continuum of sensitivity to distress cues and other types of stimuli in the normal population.

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But the schizophrenia connection . . .

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Abstract: As well as data indicating relationships (emphasised in the target article) (1) between dopaminergic transmission in the nucleus accumbens and positive incentive motivation, and (2) between dopaminergic transmission and extraversion, other data (not accounted for by the hypotheses developed in the target article) indicate relationships (3) between accumbens dopaminergic transmission and cognitive, especially perceptual, processes that are disrupted in schizophrenia, and (4) between dopaminergic transmission and psychoticism. The tension between relationships 1 + 2 and 3 + 4 is discussed and a tentative resolution proposed.

Depue & Collins (D&C) make an important contribution to the tradition that seeks a neurobiological basis for behavioural differences between individuals within a species, impressive in scope in knitting together data from different species, disciplines, and methodologies and in careful attention to detail. It should serve as a storehouse for detailed empirical investigations in the field of personality with both human and animal subjects for many years. Despite its breadth, however, an important aspect of the topic addressed is given scant attention, affecting the interpretation of the data at several points. At the level of human personality, there are data which suggest a relationship between the intensity of dopaminergic transmission and psychoticism, not extraversion as proposed by D&C. At the neurobiological level, there are matching data suggesting a relationship between dopaminergic transmission in the nucleus accumbens and, not incentive motivation as emphasised by D&C, but cognitive processes which suffer disruption during acute psychotic breakdown. These two bodies of data give rise to an alternative hypothesis concerning the relationship between neurobiology and personality.

The "missing" bodies of data are neither obscure nor limited. Unfortunately, there is a dichotomy in discussions of the role of dopamine in behaviour between those who (like D&C) concentrate on evidence linking this to reward and (positive) incentive motivation, and others who concentrate on evidence linking it to schizophrenic cognitive dysfunction. The two groups of workers rarely cite the other body of evidence or the alternative interpretation of the functions of dopaminergic transmission. Yet, without radical revision of at least one of these two competing views, they cannot both be right. Since it is the "schizophrenia connection" that is missing from the target article, I shall discuss only that (see Gray et al., in press, for a model capable in principle of encompassing both bodies of data).

The general hypothesis and supporting data which suggest hyperdopaminergic activity in acute schizophrenia characterised by positive psychotic symptoms (Crow 1980) are well known (Carlsson 1988; Gray et al. 1991). Here I concentrate only on evidence indicating a role for enhanced dopaminergic transmission specifically in the nucleus accumbens, and specifically in cognitive dysfunction observed in acute schizophrenia (for a more general discussion, see Gray 1998). This evidence goes to the heart of D&C's argument. They claim that the degree of extraversion is a positive function of behavioural facilitation resulting from positive incentive motivation and that the behavioural facilitation resulting from positive incentive motivation is a positive function of the intensity of intra-accumbens dopaminergic transmission. Evidence that such transmission is related to something else is accordingly in critical opposition to D&C's argument. This evidence is abundant and readily to hand; I therefore refer only to secondary sources.

Two phenomena are of particular interest: prepulse inhibition (PPI) and latent inhibition (LI). PPI is a reduction in the amplitude of the startle response to a high-intensity "pulse" stimulus if this is preceded by a "prepulse" of lower intensity at a prepulse-to-pulse interval of about 100 msec. LI is a loss of associability if a to-be-conditioned stimulus is first presented, prior to conditioning, a number of times without other consequence. Both PPI and LI are reduced in schizophrenia (Gray 1998; Swerdlow & Geyer 1998; Swerdlow et al. 1992; Weiner 1990). PPI appears to serve a sensory gating function, allowing time for the prepulse to be processed. LI appears to serve a perceptual selection function, weakening processing of previously uninformative stimuli. Thus, loss of PPI and LI in schizophrenia is reasonably interpreted as related to the difficulties experienced by psychotic patients in stimulus selection and focussing of attention (Hemsley 1987). In animals, both PPI and LI can be disrupted by treatments that increase dopaminergic transmission specifically in the accumbens (Swerdlow et al. 1992; Gray 1998; Gray et al. 1997; Swerdlow & Geyer 1998).

Impairment in neither PPI nor LI can plausibly be related to alterations in incentive motivation, contrary to D&C's arguments. These effects suggest, rather, that enhanced accumbens dopaminergic transmission alters *perceptual* processing. A pathway by which such perceptual effects may be produced is described by Grace (Lavin & Grace 1994; O'Donnell & Grace 1998): the projection from the accumbens to the ventral pallidum (see Fig. 6 in the target article), and thence to the nucleus reticularis thalami, which in turn projects to the entire set of ascending thalamocortical sensory relay pathways. This "perceptual" output from the accumbens complements that shown in D&C's Figure 6 to motor systems (via the mediodorsal thalamic nucleus). Thus the dichotomy in views of accumbal function, noted above, is reflected in two different output pathways from the accumbens, one to motor and one to perceptual systems.

There are other features of these experiments which fit ill with any equation of accumbens dopamine release with incentive motivation. In line with other evidence that aversive stimuli elicit such dopamine release (Salamone et al. 1997), experiments applying intracerebral microdialysis to behaving animals during the LI paradigm have demonstrated this effect after both footshock and conditioned stimuli previously associated with footshock (Young et al. 1993). D&C acknowledge the problem posed by such data (sect. 4.7), proposing that (1) there may be functional and anatomical heterogeneity in the circuitry involved and/or (2) goal-directed behaviour is necessary to avoid negatively reinforcing aversive stimuli. Evaluation of solution (1) is difficult without clarification of how dopamine release can differentially affect the proposed heterogeneous circuits. Solution (2) is weakened by further data from experiments applying microdialysis to the accumbens in a sensory preconditioning paradigm. In these, we demonstrated increased accumbens dopamine release after Pavlovian pairing of two stimuli, a light and a tone, which do not possess biological reinforcer properties, either positive or negative; which did not elicit dopamine release prior to pairing; and which did not elicit dopamine release if presented an equivalent number of times but without a Pavlovian associative link (Young et al. 1998). These results imply that accumbens dopamine release reflects associations between stimuli (perhaps, more generally, between events of all kinds) rather than incentive motivation, either positive or negative.

These, then, give rise to a view of accumbens dopaminergic transmission as related (1) to "stimulus salience" (Young 1993), and (2) to cognitive processes affected in schizophrenia. This view suggests that D&C's proposed neurobiology may underlie, not extraversion, but psychoticism. Consistent with this extrapolation, both PPI (Kumari et al. 1997; Simons & Giardina 1992) and LI (Baruch et al. 1988, and many replications) are reduced in normal individuals scoring high on psychometric measures of psychoticism or schizotypy; and, in neuroimaging studies, degree of dopamine receptor binding is related to scores on psychoticism scales (Farde et al. 1997; N. S. Gray et al. 1995). Also, as indicated by D&C, a polymorphism in the dopamine D4 receptor gene is related to scores on the trait of Novelty Seeking (Cloninger et al.

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1991). D&C interpret this as reflecting an extraversion component to this trait; however, it may also reflect a psychoticism component. This ambiguity at the level of human personality description parallels the dichotomy, considered in this commentary and elsewhere (Gray et al., in press), between two very different views of the functions of the mesolimbic dopaminergic projection. A possible resolution (Pickering & Gray, in press) is that the personality dimension most directly linked to accumbens dopaminergic transmission is impulsivity, this being reflected in existing questionnaires as a blend of extraversion and psychoticism.

Neurobiology of extraversion: Pieces of the puzzle still missing

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Abstract: The neurobiological mechanisms associated with affiliation, that Depue & Collins argue are a central component of extraversion are not specified in their model. In addition, only the involvement of the prefrontal cortex in extraversion is discussed, although recent evidence suggests that activity associated with additional cortical regions may be related to this trait. Finally, the assumption that neurobiological mechanisms underlie or play a causal, and therefore, more fundamental role than psychological constructs in the trait is challenged.

The model presented by Depue & Collins (D&C) is to be commended for its integration of behavior, affect, and both cortical and subcortical mechanisms in addressing extraversion. As a theory of the neural circuitry associated with a complex human trait, it explicates more thoroughly than most models the possible collaboration of diverse brain regions that may play a role in a particular pattern of behavior. However, it is questionable whether a model based almost exclusively on animal research can fully characterize a trait such as extraversion. Theoretical gaps remain to be addressed on both psychological and neurobiological levels.

For example, D&C provide substantial theoretical and empirical support for the mechanisms associated with the agency component of interpersonal engagement, argued to be one of the central characteristics of extraversion. However, a potential limitation of the model is that it does not specify the neurobiological mechanisms involved in the other lower-order trait associated with interpersonal engagement, sociability or affiliation, which "reflects enjoying and valuing close interpersonal bonds, and being warm and affectionate," (sect. 2.1). Although D&C note that affiliation is a central component of extraversion and is likely to be associated with a separate motivational and neurobiological influence (sect. 2.4), the mechanisms that relate this trait to extraversion are not elaborated. D&C noted a number of criteria as essential to a comprehensive neurobehavioral model of a personality trait: a description of the behavioral and emotional characteristics of the trait; the motivation inferred to underlie central characteristics; the network of brain structures that integrates that motivation; the neurobiological variables that account for differences in functioning of the network; and the sources of individual differences. For extraversion's lower-order trait of affiliation it appears that only the first point is specified in this model. Since many personality theorists include affiliation as an essential part of extraversion, a comprehensive model would be expected to meet these criteria for all aspects of the trait.

In addition, a problem associated with models of human behavior based on animal data is the emphasis on subcortical mechanisms. Although the present model is notable in its attention to prefrontal cortex, it is unlikely that this is the only cortical region associated with extraversion. A model of regional cortical brain activity and affect (Heller 1993) recently extended to include brain activity associated with the major personality traits of extraversion and neuroticism (Isom 1999) makes clear predictions that increased cortical activity in specific regions of both the frontal and posterior areas would be associated with extraversion. Supporting the prediction of cortical involvement, several studies examining regional cerebral blood flow (rCBF) associated with extraversion have obtained differences in rCBF in secondary visual cortex (Fischer et al. 1997), the bilateral temporal lobes and the left frontal lobe (Stenberg et al. 1990), and the anterior and posterior cingulate cortex (Ebmeier et al. 1994).

It has also been well established that the posterior right hemisphere is specialized for the processing of emotional information (Heller 1997). D&C assert that individual differences in extraversion are a function of differences in encoding incentive salience of stimuli (e.g., is it positive or aversive?). If this is the case, it is likely that the posterior right hemisphere contributes to the process of judging the affective salience of incoming stimuli. Moreover, variation in the process of encoding incentive salience that is described as the basis of individual differences in the frequency and intensity of incentive motivation and as the main source of individual differences in extraversion may also be a function of cortical input from the right posterior hemisphere. In modeling extraversion it will therefore be important to describe the roles and interactions of these additional cortical regions that have been identified as associated with the trait.

A final, but important concern is the assumption that neurobiological mechanisms are "causal" (sect. 2.4) or "underlie" (sect. 4) extraversion. It is conceivable that the causal arrow may go in both directions; although neurobiology may influence behavioral manifestations of extraversion, behavior and psychological constructs may also influence neurobiology (Miller 1996). For example, cognitive-behavioral intervention has been demonstrated to be as effective as pharmacological therapy in modifying biological measures off brain activity (Foa & Kozak 1996). It is therefore evident that variations in psychological constructs (e.g., optimism), and in behaviors (e.g., social interaction) associated with extraversion may influence the activity of the neurobiological systems embodying this trait. Although biogenic amines (such as dopamine) "may provide a powerful predictor of human behavioral variation" (sect. 8), human behavioral variation itself may also serve as a powerful predictor of biogenic amines. In addition, the statement that neurobiological mechanisms "underlie" the trait of extraversion implies that the neurobiological phenomena are somehow more fundamental than psychological phenomena. However, no strategy that focuses on either explanation to the exclusion of the other can be considered comprehensive (Miller 1996); an account of the neural systems associated with extraversion is not a comprehensive explanation of the psychological constructs comprising the trait. A comprehensive model of a trait should integrate both psychological and biological phenomena without assuming that psychological phenomena are reducible to brain events. Moreover, such a perspective limits the degree to which other factors (cultural, environmental, social) are acknowledged as important, despite strong evidence that they play a role.

In sum, although Depue & Collins have presented a well-researched and thoughtful model of extraversion, there is further work to be done if we are to understand fully the human expression and experience of extraversion. A comprehensive model of extraversion must be able to account for all behavioral aspects of the trait, such as sociability and affiliation, as well as the evidence that cortical regions other than the pre-frontal area may be involved. More fundamentally, to the degree that such research recognizes the "agency" in psychological constructs and behaviors as well as in the neurobiology that implements them, models will be better able to integrate the psychological and biological phenomena associated with human personality traits.

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The limbic basal-ganglia-thalamocortical circuit and goal-directed behavior

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Abstract: Depue & Collins's model of incentive-motivational modulation of goal-directed behavior subserved by a medial orbital prefrontal cortical (MOC) network is appealing, but it leaves several questions unanswered: How are the stimuli that elicit an incentive motivational state selected? How does the incentive motivational state created by the MOC network modulate behavior? What is the function of the dopaminergic input to the striatum? This commentary suggests possible answers, based on the open-interconnected model of basal-ganglia-thalamocortical circuits, in which the limbic circuit selects goals and, via its connections with the motor and the associative circuits, directs behavior according to those goals, elaborating on the role of dopamine.

Depue & Collins (D&C) have accomplished a commendable task in integrating a broad spectrum of data and theory to arrive at a neurobehavioral model of extraversion. Their key assumption is that extraversion is closely related to a behavioral approach system based on positive incentive motivation. A medial orbital prefrontal cortical (MOC) network is said to integrate and regulate incentive-motivational modulation of goal-directed behavior. Based on our "split-circuit" model of basal-ganglia-thalamocortical circuitry which describes interconnected (split) motor, associative and limbic basal-ganglia-thalamocortical circuits (Fig. 1; Joel & Weiner 1994; 1997), D&C further suggest that the MOC network likely interacts with a parallel motor network involved in translating motivational states to motor acts.

We proposed that the three split circuits provide the brain machinery for the selection and execution of goal-directed routine behavior, the connections within each circuit subserving the selection of specific behavioral elements (motor acts, motor programs and goals, respectively) and the connections between the circuits serving to coordinate their actions so that the production of complex goal-directed behavior is possible (Joel & Weiner, in press). Of direct relevance to the MOC network is the part of our model dealing with the limbic split circuit (i.e., the connections involving the limbic striatum and the limbic prefrontal cortex [PFC]), which is involved in the selection of goals and their translation to behavioral output. In the following we will highlight some points of possible synthesis between the two models.

1. How are the stimuli that elicit an incentive motivational state selected? The MOC network is composed of first, the nucleus accumbens shell (NASshell, part of the limbic striatum) which encodes the motivational intensity or salience of incentive stimuli, second, a motive circuit which forms an intensity encoded incentive motivational state, and third, MOC 13 (part of the limbic PFC), which constructs reinforcement priorities and behavioral outcome expectations and performs higher-order regulation of network processes. Two different modes of action of the MOC network are described: a continual iterative updating which takes place between MOC and the NASshell, and a collaboration of MOC with the amygdala and hippocampus when behavioral responses evoke unexpected reinforcement outcomes.

An essential question left unanswered in this scheme regards the mechanism by which the stimulus eliciting an incentive motivational state is selected from the multiple stimuli continuously impinging on the organism. Based on hodological, electrophysiological, and behavioral data, we have attributed this selection function to the limbic basal-ganglia-thalamocortical split circuit. The limbic striatum subserves the automatic selection of goals, whereas the limbic PFC subserves a supervisory-like function – it is recruited in ill-learned or non-routine situations, and subserves the deliberate process of deciding what to do. Information regarding the motivational significance of stimuli, provided to the limbic striatum by the limbic PFC and other limbic structures, activates subsets of striatal neurons, which encode goals. The selection between activated goals is based on inhibitory mechanisms in the limbic striatum which subserve competition between activated sets of striatal neurons.

This selection process is molded by reward-driven association learning, which takes place via long term changes in corticostriatal synaptic efficacy guided by a reinforcement signal provided by the dopaminergic (DA) input to the striatum. Learning occurs when in a specific cortical context (representing a specific external and internal environment) a set of striatal neurons is activated (encoding a goal) and the resulting behavior leads to outcomes favorable to the organism, signaled to the striatum by increased DA input. As a result, the activated corticostriatal synapses onto these activated striatal neurons are strengthened, so that in the future the same set of neurons is more likely to be activated, that is, the same goal is more likely to be selected, in the same context. In this way the limbic striatum "learns" to select the "most appropriate" goal in a given situation. That is, the goal whose attainment is expected, according to past experience, to maximize reward in this situation.

Limbic striatal information about the most appropriate goal in the current context is continuously channeled to the limbic PFC where it acts to bias the activity patterns of cortical neurons towards the selection of this goal. This information does not necessarily translate into behavioral output, however, because the limbic PFC receives in addition information about the current context from other cortical and subcortical regions. Under well-learned/routine situations, the biasing effect of the striatum is strong and leads to the automatic selection in the limbic PFC of the goal encoded in the striatum. In contrast, when a strong biasing effect of the striatum is in conflict with a strong cortical biasing effect (e.g., new intentions in a familiar situation), or when the striatal biasing effect is relatively weak (e.g., in novel situations), the automatic selection of goals in the limbic PFC is not possible and goal-selection is the result of a supervisory process, subserved by the interaction of the limbic PFC with other brain regions (e.g., other association cortical regions, amygdala, hippocampus). This mode of functioning of the limbic PFC parallels that suggested to take place in MOC when behavioral responses evoke unexpected reinforcement outcomes. Likewise, information from the limbic PFC is continuously channeled to the limbic striatum, so that continual iterative updating takes place between the limbic striatum and the limbic PFC, as described in the D&C target article.

2. How does the incentive motivational state created by the MOC network modulate behavior? As noted above, D&C state that the translation of goals into motor programs probably involves channeling of information between the basal-ganglia-thalamocortical circuits, but they do not elaborate on how this could be achieved. In our scheme, the limbic split circuit selects goals without specifying the specific motor program whereby they are to be achieved, whereas the coordinated activity of the associative and motor split circuits serves the selection and execution of motor programs. Via its connections with the associative and motor split circuits the limbic split circuit directs and "energizes" the selection and execution of motor programs towards achieving the selected goals (see Fig. 1; for a comprehensive description see Joel & Weiner, in press).

More specifically, via its connections with the associative split circuit, the limbic striatum can bias information processing within the latter, so that the selection of motor programs is in accord with current goals. Via its connections with the DA system, the limbic striatum can modulate its own DA input as well as the DA input to the motor and associative striatum. The latter enables the limbic split circuit to direct learning and to regulate the "energizing" DA effect in the motor and associative striatum according to the current goal (see also below). Finally, via corticocortical projections from the limbic PFC to the associative PFC, the former may directly bias the selection of motor programs by the associative PFC according to current goals.

A note on constraint and impulsivity: in addition to the connections described above, there may be a pathway connecting the as-

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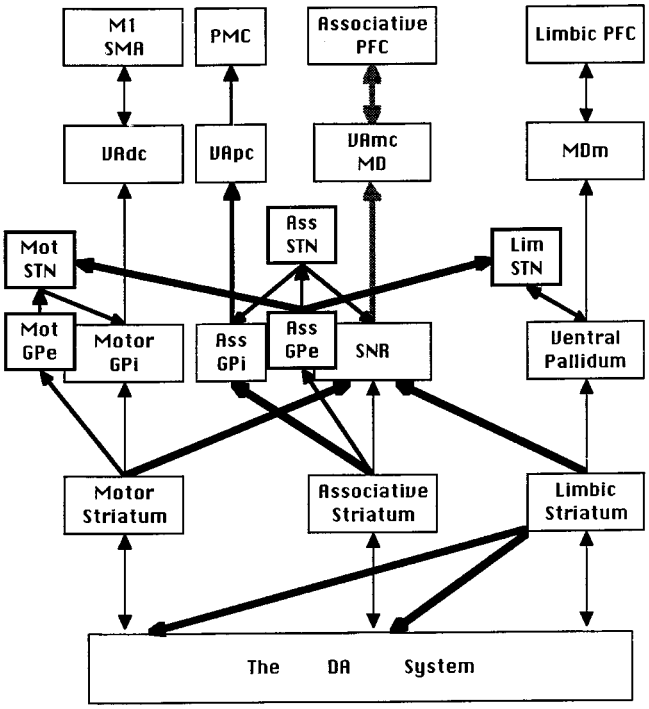


Figure 1 (Joel). A summary diagram of the structural organization of the interconnected motor, associative, and limbic split circuits. (For details see Joel & Weiner 1994; 1997; in press). Pathways connecting circuits are demarcated in thick lines. Abbreviations used: Ass – associative; GPe – external segment of globus pallidus; GPi – internal segment of globus pallidus; Lim – limbic; M1 – primary motor cortex; MD – mediodorsal thalamic nucleus; MDm – medial MD; Mot – motor; PMC – premotor cortex; SMA – supplementary motor area; SNR – substantia nigra pars reticulata; VAdc – ventral anterior thalamic nucleus, dencicellular subdivision; VAmc – ventral anterior thalamic nucleus, magnocellular subdivision; VApc – ventral anterior thalamic nucleus, parvicellular subdivision.

sociative split circuit to the limbic split circuit, via which the former may limit information flow in the latter. A similar pathway connects the associative split circuit to the motor split circuit. These pathways may correspond to "constraint." If this is so, this organization can account for the relative independence of constraint (which depends on the associative split circuit) and extraversion (which depends on the limbic split circuit) as well as for the association of both constraint and extraversion with trait measures of impulsivity that incorporate positive affect (which depend on the interaction between the associative and the limbic split circuits).

3. What is the function of the dopaminergic input to the striatum? Both models incorporate two of the central functions ascribed to striatal DA input, namely, governing striatal learning and enabling or "energizing" the execution of well-learned behaviors, although each model emphasizes a different function. The involvement of striatal DA input in learning and in the striatal selection process were detailed above. With regard to the facilitating role of DA, combining our view of the limbic split circuit as subserving the selection of goals with the findings cited by Depue & Collins on the relation between striatal DA levels and the motivational feelings of desire, wanting, and craving, it may be suggested that DA input to the striatum encodes the intensity of the motivational state or goal selected by the limbic striatum, and thus modulates the degree of effort that will be invested in attaining it. This is in accord with the bulk of evidence pointing to the critical involvement of DA activity in the control of behavior by conditioned incentive stimuli, whereby increased DA transmission markedly enhances responding to conditioned reinforcers (see target article for references). It follows that via its connections with the DA system (via limbic striatal and limbic PFC projections to the DA system) the limbic split circuit not only selects the current goal but also modulates the degree of effort that will be invested in attaining it.

The neurobiology of attention-deficit/hyperactivity disorder (ADHD) as a model of the neurobiology of personality

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Abstract: The Depue & Collins model is intended to explain a normal human personality trait: extraversion. In contrast, attention-deficit/hyperactivity disorder (ADHD) is generally considered to be a type of psychopathology not found in so-called normals; however, the clinical and neurobiological research done on ADHD seems to amplify and support Depue & Collins's model.

In the penultimate section of their target article, Depue & Collins (D&C) relate their neurobehavioral model of extraversion to the small amount of research on similar human behaviors, such as sensation-seeking. Although they find a modest amount of relevant data, one senses their disappointment in the number of nonsignificant trends and modest correlations found in the cited literature. My contention in this commentary is that they were looking in the wrong place. If they look beyond the range of "normal" human behavior (extraversion and sensation-seeking), into the realm of psychopathology, they will find added support for their thought-provoking model. Attention-deficit/hyperactivity disorder (ADHD) is a clearer manifestation of behavioral facilitation than is extraversion/sensation-seeking, and research on its neurobiological basis is consistent with the data they marshalled to illustrate their model.

Readers unfamiliar with childhood psychopathology may not immediately perceive the relevance of ADHD. The core symptoms of ADHD are inattention, impulsivity, and (sometimes) hyperactivity. Russell Barkley, undoubtedly the leading theorist in the ADHD research field, has recently conceptualized the disorder as being one of "behavioral inhibition" (the inverse of D&C's behavioral facilitation; Barkley 1996). As Barkley and many others have contended for over a decade, ADHD is a disorder of "executive function," the seat of which is in the prefrontal lobe and its connections. Deficits in behavioral inhibition have ramifications for many facets of human behavior, ranging from motor control systems to emotional regulation. Impulsivity and poor self-regulation are hallmarks of ADHD, and D&C's description of impulsivity is, in fact, an excellent portrayal of ADHD: "Impulsivity comprises a heterogeneous cluster of lower-order traits that includes terms such as impulsivity, sensation seeking, risk-taking, novelty seeking, boldness, adventuresomeness, bordeom susceptibility, unreliability, and unorderliness." This is an accurate (though incomplete) litany of the cluster of traits often associated with ADHD.

Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed type of mental disorder in childhood. Estimates of its prevalence vary, but currently it is thought to afflict around 3–5% of children in North America (American Psychiatric Association 1994). It represents an enormous family and social burden (Kaplan et al. 1998). Long-term followup studies reveal that children with ADHD are at risk later in life for other forms of psychopathology, especially affective disorders (Farone & Biederman et al. 1990; 1991). Predisposing genes have not yet been

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identified, although dopamine transport genes have been implicated (Cook et al. 1995).

Most relevant to D&C's model is the large amount of data demonstrating reduced blood flow and electrophysiological activation of the prefrontal cortex (especially its striatal connections to the limbic system; for an overview, see Barkley 1996). The data on the dopaminergic basis of such impaired activation are more contradictory, but as D&C point out, the relationship between urinary levels of DA or its metabolites and central DA functioning is questionable, and of course it is difficult to obtain direct measures of central DA functioning in live humans. Certainly, the overriding view of ADHD researchers at the current time is that there is deficient regulation of dopaminergic systems in the same areas of the brain central to D&C model.

Another central point to be made about ADHD is that it is part of a continuum of human behavior. Murphy and Gordon recently expressed this most eloquently (Murphy & Gordon 1998): "the core symptoms of the disorder are also core symptoms of human nature" (p. 347). Levy and her colleagues examined this question in a large cohort from the Australian Twin Registry, and demonstrated empirically that ADHD is best viewed as the extreme end of a continuum of human behavior (Levy et al. 1997).

In summary, the D&C target article is an exhaustive account of the neurobiological basis of behavioral facilitation. At the extreme end of the continuum of behavioral facilitation lies the syndrome we currently know as ADHD. The neurobiology of ADHD is consistent with the Depue & Collins model.

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Dopamine and serotonin: Integrating current affective engagement with longer-term goals

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Abstract: Interpreting VTA dopamine activity as a facilitator of affective engagement fits Depue & Collins's agency dimension of extraverted personality and also Watson's and Tellegen's (1985) engagement dimension of state mood. Serotonin, by turning down the gain on dopaminergic affective engagement, would permit already prepotent responses or habits to prevail against the behavior-switching incentive-simulation-driven temptations of the moment facilitated by fickle VTA DA. Intelligent switching between openly responsive affective engagement and constraint by long-term plans, goals, or values presumably involves environment-sensitive balancing of these neuromodulators, such as socially dominant primates may show.

The ventral tegmental area (VTA) dopamine projection, although not the only mediator of positive affect or pleasure (Berridge 1996), seems to be at least among its chief facilitators, as Depue & Collins (D&C) claim, even if their claim for it is not intended to go much farther than this. While it may seem that the VTA DA response to neutral stimuli in orienting reactions and to aversive stimuli in avoidance behavior shows it not to be specialized for positive affect, such a conclusion, even if justified, may make a difference that is less than it seems.

As Salamone et al. (1997, p. 352) observes in rejecting older "reward," "reinforcement," and "anhedonia" interpretations that made dopamine mediate even the primary pleasures of taste, feeding when hungry, and their like, "accumbens DA . . . is involved in higher order motor and sensorimotor processes that are important for activational aspects of motivation, response allocation, and responsiveness to conditioned stimuli" (p. 352). But one may then go farther to acknowledge that such affective engagement with one's environment, whether perceptual, cognitive, planning, motor, or mixed, is most often pleasant and may be so even where the initially engaging stimulus is aversive and the behavior avoidant. There may thus be more active pleasures than those of pure sensory pleasure or tranquility that are more important determinants of individual differences in behavior and mood. The VTA DA system would seem to be the major facilitator of these.

Interpreting VTA DA activity as a facilitator of affective engagement comports well not only with D&C's account of personality but also with Watson's and Tellegen's (1985) closely related dimensional account of state mood. I assume here that D&C's agency is to be aligned with Watson and Tellegen's high engagement and D&C's affiliation with Watson and Tellegen's pleasantness. We can do this while leaving open the question of whether a bias toward positive affect emerges out of the integrated functioning of the system, presumably in interaction with other affective systems, learning and the environment. However, identifying agency with high engagement would seem to exclude building a bias toward positive as opposed to negative affect into the agency dimension itself, as D&C's discussion seems sometimes to suggest. (However, their expository shifts of emphasis between extraversion and its agency dimension leave room for doubt about this.)

The role of serotonin in D&C's model is more perplexing, if it is to be simultaneously responsible for antagonizing dopamine's pro-extraversion-biasing incentive motivation facilitation (Fig. 8) but also for the nonaffective (legend for Fig. 3) constraint dimension that is supposed to be orthogonal to the extraversion dimension (sect. 2.4 and Fig. 3) and thus not directly opposed either to this or to its agency component, to which I take D&C's VTA DA hypothesis primarily to apply. Differences between serotonergic systems and receptors are available to the theorist, but these do not seem on call here. Perhaps constraint should be understood, at least in part, as the strength of relatively affectless habits formed, in part, by the past incentive motivational teaching of the VTA DA system. Serotonin, by turning down the gain on dopaminergic agency or affective engagement, would permit already prepotent responses or habits to prevail against the behavior-switching incentive-stimulation-driven temptations of the moment facilitated by fickle VTA DA.

A further doubt about D&C's job assignment to overall serotonergic tone arises from the literature on social dominance, in which high-serotonin socially dominant primates often appear to act the role of extraverts in a manner responsive to their serotonin levels (Mehlman et al. 1995; Raleigh et al. 1983). More dominant animals indeed move about less, yet they may approach their groupmates more and interact with them more than do less dominant ones. Perhaps their acting the extravert is in part just acting, however, as more recent ethological work sensitive to the quality and brevity rather than only to the number of their interactions is beginning to suggest (Shively et al. 1991). Rather than behaving simply as incentive motivated extraverts sensitized to social stimuli, they may be acting strategically, using for their long-term mature political ends the superiority in social skills that a high level of serotonin while growing up allows (Mehlman et al. 1995). In both this learning and its later exercise an ability to step back from affective engagement for a cool moment of strategic reflection may be essential and it is this ability that high serotonin levels may confer.

For an animal to have the ability thus to call and use more affective engaged knowledge and behavior appropriately, however, something must have learned when and how much to modulate the modulators in keeping with what is known of the relevant extended context of behavior, if the midbrain's reach is not to disastrously exceed its grasp. Presumably the intelligent switching between openly responsive affective engagement and taking a less affective and more habitual view constrained by long-term plans, goals, or values is one of the things that our large prefrontal cortex, which enters into D&C's scheme, is for. Even so, integrating the demands of love and loyalty, of spontaneity and commitment, is seldom an easy task.

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Anterior asymmetry and the neurobiology of behavioral approach circuitry

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Abstract: Depue & Collins [D&C] propose a well-conceived and nicely detailed theory of the involvement of dopaminergic connections in extraversion. Since these systems are hypothesized to be associated with reward sensitivity, other neural systems that are involved with reward sensitivity should be considered as well. In this commentary it is argued that there is now enough evidence for the involvement of the left and right frontal regions of the brain in approach and withdrawal behavior that it should also be considered in theories of personality such as D&C's. Integration of predominantly subcortical and cortical theories of personality/brain function may produce a more comprehensive picture of temperament and personality.

Depue & Collins (D&C) have provided a nicely detailed neurobiological model for extraversion that is solidly based on extant literature concerning the interaction of mesolimbic dopaminergic pathways, particularly ventral tegmental area (VTA) projections to the nucleus accumbens (NAS), the ventral pallidum (VPM), and the medial orbitofrontal cortex (MOC13). To their credit, D&C also discuss modulation by other transmitter systems such as inhibitory serotonergic projections from the raphe nucleus. The theory is unique, well conceived, and based on a solid theoretical foundation. The authors should be lauded for this work.

Although D&C's theory is essentially well conceived, there appears to be no mention of the literature concerning lateralization of emotion, especially of the left and right frontal regions of the brain. This is particularly important for extraversion, which is hypothesized by D&C to result from neural circuitry involved in incentive motivation. There is now an ample literature on emotional lateralization and its correlations with approach and withdrawal behaviors that might require expanding D&C's incentive motivational circuits to differences in the left and right frontal regions of the brain.

The experience of positive, approach-related emotion is hypothesized to be associated with relative left-frontal and anterior temporal activation, while the experience of negative emotion has been hypothesized to be associated with higher relative activation of the right frontal and anterior temporal regions (Ahern & Schwartz 1985; Davidson 1995; Heller 1990; 1993; Jacobs & Snyder 1996; Tomarken et al. 1990). Victims of left and right frontal strokes, and patients undergoing unilateral hemispheric anesthesia during the intracarotid sodium amobarbitol (Wada) test have shown affective changes consistent with the hypothesis (for a review see Liotti & Tucker 1995). Perhaps the most extensive literature on this hypothesis concerns emotional responses, emotional style, and anterior activation of the electroencephalogram (EEG; see Davidson 1995 for a review).

Left frontal EEG activation (i.e., less alpha in left than right regions) has been related to decreased vulnerability to depression (Kline et al. 1998; Tomarken & Davidson 1994), and relative right frontal activation to increased vulnerability to depression (Allen et al. 1993; Davidson 1995; Henriques & Davidson 1990). Anterior asymmetries recorded during baseline conditions have predicted subsequent emotional responses in infants (Davidson & Fox 1989) and adults (Tomarken et al. 1990), and correlate with personality traits thought to relate to vulnerability to depression (Harmon-Jones & Allen 1997; Kline et al. 1998; Sutton & Davidson 1997; Tomarken & Davidson 1994), as well as depression per se (Allen et al. 1993; Henriques & Davidson 1991).

The left and right frontal regions of the brain appear to be sensitive respectively to positive and negative stimuli (Davidson & Fox 1982; Fox & Davidson 1986), to the expression of happiness and disgust (Davidson et al. 1990), and to reward and punishment (Sobotka et al. 1992). Especially relevant to individual differences in incentive motivational circuits and extraversion are data relating individual differences in behavioral activation and inhibition as assessed by the Behavioral Inhibition/Behavioral Activation (BIS/BAS) scale (Carver & White 1994) to left and right frontal activation (Harmon-Jones & Allen 1997; Sutton & Davidson 1997). Carver and White (1994) have reported moderate correlations of the BIS with manifest anxiety, and moderate correlations of the BAS with extraversion. Furthermore, Carver and White (1994) have argued that their view of BIS/BAS is very similar to that developed by Depue and colleagues.

The evidence implicating the left and right frontal regions of the brain in approach and withdrawal is sufficient to warrant considering theories of personality relating to reward sensitivity, extraversion, depression vulnerability, and related concepts. In particular, it would seem fruitful to explore the integration of transmitter systems and brain laterality. For example, we recently found that higher spontaneous blink rates, a peripheral correlate of dopamine function, were associated with relatively greater left frontal activation (Myers et al. 1997). Such a relationship might be expected, given that dopamine projections may be slightly more abundant in the left hemisphere than in the right (for a review see Liotti & Tucker 1995). A second example involved transient and rapid reduction of available serotonin using rapid tryptophan (TRP) depletion. Rapid TRP depletion alters frontal EEG asymmetry in euthymic individuals with a history of depression, but not in never depressed controls (Allen et al. 1995).

Although sufficient commonalities between the EEG asymmetry literature and D&C's hypothesis exist to warrant attention to the issue of their integration, there are some notable limitations and inconsistencies. For example, there are no published studies on extraversion and left frontal activation, possibly because there is in fact no relationship. Consistent with this hypothesis, in substantial unpublished raw data on resting EEG and the Eysenck Personality Questionnaire (EPQ), and has no significant relationships between extraversion and EEG asymmetry were observed (Kline 1998). The only significant relationships with the EPQ and asymmetry involved the L scale (see Kline et al. 1998).

It could accordingly be that brain laterality has little or nothing to do with extraversion, and that D&C are justified in leaving it out of their theory completely. On the other hand, it may be that no relationship between frontal EEG asymmetry and extraversion exists when measured by widely used and higher-order measures of the construct. As suggested by D&C, it might be more fruitful to try to integrate neurobiological measures (e.g., EEG) with lower-order constructs in the extraversion domain. Alternatively, approach and withdrawal may be the more fundamental dimensions of emotion (Davidson 1995) and extraversion must nevertheless be interpreted in context. In any case, the laterality puzzle has clearly been omitted from an otherwise comprehensive discussion by Depue & Collins.

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Steps to a neurochemistry of personality

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Abstract: Depue & Collins's (D&C's) work relies on extrapolation from data obtained through studies in experimental animals, and needs support from studies of the role of dopamine (DA) neurotransmission in human behaviour. Here we review evidence from two sources: (1) studies of patients with Parkinson's disease and (2) positron emission tomography (PET) studies of DA neurotransmission, which we believe lend support to

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Depue & Collins's theory, and which can potentially form the basis for a true neurochemistry of personality.

Depue & Collins (D&C) rightly lament the absence of corroborative evidence from human cognitive neuroscience for their theories. However, we believe that there are data from human psychopharmacology, which provide support for their work, and may help to form the basis for an integrated neuroscience of personality.

In an important article, Robbins and Everitt (1992) detail their work on the functions of dopamine in the striatum using the two classic methodologies of comparative psychopharmacology: (1) examining the effects of altering dopamine neurotransmission on behaviour and (2) investigating how behaviour and environmental circumstances change dopamine transmission. These methodologies, when transferred to human studies, provide powerful tools for characterizing the functions of dopamine in human behaviour.

Studies in Parkinson's disease patients. Obviously, selective neurochemical manipulations cannot be made in humans, but patients with Parkinson's disease (PD) provide a useful model of the effects of dopamine depletion in humans. PD is characterised by degeneration of both the nigrostriatal and mesolimbic/mesocortical DA systems (Agid et al. 1987), and, as would be predicted from C&D's work, patients show both reduced novelty seeking (Menza et al. 1993) and impaired exploratory behaviour in a task analogous to the radial maze (Owen et al. 1997). Novelty seeking scores in PD patients correlate with striatal dopaminergic status, as measured by ^{18}F-Dopa uptake (Menza et al. 1995), and exploratory behaviour is influenced by L-Dopa medication status (Lange et al. 1992), suggesting that both deficits do indeed relate to altered DA transmission. Furthermore, we have recently shown that impaired novelty seeking and exploratory behaviour in PD are themselves correlated (Hutton 1998), suggesting a common linkage between the two.

PET neurotransmitter "activation studies." Previous PET studies aiming to explore links between DA transmission and behaviour have relied on correlating scores on cognitive tasks and personality inventories with resting levels of dopamine binding in the striatum (e.g., Farde et al. 1997; Grant et al. 1998; Lawrence et al. 1998; Menza et al. 1995). These studies have generally shown correlations between levels of striatal dopamine binding and measures related to the extraversion construct. However, the studies are somewhat limited, in that they are unable to tell us anything about the dynamics of DA transmission in relation to specific behavioural challenges, in the way, for example that has been so successful in brain mapping studies examining changes in blood flow in relation to specific behavioural challenges. However, recent developments in PET neuroreceptor mapping techniques have, for the first time, provided a method for examining dynamic alterations in DA transmission in the living human brain during behavioural challenge.

The basic idea behind PET neurotransmitter "activation" studies, is that a behavioural (or pharmacological) challenge should result in increased release of endogenous neurotransmitter, which will reduce the number of receptors available for binding to the injected PET radio tracer (Grasby et al. 1996; Kegeles & Mann 1997). Until recently, the question has been whether the resulting decrease in receptor binding of the radiotracer caused by an increased concentration of endogenous neurotransmitter produces a detectable signal change in the PET images. Morris et al. (1995) used numerical simulation to investigate the possibility of measurable effects produced in the DA D_2 system by an activation task; their results suggested that activation of DA was detectable with PET and ^{11}C-raclopride.

Recently, we (Koepp et al. 1998) used ^{11}C-raclopride to detect, for the first time in the living brain, changes in the kinetic behaviour of the tracer *in vivo,* consistent with changes in levels of extracellular dopamine induced by a behavioural task. During one scan, male volunteers played a video game, which involved learning to navigate a tank through a computer-generated environment in order to obtain a financial reward. This task is comparable to tasks in the animal studies described by D&C, in which dopamine is released during the anticipatory or appetite phase of motivated behaviour. During a second scan, subjects viewed an empty screen. Differences in ^{11}C-raclopride binding potential between baseline and activation scans were used to infer changes in levels of extracellular dopamine (Morris et al. 1995). Our results showed that striatal ^{11}C-raclopride binding potential was reduced during the video game, particularly in the ventral striatum; results which are compatible with a task-related increase in levels of extracellular dopamine reducing the number of D_2 receptor sites available for binding to ^{11}C-raclopride. These results thus complement electrophysiological studies of dopaminergic neurotransmission in animal studies, and provide a bridge linking human and experimental animal data on the role of DA neurotransmission in motivated behaviour.

We believe that these complementary methodologies provide a useful framework in which to explore, in humans, neurobiological theories of personality, of which D&C's is a paragon. For example, studies of personality, in subjects with phenylketonuria (PKU) who have a developmental disorder characterised by a selective reduction in DA neurotransmission (Diamond 1996) could provide important data on the developmental neurobiology of personality; and variability in neurotransmitter release detected during behavioural (or pharmacological) neurotransmitter "activation" studies could be related to individual differences in personality traits such as extraversion. Perhaps one day we may even be able to agree with Freud (1920) that "The deficiencies in our description [of the psyche] would probably vanish if we were already in a position to replace the psychological terms by physiological or chemical ones."

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Reconciling discrete psychological typology with a psychobiological continuum

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Abstract: Structure entails arrangements and interrelations of parts that organize the whole (i.e., personality). It involves stability of traits over time. Extraversion varies along a continuum towards introversion. Multiple behavioral and biological variables in several systems vary and are regulated homeostatically within the normal range. If there is a fixed point for an individual, what inhibits variation in the biological parameter?

Given the impressive scope of Depue & Collins's (D&C's) review – bringing together, as it does, such a wide array of disciplines such as personality psychology, social psychology, and neurochemical pharmacology – it might seem over-fastidious to blame the authors for leaving out certain important aspects of the topic, but among the definitions D&C begin with, there is one I would like to have seen more fully discussed, the "structure" construct. What is this, not anatomically, of course (for neurobiologists have alas banished this word), but psychobiologically? (Kagan 1994). Given the hypothesis that there exist relatively stable traits, the challenge is to explain how neurochemical, neuroendocrinological or other organ system parameters correlate with psychological-behavioral ones in such a way that, for a given individual, a certain level of dopamine utilization or a certain amount of stress hormone released in a specific situation, predicts a corresponding

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spectrum of psychological responses (or vice versa) with a certain degree of stability across time.

Depue & Collins (D&C) refer to a now widely accepted dichotomy in the rat: HR vs. LR, based on reactivity to stress (Piazza et al. 1989). It is important to remember, however, that reactivity to stress varies along a continuum. The reactivity parameter has the same basic characteristics as other biological data, covarying with parameters from other systems, biochemical, endocrinological and behavioral, all derived from data on individuals. When correlations are significant enough, they can be used to make predictions (Piazza et al. 1990; 1991a; 1991b). A related concept is that of normality: Where, on the continuum, is the optimal point? One cannot understand the factor interactions and between-systemic covariation for a given individual without likewise considering other individuals. To understand psychobiological structure for a given subject, one must take individual differences into account (Bates & Wacks 1994; Costa & Widiger 1993).

It is important to approach the underlying psychobiological laws that order variation in systems towards stability for a given organ. The HR rat cannot be understood without understanding the LR rat, just as thyroid function cannot be understood by studying either hypothyroidism or hyperthyroidism (Piazza & LeMoal 1996). It is impossible to study extraversion without studying introversion and considering their relation on the same psychobiological continuum. The concepts of structure and of temperamental stability leave open the possibility for change, a matter of intense debate (Heatherton & Weinberger 1994). There is evidence from animal studies that, at least under certain conditions and during certain critical periods, it is possible to transform LR rats into HR ones and vice versa. What about extraversion and its underlying biological parameters?

It would be interesting to dissect the "agency" construct and its motivational components, such as achievement. It is thought that many philosophers, poets, novelists, and creative and productive artists have been introverts (if not depressed). Impulsivity also merits more discussion; from a psychiatric and clinical point of view, and perhaps also in animal pharmacology, it has negative connotations. This trait may be the extreme of a continuum. It would also have been of interest to consider how the ability to inhibit is related to attention; this might be impaired in extreme extraversion with hyper-reactivity and impulsivity.

To conclude this commentary with some neurobiological considerations, I still think dopamine neurons are assembled in a complex interactive network in which the frontal cortex (mesoprefrontal dopamine) exerts a pontifical role even in motivational problems (Le Moal 1995).

What about sex differences? An adaptationist perspective on "the lines of causal influence" of personality systems

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Abstract: The evolutionary theory of sex implies a theoretically principled account of the causal mechanisms underlying personality systems in which males pursue a relatively high-risk strategy compared to females and are thus higher on traits linked to sensation seeking and social dominance. Females are expected to be lower on these traits but higher on traits related to nurturance and attraction to long-term relationships. The data confirm this pattern of sex differences. It is thus likely that these traits have been a focus of natural selection rather than the traits of gregarious/aloof and arrogant/unassuming hypothesized by Depue & Collins.

My commentary focuses on conceptualizing personality traits as adaptive systems. As Depue & Collins (D&C) note, "theoretical arguments far exceed data in the debate over where to place the lines of causal influence within the relational structure of personality." True, but by using the evolutionary theory of sex it is possible to make theoretically principled arguments on how to conceptualize personality traits as adaptations (see MacDonald 1988; 1995). Personality systems are sex differentiated in a manner that is predictable from the evolutionary theory of sex and the "lines of causal influence" are not as proposed by D&C.

Evolutionary theory predicts that in species with sex-differentiated patterns of parental investment, the sex with the lower level of parental investment (typically the male) is expected to pursue a higher risk strategy compared to females, including being prone to risk taking, neophilia, and exploratory behavior. This follows because the high-investment sex (typically female) is expected to be able to mate relatively easily, is highly limited in the number of offspring, and does not typically benefit from additional matings (Buss & Schmitt 1993; Symons 1979; Trivers 1972). Males do typically benefit from additional matings, however, with the result that males must often compete with other males for access to females. Successful males are able to sire a highly disproportionate number of offspring, and unsuccessful males are often without access to mating opportunities.

Mating for males is thus expected to be a much higher-stake enterprise, with more to gain and much more to lose than is the case with females. Risk taking directed at resource acquisition can therefore have high payoffs for males compared to females. Males in general are expected to be higher than females on behavioral approach systems (including sensation seeking, neophilia, exploratory behavior, risk-taking, boldness, sensitivity to reward, and impulsivity). D&C claim that this is a heterogeneous list of traits, but within the evolutionary theory of sex they form a conceptual unit: they all involve risky behavior that would benefit males more than females. Similarly, evolutionary theory predicts that in species with sex-differentiated patterns of parental investment, males would gain more from aggression and social dominance because engaging in these behaviors would be more likely to lead to increased mating opportunities whereas females do not benefit from increased mating opportunities.

Given the clear predictions based on the evolutionary theory of sex, it seems reasonable to suppose that sex-differentiated personality systems conforming to these theoretical expectations have indeed been a focus of natural selection. This in turn implies, in agreement with the pioneering work of Jeffrey Gray, that extraversion should not be viewed as the causal basis of behavioral approach [see also Gray: "On Mapping Anxiety" *BBS* 5(3) 1982; Gray et al. "The Neuropsychology of Schizophrenia" *BBS* 14(1) 1991.] An adaptationist perspective is much more compatible with a factor rotation in which dominance as well as several other highly sex differentiated, approach behaviors, including sensation seeking and impulsivity, form one axis, while the trait of nurturance/love, which includes pair bonding and close emotional attachments, forms the other. Thus the circumplex model of interpersonal descriptors results in the dimensions of dominance and nurturance/love and covers the same domain as extraversion and agreeableness on other five factor model (FFM) measures (Briggs 1992; Trapnell & Wiggins 1990). As Trapnell and Wiggins (1990) point out, the difference amounts to a rotational difference between two different ways of conceptualizing the same interpersonal space.

There are no sex differences in extraversion or gregariousness, in accord with evolutionary expectations, but men score significantly higher on the IAS-R-B5 DOM (dominance) scale (Trapnell & Wiggins 1990) and on the thrill and adventure seeking, disinhibition, and boredom susceptibility subscales of the sensation seeking scale (Zuckerman 1979). [See also Zuckerman: "Sensation Seeking" *BBS* 7(3) 1984.] These scales tap variation in attraction to physically dangerous activities, lack of fear of physical harm, gambling, reward-seeking behavior (e.g., promiscuous sexual activity, drinking) and aversion to repetitive experiences. On the other hand, there are no sex differences for experience seeking which involves seeking a variety of experiences (e.g., attraction to visual and olfactory experiences; attraction to non-conformist

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lifestyles) and thus not expected to be sex-differentiated on an evolutionary account. In factor analytic studies, sensation seeking and IAS-R-B5 dominance line up in the same factor analytic space (Zuckerman 1989). Taken together, the data indicate a highly sex differentiated interpersonal and non-interpersonal space tapped by IAS-R-B5 dominance and several central aspects of sensation seeking.

Although there is little evidence for age changes in NEO-PI-R Extraversion (McCrae & Costa 1990), sensation seeking (including the promiscuous sexual activity loading on the disinhibition subscale, Zuckerman 1979) and aggression peak in late adolescence and young adulthood, followed by a gradual decline during adulthood. This "young male syndrome" is highly compatible with evolutionary thinking: sex-differentiated systems are expected to be strongest at the time of sexual maturation and maximum divergence of reproductive strategies (Wilson & Daly 1985). Because mating is theorized to be relatively problematic for males, it is during young adulthood, when males are attempting to establish themselves in the wider group and to accumulate the resources necessary for mating, that the male tendencies toward sensation seeking, risk taking, and aggression are expected to be at their peak.

Similarly, at the functional level, nurturance/love is a much better candidate as a fundamental human adaptation than sociability, gregariousness, or extraversion. Nurturance/love is proposed to underlie adaptive relationships of intimacy and other long term relationships, especially family relationships, involving reciprocity and transfer of resources to others (e.g., maternal and paternal investment in children). Secure attachments and warm, affectionate parent-child relationships have been found to be associated with a high-investment style of parenting characterized by later sexual maturation, stable pair bonding, and warm, reciprocally rewarding, non-exploitative interpersonal relationships (Belsky et al. 1991). If the main evolutionary impetus for the development of the human affectional system is indeed the need for high investment parenting, females are expected to have a greater elaboration of mechanisms related to parental investment than males. Females, because of their very high, morphologically imposed investments in pregnancy and lactation are expected to be highly discriminating matters compared to males. Females score higher on the IAS-R-B5 LOV scale by a very robust 0.88 standard deviations (Trapnell & Wiggins 1990). Moreover, IAS nurturance involves the tendency to provide aid for those needing help, including children and people who are ill (Wiggins & Broughton 1985), and would therefore be expected to be associated with ideal child-nurturing behaviors. This dimension is strongly associated with measures of femininity, and is associated with warm, empathic personal relationships and dependence (Wiggins & Broughton 1985).

In summary, D&C state that the circumplex model of interpersonal descriptors consisting of orthogonal dimensions of dominance and affiliation is "consistent" with their perspective, but they interpret these two dimensions as components of extraversion. Social dominance and nurturance/love are very different adaptations, however, with very different functions in the human environment of evolutionary adaptedness, and they have very different patterns of evolutionarily expected sex differences. Within D&C's perspective, we must suppose that the non-sex differentiated dimensions of gregarious/aloof and arrogant/unassuming has been the primary focus of natural selection. There is no question that all phenotypes have a biological substrate. However, there are acknowledged methodological difficulties involved in psychopharmacological studies (Depue et al. 1994), and there are relatively few studies linking dopamine mechanisms with extraversion but not sensation seeking. Indeed, despite significant associations with Tellegen's PEM (a measure of extraversion), Depue (1996) failed to find a significant association between DA PRL response and Eysenck's EPQ extraversion. Further confusing the picture, there were associations between dopamine mechanisms and Eysenck's venturesomeness and risk-taking, which are conceptually linked with sensation seeking and expected on an evolutionary account to be under differential selection between the sexes. However, this study reported no associations between dopamine mechanisms and the disinhibition and boredom susceptibility subscales of the sensation seeking scale. It therefore seems at least premature to insist that extraversion should be viewed as an adaptation and a primary focus of natural selection while traits like sensation seeking and nurturance/love, whose patterns of sex differences show a clear evolutionary logic are relegated to a secondary status resulting from a hodgepodge of neurobiological mechanisms.

Moderators and mechanisms relating personality to reward and dopamine: Some findings and open questions

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Abstract: Data from further human experiments touch four open questions in the target article. (1) Extinction of reward acquisition postulated by Depue & Collins's model could not be confirmed if correlating craving for, liking of, and satisfaction from smoking. (2) Intraindividual correspondence between responsivity to dopamine agonists and antagonists could likewise not be confirmed. (3) Nicotine craving and drug-induced hormone responses were not substantially correlated. (4) Low serotonin can be the cause and not just the moderator of dopaminergic sensitivity, and personality correlates of low dopamine/low MAO (aggressive impulsive traits) can hardly be related to the positive emotion associated with dopaminergic activity.

Depue & Collins (D&C) have convincingly accumulated and evaluated the available literature on the role of dopamine in incentive behavior in animal as well as human research, but there are some open and puzzling questions which need elucidation from human studies. D&C themselves state in section 7 that "there is a paucity of work on individual differences in DA functioning in normal humans." The present commentary addresses four points by providing some further findings from research in humans.

(1) How to separate the role of dopamine in wanting and enjoying substances. A question frequently addressed in addiction research concerns whether positive affect is the vehicle to induce dopamine release via motivated behavior, or whether dopamine release can also induce positive affect. The latter would be suggested by (a) the lack of enjoyment of substances of abuse upon dopamine depletion in humans (Ahlenius et al. 1973) and by (b) the lack of drug seeking behavior and the development of depression (Willner et al. 1991) upon dopamine (DA) depletion in animals, as described in the target article. It is not quite clear however, why the application of DA precursors or agonists does not induce elation or incentive behavior (Netter & Rammsayer 1991), although it is claimed that self-administration of drugs like amphetamine and nicotine occurs for the sake of DA release as a rewarding process. It is accordingly unclear why subjects self-administering drugs of abuse do not get satisfaction from the dopamine release elicited by the substance but tend to try to supply even more. The Depue & Collins (D&C) model depicted in Figure 8 implies that subjects with high dopamine receptor activation show resistance to extinction of reward acquisition, so one would have to expect that DA state activation (by a DA agonist) as well as trait activation (by extraversion-related traits) to be associated with higher craving for, more enjoyment of, and less satisfaction from the corresponding drug.

This was tested in a human model (Netter et al. 1998) using the DA agonist lisuride (L, 0,2 mg), the D1/D2 antagonist fluphenazine (F, 2 mg), and placebo (P) in a balanced cross-over design in

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36 smokers who were offered a cigarette after 3½ hours of deprivation. If one may assume that craving measures in humans reflect incentive motivated behavior in animals, one should have expected a higher induction of craving by L, but none of the three measures applied yielded significant drug differences during the deprivation period. For satisfaction smoking would have been expected to reduce craving more in F-treated than L-treated subjects, but the order of magnitude of reduction in craving tested for significance of observed versus expected frequencies was not significant for the order F > P > L but rather for the reverse order L > P > F.

This indicates that the agonist lisuride does not induce craving but rather reduces it more than placebo and more so than the DA blocker in the same individual. Furthermore, enjoyment of the substance (i.e., rated taste and positive effects of a cigarette) was not differently influenced by the three drugs. This leaves the question open why satisfaction was more readily obtained in these subjects, and why craving was not increased by L. The trait of DA activation was also tested for effects on craving: In a second study dividing subjects according to novelty seeking into high and low scorers under similar conditions of nicotine deprivation, high novelty seekers developed significantly less craving than low novelty seekers (unpublished data).

So neither trait nor state by themselves seem to elicit drug seeking behavior. Rather, the combination of the two (trait and state) induces incentive motivation, as shown by the lisuride induced increase of craving in high experience seekers (Netter et al. 1996). In the same study, low experience seekers and subjects high in hedonic tone, (i.e., those who can enjoy sensory stimuli as assessed by a questionnaire) supported the assumption that dopamine receptor stimulation reduces craving and yields satisfaction per se, whereas the D&C model of Figure 8 fit the data of high experience seekers and those who fail to enjoy sensory stimuli (increase in craving by the DA agonist).

(2) The relationship between responses to dopamine agonist and antagonist in the same individual. The target article only mentions separate studies of agonists and antagonists. A previous study on the precursor L-Dopa and the D2-antagonist haloperidol (Netter & Rammsayer 1991) revealed that subjects who were sensitive to the blocker were not necessarily sensitive to the precursor too. In inspecting prolactin release in identical subjects by the agonist lisuride and antagonist fluphenazine in the study mentioned above, it became evident that of 34 subjects who could be evaluated according to unambiguous prolactin responses 22 were either responders (n = 14) or nonresponders (n = 8) with both substances, whereas only 6 subjects were exclusive F or L responders, respectively. So the question whether the same subject is sensitive to the agonist and the antagonist is not conclusively answered. Further studies should investigate whether different sensitivity is due to differences in dosages for agonist and antagonist effects interacting with personality.

(3) The relationship between prolactin and behavior responses. In section 7 the target article reports highly significant correlations between extraversion and DA agonist responses, but it is not clear whether DA-induced state variables too are related to the respective hormone responses by the drugs. We screened our data in the cross-over design study, and although decrease and increase of PRL by L and F respectively were associated with increase and decrease of craving as predicted, the total number of correlations computed between different measures of craving and prolactin during deprivation were not convincing enough to suggest that the hormone response is a good predictor of the motivational response. Further studies are necessary to explain whether this is due to the fact that emotional and hormone responses are mediated by different brain areas and that receptor densities in these different areas require different amounts of the substance for response facilitation.

(4) The relationship of personality to dopamine as opposed to MAO-B and serotonin. In section 8, the target article states that low levels of MAO-B and 5-HT are associated with aggression and impulsivity but also with extraversion. The latter relationship is explained by the role of MAO-B in DA metabolism yielding the high DA-activity characteristics of extraverts. The role of low 5-HT activity resulting in a lack of DA-inhibition is not discussed in this section. It cannot be excluded that the 5-HT deficit represents the "chicken" and DA the "egg." In both instances (low MAO-B and 5-HT), aggression and lack of impulse control represent aspects not to be expected in high scorers on extraversion according to Depue & Collins.

Further studies need to elucidate whether a combination of low MAO-B / 5-HT levels with high DA sensitivity is possible and whether these individuals would be characterized by positive affect *plus* impulsive aggression.

Dopamine: Go/No-Go motivation versus switching

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Abstract: Sensitivity to incentive motivation has a formative influence on extraversion. Mesoamygdaloid dopamine (DA) activity may, at one level, act as a micro-gate permitting an incentive to influence behavioral organization – "Go/No-Go" in this scheme. Data on function elsewhere in the mesocorticolimbic DA system are taken to support this particular function. At another level of analysis, the data in Depue & Collins's review, along with those on the rest of the ventral tegmental area (VTA) system, may fit better with a "switching" function in information processing. This link is supported by correlations between measures of extraversion, learned inattention, and overall DA activity. The point is extended to the novelty-seeking feature of the extraverted personality.

The neurotransmitter dopamine (DA), in areas innervated by the VTA, is undoubtedly an important part of the substrate for motor activation and responses to novelty, as expressed in the mesolimbic and modulated by the mesocortical system. Thus, it is not disputed that via activation and impulsivity (Depue & Collins's [D&C's] terms), modulation by DA of limbic and neocortical activity occurs in the expression of extraversion. We support this in the animal model with psychostimulants (rearing, head-turning, and orienting movements, Oades et al. 1985; 1986) as well as normal young adult humans, where ratings of "outgoing-behaviour" correlated with the levels of DA excreted (n = 29, Spearman r = +0.5, p = 0.015, data in Oades et al. 1996a).

What is in dispute is the exclusive role of the VTA-DA projection system in "incentive motivation." D&C (sect. 3.3) specifically state that the approach of a rewarding goal is the essence of incentive motivation and that this is facilitated by VTA-DA activity. They then qualify this (sect. 4.1) by saying that this facilitation does not consist of mediation (the strong version of the postulate); it should instead be seen as modulation. This "weak" version conflicts with the "strong" version promulgated by Schultz and colleagues (e.g., 1995b), whom they so willingly cite in section 4.2, (the titles alone illustrate the point). Both versions are a kind of Go/No-Go theory to explain the extraversion/introversion conflict over signals of reward and punishment described in section 2.4. A more widely applicable and more parsimonious alternative lies in selective information processing.

D&C draw on this interpretation (Oades 1985) without resorting to the underlying idea. The proposal was and remains that an increase of DA activity in a DA-innervated nucleus increases the likelihood that the current control of the output of this nucleus is switched to the influence of another input. This makes particular sense for the nodes innervated by the VTA, where there is a huge convergence of input, as described by Oades and Halliday (1987: e.g., VTA, prefrontal cortex, entorhinal cortex, septum, nucleus accumbens, and habenula). This point is selectively used (for the

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VTA) at the start of section 4.6. An argument can also be made that the basolateral amygdala is one of the nodes innervated by the VTA (see sect. 4.3.1), but this is only one branch of the system, albeit an especially relevant one for motivational matters: other branches are relevant too, for example, motor responsiveness and heteromodal processing. Thus, in the example cited above (Oades et al. 1996a), the ability of normal young adults not to attend to a new conditioned stimulus while still learning about another – a selective attentional ability called conditioned blocking – correlates with the general background level of DA utilization. Blocking measures an ability to select stimuli for processing and learning: as the learning and the blocked stimuli have the same consequences, attention for the one over the other reflects a selective strategy relatively unsullied by questions of incentive motivation.

To be sure, Oades et al. (1996a; 1996b) found that "outgoing personality features" correlated with improved blocking. This might be predicted, as extraversion (in part) reflects this sort of "decisive" information-processing service, provided by the mesolimbic accumbens and frontocortical VTA-DA projection system (structures shown to influence blocking in animal studies such as Oades et al. 1987) – a bottom-up argument. According to the top-down argument of D&C, the large limbic and cortical modules that put extraversion together require this sort of processing, and thus incentive motivation is the label they feel attaches best to the (part) of the VTA activity that is coincident.

It is not surprising that "switching" is a form of explanation also used to describe the influence of DA agents on latent inhibition, a task with some similarities to conditioned blocking (Weiner 1990). Even in simple visual discrimination learning we have seen an apparent relationship between the background DA activity and performance (Oades 1997). Slower initial learning but more rapid reversal was seen in subjects with higher DA activity. Both results are consistent with an explanation in terms of switching, but only the latter in terms of incentive motivation.

An example of arguably incentive-free activity may be taken from the sensation- or novelty-seeking features of an extraverted personality. Novel stimuli do not just elicit attention: direct and indirect, visual and auditory, reciprocal pathways (Dinopoulos & Parnevelas 1991; Fallon et al. 1984) ensure that there will be bursts of firing in DA neurons of the VTA (Horvitz et al. 1997; Schultz 1992), but they elicit widespread neural responses in frontal regions inhibiting ongoing neural processes (the P3a event-related potential). These changes (or switches) are adaptive, and need no recourse to explanations in terms of incentive motivation. (To so argue would be teleological, and an incentive would underlie any circuit that functioned. Novelty does not just pertain to stimuli that could indicate the proximity of a predator, but to seeking out new versus old stimuli [Berlyne 1960]; and high ratings of curiosity have been related to an increased life span [Swan & Carmelli 1996]). Hugdahl and Nordby (1994) argued that the larger P3a potential to an invalid versus a valid cue during the covert orienting of attention should be interpreted as indicating the attention-switch, a feature that is integral to orienting and exploring (Pribram & McGuinness 1993) and that can be enhanced by dopaminergic agents like methylphenidate (Lazzaro et al. 1997).

There need be no dispute that the amygdala is central to the orbitofrontal – hypothalamic axis controlling the appropriate application of emotional responses to sensory events in terms of physiological and behavioral indices (Downer 1962). Nor need it be disputed that the amygdala "enhances the processing resources allocated to ambient events with high emotional or hedonic valence" (Mesulam 1998, p. 1035). The norm is that incentive contributes strongly to what is learned. Meso-amygdaloid DA activity plays an important role here. This role may be a switching one, but more important, most DA in the VTA projection system lies elsewhere involved in information processing that is not of necessity guided directly by incentives.

The affiliative playfulness and impulsivity of extraverts may not be dopaminergically mediated

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Abstract: A major dopaminergic role for extraversion is compromised by the fact that affiliation and impulsivity tend to be reduced by psychostimulants. Also, the large clinical literature on the treatment of ADHD with drugs that promote dopamine activity provides little or no support for a major role for dopamine in human extraversion. Dopamine facilitation of agency may be more evident for inanimate rather than animate rewards.

Classical personality theory sought to relate human temperaments to the humoral processes of the body but left us with no lasting understanding. Without a substantive neuroscientific data base, no attempt to link the complexities of human personality to the material processes of the body could succeed. Now abundant facts are available, and investigators can outline possibilities that were unimaginable just a few decades ago. The neuroscience data base is so rich, however, that the establishment of detailed relations to human issues remains a daunting task. At present, stable bridges to human issues may need to be constructed at much lower levels of resolution than the details afforded by the most recent findings from behavioral neuroscience. An optimal strategy may be to relate pharmacological modification of human personality traits to the global functions of certain neurochemical systems shared by all mammals (Panksepp 1986b; 1993a). For example, certain personality dimensions such as negative affect can be attenuated by pharmacologically elevating brain serotonin activity (e.g., Knutson et al. 1998), and this is the level of analysis that is likely to be most informative at the present time.

Depue and Collins (D&C) have entered the den of neuroscientific complexities with confidence and have put forward a bold and credible perspective on how brain dopamine may contribute to extraversion. As they skillfully detail, the dopaminergic basis for generalized appetitive motivational responsivity in the animal brain is now well established and the data base can be credibly linked to psychological agency, one of the three main aspects of extraversion. However, as D&C recognize, their ideas may not apply to other key features, namely, social affiliation and impulsivity. To the extent that these aspects are at least as important as agency in defining extraversion, D&C's treatment of that concept must be deemed provisional and incomplete. Although they acknowledge such shortcomings, I would like to draw them out a bit further on those outstanding features, especially because one can readily argue that brain dopamine influences social affiliation and impulsivity in ways diametrically opposed to that of agency.

The childhood problem presently subsumed in the diagnostic category of Attention Deficit/Hyperactivity Disorder (ADHD) is a human condition in which both of these features of extraversion as well as relevant brain neurochemical differences come together, along with a massive societal data base on drugs that promote dopamine activity. This condition of human diversity appears to be characterized by decreased development of frontal lobe areas (Castellanos et al. 1996) and mild differences in the activity of ascending brain catecholaminergic arousal (Pliszka et al. 1996). It might be informative to consider how such children, prior to being placed on dopamine promoting medications, fare on the various dimensions of extraversion. Are ADHD kids more or less extraverted than normal? From the dopaminergic viewpoint advocated by D&C, we might expect them to be less extraverted. Likewise, how do they fare on affiliative and impulsive tendencies when their catecholamine systems are aroused with psychostimulants? The literature tends to suggest that both are diminished (Barkley 1997). Because such observations do not square well with D&C's views, let me develop this perspective in greater detail.

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A basic form of outgoing social engagement is rough-and-tumble social play. On the face of it, play rates high on the dimension of agency. This instinctual behavioral process is characterized by assertiveness, potency and tendencies toward social dominance (Panksepp 1993b; 1998a). From D&C's view one might expect dopaminergic agents to promote such behaviors, but just the reverse has been commonly observed (Panksepp et al. 1979). Indeed, every drug that promotes dopamine activity markedly reduces playfulness (Panksepp et al. 1987; Vanderschuren et al. 1997).

It is reasonable to view children with ADHD as reflecting, at least in part, a natural variant of human diversity characterized by high levels of playful impulsivity (Panksepp 1998b; 1998c). One implicit reason psychostimulants may be so widely used in these children could reflect the simple fact that such drugs can markedly reduce outgoing, playful urges, while promoting more adult-like attentive approaches to the world. I am not aware of any data indicating that treatment of ADHD children with psychostimulants makes them more extraverted; there are good reasons to suspect that just the opposite occurs, because their frontal lobe functions can be amplified by psychostimulants (Barkley 1997; Chabot & Serfontein 1996). Thus, this condition and its treatments seem to provide evidence contrary to the views advocated by D&C.

In a similar vein, we might consider the adult emotional problem of mania, which seems to be characterized, at least on the surface, by heightened extraversive tendencies. Although there are a lot of data suggesting that mania is accompanied by high levels of brain norepinephrine activity, there is no consistent evidence for a hyperdopaminergic state in mania (Buki & Goodnick 1998). Thus, it might be interesting to consider that extraversion is related more to brain norepinephrine rather than dopamine activity. Indeed, the condition where there is some evidence for an excess of dopamine activity in the brain, namely, certain forms of adult-onset schizophrenia, has never been reported to be accompanied by heightened extraversion or agency.

It is very likely that many other brain neurochemical systems are more influential in the generation of extraversion than dopamine. Various outgoing social tendencies in animals have been clearly linked to brain norepinephrine, opioid, and oxytocin activities (for review, see Nelson & Panksepp 1998). It will be interesting to consider how these neurochemical systems contribute to socially outgoing dispositions. We already know that trait differences in oxytocinergic activity in wild mice have profound consequences for their affiliative tendencies, with abundant oxytocin receptors in the brain being correlated with the more social temperaments (Insel 1992). We know that the facilitation of brain opioid activity can increase playfulness and social dominance (Panksepp et al. 1985).

These dilemmas are important for D&C to consider and to resolve in theoretically coherent ways. Perhaps agency is only of secondary importance in the concept of extraversion. Perhaps agency is merely a derivative outgrowth of core issues, such as strong and consistently positive affiliative tendencies. More developmental personality research may help resolve such issues. In any event, high dopamine activity in human children tends to reduce social motivation, while promoting more self-centered studious activities (Barkley 1997). Thus, even though dopamine certainly seems to control the engagement of organisms with a large variety of environmental incentives (most of them inanimate), I would like to see convincing data that drugs which promote dopamine activity can specifically increase social agency as opposed to simply many other forms of action readiness.

Despite the many dilemmas that can be posed for views like theirs, Depue & Collins's work is an excellent example of how we should proceed in this difficult intellectual arena. The abundant data on brain systems that all mammals share are related to a careful analysis of human personality traits, and critical predictions are generated. Developing such creative ideas will continue to require intellectual courage, for all we can really be confident of is that the complexities of the brain will, for the foreseeable future, put all of our theories to shame.

Personality correlates of the dopaminergic facilitation of incentive motivation: Impulsive sensation seeking rather than extraversion?

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Abstract: Depue & Collins associate dopaminergically mediated incentive motivational processes with extraversion. In this commentary I consider dopaminergic indices from neuroimaging investigations which correlate more closely with impulsive sensation seeking personality traits than with extraversion. Measures of relevant behavioural processes also appear to correlate with personality measures other than extraversion.

The target article by Depue & Collins (D&C) represents a continuation of the distinguished lineage in personality theory that runs from Pavlov through Eysenck and Gray to the present day (see Pickering 1997). Most impressive is the range of research domains from which the model draws data, although this is as it should be for a model of this scope ("to provide a comprehensive neurobehavioral model of a personality trait"). My comments here suggest that D&C may be wrong in relating dopaminergic neurotransmission to extraversion.

1. Extraversion versus impulsive sensation seeking (ISS). As D&C acknowledge, they are at odds with Gray, Zuckerman, and Cloninger in aligning the causal neurobiological axis of personality with extraversion rather than with the cluster of ISS personality traits which lie rotated approximately 45 degrees from extraversion in the direction of low constraint. D&C suggest that ISS traits, emergent from interactions between the fundamental extraversion and constraint dimensions, would be expected to have heterogeneous neurobiological influences. Hence, D&C expect that dopaminergic correlates of ISS traits would tend to be weak and inconsistent, whereas more consistent correlations should be found with extraversion.

D&C concede (sect. 7) that the data are pretty indecisive. Depue's own studies of prolactin and eye blink indices of D2 dopamine receptor effects (Depue 1995; 1996; Depue et al. 1994), replicated by another group (Netter et al. 1996), provide the clearest evidence of strong associations with extraversion in the absence of the significant relationships with ISS traits or constraint. However, their review did not include our own single photon emission tomography study in a small group of healthy volunteers (N. S. Gray et al. 1994). We found significant negative correlations between D2 binding in the basal ganglia and (EPQ) psychoticism, but no significant associations with other EPQ personality measures including extraversion. Farde et al. (1997) independently reported correlations between a positron emission tomography (PET) D2 binding index and the Karolinska Scales of Personality. Significant negative correlations were obtained for the dimensions of detachment and irritability, which index some of the same personality facets as EPQ psychoticism. Finally, a further PET study in a small group of Parkinson's disease patients (Menza et al. 1995) found that uptake of [^{18}F]dopa in the left caudate, but not other measured regions, was significantly correlated with Cloninger's Novelty Seeking. Scanning measures of dopaminergic function appear to align more closely with ISS traits than extraversion. In addition, the findings of *reduced* D2 binding in high impulsives needs to be squared with evidence of stronger psychophysiological responses to a D2 agonist in extraverts than in introverts (Depue et al. 1994).

2. Testing the model. The model in its present form specifies, at the human level, little more than an expected pattern of correlations between trait measures and indices of dopaminergic neurotransmission. In section 6.2 D&C discuss six "behavioural predictions that have implications for conceptualizing extraversion." The first four appear to be restatements of the model rather than true predictions. For predictions five and six, which are amenable to test, the data indicate once again that extraversion may be the

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wrong trait. D&C (prediction 5) state that introverts should show earlier extinction of reward acquisition behaviour than extraverts, particularly under conditions such as intermittent reinforcement. In the late 1980s, using a simple appetitive paradigm (Vogel-Sprott 1967), N. S. Gray and I (unpublished observations) explored personality correlates of learning in two groups of healthy subjects: one was given continuous reinforcement (CR) during acquisition followed by extinction; the other received intermittent reinforcement (IR; random 50%) prior to extinction. Using the EPQ, extraversion revealed no significant correlations. Instead, two findings emerged: (1) in the CR condition high neuroticism subjects were much slower to acquire the correct response than low neuroticism subjects (there were no neuroticism effects in extinction or for IR-trained subjects in acquisition); (2) amongst CR-trained (but not IR-trained) subjects, high psychoticism subjects extinguished more rapidly than low psychoticism subjects. Clearly, as with the scanning data, extinction effects may not relate as closely to extraversion as to (proxies for) ISS personality traits.

Prediction six is more vague: extraverts (cf. introverts) should manifest "more flexible adaptation to environmental contingencies as they fluctuate over time." Latent inhibition (LI) measures this adaptation: a subject pre-exposed to a stimulus which has no consequences is slow to learn when that stimulus subsequently predicts another salient stimulus (such as a biological reinforcer). Human LI tasks are sensitive to dopaminergic manipulations (N. S. Gray et al. 1992) and show similar personality effects in several studies (Lubow & Gewirtz 1995). Subjects with high scores on schizotypal personality inventories – typically including EPQ-Psychoticism – show more flexible adaptation to changing environmental contingencies (they show less interference with learning from the prior irrelevant pre-exposure). The LI-personality findings may reflect another influence of ISS personality traits given the correlations between schizotypal personality and ISS traits (Mason et al. 1995). However these results should be interpreted, they are at odds with D&C's model in its current (somewhat underspecified) form.

Dopamine and extraversion: Differential responsivity may be the key

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Abstract: Depue & Collins's general idea of a functional relationship between DA activity and extraversion is an important step toward an integrative biological model of personality. However, focusing primarily on incentive motivation and variations in VTA DA activity as basic behavioral and biological components underlying extraversion appears too limited. Existing data suggest that responsivity to changes in DA activity is higher in introverts than in extraverts. This may reflect a general, extraversion-related characteristic of the entire dopaminergic network in the brain.

Depue & Collins (D&C) introduce a new view of extraversion based primarily on incentive motivation (sect. 1.2, para. 4) and arrive at the conclusion that variation in encoding incentive salience represents the main source of individual differences in extraversion (sect. 1.2, para. 6). This places too much importance on the mesolimbocortical DA system and is at risk of ignoring certain behavioral characteristics of extraversion not related to this DA subsystem.

Existing data provide convincing evidence that the mesotelencephalic DA system comprises two major, functionally distinct, subsystems: the mesostriatal and the mesolimbocortical DA system (e.g., Amalric & Koob 1993; Robbins & Everitt 1995). Unlike mesolimbocortical DA neurons, mesostriatal DA neurons appear to act as an inhibiting modulatory system on the striatum (Björklund & Lindvall 1986), which in turn exerts a powerful inhibitory effect on the thalamus and the reticular formation (Carlsson & Carlsson 1990). Therefore, any increase in mesostriatal DA activity will counteract the inhibitory effect of the striatum, thus resulting in increased reticular arousal and (for example) enhanced sensory sensitivity. Superior sensory sensitivity in introverts compared to extraverts (e.g., Smith 1968; Stelmack 1996; Stelmack & Campbell 1974) supports the view that extraversion-related functional differences may also exist in the mesostriatal DA system.

Although D&C make a commendable effort to provide the reader with a comprehensive review of work on individual differences in DA functioning in normal humans (sect. 7), they do not evolve any clear idea of the functional relationship between individual differences in DA reactivity and extraversion. Significant relations between behavioral or biochemical indicators of DA activity and extraversion (see sect. 7) have only been found after experimentally induced changes in DA activity, whereas under normal physiological conditions no such relation could be established (Depue et al. 1994; Rammsayer et al. 1993). These findings suggest differential responsiveness or susceptibility to *changes* in DA activity, rather than differences in the *general level* of DA activity, as a possible neurobiological mechanism mediating extraversion-related individual differences.

Rammsayer et al. (1993) addressed the question of whether a pharmacologically induced decrease in DA activity in the brain would differentially affect reaction times of extraverts and introverts. After pharmacological blockade of DA synthesis by means of alpha-methyl-para-tyrosine (AMPT), performance on both lift-off time (i.e., time required to lift the hand from a start button) and movement time (i.e., time required to move the finger from the start button to a response button) was markedly impaired in introverts but not in extraverts. Since AMPT produced a nonspecific decrease in brain DA activity, in a very recent study (Rammsayer 1998), the DA D2 receptor blocker remoxipride was chosen to more selectively affect the homeostasis of dopaminergic neurotransmission. Remoxipride primarily inhibits dopaminergic neurons of the VTA that project to limbic and cortical regions (Köhler et al. 1990). In introverts, remoxipride caused a pronounced increase in lift-off time compared to extraverts while movement time was not affected in either group. These findings indicate extraversion-related differences in responsivity to deviations from the physiological level of mesolimbocortical D2 receptor activity. Thus, introverts appear to be more responsive and more susceptible to pharmacologically induced changes in D2 receptor activity than extraverts. Furthermore, the absence of an effect on movement time suggests that lift-off time and movement time represent largely independent processes modulated by the mesolimbocortical and mesostriatal DA systems, respectively.

Converging evidence for differential dopaminergic responsivity of introverts and extraverts can also be derived from the study by Depue et al. (1994). In this study, a significant correlation was obtained between PE scores and the inhibitory effect of bromocriptine on prolactin secretion (see sect. 7, para. 6). This correlation may indicate that DA activity is positively related to PE, as proposed by Depue et al. (1994). In a recent animal study, however, Rots et al. (1996) provided direct experimental evidence that high dopaminergic activity is associated with reduced prolactin responses to stress. Consequently, subjects showing a strong response to a DA agonist, such as bromocroptine, should be characterized by functionally low dopaminergic activity. The reverse applies to subjects showing a weak response to DA agonists. Therefore, the positive correlation between PE scores and the inhibitory effect of bromocriptine on prolactin secretion reported by Depue et al. (1994) would rather point to higher dopaminergic responsivity in low PE than in high PE subjects. Finally, in a PET study, Fischer et al. (1997) obtained measures of regional cerebral blood flow to investigate neurobiological differences in extraverts and introverts. Their data indicate substantially increased DA activity in the caudate nucleus and the putamen in introverts compared to extraverts.

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Regardless of the exact nature of the relationship between DA activity and extraversion, the available data support Depue & Collin's basic assumption that the neurotransmitter DA may represent a biological basis of extraversion-related individual differences. However, the observed extraversion-related differences in peripheral physiological responses, mediated by the tuberoinfundibular and tuberohypophysial DA systems, as well as in behavioral responses primarily modulated by the mesolimbocortical or mesostriatal DA subsystems suggest that differences between extraverts and introverts in dopaminergic responsivity and/or DA activity are not confined to a specific DA subsystem but rather represent a general feature of the entire dopaminergic network in the brain.

Is depression a dysfunction in self-regulating the brain/behavior system for approach?

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Abstract: This commentary examines the implications of the Depue & Collins model for the etiology and treatment of depression, specifically, whether it can account for findings concerning neurobiological, behavioral, and phenomenological facets of depression. Drawing upon the construct of *self-regulation*, I explore the fit of the model to current knowledge about depression, conceptualized as a dysfunction within a hypothetical brain/behavior system for maximizing positive outcomes.

What is known about depression? I offer the following as representative of our knowledge regarding depression in its nonbipolar, nonpsychotic manifestations:

1. Depression is associated with temperament and personality variables that can be clustered under the labels of *extraversion* or *positive affectivity* (Clark et al. 1994).

2. Depression is preceded by or associated with experiences of loss and failure (Brown & Harris 1978; Kessler 1997).

3. Depression is associated with changes (at varying levels of representation) in the perceived incentive value of reward and the perceived likelihood of attaining desired outcomes (Abramson et al. 1989; Blatt & Zuroff 1992; Roberts & Monroe 1994).

4. Depression is associated with hypoactivation in brain regions (e.g., left prefrontal cortex) hypothesized to subserve approach-related behavior and positive affect (Davidson 1992; Depue & Iacono 1989).

5. Both biological and psychosocial interventions are efficacious in treating depression (Craighead et al. 1998; Nemeroff & Schatzberg 1998).

Although these statements do not capture the entirety of knowledge regarding depression, they nonetheless account for an enormous quantity of data. Correlations across classes of observations are intriguing, but as yet a unified theory accounting for all five sets of data is unavailable. A brain/behavior model which could explain the entire spectrum of knowledge regarding depression would be of enormous value. Is the model of individual differences in extraversion proposed by Depue & Collins (D&C) a step in that direction?

The D&C model is an impressive and scholarly thesis which offers a compelling neurophysiological template to integrate observations about depression, albeit one for which the critical tests of relevance to depression have yet to be conducted. More important, the model offers a basis for conceptualizing depression (and vulnerability to depression) as a *disorder of self-regulation*, specifically the perceived availability, incentive value, or likelihood of receiving positive outcomes (a term I prefer to "reward").

It has long been proposed that depression can result from a breakdown in neurophysiological, cognitive, or behavioral mechanisms of maximizing positive outcomes (e.g., Costello 1973; Meehl 1975). More recent work by Carver and Scheier (cf. 1998) and others demonstrates how individual differences on psychological or neurophysiological dimensions of self-regulation – for example, approach or avoidance goals, sensitivity to positive or negative outcomes, and strength of self-regulatory orientations – can predispose individuals to dysphoric affect and loss of approach motivation. Contemporary theories of self-regulation draw heavily from attachment theory (Bowlby 1988) as well as developmental psychology and neurobiology (Cicchetti & Tucker 1994; Derryberry & Reed 1994b) to account for the reciprocal impact of socialization and neural development on personality structure and vulnerability to mood disorders.

Our own recent studies of self-regulation in depression (cf. Strauman 1996) take a similar integrative view. Based upon studies of self-discrepancies in normal, analog, and clinical populations, we have proposed that depression can result from chronic perceived failure to attain promotion (approach) goals. Whereas both biological and psychosocial interventions can alleviate depressive symptoms, treatments differ substantially in their impact on conscious and unconscious self-regulatory cognition – differences that we predict ultimately influence the likelihood of relapse or recurrence (Strauman et al. 1998).

What is gained by conceptualizing depression as a breakdown in the self-regulation of a brain/behavior system for approach? One important advantage is that a self-regulatory perspective allows us to consider simultaneously – at appropriate levels of analysis, from cellular to societal – how the human organism pursues positive outcomes, and how that normally adaptive process can go awry at any level. Indeed, it *forces* us to consider depression hierarchically, so that (for instance) *both* biological and cognitive theories of loss of approach motivation might be valid, even within the same depressed person.

What, then, does the D&C model offer with regard to existing theories of depression and setting agendas for future research? I see both an advantage and a disadvantage. The strength of the model, with regard to depression, is the scholarly and thorough manner in which D&C draw parallels in the literature on extraversion, behavioral facilitation, and neurobiological facilitation. In this respect their *tour de force* extends the seminal work of Gray and generates a number of additional questions for research. [See Gray: "On Mapping Anxiety," *BBS* 5(3) 1982; Gray et al. "The Neuropsychology of Schizophrenia" *BBS* 14(1) 1991.] The potential disadvantage, which D&C themselves noted, is that the neurobiological facilitation literature upon which they draw is not based on the kinds of reinforcers – achievement, esteem, communion, intimacy, popularity, to name a few – which appear to be "primary" among humans. Although animal studies of self-reinforcement with stimulants or other drugs are invaluable (e.g., in maximizing internal validity), there is a tremendous span from such investigations to the phenomenology of depression.

Nonetheless, the model's prospects are exciting. One question of particular interest which could be pursued via the D&C framework is "Can treatments for depression reverse the underlying dysfunction in self-regulation in addition to alleviating symptoms? Assuming that depression is indeed a disorder of self-regulation, alleviating symptoms is not sufficient to decrease the risk of relapse or recurrence. Rather, if the specific breakdown – which might occur in a particular individual at any number of levels – is repaired, the individual should be less likely to suffer subsequent episodes. Our own work on the impact of various treatments on self-regulatory cognition is but a first step in this direction. Given the controversy regarding the utility of psychosocial versus pharmacological treatments for relapse prevention (e.g., Jacobson & Hollon 1996), it is essential to develop a clearer understanding of *how* antidepressant treatments work.

The D&C model is a potentially important piece of the depression puzzle, one that may allow investigators to view depression in a clearer Gestalt. The model has significant incentive value for researchers concerned with the etiology and treatment of depression. Achieving the desired positive outcome – better under-

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standing of and treatment for depression – has never been a more salient goal for our field.

Extraversion, sexual experience, and sexual emotions

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Abstract: Sex differences in motivation and emotional reactions to casual sex suggest that the links to extraversion, constraint, impulsivity-sensation seeking, and sexual behavior differ for men and women. Because both testosterone and dominance, and dominance and number of sex partners appear to correlate in men but not in women, it is plausible that testosterone is involved in the creation and maintenance of these sex differences in linkage among the behavioral subsystems involved in sexuality and extraversion.

Depue & Collins (D&C) propose that behavioral systems vary along a dimension of increasing generality. At lower levels specific stimuli related to biological aims elicit behavior and emotions that are relatively specific to those conditions. At the highest level are a limited number of general behavioral systems that are more flexible and have less immediate objectives. Extraversion is a general behavioral system that is based on underlying processes and behavior, and behavioral systems are fundamentally emotional systems (sect. 3.2).

All psychological theories imply that some brain/mind systems are typical of *Homo sapiens,* but theories differ in the extent to which these systems are thought to be few and general or many and specialized. Darwinism strongly favors the latter, and a corollary of this expectation is that in the human brain these systems are sexually dimorphic – particularly those systems that moderate sexuality and emotions related to sexuality (Symons & Ellis 1989).

Townsend and Wasserman (1998) found that men's sociosexual orientation inventory (SOI) scores correlated negatively with interest in target persons' status traits, and positively with expressed willingness to copulate with target persons solely on the basis of a visual appraisal of physical attributes; for women, these correlations were nonsignificant. Women were also more likely than men to worry about partners' willingness to invest and to have thoughts about marriage (investment thoughts) – even when they had voluntarily decided not to get emotionally involved with a particular partner. Women's investment thoughts were not associated with number of sex partners and permissive attitudes, whereas men's investment thoughts correlated negatively with number of partners and permissiveness of attitudes (Townsend 1995; 1998; Townsend & Wasserman 1998). In contrast to these measures, researchers have consistently reported *comparable* correlations for men and women between sexual behavior and conventional measures of sexual attitudes (Simpson & Gangestad 1991; 1992; Townsend 1995).

Numerous studies indicate that men's thoughts, fantasies, and emotions motivate them to engage in low-investment relations with a variety of partners (Bailey et al. 1994; Ellis & Symons 1990; Kinsey et al. 1953; Townsend 1998). We would therefore expect the feedback that men and women receive when they engage in casual relations to differ. For women, these feelings and memories can be very negative; for men, they are more often positive, and they stimulate men to attempt to repeat the experience (Ellis & Symons 1990; Kinsey et al. 1953; Townsend 1987; 1995).

Cross-sectional data cannot establish whether this type of differential feedback is responsible for sex differences in associations between attitudes and behavior. It is likely, however, that the attitudes and thoughts and feelings of men with more experience in casual relations diverge from those of less experienced men (and from those of women) as they gain familiarity, confidence, and experience (Townsend 1987; 1995; 1998). A longitudinal study of West German school children is consistent with this view (Schoof-Tams et al. 1976).

Gangestad and Simpson (1990) argue that, as measured by their sociosexual orientation inventory (SOI), permissive sexual behavior in women (and men) correlates with extraversion, lack of constraint, and other measures of social assertiveness and risk taking, and that the broad dimensions of these measures are substantially heritable (1990, p. 72). Our results indicate that even when women voluntarily engage in casual sex, their motivations and their emotional reactions differ from those of men (Townsend 1995; 1998; Townsend et al. 1995). Viewing our findings in the light of these other studies, we suggest the following. Women with multiple partners (and thus high SOI scores) have the same mental mechanisms for assessing quality of investment as do women with fewer partners. Given their extraversion and lack of constraint, however, multiple-partner women are more willing to take risks and to use their sexuality than fewer-partner women to obtain what they perceive as partners with high investment potential. In their pursuit of highly attractive partners, however, they sometimes overestimate their ability to acquire sufficient investment and underestimate the power of their emotional reactions when they eventually fail to obtain sufficient investment – hence their surprise, anger, and pain when this happens (Townsend 1987; 1995; 1998).

Although extraversion and nonaffective constraint are orthogonal, impulsivity/sensation-seeking traits associated with strong positive affect arise as a joint function of the interaction of extraversion and constraint (sect. 2.3). Given the observed sex differences in motivation and emotional reactions to low-investment sex, it appears that the links among extraversion, constraint, impulsivity-sensation-seeking, and sexual behavior differ for men and women. Because testosterone and dominance, and dominance and number of sex partners appear to correlate in men but not in women (Mazur et al. 1994; Mazur & Booth 1998), it is plausible that testosterone is involved in the creation and maintenance of these sex differences in linkage among the behavioral subsystems involved in sexuality and extraversion.

Dopamine tightens, not loosens

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Abstract: Depue & Collins propose that extraversion should be separated from the impulsivity-constraint dimension of personality, and that the VTA dopamine system is the primary engine of extraversion. Although their focus is on personality traits, it may be useful to consider the evidence on psychological state changes, related both to affective arousal and to drug effects. This evidence shows that there are inherent relations between extraversion and impulsivity-constraint, and that there are influences of dopamine on impulsivity-constraint that are not consistent with the Depue & Collins model. Increased positive affect leads to increased extraversion, and this is associated with more impulsivity and less constraint. The evidence on drug effects shows that greater dopaminergic control is associated with more constraint, and with anxiety and vigilance rather than positive affect.

A dimension of extraversion (emphasizing social affiliation, agency, and positive affect) may be separable from an impulsivity-constraint dimension in a psychometric analysis. But is it accurate to assert that these dimensions are truly orthogonal? In both psychological theory and everyday usage, we accept Jung's definition that extraverts are inherently impulsive. Are we to believe they are as likely to be constrained as impulsive? People in a strong state of positive affect, such as children who are socially aroused, or bipolar patients in a manic state, become more extraverted in

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terms of both social affiliation and agency. In this state, people become impulsive, not constrained.

In animal studies, increasing doses of dopamine agonists impose increasing constraints on behavior. Animals first reduce exploration, then with higher doses begin repetitive actions, then with still higher doses show behavioral stereotypy (Klawans & Margolin 1975; Kokkinidis & Anisman 1983). Human amphetamine abusers show a similar progression (Kokkinidis & Anisman 1980). The initial euphoric state wanes as norepinephrine depletes and the remaining active neuromodulator is dopamine (Antelman & Caggiula 1977). In this chronic state of behavioral activation, behavioral stereotypies appear along with hypervigilance and paranoia, suggesting that dopaminergic constraint is associated with anxiety and vigilance (Ellinwood 1967). The amphetamine evidence is consistent with the dopamine theory of schizophrenia, in which high dopamine levels are associated with symptoms such as autism, stereotyped self-verbalizations, and paranoia (Antelman & Chiodo 1984). Not extraversion. The efficacy of specific dopamine blockers in schizophrenia supports the dopaminergic basis of these systems (Carlsson 1988).

A similar effect is seen with stimulant treatment of hyperactive children. These dopamine agonists cause loose and impulsive boys to become behaviorally constrained, affectively restricted, and socially introverted (Malone et al. 1988; 1994).

The VTA dopamine projections are certainly important to motivated actions in appetitive as well as aversive contexts. But the consensus in many neuroscience and pharmacology studies – that dopamine is the basis of the reward system – is simplistic and misleading. As shown by the balanced review provided by Depue & Collins (D&C), dopaminergic activation is integral to aversive states as well. However, they conclude this review with the rather weak speculation that there may be different VTA-nucleus accumbens circuitries for positive and aversive motivational processes. This may be right, but it provides little justification for emphasizing only the positive incentive function of the dopamine projections while ignoring the role of these projections in aversive responses.

By associating dopaminergic activation with the state of anxiety, Williamson and I (Tucker & Williamson 1984) attempted to extend the Pribram and McGuinness (1975) concept of tonic motor readiness to aversive as well as appetitive contexts. Whereas psychologists seem to assume that anxiety is aversive, in everyday language we use the term anxiety to describe positive as well as negative anticipation. A state of vigilance and motor preparation would be integral to both.

Although there may not be a consistent valence bias toward positive or negative motivational orientations with dopaminergic modulation, there does appear to be a consistent structural bias. Dopamine tightens. In the behavioral domain, the redundancy bias of dopaminergic activation causes motor sequences to become restricted, constrained, and routinized. In the cognitive domain, this bias appears to operate as well, causing the anxious person to constrict memory, focus attention, and ruminate.

Given these disagreements with the Depue & Collins model, I do resonate favorably with the breadth of their speculations. Now that we have recognized the isomorphism of psychological and neurophysiological domains, science must formulate mechanisms that work in both.

Conditioned stimuli and the expression of extraversion: Help or hindrance?

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Abstract: Upon consideration of the unconditioned and particularly the conditioned stimuli that have been proposed to participate in the generation of incentive motivational states and, by extension, of extraversion, the nature of the contribution of NAS DA becomes less clear. Different kinds of conditioned stimuli can also exert strong control over the expression of behavioral sensitization. How might such stimuli affect the ability of experience-dependent processes to introduce stable individual differences in the development and expression of extraversion trait levels?

Depue & Collins (D&C) are to be commended for undertaking the seemingly Herculean task of attempting to derive a neurobiological model of extraversion. Although they themselves acknowledge that models of personality traits based on only one neurotransmitter are clearly simplistic, their focus on the ascending midbrain DA systems and, in particular, the VTA-NAS DA pathway as a predominant contributor to extraversion represents a good starting point. DA neurons originating in the VTA project to a large number of forebrain sites and are subject to a rich and diverse afferent regulation. On the one hand, this arrangement positions them well to provide forebrain neuromodulation of motor and affective responding. On the other, variations from one individual to another in the afferent regulation of these neurons may provide the basis for individual differences in the extent to which such neuromodulation is afforded and, by extension, to which extraversion is expressed. Considering the challenges inherent in the authors' task (see sect. 5 of the target article), these characteristics of the ascending VTA-NAS DA system are a definite asset. Upon closer examination, however, such characteristics also introduce some difficult questions for a model in which NAS DA, particularly when it is tied to conditioned stimuli, is the predominant facilitator of incentive motivation and extraversion.

Dopamine, incentive motivation, and conditioned incentive stimuli. There are many data (as illustrated by D&C) that support a critical role for the VTA-NAS DA pathway in the generation of incentive motivational states and the ensuing goal-directed behaviors that are promoted by such states. The nature of this pathway's contribution and how it relates to the impact on the individual of conditioned and unconditioned stimuli is less well understood, however. Thus, although there have been a number of reports (see also target article, sect. 4.2, para. 4) demonstrating that *increased* levels of extracellular DA in the NAS can become associated with the stimuli that predict as well as the behavioral activation that precedes the acquisition of food (Kiyatkin & Gratton 1994) or drug (Gratton & Wise 1994; Kiyatkin et al. 1993), it has also been reported that a *decrease* in these same levels can precede responding for drug and therefore serve to trigger its pursuit (Wise et al. 1995). In the latter case, it is not clear how NAS DA can be critical to the control of appetitive behaviors by conditioned incentive stimuli (i.e., those stimuli predictive of or surrounding the acquisition of the drug). Similarly, DA receptor blockade has been reported to spare the ability of drug-paired stimuli to elicit conditioned locomotor activity (Beninger & Hahn 1983) and to leave unaffected discriminative stimulus induced behaviors directed at acquiring food (Horvitz & Ettenberg 1991) or drug (McFarland & Ettenberg 1995). Again, while the latter reports support a role for NAS DA in the establishment of associations between conditioned incentive and unconditioned stimuli (perhaps via interactions with the basolateral amygdala and other nuclei; Everitt & Robbins 1992), they clearly suggest that it is not necessary for the behavioral expression of an incentive motivational state and, by extension, of extraversion. Furthermore, it is not clear under what conditions evocation of this state/trait by conditioned incentive stimuli would be associated with increases

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in NAS DA or with changes in neurotransmission perhaps previously established by DA in other areas of the motive circuit that D&C propose.

Behavioral sensitization as a source of experience-dependent variation in DA facilitation: Contribution of conditioned stimuli. The capacity of VTA-NAS DA neurotransmission to undergo sensitization is an attractive feature of this system and provides one experience-dependent mechanism by which individual differences in DA reactivity can be introduced. The implication in the authors' model (see target article, sect. 5.3) is that the development of such sensitization in some individuals but not in others could subsequently provide the basis for *stable* individual differences in responsivity to incentive stimuli, in the facilitation of incentive motivational states and, theoretically, in the expression of extraversion trait levels. It is interesting to consider the impact conditioned stimuli may have at this point. It has, for example, been known for some time that the expression of behavioral sensitization can come under strong conditioned stimulus control (Stewart & Vezina 1988) and this appears to be the case for sensitized NAS DA responding as well (e.g., Fontana et al. 1993). If it is assumed that this stimulus control is achieved via occasion-setting or facilitation by a conditioned stimulus complex (Anagnostaras & Robinson 1996), it follows that sensitization will be evoked by an eliciting stimulus appearing in the situation surrounding or following the individual's experience of this stimulus complex. Because occasion-setting stimulus complexes more often than not accompany or precede eliciting stimuli, they have often been identified with the expression of sensitization. This perception would be consistent with the view that sensitization of NAS DA reactivity represents a stable condition in the individual that guarantees enhanced motivational responding to appropriate eliciting incentive stimuli.

It is difficult to maintain this view, however, if one considers that in the absence of the occasion-setting stimulus complex, these incentive stimuli fail to evoke sensitization. A similar state of affairs is suggested by studies demonstrating that stimuli specifically unpaired with the unconditioned stimulus can *inhibit* the expression of sensitization (Stewart & Vezina 1988). Such conditioned inhibition (which, incidentally, has been likened more to the opposite of facilitation or occasion-setting than to the opposite of an excitatory conditioned stimulus; Rescorla 1985) can be reversed with proper extinction procedures to reveal sensitized responding (Stewart & Vezina 1991; Vezina et al. 1998). It would seem, therefore, that unlike the modulation of sensitization afforded by stable individual differences in VTA-NAS DA neurotransmission the authors as well as others propose (see target article, sect. 5.3.2, para. 4), stimuli endowed with occasion-setting or conditioned inhibiting properties are well positioned to influence the expression of sensitization in a more discrete, selective, and environment-dependent manner. It is conceivable that such stimuli may produce their effects by virtue of their access to and ability to influence activity in VTA-NAS DA neurons. Given that the pathways providing such access would be non-dopaminergic, D&C are right in their concluding remarks to evoke the contribution of other neurotransmitter systems. Needless to say, much remains to be determined. For example, what is the identity of these neurotransmitter systems? Might they contribute to motivational responding in a DA-dependent and, given the above results, DA-independent manner as well? What is their load contribution (relative to NAS DA) to the extraversion trait and the implications for the stability and the neurobiological substrates of such a trait of the ability of conditioned stimuli to control its expression?

As such, Depue & Collins's model mirrors well the challenges facing the areas of research it attempts to integrate.

Incentive motivation: Just extraversion?

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Abstract: Is a generalized positive incentive motivation a construct appropriate to the human level of behavior or would sensation or novelty seeking be a more appropriate one? Is positive incentive motivation, or susceptibility to signals of reward, a mechanism related only to extraversion traits including sociability, activation, social potency, and positive affect? Research shows that susceptibility to reward is related to impulsive sensation seeking and aggression as well as sociability and an aroused type of positive affect. Comparative and indirect human correlates suggest an involvement of dopaminergic reactivity in sensation seeking *and* sociability.

Personality studies across levels may start from the top (human behavior and traits) and work down (animal behavior and its biological bases), or from the bottom and work up (Zuckerman 1984; 1993). If it is the former, one starts with the basic traits of personality as established through theoretically informed factor analyses and then looks down to find their animal analogues and biological bases. If it is the latter, one starts with behavioral paradigms studied in other species in controlled laboratory settings and the brain mechanisms associated with these behaviors and attempts to find where they fit in the trait dimensions established for humans. I sense some ambivalence in Depue & Collins (D&C) as to which direction to go. But the problem is that the constructs derived from Gray's theories are based on research with other species, primarily rats, and are somewhat limited by the species specific characteristics of the chosen subjects. This is particularly true of *positive incentive motivation* as the behavioral mechanism underlying extraversion. But let us first begin at the top: the structure of human traits.

D&C focus on two higher-order traits, extraversion and constraint, and subsume others like impulsivity, sensation seeking, positive emotions, optimism, and so on, as combinations of these basic two. Although there is a great deal of agreement on the general nature of three of the major factors of personality, there is disagreement on which are primary and which are lower-order components of the primary factors (Zuckerman 1995; Zuckerman et al. 1993). Constraint, the term used by Tellegen (1985) to describe the third dimension of personality, is most equivalent to Eysenck's (1967) psychoticism, Costa and McCrae's (1992) conscientiousness and our impulsive sensation seeking (Zuckerman 1994b; 1994c).

Some years ago we asked how Gray's (1973; 1982; 1991) motivational constructs, susceptibility to signals of reward, and susceptibility to signals of punishment – as well as cognitive constructs like generalized reward and punishment expectancies, and affect traits like anxiety, depression, hostility, and positive affects – fit into the personality structure (Zuckerman et al., in press). The motivational measures were obtained from a questionnaire developed around Gray's model, with some validity established in behavioral performance studies of reward and punishment (Torrubia et al. 1995).

D&C are specific in the types of subtraits associated with positive incentive motivation and do not include sensation seeking, impulsivity, and aggression, leaving only sociability (affiliation), activity, social potency, and positive affect. Table 1 shows the bivariate correlations between SuRe and SuPu scales and the personality and affect scales in our study. In both the derivation and replication samples SuRe correlated about equally with extraversion (E), sociability (Sy), impulsive sensation seeking (ImpSS), aggression (Agg), and the sensation seeking or surgent type of positive affect (SS-PA). Positive incentive motivation, as measured by this scale, is related to a much broader range of traits than allowed for in their model.

Of course positive incentive motivation is defined from the bottom-up and includes social, sexual, food, and safety motivations

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Table 1 (Zuckerman). *Correlations between susceptibility to reward (SuRe) and susceptibility to punishment (SuPu) scales and personality and affect trait scales*

	Sample 1 (n = 207)		Sample 2 (n = 189)	
Personality and Affect Scales*	SuRe	SuPu	SuRe	SuPu
EPQ: Extraversion	**.35**	**−.39**	**.38**	−.05
EPQ: Neuroticism	.08	**.58**	.21	**.70**
EPQ: Psychoticism	.21	−.07	.22	−.11
ZKPQ: Sociability	**.34**	−.24	**.35**	−.20
ZKPQ: Neuroticism	−.01	**.61**	.13	**.61**
ZKPQ: Imp. Sensation Seeking	**.36**	−.18	.29	−.22
ZKPQ: Aggression	**.30**	.04	**.42**	.08
ZKPQ: Activity	.02	−.24	.09	−.21
MAACL-R: Anxiety	.00	**.50**	.19	**.64**
MAACL-R: Depression	−.02	**.36**	.08	**.53**
MAACL-R: Hostility	.04	.15	.26	**.38**
MAACL-R: Positive Affect (PA)#	.09	−.26	−.04	**−.37**
MAACL-R: SS(Surgency) PA^	**.30**	**−.46**	**.34**	**−.41**

*EPQ = Eysenck Personality Questionnaire; ZKPQ = Zuckerman-Kuhlman Personality Questionnaire; MAACL-R = Multiple Affect Adjective Check List-Revised (Trait form).
#PA Adjectives, e.g., glad, good, happy, joyful, peaceful, pleasant, satisfied, secure.
^SS Adjectives, e.g., active, adventurous, aggressive, daring, energetic, enthusiastic, merry, wild.
Correlations .30 or higher in bold-face. Sample 1: $r = .18$, $p < .01$; Sample 2: $r = .19$, $p < .01$.

(see their Fig. 4). The general behavioral pattern in response to cues associated with rewards in these areas are "approach, exploration, and engagement." In my system, the approach mechanism is shared by sociability and impulsive sensation seeking, but the weak constraint or inhibition mechanism is more specific to impulsive sensation seeking (Zuckerman 1995). At the behavioral level in humans all incentive motivations are not necessarily correlated. What is generalized in the sensation seeking motive is the interest in novel and intense stimulation and the willingness to seek it despite the risk that may be involved (Zuckerman 1979; 1994b). The motivation is not unique to humans. Other species explore novel situations and objects in the absence of primary drives like hunger, and dopamine activity has been implicated as a source of variation in such exploration (Panksepp 1982; Zuckerman 1984).

Siegel et al. (1993) found that a psychophysiological marker that differentiates high from low sensation seekers, augmenting or reducing of the cortical evoked potential (EP), also clearly discriminated two selectively inbred strains of rats. The augmenting strain were shown in other studies to differ from the reducing strain on a number of significant behavioral traits including: exploration, aggression, acceptance of alcohol and barbiturates, operant responsiveness to intense levels of brain stimulation in the reward areas of the brain, and weaker emotionality and stress response. Although the serotonergic stress response in the augmenting strain is weaker, their dopaminergic stress reaction in the forebrain is stronger than in the reducing strain.

The association between dopaminergic activity in the human and the sensation seeking trait is not supported by direct correlational evidence as pointed out by D&C. Any correlational studies in humans depend upon uncertain metabolite indicators of central neurotransmitter activity and therefore are problematic as biological trait indicators. The same reservations must hold for the fairly consistent negative correlations found between platelet MAO-type B and sensation seeking trait in humans (Zuckerman 1994b). The significance of MAO-B to the dopamine hypothesis is the suggestion that brain MAO-B is relatively more specific to the catabolic regulation of one monoamine, dopamine (Murphy et al. 1987).

Behavior genetic studies of twins, whether raised together or apart, show a high heritability for sensation seeking (60%) relative to other personality traits (typically about 30–50%) (Zuckerman 1994b; 1994c). Two independent studies found relationships between a dopamine receptor (D4DR) gene and Cloninger's novelty seeking (NS, Benjamin et al. 1996; Ebstein et al. 1996). NS is highly correlated ($r = .68$) with ImpSS (Zuckerman & Cloninger 1996). Some failures of replication for the D4-NS relationship have been reported, but so also have some new replications, as well as finding the same characteristic variant of the D4 in three different samples of opiate abusers (Ebstein & Belmaker 1997).

An involvement of a dopamine receptor gene with sensation seeking at the genetic level suggests that it may be premature to dismiss the monoaminergic hypothesis (strong dopaminergic, weak serotonergic and adrenergic reactivities) underlying this trait and limit the positive incentive or novelty seeking motivations to the human trait of extraversion defined in the narrow sociability sense. Our trait correlational evidence suggests that a number of relatively independent traits like sociability, impulsive sensation seeking, and aggression, as well as surgent positive affect, are related to susceptibility to cues for reward. If the high activity in the VTA DA projection system underlies incentive motivation then it must underlie some higher order of personality traits divided into those involved in approach (E, P, Imp-SS, Agg, Act) and those involved in inhibition (N) of behavior.

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Authors' Response

On the psychobiological complexity and stability of traits

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Abstract: The commentaries on our target article address three main areas: (1) the relative importance of extraversion and other related traits to DA functioning, (2) how the long-term stability of extraversion can be conceptualized within a highly plastic central nervous system, and (3) the nature of DA functioning in the MOC network and in extraversion. We have organized our Response, therefore, into three major sections.

R1. The need for greater clarity and precision in human trait research

Derryberry & Reed make a good point in their first paragraph in stating that "The discussion [in the target article] would benefit from considering experiments on human extraversion, particularly those dealing with the proposed motivational and response processes." Actually, some years ago we reviewed the human *non*biological research literature on extraversion. We concluded that there was a substantial lack of clarity about the constructs thought to underlie many personality traits, and an equal lack of critical analysis of their phenotypic and hence neurobehavioral heterogeneity. The importance of such imprecision is that it can be reflected in psychometric measures and in the experimental tasks designed to assess those traits. With such variance at play, the number of positions about the nature of a trait that one can support using a conceptual, and in some cases extremely limited, selection of the research literature is fairly high.

Accordingly, we modified our strategy in line with Gray's (1973) initial intent, and attempted to approach the conceptualization of traits by relying heavily on the animal behavioral neurobiology literature. Realizing the limitations of this approach, each step of the way, from trait to behavioral system to animal neurobiology, we attempted to be very clear about the analogies being drawn, as outlined in our strategy in Figure 1 of the target article. Furthermore, our experience with the human trait literature encouraged us to devote the entire first section of the target article to the issue of the nature and heterogeneity of extraversion in order to be clear in our definition of the trait and which aspects of the trait we were modeling neurobiologically. Thus, it is particularly frustrating to us that approximately half of the commentaries address the nature of extraversion and other related traits in the same manner as found in the extant human trait literature, as if the first section of the target article did not exist, or as if the current understanding of traits is so engrained that alternative views are not fully considered. We assume that our target discussion must have been insufficiently clear on these issues, so we will attempt to reclarify them: not in a point by point listing, but rather by categorizing the issues we believe to be involved, citing the relevant commentary accordingly.

R1.1. The complexity of trait concepts and phenotypes. The general issue here to us is that psychometrically derived traits often have heterogeneous phenotypes that can be associated with two or more behavioral systems and neurobiological networks. We wish to repeat that such trait indexes may indeed turn out to be the best way to characterize behavioral expression in the natural world. Thus, it may be that the heterogeneous, emergent trait of impulsive sensation seeking is a much richer way to index behavior than, for instance, using extraversion and constraint in a combinatorial way. But, when the focus is changed to what is the best way to discover the underlying neurobiological networks and neurotransmitters associated with phenotypic traits, we believe that less heterogeneous traits that are defined by reference to evolutionarily preserved behavioral systems will provide the clearest path toward defining the neurobiological foundations of personality.

Against this backdrop, let us consider points raised by the commentaries. First, just some direct clarification of what we stated about the trait of extraversion in the target article, then on to more complex points. **Corr** states (para. 6) that we "conjecture that extraversion is a homogeneous trait linked to a single motivation system." The purpose of the entire first section of the article was to indicate that extraversion is heterogeneous, being traditionally comprised of several phenotypes (agency, affiliation, and impulsivity-sensation seeking) that are likely associated with several different neurobehavioral systems. Thus, we agree with **MacDonald** that affiliation (what he calls "nurturance/love") ought to be distinguished from dominance (which in contradiction to MacDonald's statement [paras. 2 and 3] lines up more closely with extraversion than sensation seeking; see Figs. 2 and 3.

Corr continues in the same sentence "it follows that extraversion should not be related to other neurobiological processes. However, the one consistent finding in experimental studies of extraversion is its mediating role in nonspecific arousal." Three things are important here: (1) we believe the agency form of extraversion is associated with a particular neurobehavioral system (positive incentive motivation and approach behavior), (2) such specification of the neurobehavioral *system* associated with agentic extraversion does not preclude the concurrent activity of other neurobiological *processes,* such as nonspecific arousal (obviously the brain requires and can operate more than one process at a time), and (3) we specifically state that nonspecific arousal or activation has been and likely is a process associated with (not "mediated" by) agentic forms of behavior (see sect. 1.2, para. 2, column 4 of Table 1, and the left-most box in the bottom row of Fig. 4 A, B, and C). Nonspecific emotional arousal accompanies all forms of behavioral engagement (hence the term nonspecific), with the ascending locus coeruleus norepinephrine projections strongly involved in the cortical component of such arousal, and the descending projections from the medullary nucleus paragigantocelluaris and rostroventrolateral medullary integration zone in the autonomic component (Aston-Jones et al. 1996). Nevertheless, Corr then suggests (para. 8) that the joint occurrence of positive incentive motivation and nonspecific arousal makes extraversion a "heterogeneous, emergent trait that does not fulfill (our) criterion for ho-

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mogeneous, single motivational system traits." According to what we have just discussed, this does not follow as a logical consequence. In terms of underlying systems, one point that Corr suggests (para. 6) can probably be ruled out if incentive motivation and DA play a role in agentic extraversion: that extraversion may relate "to the emotional states experienced upon consummation of an appetitive act." As indicated in the target article, incentive motivation and DA appear to contribute very little to consummatory behavior, per se.

Zuckerman's suggestions (para. 2) that we view positive emotions and optimism as arising from combinations of extraversion and constraint, and (para. 9) that we "limit the positive incentive or novelty seeking motivations to the human trait of extraversion defined in the narrow sociability sense" are just not accurate. We view positive emotions and optimism as an integral part of agentic extraversion. The point of our extensive discussion on the distinctness of agency from affiliation, and that positive incentive motivation was differentially related to agency, was to indicate that extraversion should *not* be narrowly defined as sociability.

Furthermore, **Zuckerman** emphasizes an important point that is echoed in many of the other commentaries, and which seems to us one of the more consistent misinterpretations of our position. This involves the dichotomous, black-white view of our position with respect to the association of positive incentive motivation and its DA facilitation with extraversion versus the complex of traits termed impulsivity, sensation seeking, risk taking, and novelty seeking. Zuckerman suggests (para. 4) that we "are specific in the types of subtraits associated with positive incentive motivation, and do not include sensation seeking, impulsivity, and aggression, leaving only sociability (affiliation), activity, social potency, and positive affect." He asks (in the abstract) "is positive incentive motivation, or susceptibility to signals of reward, a mechanism related only to extraversion traits. . .?" Similarly, despite the evidence that "extraversion and positive emotion are related" (**Corr,** para. 6) and that "a number of studies suggest a relation between extraversion and positive incentive motivation" (**Derryberry & Reed,** para. 2), Corr concludes (para. 5) that "extraversion is not *preferentially* related to positive incentive motivation" (our emphasis). Zuckerman extends this argument to DA, stating (last para.) that "If the high activity in the VTA DA projection system underlies incentive motivation then it must underlie some higher order of personality traits divided into those involved in approach (E, P, Imp-SS, Agg, Act)."

Our position is not dichotomous. We believe that positive incentive motivation and its DA facilitation *most directly* represents the foundation of agentic extraversion. Put differently, agentic extraversion is the most homogeneous reflection of the operation of positive incentive motivation and its DA facilitation. This in no way is meant to imply that positive incentive motivation and its DA facilitation will show a specific, limited association to agentic extraversion. Any trait with a complex, heterogeneous phenotype that incorporates, at least in part, behavioral expressions that are the result, in part, of elicition by incentive stimuli will show some degree of association with positive incentive motivation and its DA facilitation. We specifically wished to emphasize this in the target article by differentiating between impulsive forms of behavior that involve a positive affective component and those that do not. The purpose of Figure 3, in part, is to show that many traits labeled impulsivity, sensation seeking, novelty seeking, and risk taking are emergent traits that incorporate positive incentive motivational processes. Despite the fact that as **Zuckerman** points out (para. 7), the extant research does not consistently support an association between DA and sensation seeking, we would nevertheless predict that the same positive affectively-related traits could be correlated with DA activity. Indeed, as pointed out by **MacDonald** (last para.) as a negative finding for our model, DA functioning in our work (Depue 1995; 1996) has been related not only to extraversion, but also (albeit, much more weakly) to positive affective (e.g., Venturesomeness [0.40] and Risk Taking [0.33]) but not nonaffective (e.g., Tellegen's Impulsivity [−0.13], and Zuckerman's sensation seeking scales of Social Disinhibition [−0.12] and Boredom Susceptibility [−0.06]) scales of sensation seeking and impulsivity. This is exactly what we would predict: that forms of impulsivity that incorporate a positive affective process will bear a moderate relation to positive incentive motivation and DA activity.

Perhaps the problem here is related to level of analysis. As we argued in the target article, phenotypic traits, like extraversion and impulsive-sensation seeking, are heterogeneous behaviorally and neurobiologically, but they often tend to be discussed, as in the commentaries, as if they represent distinct entities. (Does it make sense any longer, for instance, to refer to extraversion or sensation seeking as distinct, homogeneous entities?) Therefore, if one posits that an incentive-DA neurobehavioral system underlies agentic extraversion, it is seen as a point of invalidation if such processes are also found to be related to impulsivity-sensation seeking, despite the fact that some forms of the latter traits incorporate an incentive component. Alternatively, our level of analysis involves starting with the general neurobehavioral system of positive incentive motivation and its DA facilitation, and aligning that system as specifically as possible with a homogeneous component of a higher-order trait (agentic extraversion). It should not be surprising if that narrower level of analysis (neurobehavioral system) finds expression in the broader, more heterogeneous behavioral domain of personality traits. But the point is that attempts to define the neurobiological structure of personality, which is our specific goal, will best be done by dividing the broader personality traits into more homogeneous components that relate to meaningful, specific neurobehavioral systems. To us, this would be true even if it can be demonstrated that the best *descriptive* means of defining behavior is through the use of phenotypically heterogeneous traits.

Some commentaries, such as those of **MacDonald, Zuckerman, Pickering,** and **Corr,** disagree with our view of the impulsive-sensation seeking trait as heterogeneous, arguing that it represents a distinct entity. MacDonald suggests (para. 3) that these traits ("including sensation seeking, neophilia, exploratory behavior, risk-taking, boldness, sensitivity to reward, and impulsivity) . . . form a conceptual unit," and that they, but not extraversion (not further specified), represent a behavioral adaptation that has been selected by evolution to insure resource acquisition. Zuckerman suggests (para. 5) further that there is a specific sensation seeking motive underlying this trait complex that activates interest in and exploration of novel and intense stimulation. This indicates that we should take a hard look at the concept of sensation seeking, impulsivity, and risk-taking. We count at least *five* different neurobehavioral sys-

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tems that potentially underlie this trait complex, and all of which no doubt were subject to evolutionary forces:

1. Positive incentive motivational processes that are activated by incentive stimuli and support approach to and acquisition of rewarding goals, a system found in all mammals (Schneirla 1959). Exploration of novel stimulus conditions has been shown to be dependent on this system and its DA facilitation. The "sensitivity to reward" characteristic of sensation seeking, cited by **Zuckerman, Derryberry & Reed, MacDonald, Corr,** and **Pickering** certainly relates to this incentive system, as the target article demonstrates.

2. Trait fear, as indicated in the concept of risk-taking (**Zuckerman,** para. 5), in Zuckerman's Thrill and Adventure Seeking scale (which correlated inversely with Tellegen's fear scale: r's = −0.68 in males (n = 477), −0.66 females (r = 604), p's < 0.01; unpublished data), and in **MacDonald**'s (para. 5) emphasis on "attraction to physically dangerous activities, lack of fear of physical harm." That is, sensation seeking-impulsivity and risk-taking must coincide with low trait fear of physical dangers and bodily injury. The contribution of fear and aggression, where the mean of males differ from females, to sensation seeking helps to explain why, as MacDonald notes (para. 5), males have a higher mean on social dominance and sensation seeking scales.

Of course, the neurobiology of fear is quite different from that of positive incentive motivation, and intimately involves amygdalar and bed nucleus of the stria terminalis activation of cell groups in the lateral and ventrolateral longitudinal cell columns of the midbrain periacqueductal gray region (Bandler & Keay 1996; Davis 1997; Davis et al. 1996; LeDoux 1996b; Lovick 1996).

3. **Zuckerman** and **MacDonald** both view aggression as an integral part of sensation seeking and risk-taking as a means of acquiring resources (MacDonald, para. 3, Zuckerman 1989). This seems to involve two forms of aggression, which we discuss in greater detail below: (a) affective aggression, which supports removal of obstacles to acquiring resources; and (b) competitive or instrumental aggression that specifically may be involved in striving for priority to resources, such as social dominance. These may be neurobiologically different forms of aggression, and they are clearly different neurobiologically from fear and incentive motivation (Panksepp 1998). Nevertheless, as the target article demonstrates, the incentive motivational system and its DA processes facilitate both forms of aggression.

4. As suggested in the target article and by others (Depue 1995; 1996; Panksepp 1998a; **Zuckerman** 1991 and his commentary), sensation seeking involves low constraint associated with reduced activity in the serotonin system.

We conclude that impulsive sensation seeking or novelty seeking is a complex, heterogeneous trait that emerges from the interaction of at least 4–5 independent neurobehavioral systems, each of which evolved in response to somewhat specific environmental challenges. Add to this that impulsivity is not a specific concept either. What is impulsivity? How do you get impulsive behavior? If one is highly sensitive to incentive stimuli and rewarding goals, so that aversive, constraining stimuli are perceived as relatively less potent, one may approach the rewarding stimuli when prudence suggests otherwise. That is impulsive behavior, the type that may be found at the extreme end of the agentic extraversion dimension (as **Le Moal & Piazza** suggest in their next to last paragraph, and as **Tucker** indicates in his para. 1). Thus, contrary to **Netter & Hennig**'s statement (next to last para.) that we would not expect impulsivity to be associated with high extraversion, we would expect this form of impulsivity to be so related. If one adds to this type of impulsivity low trait fear, one would be willing to risk physical danger in seeking rewarding experiences. In this case, impulsivity associated with high agentic extraversion would take on the additional phenotypic feature of risk taking and sensation seeking. On the other hand, if one has such low constraint that actions are regularly initiated prior to cognitive consideration of various alternatives (nonplanning), that is another form of impulsive behavior, lacking in affective tone and, in agreement with Netter & Hennig, not predicted by us to be related to high extraversion. In all of these cases, the term impulsivity generally applies, but it carries little specific information with respect to the underlying neurobehavioral systems involved in producing the behavior. Descriptively, the term is perhaps helpful, even perhaps predictive of general types of behavior or its consequences; but from a neurobehavioral standpoint, it only obfuscates the more specific systems contributing to the behavior. We believe that the same argument applies to Gray's conception of impulsivity, which appears to combine several neurobehavioral systems, as discussed in the target article.

Both **MacDonald** and **Townsend** raise the issue of sex differences in extraversion and sensation seeking. MacDonald suggests (para. 5) that "there are no sex differences in extraversion or gregariousness." Again, this is only accurate if one considers extraversion in an undifferentiated manner. As MacDonald (para. 5) and Townsend (para. 7) both indicate, men score higher on dominance than females, whereas the reverse pattern is found for affiliation. This indicates that sex differences, and perhaps sex steroids, are potentially important when considering agency and affiliation as separate neurobehavioral systems. We have also found important, complex sex differences related to agency and affiliation (Morrone et al., under review). When incentive motivation and positive affect were elicited by incentive-inducing film material of competitive sports scenes, trait aggression (measured by Tellegen's multidimensional personality questionnaire [MPQ]) moderated that reactivity in different ways in males and females. Males ($r = 0.37$, $p < 0.05$) but not females ($r = 0.13$, *ns*) showed a significant correlation between MPQ aggression and post-film positive affect ratings, indicating that aggression contributes in males but not females to positive affective reactivity in incentive stimulus contexts. Moreover, MPQ aggression correlated significantly with MPQ agentic extraversion (r = 0.29, $p < 0.05$) in males but not in females, who actually showed an inverse correlation between agentic extraversion and aggression (−0.28). Conversely, when MPQ aggression was removed from the calculation of MPQ extraversion, a nonsignificant correlation in males between extraversion and positive affective reactivity results, whereas an increased extraversion-positive affect correlation occurs in females.

The manner in which aggression moderates the correlation between extraversion and positive affective reactivity is complicated, but it appears to involve a differential association of aggression with different MPQ extraversion primary traits. In particular, the main significant association of aggression with the MPQ extraversion primary traits in males was with social potency (dominance) ($r = 0.37$, $p < 0.05$), but in females this association was near zero ($r =$

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0.05, *ns*). This association may in part derive from a positive correlation between testosterone levels and both social dominance and aggression in males (**Townsend,** last paragraph; Zuckerman 1991). On the other hand, the main significant association of aggression with the extraversion primary traits in females was an *inverse* correlation with social closeness (affiliation) ($r = -0.31$, $p < 0.05$), whereas in males this correlation was nonsignificant and near zero (-0.08). Thus, apparently, trait aggression and social dominance interact in males, and combine to affect the degree of activation of incentive motivation and positive affect by competitive sports scenes. This appears not to be operating in females and, in fact, trait aggression interacts negatively with social closeness or affiliation in females, thereby reducing the overall relation of extraversion with positive affective experience.

How might aggression and extraversion interact differently in males and females? Aggression may be manifested in a variety of ways, with competitive or instrumental aggression and affective aggression as the most popular distinctions used to explain sex differences in aggressive behavior (Campbell et al. 1992; 1993; Kingsbury et al. 1997; Vitiello & Stoff 1997). These forms of aggression are rooted in one's orientation toward others, and have parallels to the concepts of agency and affiliation. According to a number of researchers, masculinity is associated more with an agentic orientation toward others and an instrumental view of aggression, whereas femininity is associated more with an affiliative orientation toward others and an expressive view of aggression (Campbell et al. 1993). This line of reasoning suggests that competitive aggressive behavior gains material and social rewards or intrinsically rewarding feelings of power and control for the aggressor (Campbell et al. 1992), whereas affective aggressive behavior involves a cathartic discharge of anger (Campbell et al. 1993). Thus, rewarding stimuli generate instrumental aggressive behavior, because they cause the aggressor to expect a positive outcome (Kingsbury et al. 1997).

Rewarding stimuli that drive aggressive behavior and triumphant emotions which follow an instrumental aggressive encounter are quite similar to the reward-related goal-directed behavior and agentic positive emotions that impel the individual to seek rewards. In fact, it has been argued that instrumental aggression is facilitated specifically by incentive motivation (Kingsbury et al. 1997), and in that sense represents other forms of goal-oriented behavior (Toates 1986; Vitiello & Stoff 1997). An interesting result that highlights the different perspectives that males and females have *on average* toward aggression was the significantly negative correlation between social closeness and aggression seen in females ($r = 0.31$, $p < 0.05$) but not in males ($r = -0.08$, *ns*). Females who are high on social closeness value interpersonal relationships and thus are likely to hold an expressive view of aggression. As a result, they may avoid aggressive behavior, because it threatens those relationships (Campbell et al. 1993).

Panksepp and **Isom & Heller** both raise important questions about other forms of social-affiliative behavior. As Isom & Heller point out, it is true that we do not address the neurobiology of the affiliative component of extraversion, although we disagree with their characterization of affiliation as constituting the uniquely human aspect of extraversion. All mammals share affiliative aspects to their behavior, broadly conceived, and neurobiological research on affiliation has relied almost entirely on animals (Carter et al. 1997). Nevertheless, we agree that this is certainly an important area of research, but, as both a recent treatise on the integrative neurobiology of affiliation and Panksepp's commentary indicate, the neurobiology of affiliation takes us in very different directions than those discussed in the target article. Instead of DA, the focus has been on the generalized facililatory influence of sex steroids, oxytocin, vasopressin, and opiates on many neural structures, sensory sensitivities, and behavioral processes that are jointly involved in courtship, mating, reproduction, parenting, and, perhaps, pair bonding (Carter et al. 1997). Although DA facilitation of incentive motivation appears to be involved in the preparatory, approach aspects of social play behavior (Vanderschuren et al. 1997), as Panksepp's commentary makes clear, other neurotransmitters and neuropeptides appear to be more important modulators of this form of social behavior. But should we conclude, as does Panksepp, that the lack of DA involvement in social play behavior indicates that DA is not influential "in the generation of extraversion" (para. 7). We do not have command of the social play literature, but this form of behavior would seem to be complex, involving the expression of many fixed, species-specific behavior patterns associated with predatory aggression, affective aggression, and sexuality. We could imagine that DA modulates approach and perhaps expressive features of these patterns (e.g., intensity, velocity), but that it does not mediate these patterns. Therefore, we would not be surprised to learn that the activation of these patterns is not found to be DA-dependent.

Le Moal & Piazza (next to last paragraph) raise the very interesting question about the nature of agency itself. They note that "many philosophers, poets, novelists, and creative and productive artists have been [thought to be] introverts," which suggests that they are high in achievement but not extraverted. We suppose (not to be Clintonesque) that it depends on what "introvert" means in this case. If, by introverted, one means not people- or socially-oriented, that would not be problematic. One could be high on agentic extraversion, and hence high on achievement, and at the same time (a) be lower on affiliation, (b) find nonsocial incentives most activating, such as more abstract goals of discovery, creation, and fame (MacClean 1990), and/or (c) lower on the agentic primary trait of social dominance (e.g., intermale aggression) than on achievement and positive affective processes. Indeed, many scientists would also fit this description.

Finally, **Townsend** suggests that our view, that only a few generalized brain systems are involved in personality, is not in keeping with the fact that evolutionary forces create many specialized systems. We do not think that Townsend's and our positions are actually in conflict if one takes into account our discussion on the analogous structures of personality and behavioral systems in section 2 of the target article. As illustrated in Figure 4, the bottom row of boxes is meant to represent many specialized neurobehavioral systems that evolved to support interactions in particular environmental contexts. Figure 4 also illustrates that these specific systems are jointly facilitated by the general neurobehavioral system of incentive motivation, which also no doubt was subject to evolutionary forces (Schneirla 1959). Our point is specifically that the *higher-order traits* of personality, which are general and few, are most likely to reflect the activity of a few, general neurobehavioral systems (White & Depue, in press.).

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R1.2. Trait complexity requires extreme experimental precision. The phenotypic complexity of personality traits indicates that extreme precision must be exercised in choosing personality measures, operationalizing trait constructs as experimental tasks, choosing biological agonists and indices, and analyzing the relation of dependent variables to trait measures. We briefly address some of these problems as they relate to issues raised in the commentaries.

R1.2.1. Trait measures and biological correlates

R1.2.1.1. *Extraversion.* As we have seen above, extraversion is a heterogeneous trait that represents several different neurobehavioral systems. This fact has two implications: (a) psychometric measures of extraversion should ideally assess these different components, and (b) extraversion needs to be divided into its component parts when related to dependent variables. The importance of these points was demonstrated in the above discussion of the relation of aggression to agentic and affiliative forms of extraversion as a function of sex. Similarly, we have found that DA agonist-induced (0.3 mg/kg oral methylphenidate) increases in serum growth hormone secretion correlate strongly with agentic ($0.68, p < 0.01$) but not with affiliative ($0.21, p > 0.05$) forms of Tellegen's MPQ extraversion (unpublished data), thereby more finely differentiating our significant, strong correlations ($0.60, p < 0.01$) between DA agonist-induced inhibition of serum prolactin secretion and *total* MPQ extraversion (Depue 1995; 1996; Depue et al. 1994).

We have not found a DA relation with all measures of extraversion, where DA agonist-induced inhibition of serum prolactin secretion was found to correlate with Eysenck's EPQ Extraversion relatively weakly (0.31, *ns;* Depue 1995; 1996). How can this be: Isn't extraversion the same on any scale? **MacDonald** (last paragraph) views this inconsistency as questioning the relation between DA and extraversion. Because we have replicated the DA-MPQ extraversion relation four times, our view of the inconsistency concerns the extraversion measures. Particular care was taken during the development of the MPQ to achieve relatively independent primary scales. Factor 1 is extraversion, termed positive emotionality (PEM), which assesses the general tendency to experience feelings of incentive-reward, effectance motivation, excitement, ambition, behavioral potency, positive affect, and a sense of well-being. It is composed of four primary scales, including well being, social potency (dominance), achievement, and social closeness (affiliation). An affective interpretation of higher-order MPQ PEM is supported by convergent-discriminant relations to the state dimension of positive affect (Zevon & Tellegen 1982), which dominates measures of current mood (Watson & Tellegen 1985). Most important, the MPQ PEM scale was purposefully developed to assess an emotional system based on sensitivity to signals of reward by systematically incorporating in the item pool several subdomains that make up positive emotional experience with strong incentive motivational components. Each of these subdomains was developed into empirically-determined independent first-order dimensions, indicating that each subdomain has gained an independent contribution in the assessment of extraversion. This suggests that the MPQ PEM scale is a comprehensive measure of the extraversion construct. Furthermore, in a four-factor model of the MPQ, PEM splits into two relatively independent factors that assess agency (PEM-A) and affiliation (communal, PEM-C). Social potency and achievement most strongly define the PEM-A factor, and well-being and social closeness predominantly characterize the PEM-C factor. Thus, for these various reasons, MPQ PEM would appear to offer distinct advantages in assessing extraversion, and in determining if there is differential association between agency and affiliation components of extraversion and incentive motivation-positive affect processes. Conversely, although EPQ extraversion has been used widely owing to its early appearance on the research scene, it was not developed, nor does it provide separate indices of, different independent subdomains of the extraversion construct, including agency and affiliation. The impulsivity component of the scale was removed some years ago, leaving EPQ extraversion as predominantly a sociability index.

R1.2.1.2. *Constraint.* As noted by **Zuckerman** (para 2), "Constraint, the term used by Tellegen (1985) to describe the third dimension of personality, is most equivalent to Eysenck's (1967) psychoticism, Costa and McCrae's (1992) conscientiousness, and our [his] impulsive sensation seeking (Zuckerman 1994a; 1994b)." **Corr** and **Pickering** rely heavily on the psychoticism scale in their commentaries as representing sensation seeking. But are these really homogeneous indicators of a similar construct? First, it must be pointed out that EPQ psychoticism has low internal consistency, indicating that perhaps several subdomains are being assessed, although no separate indices of these have been developed. Furthermore, we have found that psychoticism correlates with MPQ traditionalism quite strongly (−0.61), but that Zuckerman's impulsivity-sensation seeking scale correlated with traditionalism only half as strongly (−0.32) ($n = 1081$; unpublished data). Tellegen's MPQ constraint consists of three primary scales which assess classical impulsivity, fear (harm avoidance), and traditionalism. These apparently relate to very different neurobiological systems, because we found that serotonin agonist-induced increases in serum prolactin secretion were correlated significantly only with the impulsivity primary scale (−0.44) but not with the fear (0.01) or traditionalism (0.04) primary scales (Depue 1995; 1996). Moreover, DA reactivity was not related to MPQ constraint (0.09) or any of its primary scales, nor to Zuckerman's sensation seeking scales of social disinhibition (−0.12) or boredom susceptibility (−0.06), and this is concordant with Zuckerman's acknowledgment (para. 7) that "the association between dopaminergic activity in the human and the sensation seeking trait is not supported by direct correlational evidence." But, we did find that DA activity was moderately related to EPQ psychoticism (−0.39) and sensation seeking scales of venturesomeness (0.40), and risk-taking (0.33). And, as pointed out by Zuckerman (para. 8), some but not all studies have found a relation between a DA receptor gene and Cloninger's novelty seeking, a scale that correlates with Zuckerman's impulsivity sensation seeking scale (0.68). Even here, however, results are not completely clear: although certain genotypes were related to extraversion, positive emotions, excitement seeking, and novelty seeking, the same genotypes were not related to the impulsivity subscale of Cloninger's novelty seeking scale (Benjamin et al. 1996), suggesting a possibly stronger relation with core extraversion than impulsivity, *per se.*

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The point of this discussion is that these various constraint indicators are not phenotypically or biologically "equivalent." Their complexity probably accounts for the inconsistent results across various biological variables. What, for instance, in view of the entire above discussion on trait measurement, is one to make of **Pickering's** (para. 3) statement that DA is related more to sensation seeking than extraversion because D2 binding in the basal ganglia (unspecified as to dorsal vs. ventral) has been negatively correlated with EPQ psychoticism but not EPQ extraversion, as well as with the Karolinska personality scale of detachment (which appears to tap low extraversion as much as sensation seeking). It is not surprising that **Lawrence et al.** (para. 4) concluded the opposite when considering the same and several additional binding studies: "These studies have generally shown correlations between levels of striatal dopamine binding and measures related to the extraversion construct."

R1.2.2. Biological specificity. Obviously, in assessing the relation of DA and extraversion, DA agonists and DA binding materials need to be very specific to the DA system, and in this sense amphetamine is probably not the best choice of DA agonist (see **Corr** and **Pickering**). In addition, there must be high precision in selecting the peripheral or central neural systems that are used to index DA reactivity. We would guess that nonspecific arousal is not a specific DA indicator as such (Corr), and that the use of defensive motivational (fear) contexts and startle reactions (**Derryberry & Reed**) do not assess well the VTA DA projections to the NAS that are involved in positive incentive motivation (White & Depue, in press). Tucker's argument that DA tightens rather than loosens, although not totally clear to us in meaning, is based on unnaturally high DA activation of stereotypies, a phenomenon more associated with nonmotivational aspects of behavior in the dorsal striatum than with incentive motivation in the ventral striatum. Similarly, **Rammsayer's** suggestion that DA effects on sensory sensitivity may occur via the dorsal striatal projections of the DA system overlooks the direct DA innervation of several sensory systems, most notably the direct DA innervation of the pupil which modulates contrast sensitivity. The study of DA functioning in humans in relation to motivational behavior is fairly new, and requires great precision in these early stages. In this sense, Lawrence et al.'s discussion of human DA research strategies as used with Parkinson's and PKU patients, and in PET neuroreceptor mapping studies (of which their's is an elegant example) provides a superb framework.

R1.2.3. Experimental operationalizing of trait constructs. In view of the complexity of phenotypic personality traits, and the likely heterogeneity of their underlying constructs and neurobehavioral systems, it will be a most difficult challenge to construct psychologically-relevant tasks that operationalize those constructs. There will have to be very differentiated mapping of task procedures and dependent variables to specific trait components. For instance, **Corr** argues (para. 3) that "few studies support the claim that variation in reactivity to cues of positive emotional valence are strongly related to extraversion (or impulsivity)." This is not accurate, as pointed out by **Derryberry & Reed** (para. 2), and we can add to that many other positive findings in this regard (Costa & McCrae 1980; 1984; David et al. 1997; Larsen & Ketelaar 1989; 1991; Neumanick & Munz 1997; Rusting & Larsen 1998; Watson & Clark 1984; 1996). But more important, as Robinson and Berridge (1993) have discussed, there is a distinct difference between incentive motivational cues and merely positive valence cues in that the subjective feelings generated (e.g., desire and wanting vs. pleasantness) are related to different neurobiological processes.

This distinction has also been evident in the use of film material as a means of generating emotional responses. The use of static pictures or dynamic film material has become a standard means of inducing affective states, although, in terms of the induction specifically of incentive motivation and positive affect, available film material is relatively deficient. Most studies using static pictures or moving films have mainly induced a general state of pleasantness, amusement, or happiness by use of humorous or amusing film content (e.g., Gross & Levenson 1995; 1997; Hubert & de Jong-Meyer 1991; Palfai & Salovey 1993; Tomarken et al. 1990; 1992; Wheeler et al. 1993). The problem with this approach is that, in the circumplex structure of mood space, the bipolar axis of pleasantness-unpleasantness is associated with a mood state characterized by emotional feelings that are *relatively* devoid of a motivational component. As Watson and Tellegen (1985; Tellegen 1985) convincingly demonstrated, the dominant axes in this circumplex are positive and negative affect, which are strongly motivational in nature and which are affectively unipolar, extending from a strong motivational-affective state to an absence of that state. Studies that use mood terms which measure pleasantness-unpleasantness "may yield results quite different from those obtained with the near-orthogonal Positive and Negative Affect measures used by other investigators (e.g., Costa & McCrae 1980)" (Watson & Tellegen 1985, p. 231). Therefore, film material that mainly induces pleasantness would seem less adequate for investigating the incentive motivational-positive affect nature of extraversion. Indeed, Tomarken et al. (1990) acknowledged that the amusing film clips they used did not evoke the strong incentive motivation, focused engagement in ongoing activity, or accompanying behavioral signs (e.g., movement toward a stimulus) normally associated with approach motivation. Also, Gross and Levenson (1995) found that extraversion and trait positive affect did not significantly predict amusement responses to a comedy film, although extraversion predicted increases in positive affect. Concordant with this argument, when Sutton et al. (1997) used static pictures that had appetitive or incentive motivational content, such as appetizing food, successful athletic competition, and attractive nudes, they found adequate maintenance of positive affect with the pictures. We have extended this methodology in a study of film material that specifically displays an incentive motivational context (competitive sporting events) (Morrone et al., under review). Not only did post-film positive affect ratings significantly relate to MPQ extraversion ($r = 0.34$, $p < 0.01$), but also this relation was accounted for entirely by a significant relation to MPQ agentic extraversion ($r = 0.32$, $p < 0.01$) rather than MPQ affiliative extraversion ($r = 0.18$, *ns*).

Derryberry & Reed (para. 4) have added another point of interest to task development. They indicate that extraverts show an attentional bias to rewarding cues as expected, and we suggested in the target article (next to last paragraph of sect. 5) that when such cues are weak, inter-

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mittent, or based on delayed gratification – and/or when the effort required to obtain a reward is large relative to the magnitude of the reward – individuals with low DA functioning will show less resistance to extinction. **Pickering** suggests (para. 4) that this prediction is not the case in that their 1980s unpublished study of EPQ extraversion was unrelated to rate of extinction when acquisition occurred under intermittent versus continuous reinforcement conditions. It can be asked whether a 50% intermittent reinforcement schedule in humans validly operationalizes our prediction. That is, has the task operationalized all of the variables we suggested were important? The key is to make certain that the *frequency of rewards are low, relative to the effort required to respond.* In animal work, where DA functioning is positively related to resistance to extinction, high rates of response (i.e., effort) are required in order to obtain reward. A 50% intermittent schedule seems to us a high frequency of reward for humans who can symbolically span the short delays between reward, unless the corresponding effort is extremely high. Thus, this is a good example of the need to attend to all aspects of a construct in order to test it adequately. We suggest that **Lawrence et al.**'s operationalization of incentive-activated responding via a competitive video game, which was specifically associated with DA tracer binding in the ventral striatum, serves as a model for us all (see Lawrence et al. commentary).

R1.2.4. Sample selection and normal and pathological composition. Two points seem worth mentioning very briefly with respect to samples. First, in behavioral neurobiology research with humans samples tend to be small, as indicated by **Pickering** and **Corr** in describing studies in their commentaries. When selected in a completely random manner, small samples will rarely adequately represent a full range of the trait being studied, which will markedly affect the magnitude of correlations between biological variables and trait scores. It seems wise in such cases to select samples within a stratified manner, for instance by selecting randomly from each decile of a trait's score distribution. This will require, however, that the larger group from which one is selecting the small sample be relatively large and representative of the distribution of trait scores in the general population. Second, it is unclear how much one can generalize from small samples of disordered individuals, especially when the neurobiological features of that group are not clear. For instance, we do not know exactly what to make of the unpublished latent inhibition findings presented by Pickering (para. 5), since the study is based on a small sample of schizotypal personality disordered individuals whose DA status is unknown.

This latter study of schizotypes raises a more general issue echoed by **Panksepp, Kaplan, Lawrence et al.** and **Strauman.** We believe, being very conservative on this point, that our model will gain support from populations that have clear DA dysfunctions that affect the VTA projection system as a major, if not sole, causative factor, as Lawrence et al. suggest with respect to Parkinson's and PKU diseases. Whether attention deficit disorder with hyperactivity (ADDH) also lies within this group of disorders, as Panksepp and Kaplan suggest, is less clear to us, but Kaplan makes a good case for its relevance. But we do not agree with the approach offered in Panksepp's commentary that suggests that, because DA agonist treatment of ADDH does not promote extraversion in these children, or that because DA hyperactivity occurs in introverted schizophrenics, the model is in jeopardy. These are extremely complicated human disorders which we doubt reduce to simple level differences in DA functioning. For instance, DA hyperactivity in schizophrenia does not appear to be a chronic condition but rather represents a transient increase in DA release in the NAS that is associated with positive symptoms at times of increased stress. In turn, DA hyperactivity may result from fundamental deficits in prefrontal cortex in schizophrenia, which result in a loss of prefrontal inhibitory regulation of DA release in the NAS. Moreover, is the long premorbid and postmorbid history of negative symptoms in schizophrenia the same as introversion?

We believe that **Strauman**'s approach is closer to the mark: that our model may enlighten understanding of the dysfunctions found in relevant disorders. In Strauman's case, our model would be used to understand the dysfunctions in self-regulation of incentive motivation and approach to reward. We have proposed similar applications of our model to affective disorders in terms of dysregulation (Depue 1995; Depue & Iacono 1989; Depue et al. 1987), but Strauman's addition of a *self*-regulatory deficit is novel and interesting. We would add that, in behavioral disorders relevant to DA functioning, DA trait levels associated with personality traits may relate more directly to variation in clinical characteristics of the disorders, such as course, severity, suicidal risk, and impairment, rather than to the specific etiology of the disorders, *per se.* For instance, we have shown that in bipolar affective disorder, where DA dysregulation may be directly involved in symptom generation (Depue & Iacono 1989), the level of extraversion is related strongly to the natural variation of clinical course observed in bipolar disorder, that is, extraversion is related positively to the relative frequency of manic to depressive episodes experienced by an individual over time (Depue et al. 1987). This is concordant with our model of DA facilitation of positive affective experience like that found in mania.

R2. Stability of traits within a plastic central nervous system

Three intriguing commentaries (**Cabib & Puglisi; Le Moal & Piazza; Vezina**) zero in on what to us is the most interesting, but simultaneously the most complex and least understood, aspects of our model. Le Moal & Piazza put it simply but precisely in their abstract (last line): "If there is a fixed point for an individual, what inhibits variation in the biological parameter?" Put differently, how can it be that individuals are stable in extraversion, "because development is a life-long phenomenon defined by the ability of the organism to recognise and *change* in the face of a changing environment (Schneirla 1966)" (Cabib & Puglisi-Allegra, para. 8). Neuroscience has demonstrated a vast potential for neuroplasticity in the central nervous system, so that it is difficult to imagine that behavioral stability is possible outside of narrow temporal windows. But the facts are clear on this, and cannot be ignored: many personality traits, including extraversion, have a strong genetic influence (Bouchard 1994; Tellegen et al. 1988), and are stable (in terms of an individual's rank order) over as many as 20 years (Costa & McCrae 1994). Furthermore, twin studies have shown a genetic contribution to the stability of positive affective trait levels, that severe stress-induced changes in

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those levels are temporarily quite limited, and that positive affective levels return to pre-stress trait levels as if a set-point influence were operative (Lykken & Tellegen 1997). The same perplexing finding occurs with respect to intelligence: IQ levels (which here can be thought of as a trait) of identical twins reared apart show equally high heritability (.74) as those for identical twins reared together (Bouchard 1994). Clearly, the development of intelligence, or emotional behavior as in extraversion, must be dependent on many powerful neuroplasticity processes that are environment activated. How is stability, therefore, even when individuals are raised in different environments, achieved?

We have asked ourselves these questions many times, and the answer keeps evolving (some things are not stable). We present here, with reference to the commentaries, our latest understanding of this dilemma. In the case of extraversion, we propose that stability occurs for the following reasons:

1. Genetic factors strongly influence a biological variable that plays a central role in the trait's phenotype. As in the target article, let us use the number of VTA DA neurons as the biological variable, since their number has been shown to be genetically influenced and to strongly influence extraversion-relevant, incentive motivated behaviors. This factor, we presume, is the lowest-order foundation of the concept of trait.

2. This biological foundation strongly influences the impact of the environment. According to our model, VTA DA neuron number would presumably influence the mean *range* of incentive stimuli that will normally (i) activate VTA DA projections sufficiently strongly to (ii) generate their effects on neural and behavioral processes.

This is illustrated in Figure R1-A of this Response, which we emphasize is a very simplistic rendition of nature. Arbitrary units of VTA DA neuron number are shown on the vertical axis, whereas arbitrary units representing the mean magnitude of environmental incentive stimuli are illustrated on the horizontal axis. The dashed diagonal line demarcates the lowest magnitude in the range of incentive stimuli which are, on average, effective in activating incentive motivational and behavioral processes. This threshold for activation of behavior is greatly influenced by VTA DA neuron number.

3. The product of this positive genotype x stimulus efficacy interaction will develop during early life via experience expectant processes. Under environmental conditions that fall within the normal range of life's experiences, a relatively stable psychobiological foundation (synaptic network) will be established within structures of the MOC network, which mediates the connection between salient incentive contexts and incentive motivational processes. This psychobiological foundation serves as the background upon which future experience-dependent processes will act. We view this psychobiological foundation as the basis of the extraversion *temperament*.

Figure R1-B of this Response illustrates the range of individual variation that can obtain in this psychobiological foundation, where VTA DA neuron number units are shown on the vertical axis, and arbitrary units of synaptic density across MOC network structures are shown on the horizontal axis. Synaptic density was calculated by multiplying each VTA DA number unit by each of the incentive magnitude units falling within the effective range associated with that VTA DA unit. Then, because all incentive

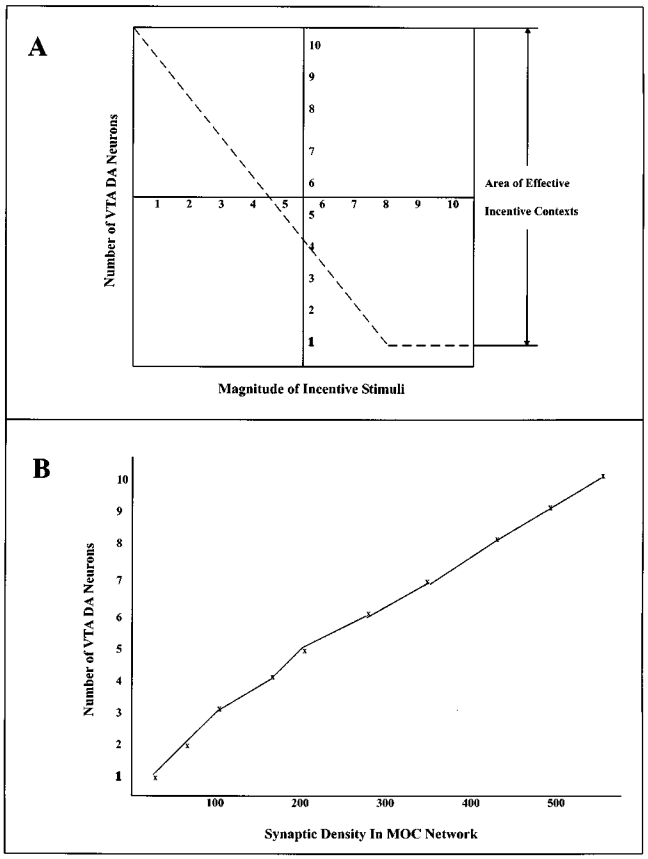


Figure R1. Incentive stimulus sensitivity and synaptic density in the MOC network as a function of number of VTA DA neurons. (A) Sensitivity to magnitude of incentive stimuli as a function of number of VTA DA neurons. The dashed diagonal line demarcates the lowest magnitude in the range of incentive stimuli which are, on average, effective in activating incentive motivational and behavioral processes. From this lowest magnitude to the right border of the figure represents the range of incentive magnitudes that activate VTA DA neurons. Both the range and the threshold for activation of behavior are greatly influenced by VTA DA neuron number. (B) Increasing synaptic density in the MOC network as a function of the number of VTA DA neurons. See text for a discussion of the calculation of data points.

units falling within an effective range will hypothetically contribute to synaptic formation (albeit in proportion to their magnitude), the individual products of each multiplication were summated (e.g., a VTA DA unit of 10 is multiplied by each of the 10 incentive magnitude units, and these 10 products were summated). This scenario makes the unlikely assumption that individuals with different numbers of VTA DA neurons have equal exposure to environmental incentives: that is, no active genotype x environment interaction (differential selection of incentive environments) is occurring. The latter is, indeed, likely to occur, and would only serve to increase the range of synaptic density values.

4. Stability of this psychobiological foundation or temperament level is assumed to be maintained by at least two factors: (i) the psychobiological foundation of the extraversion temperament has now established the mean range of effective incentive stimuli more strongly (the range of effective incentive environments in Fig. R1-A has become increasingly set), thereby further influencing the extent to which the environment has access to experience-dependent neuroplastic processes. By this stage of development,

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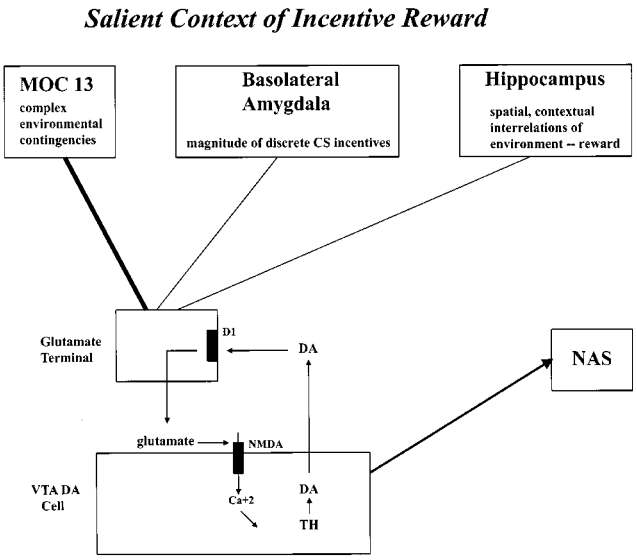


Figure R2. Dopamine facilitation of heterosynaptic plasticity at the level of individual VTA DA neurons. The connection of glutamatergic inputs representing the salient context of incentive reward are facilitated by somatodendritic DA release from VTA DA neurons. Via D1 receptors located on the glutamate terminals, somatodendritic DA increases the release of glutamate, thereby facilitating long-term potentiation and the *development* of behavioral sensitization. Burst firing of VTA DA neurons under the influence of strong input activation promotes intense DA release from VTA DA-NAS projections, a DA release that facilitates heterosynaptic plasticity of salient inputs to NAS spiny neurons and the expression of behavioral sensitization. See Figure 5 and discussion in the target article and in this Response.

one can presume that the operation of an active genetotype x incentive environment interaction will play an important role in maintaining initial differences. But most important, (ii) individual differences in VTA DA functioning (e.g., due to variation in neuron number) will strongly influence the neuroplastic processes *themselves,* thereby influencing the extent to which even effective subsequent incentive stimuli gain control of incentive motivational and behavioral processes.

In the target article, we attempted to operationalize this last point through the use of a behavioral sensitization framework of experience-dependent processes. We take behavioral sensitization to be an experimental example of a primary means by which the salient context of incentive reward (including neutral-conditioned and unconditioned incentives) in *natural* environments gains control over incentive motivational and behavioral processes. The important point for stability is that VTA DA functioning plays a critical role in these processes via its participation in heterosynaptic plasticity. In Figure 5 of the target article, we attempted to illustrate this role for DA in facilitating the connection of the salient context of reward to NAS spiny neurons, a process that appears to be important for the *expression* of behavioral sensitization. As illustrated in Figure R2 of this response, the *development* of behavioral sensitization also relies on DA facilitation of the connection of the salient context of incentive reward with VTA DA neurons. In both cases of heterosynaptic plasticity, DA facilitates the connection of glutamate efferents from the MOC, hippocampus, and amygdala carrying the salient context of reward to VTA DA and NAS neurons.

Thus, when a stimulus of sufficient salience occurs in a manner that predicts the occurrence of an incentive goal, it is critical that that stimulus gains access to, and hence subsequently gains influence over, the VTA and NAS circuitries that activate incentive motivational and behavioral processes that support goal acquisition. This is concordant with **Vezina**'s hypothesis (penultimate paragraph): "It is conceivable that such stimuli may produce their effects by virtue of their access to and ability to influence activity in VTA-NAS DA neurons." As reviewed in the target article, VTA DA plays a critical role in the processes by which salient stimuli gain control of responding. In this sense, behavioral sensitization is the product of the now joint action of contextual inputs and increased DA facilitation. As the behavioral sensitization literature demonstrates, and as we reviewed in the target article, the salient contextual inputs to the *VTA DA neurons* provide the predominant means by which the environment activates sensitized responding, which is subsequently expressed via the interaction of contextual inputs (glutamatergic release) and DA release in the NAS. Take away the contextual input (to the VTA DA neurons), and the still sensitized system is not typically expressed.

In a nutshell, our theory of the development of extraversion is that individual differences in the expression of agentic affect and behavior are due in large part to the effects of individual differences in the extent to which VTA DA functioning facilitates the connections of salient contextual inputs to VTA DA and NAS neurons. Moreover, we assume that VTA DA individual differences have an equivalent influence on heterosynaptic plasticity in other brain regions, and, in our case, especially in structures of the MOC network. For instance, according to research presented in the target article, VTA DA projections to the basolateral complex of the amygdala may facilitate the synaptic connections between conditioned and unconditioned incentive stimulus inputs (also suggested by **Vezina**). Similarly, VTA DA projections to the central nucleus of the amygdala may facilitate synaptic connections between conditioned stimulus inputs to central nucleus output neurons to the NAS, thereby contributing salient contextual input to NAS spiny neurons, the connections of which may then be facilitated by VTA-NAS DA activity.

Studies described in the target article (sect. 4.3.2) illustrate the extent to which individual differences in VTA-NAS DA functioning may modulate these plastic processes, and thereby, in our opinion, maintain individual differences in the extent to which the environment can influence incentive motivational and behavioral processes. Two groups of rats created by a median split of locomotor response to novelty (low [LR] and high [HR] responders) differ substantially in the magnitude and duration of VTA-NAS DA functioning, a finding that is dimensionally related under stress conditions across the range of motor scores ($r = 0.86$). The locomotor differences under normal environmental conditions are very stable or trait-like (**Le Moal,** personal communication, October, 1998). Across a wide range of doses, high responders exceed low responders in the rate of responding, and in the amount of drug administered, during the acquisition of psychostimulant self-administration, and in levels of intra-VTA self-stimulation. These differences appear to be influenced by genetic variation, and by the number of DA neurons in the VTA region. In many studies, *pretreatment* novelty-induced locomotion

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is positively correlated *across* animals with locomotor reactivity to psychostimulants administered systemically or into the NAS or VTA. All of these findings suggest that these animals have differential ranges of effective incentive stimuli, as shown in Figure R1-A of this response. Clearly, these two groups have a differential psychobiological foundation or extraversion-relevant temperament.

But will the neuroplastic processes of these two groups respond differently in connecting salient incentive context to VTA DA and NAS neurons, thereby maintaining their temperamental differences? Two findings suggest that they will (see target article). First, at low to moderate doses of stimulants, a correlation between *pretreatment* novelty-induced locomotion and degree of subsequent sensitization was observed in several studies, which may be influenced by genetic variation in DA concentrations in the NAS. Second, the inbred strain of C57 mice, which shows enhanced DA transmission, showed enhanced context-dependent sensitization relative to DBA mice, although the two did not differ in degree of context-independent sensitization. Similar findings favoring context-dependent sensitization in a selected line of rats with enhanced responses to novelty have been reported.

Thus, the *important point concerning stability* is this: because VTA DA functioning plays an integral part in (a) determining the range of effective incentive stimuli that have access to an individual, and (b) the extent to which those stimuli are connected to and gain influence over VTA DA and NAS neurons (behavioral sensitization), then individual differences in VTA DA functioning will modulate both of these processes and, hence, the extent to which salient incentive contexts facilitate incentive motivational and behavioral processes over time.

The three commentaries related to this issue demonstrate how complex the modeling of the development of personality traits can be. **Cabib & Puglisi-Allegra** provide a wonderful example of the complexities, where two inbred mouse strains (C57 and DBA) have genotypes associated with differential DA transmission and incentive motivated behaviors (high vs. low, respectively), but due to inverse responses of their DA system to stress, end up displaying DA and behavioral functioning that initially characterized the opposite strain. This is certainly an elegant demonstration of the fact that problems for any model proposing stable behavioral traits will arise when negative genotype-environment correlations are operative.

It is difficult to know how generalizable these findings are to non-inbred strains when considering modifiability of stable individual differences in VTA DA functioning. One problem with an inbred-strain research strategy is that behavioral differences in inbred strains of disparate origins could reflect many genetic and neurochemical differences between strains, and cosegregation of traits could be due to the occurrence of genetic differences at the same or different loci (Phillips 1997; Robinson 1988). These complexities are particularly difficult when dealing with behavioral traits, which tend to be polygenic in nature (Plomin 1990). In this case, any particular behavioral contrast between strains may reflect disparate epigenetic influences of various components of the overall differences in inter-regulated expression of polygenic complexes (Phillips 1997). For instance, C57 and DBA mice are among the most studied inbred strains in the behavioral pharmacology of DA, and they differ in several structural parameters of the DA system in a way that appears to relate directly to behavioral differences (Puglisi-Allegra & Cabib 1997). Nevertheless, they also exhibit several qualitatively different behavioral patterns that, at a finer level of analysis, are supported by separable DA-related neurobiological networks (e.g., mesoaccumbens vs. nigrostriatal) and different modes of inheritance.

Other research supports a positive interaction of stress and stress-related steroids with DA functioning. For instance, in rats, novelty-induced locomotion is positively correlated with basal and stress- and novelty-induced corticosterone secretion, which in turn is related to the amount of drug administered during the acquisition of self-administration of amphetamine and cocaine (Piazza & Le Moal 1996). Functionally, corticosterone in rats enhances firing of VTA DA neurons projecting to the NAS, sensitivity of D_1 and D_2 receptors, DA release in the NAS, and DA release to stressors (Piazza & Le Moal 1996). To the extent that VTA DA functioning is related to extraversion and trait levels of positive affect, the findings in human twins cited above which showed that life stress affects positive affect levels only temporarily and that individuals subsequently return to their pre-stress levels, suggests that no prolonged modification of VTA DA functioning, at least in adults, occurs under conditions of life stress that are *within the normal range.* As the literature on post-traumatic stress disorder indicates, however, extremely stressful conditions, or stressors occurring during early stages of development, may indeed cause long-term modifications of neurotransmitter and/or neuropeptide functioning that can be accompanied by "personality" changes (Yehuda & McFarlane 1997). Moreover, as we discussed in the target article, when LR rats were provided DA-enhancement via sensitization to amphetamine, subsequent acquisition of self-administration of amphetamine was equivalent to HR rats. Similarly, when a high dose of amphetamine was employed, Hooks et al. (1992c) observed robust sensitization in LR rats who had failed to sensitize at lower doses. Thus, individual differences in DA functioning, even if influenced by fixed characteristics in DA systems, may be modifiable by *strong* experiences acting through experience-dependent processes. But, again, such effects do not appear to be the general rule in rats and perhaps humans when life conditions are within the normal range.

Vezina raises important issues about the role of conditioned stimuli (CSs) in activating incentive motivational processes. It is clear that conditioned positive incentives that bear a predictive relation to reward strongly activate VTA DA neurons prior to behavioral responding, and are associated with an increased release of DA in the NAS even in experiments of behavioral sensitization, as amply demonstrated in the target article. As Vezina points out, however, incentive motivated behavior has been found to occur in the presence of CSs during DA receptor blockade, although it should be noted that this is often not the case (Benninger 1983). Two findings may help to explain this result. First, well demonstrated in extensive reviews of DA and behavior (Le Moal & Simon 1991; Oades 1985) is that DA does not *mediate* the effects of CSs in activating incentive-induced behavior. Rather, DA appears to provide facilitatory *modulation* of incentive states, in part by facilitating heterosynaptic plasticity between CS inputs and NAS neurons. As Oades (1985) noted, animals with DA receptor blockade seem to have difficulties initiating incentive-induced be-

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havior, but, once moved or pushed by the experimenter, are able to perform quite effectively. Within the framework of our discussion, this may mean that DA facilitates the activating effects of the CS in both the VTA and NAS. Presumably, because the performance of incentive behavior under DA receptor blockade conditions is not consistently observed, only in some cases is the CS salient or intense enough to activate the behavior in the absence of DA facilitation. It is important to note that even in the latter circumstances one would expect, on the basis of the target discussion, that a lack of DA facilitation will influence the *expressive* features of the performed behavior, including its vigor, intensity, and velocity. It is the latter features that appear to be most sensitive to DA manipulations, and VTA DA neuron activity is well correlated with the velocity of incentive-motivated behavior.

Second, Schultz's studies showed that VTA DA neuron responses to incentive stimuli may play a role in facilitating the association between stimuli that predict reward and behavioral responses that obtain reward (Schultz et al. 1997). The optimal stimuli for activating DA neurons are phasically occurring *unpredicted* unconditioned rewards, whereas fully predicted stimuli are ineffective (Schultz et al. 1995b). DA neurons show increased activity in the presence of neutral stimuli that consistently predict reward, but sequentially transfer that activity to earlier and earlier occurring stimuli that are predictive of the primary incentive stimulus (Schultz et al. 1997). Thus, DA activity is critical to the control of appetitive behavior by conditioned incentive stimuli – specifically, by linking stimuli predicting reward to the response-facilitation mechanism in the NAS. Therefore, in experiments where predictive CSs have been strongly linked to the NAS during acquisition, and then DA receptor blockade is instituted in the test phase of the study, CSs may be able to elicit behavior without DA facilitatory effects. It is blocking DA receptors in the acquisition phase that should impair the subsequent ability of the CS to elicit behavior (Beninger 1983).

Vezina also notes (para. 3) that drugs that activate DA functioning do not activate sensitized behavioral responding in the absence of the salient context present during the development of sensitization. He believes that this is problematic for our model because "sensitization of NAS DA reactivity represents a stable condition in the individual that guarantees enhanced motivational responding to appropriate eliciting incentive stimuli." This does not completely capture the meaning of our position, however. We do not imagine that variation in extraversion is accounted for merely by variation in a stable condition of sensitization of NAS DA reactivity. Again, behavioral sensitization was taken as a model of experience-dependent processes; we believe that it provides an understanding of heterosynaptic plasticity processes whose magnitude may be related dimensionally to variation in VTA DA functioning. It is the effects of individual differences in VTA DA functioning on facilitation of stimulus linking in the NAS, as well as variation in DA facilitation at the time of subsequent occurrence of the stimuli, that together represent differences in extraversion. Actually, Vezina finds his way to the same conclusion (para. 4): "stimuli endowed with occasion-setting or conditioned inhibiting [facilitatory] properties are well positioned to influence the expression of sensitization in a more discrete, selective, and environment-dependent manner. It is conceivable that such stimuli may produce their effects by virtue of their access to and ability to influence activity in VTA-NAS DA neurons." We would add that the *conditioned* access of those stimuli to the VTA DA and NAS neurons will vary with individual differences in VTA DA functioning, as will the intensity of VTA DA activity that is subsequently activated by those stimuli.

R3. Neurobiological aspects of a dopamine-extraversion model based on an MOC network

A number of the commentaries relate to our proposed MOC network (**Joel, Bond & Raleigh, Fine & Blair,** and **Katz**) or components of that network (**Gray**), while others concern the role of DA more generally (**Oades**) and in relation to extraversion more specifically (**Gray, Netter & Hennig, Oades, Rammsayer**). We will address them in that order.

R3.1. The MOC network model. For us, **Joel**'s commentary, is extremely exciting, because it takes our MOC network model to new conceptual levels with seemingly very minor modifications, and helped us to clarify problems we had trouble getting straight. Joel asks two critical questions that we believe may be interrelated, but which our model did not address. While we may conceive of the issue a bit differently from Joel, we are not in disagreement with her model. We would rephrase her first and third questions this way: From several simultaneously present representations of goals (i.e., newly-constructed or stored stimulus context-reinforcement ensembles) that we presume are formulated and held in working memory in the MOC, how does the MOC network select among the goals, and what role does DA play in this selection process?

We suggested that the salient context of incentive reward converged on the NASshell from the MOC, amygdala, and hippocampus. The NASshell then served as the site of integration of the thousands of such contextual inputs. Also important, the NASshell was also viewed as the site where that integrated ensemble was associated with a motivational state, and perhaps eventually behavior, through a DA facilitated heterosynaptic plasticity process linking contextual inputs to NAS spiny neurons. Because the learning capabilities of the isolated striatum are limited, in this way, DA plays an important role in selective strengthening of cortical and limbic efferents to the NAS, thereby amplifying the cortical and limbic antecedents of previously successful responses. In addition, Graybiel et al. (1994) suggested that DA also plays a critical role in facilitating the *binding* or coordination of the numerous inputs to the striatum in order to provide an integrated output to pallidal structures. This represents a DA facilitated learning process that takes place in the NASshell, and the product can be stored for retrieval and possible modification when that context is next encountered.

As **Joel** notes, this account is insufficient, because the problem of how the MOC network selects between goals is not explained. She suggests that the selection of the many contextual stimuli concurrently present in the environment occurs in the NASshell. We believe that that is not really the problem, since our account essentially explains how variation in contextual saliency is handled. What we do not address, and which we suggest is the more significant impli-

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cation of Joel's astute observation, is how the entire MOC network selects a goal for current attention among several concurrent goals.

We would suggest that, using **Joel**'s modifications, the goal representations in the MOC, which are stimulus context ensembles associated with reinforcement, are passed through the NASshell, wherein each ensemble is either (a) encoded for incentive saliency or intensity anew if it represents a novel context, and/or (b) activated as a stored, incentive encoded ensemble. If the NASshell operates in a similar manner to other striatal areas, the contextual ensemble of highest incentive coding would be selected via collateral inhibition within the NASshell. Besides activating a comparable incentive motivational state associated with the selected context ensemble via reverberation around the motive circuit, the product of the NASshell's processes would be looped back to the MOC, biasing MOC output toward excitation of motor program circuits relevant to the selected goal, as Joel describes.

The role of DA in these processes would be to encode and bind the incentive salience of each contextual ensemble, so that whenever an array of context-reinforcement ensembles are represented as goals in the MOC, the selection process in the NASshell can use the salience weight as a guide. The means by which DA encodes incentive salience perhaps involves two processes: (a) the degree of facilitation of heterosynaptic plasticity, thereby varying the extent to which each contextual ensemble at any point in time biases the eventually selected ensemble in the NASshell, and (b) the degree to which each contextual ensemble activates NASshell–VTA DA efferents, thereby in turn activating VTA DA projections throughout the MOC network (suggested in Alexander et al.'s loops, see target article). We discuss below how different affective feeling states might accompany incentive salience encoding.

Joel's second question concerns how the selection of goals in the MOC network is relayed to motor programming and performance circuitries. We find her model very appealing, but perhaps one more circuit is needed that is able to translate incentive motivational information into an expressive code (motivational encoding of motoric acts) that the motor circuitries can more readily use. It is asking a lot of motor programming circuitries to do both translation of affect to motor codes and also program the actual motor movements. Deutch et al.'s (1993) suggested circuitry associated with the *core* region of the NAS appears to represent such an interface between motivation and movement.

The commentaries by **Fine & Blair** and by **Bond & Raleigh** have noted problems of the MOC network somewhat related to those noted by **Joel,** but their modifications are framed within computational and control system terms. Bond & Raleigh provide basically a rewording of our neuroanatomical model in the language of control systems, but especially address the problem of interactions between control systems, just as Joel addressed these issues via interacting striatal circuitries. Fine & Blair address the problem of matching the correct contextual stimuli with the appropriate response pattern, while at the same time jading all of our future Thanksgiving dinners. Our response to Joel on the manner in which the MOC network selects goals, and binds context to behavior, seems to address the problem of selection raised by Fine & Blair. What we find unappealing about these computational models is their lack of contact with neurobehavioral content. For instance, Blair's (1995) violence inhibition model lacks a connection between distress cues and a hypothesized neurobehavioral system that is elicited by such cues. But that connection seems necessary in order to discover the neurobiological meaning of *sensitivity* to distress cues and an understanding of the neurobiological basis of psychopathy. Finally, Fine & Blair are correct in indicating that the MOC does not support instrumental learning. In line with our response to Joel, we believe that the MOC is involved in constructing a representation of goals. This incorporates not just a stimulus context-reinforcement expectation, but also the stored representation of responses that led to reward in the past under those stimulus context conditions.

Katz enlarges on the interactive role of serotonin in incentive motivational activation of extraverted engagement with the environment. Two clarifications first. Katz (para. 2) raises the question of where in the Watson and Tellegen circumplex of mood space would agency fall? If with high engagement, then how do we arrive at a bias toward positive incentive motivation in extraversion? We interpret the circumplex differently from Katz. Agentic extraversion would be comprised of all three dimensions associated with positive engagement. Agency would align most strongly with the positive affect dimension, which is dominated by adjectives that represent a combination of positive feelings plus incentive motivation (e.g., peppy, strong, excited, elated, euphoric, active, energetic). This is in essence the subjective representation of positive incentive motivation, and the reason that Watson and Tellegen labeled the axis as "positive affect" rather than simply positive mood. Associated with that positive affective state are the characteristics associated with the two related diagonals in the circumplex: pleasant feelings, and high arousal and engagement.

With respect to serotonin, **Katz** (para. 3) wonders how serotonergic activity could be related to both the inhibition of DA and positive affect on the one hand, and simultaneously to the orthogonal nonaffective constraint dimension on the other, the latter implying a lack of direct opposition to DA and positive affect. The representation of serotonin in our target article's Figure 8 is not meant to represent a direct or special relation of serotonin to inhibitory modulation of DA and incentive motivation. In that figure, serotonin represents a modulating factor that influences a central nervous system threshold for the facilitation of any motivational system. Thus, we view serotonin as underlying the constraint dimension, which is a nonaffective dimension of behavior. That is, serotonin is not viewed as being preferentially associated with any particular affective system. The constraint dimension, and its serotonin foundation, is thus orthogonal or independent of the agency dimension in that one's trait levels in agency and constraint are independent, though functionally serotonin and DA interact.

Katz (paras. 3–5) does offer a very interesting extension of serotonin's functioning in relation to agency not covered in the target article. Adequate levels of serotonin permit control over the reward-biased facilitation of "fickle" VTA DA and impulsive, affective-driven responding, so that prepotent or dominant appropriate responses may be selected despite the fact that they may not be related to the highest reward. We can step back from affective engagement for a cool moment of strategic reflection." These effects of adequate serotonergic functioning no doubt are the product of serotonergic modulation throughout the structures of the

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MOC network, which all receive substantial serotonergic input. Katz's conjectures seem right, and add new light to certain human conditions. Human behavior associated with a combination of elevated DA and reduced serotonin functioning, as perhaps in histrionic and antisocial personality disorders, is characterized by labile affective responsivity (responding quickly and with high magnitude to affective stimuli without measured consideration), cognitive nonplanning, impulsive responding in the presence of strong rewards (e.g., excessive spending, sudden "wild" relationships or marital affairs) and aversive stimuli (e.g., suicidal behavior as escape or avoidance, Coccaro & Siever 1991; Depue 1996).

Kline provides a concise, valuable summary of the robust findings collected over a 20 year period relating anterior asymmetry to emotion, the important finding for extraversion being that relative left frontal activation is related to positive emotional and approach tendencies. We did not include this literature in our model, because no consistent findings of asymmetry of DA projections are evident (Le Moal & Simon 1991). More important, it is difficult to incorporate asymmetry notions in neuroanatomical network models, because there is little specificity as to cortical fields or areas outside of "frontal," or as to which functions are reflected in the activation patterns (e.g., motor preparation, attentional, working memory, emotional evaluation). We look forward to such specificity.

Gray's commentary relates to a number of issues, including those already discussed on trait concepts and task complexity. Because his commentary is in direct disagreement with our model, we need to take it seriously and discuss it at some length. A central focus of Gray's commentary is the nature of DA functioning in the NAS. He suggests (para. 2) that if NAS DA functioning is related to anything other than the facilitation of positive incentive motivation, this represents "critical opposition to D&C's argument." This strikes us as an unnecessary position to take, because many brain structures are involved in several different functions, although those functions may have a central organizing principle. For instance, whereas the amygdala is involved in fear conditioning and activation of freezing responses in the periacqueductal gray's ventrolateral longitudinal cell column, the amygdala is also involved in (a) positive reinforcement associations, and (b) output activation of many other affective response patterns.

Gray's concern is with the fact that NAS DA activity is related to three findings that are not associated with positive incentive motivation in any direct way, thus potentially totaling four NAS DA functions: (a) aversive stimuli can elicit NAS DA functioning, (b) NAS DA release can be elicited by the Pavlovian pairing of neutral stimuli not associated with reinforcement, and (c) increased NAS DA functioning is associated with sensory modulations that are reflected in prepulse inhibition (PPI) and latent inhibition (LI). It is noteworthy that Gray does not apply the same logic to his own conclusions: he concludes that NAS DA activity is related to the latter sensory processes, without finding the presence of the other two, plus NAS DA relations to positive incentive motivation, as being in "critical opposition" to that argument. Nevertheless, our position with respect to the findings raised by Gray are twofold: (a) that complex structures like the NAS do not have to serve one function, and (b) perhaps all four sets of findings have a common base.

First, in view of the enormous body of literature reviewed in the target article, it seems impossible to conclude that NAS DA does not *facilitate* positive incentive motivation. **Lawrence et al.,** in their commentary and *Nature* article, likewise show convincingly that DA binding specifically in the human ventral striatum is associated with a positive incentive motivational task, and Volkow (Volkow et al. 1997) for the first time demonstrated that the proportion of binding of methylphenidate to the DA transporter in the human striatum is correlated specifically with subjective positive affect. Rather than try to dismiss that evidence, perhaps the other three findings can be integrated with the functioning of the NAS and DA in the MOC network as laid out in the target article and in this Response.

In the target article, we suggested a number of possible reasons why aversive stimuli would also increase NAS DA activity. These reasons included the possibility that aversive stimuli may be processed in a similar manner to positive incentive stimuli. **Gray** states that "evaluation of [this] solution is difficult without clarification of how dopamine release can differentially affect the proposed heterogeneous circuits." We did not propose, however, that DA *per se* had differential effects within different circuits. We would view DA to function similarly in distinct circuits located in the MOC structures. In cooperating in the selection of goals (see above discussion), DA would have the same effect of facilitating the linkage of salient contextual inputs (in this case, negative incentive contextual stimuli) to NAS neurons, and of encoding the incentive salience of those contextual assemblies in order to provide the motor system with an expressive code for the behavior needed to deal with those circumstances. For instance, if avoidance or affective aggression were to be enacted, the DA facilitated coding of incentive salience of the contextual ensemble would provide incentive motivational support according to that code.

The critical problem here is not dichotomously Which function does DA subserve: aversive, negative incentive or positive incentive motivation? The important issue, to us, is how does the DA facilitated incentive salience code get translated subsequently into *positive* incentive motivation versus *negative* incentive motivation. Our current view of this complex issue is that in both the negative and positive incentive contexts, NAS DA encodes incentive motivational salience in the same manner as discussed above in relation to **Joel**'s commentary (although perhaps within distinct MOC, NAS circuitries). However, via separate MOC network outputs to distinct emotional circuitries (e.g., from MOC to amygdala), distinct subjective emotional experiences (e.g., positive feelings of desire, wanting, joy, and triumph vs. fear vs. anger) might be activated in order to accompany the incentive motivated behaviors of approach, avoidance, or affective aggression. Indeed, this may be the reason incentive motivated states can have mixed affective feelings (e.g., the fear as well as desire and excitement that accompany the soldier racing for his fox hole under fire).

The fact, as **Gray** notes, that there is an increased NAS DA release after the Pavlovian pairing of two neutral stimuli seems to us to fall within the same conceptual framework for NAS DA functioning that we have been discussing in this Response. In nature, the pairing of stimuli may be potentially a meaningful event. As such, the pairing will likely lead to orientation, with the expectation that an important event could follow. Under such circumstances, one

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might expect the MOC to develop a provisional contingency of "potential emotional significance," and activate (a) VTA neurons giving rise to VTA DA-NAS projections, as well as (b) NAS neurons directly. This would provide a rapid, phasic DA response (which is typical of DA dynamics, Oades 1985) to begin to link the paired stimulus ensemble to NAS neurons, in the event that salience encoding and a motor response are to follow. Conceptually, this would be a preparatory process for establishing a predictive relation between stimulus context and eventual outcome, just as locus coeruleus neurons release norepinephrine into all areas of the cortex as a preparatory response to increase signal-to-noise processing ratios when unexpected environmental events occur (Aston-Jones et al. 1996). No doubt, if nothing significant follows the pairing, such preparatory processes cease.

Gray proposes that enhanced NAS DA transmission alters perceptual processes, although his discussion seems to refer more to sensory processes (would not perceptual processes be more closely associated with the development of polymodal sensory representations in paralimbic cortical areas? LeDoux 1996b). This proposal is based on the fact that increased NAS DA functioning is associated with reduced PPI and LI effects. Note, however, that these effects are proposed by Gray to occur as a result of NAS-VP-thalamic reticular nucleus output circuitry rather than as a result of any particular processing within the NAS. In other words, as we understand his argument (although we must state that we have not read Gray's full account), this proposal tells us more about the subsequent effects that NAS output can have than about the functioning of the NAS *per se.* Indeed, one might expect numerous NAS or NAS-VP output pathways as a means to modulate other brain processes as a function of encoded incentive salience.

Why output to the thalamic reticular nucleus? One would wish motivational information to modulate sensory processing perhaps for two specific purposes. First, as **Gray** notes (para. 5), NAS-VP projections to the thalamic reticular nucleus may allow a motivational influence to activate generally the "entire set of ascending thalamocortical sensory relay pathways." Second, the reticular nucleus of the thalamus is composed of gatelets, each of whose open-closed status is modulated by a number of inputs (Stuss & Benson 1990). When a gatelet is opened, it will pass information to other thalamic structures that process the information and relay it to the cortex. It is thought that only those gatelets are opened that carry information relevant to the current environmental conditions. For instance, imagine a tiger in a cage who is always fed through a door in a specific spatial location. As feeding time approaches, the tiger's brain directs attention to the relevant parts of extrapersonal space, which are determined, for instance, by their position in the visual field at any particular moment and their motivational significance. This means that the tiger's brain, in order to attend to what is relevant, needs to emphasize those visual parts of space that are currently relevant and guide the motor system accordingly. In this case, we wish to open the reticular gatelets that pass biasing information to the medial pulvinar of the thalamus, because the latter provides visual information that is weighted for salience to cortical regions concerned with mapping extrapersonal space (e.g., visual sensory receptive area, inferior parietal area, and dorsolateral prefrontal cortex) (Andersen 1987). Thus, the point is that, if the NAS and its DA facilitation is involved in developing the selection of goals through incentive encoding of contextual stimuli (as discussed above), motivational output from the NAS to reticular gatelets or to the MOC (which has strong input to the gatelets), would help to bias subsequent sensory processing to relevant modalities. The existence of such output, however, does not invalidate our incentive motivation function for the NASshell.

In having settled on a perceptual function for NAS DA processes, **Gray** (last para.) suggests that our model underlies "not extraversion, but psychoticism." He then presents the logic behind this conclusion, which we have great difficulty following. First, to assume that the trait of EPQ Psychoticism (an unfortunate term selected by Eysenck years ago) measures some construct or phenotype related to schizophrenia requires evidence that we are not aware of and which Gray does not cite, and represents a position others have thoroughly refuted (Watson & McNulty 1994). Psychoticism is, as thoroughly discussed above, a complex trait that assesses impulsivity and aggression.

Gray asserts that "Consistent with this extrapolation [that the D&C model relates to psychoticism not extraversion], both PPI and LI are reduced in normal individuals scoring high on psychometric measures of psychoticism *or* schizotypy [our emphasis]." The studies cited appear to have used the psychosis-proneness scales of Chapman (e.g., perceptual aberration). As far as we are aware, these scales are not the same, nor can they be used interchangeably with, EPQ Psychoticism for the purpose of measuring psychosis-proneness (Watson & McNulty 1994). Thus, we find no plausible relation between PPI-LI and Psychoticism from this discussion.

Next, **Gray** notes that EPQ Psychoticism and Cloninger's novelty seeking scale (which are, in this case, related) are associated with DA functioning. We discussed these findings in detail above, and we see no logical relation of this association to DA functioning in the NAS and schizophrenia, because to the best of our knowledge, psychoticism and schizophrenia are not related.

Gray concludes that the extraversion versus psychoticism ambiguity in personality (just discussed) parallels the dichotomy of function proposed for NAS DA, meaning incentive motivational and perceptual. This is resolved in the next sentence by concluding that it is impulsivity, as a blend of extraversion and psychoticism, that relates to NAS DA function. But this is not different from that which Gray has proposed for many years, and which we discuss at length above. Thus, in the end, we see no logical connection between NAS DA functioning, schizophrenia, and the complex of impulsivity, psychoticism, and extroversion traits.

R3.2. DA dynamics and extraversion. On the basis of his work cited in the target article in section 6, **Rammsayer** proposes that high extraversion may be related to less responsive D2 receptor activity. We provided an alternative explanation of the data in the target article which Rammsayer does not address. Therefore, we still favor that explanation, and leave it to further studies to resolve. Rammsayer does raise an important question as to how generalized a DA association with extraversion is across DA cell groups. Combining the results of our work and studies cited in **Rammsayer's, Tucker's,** and **Pickering's** commentaries, it appears that extraversion may be associated with DA functioning in VTA DA-NAS projections (positive affective

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response to incentive-inducing film material), VTA DA-cortical projections (working memory), hypothalamic DA projections (prolactin and growth hormone secretion), and SN DA-dorsal striatal projections. (We have found no relation to extraversion, however, of DA functioning in the anterior preoptic area [DA-induced heat loss, unpublished data]). Such generalized characteristics in DA functioning could be due to a common genetic factor: for instance, the number of DA neurons across the different DA cell groups due to genetic variation, has been found to correlate highly (Fink & Reis 1981; Oades 1985; Sved et al. 1984; 1985).

Netter & Hennig raise an important issue in noting that 65% of subjects receiving both a DA agonist and a DA antagonist responded similarly. We found data suggesting that both D2 presynaptic autoreceptors and of D2 postsynaptic receptor sensitivity to a D2 agonist was significantly correlated with extraversion (Depue et al. 1994). These represent initial, encouraging attempts to dissect, as well as possible in humans, sensitivity of different types of DA receptor systems in relation to personality. Much more precise work in this area, in which Netter & Hennig are pioneers, is now needed, particularly on the D1 family of receptors. In pursuing this work, Netter & Hennig raise another important issue that as yet remains unexplored: whereas most work in this area assesses DA reactivity indexed by hormonal secretions that are activated by hypothalamic DA cell groups, it is unknown if this reactivity is correlated with the reactive characteristics of the VTA DA neurons which influence affect. Whereas genetic influence can result in positive correlation between number of DA neurons across DA cell groups (see above), as Netter & Hennig point out, it is unknown if thresholds of responsivity vary across cell groups, thereby requiring differential DA agonist dosing depending on the indicator under study (e.g., hormonal vs. affective).

Netter & Hennig raise yet another difficulty in noting that smoking a cigarette reduced craving for nicotine more in human subjects having received a DA agonist or who were higher in novelty seeking (presumably also high in DA functioning) than in placebo and DA antagonist conditions. These findings, however, would not appear to be problematic. Nicotine increases DA neurotransmission and thereby reduces craving for some period of time, presumably by increasing the rewarding experience associated with DA transmission. Hence, the combination of a DA agonist and nicotine should result in an enhanced reduction in craving. After nicotine reduction in blood, the need to increase DA once again should increase with time, as in cocaine addiction. On the other hand, if a DA antagonist is administered well ahead of the temporal onset of craving, one might expect blockade of the development of craving. This is what Dewey et al. (1992; 1997; in press) have found for both nicotine and cocaine craving in rats and baboons. Thus, craving appears to be a complex experience that involves a time-dependent process of change in DA neurotransmission; prior blockade of DA appears to inhibit the development of craving, whereas once craving has developed, enhancing DA transmission may promote the reduction of craving via increased reward activation. Netter and Hennig's finding that enjoyment of nicotine was not affected by DA modulation is consistent with the argument made in the target article and by Robinson and Berridge (1993) that the experience of enjoyment and liking is a fundamentally different subjective phenomenon than craving and likely related to different neurobiological foundations.

Finally, **Oades** raises three points, the first two of which have been discussed above (DA's mediation vs. modulation role and exclusivity in incentive motivational processes; and the role of VTA DA projections to the amygdala in modulation of emotion). The third comment extends Oades (1985) insightful integration of the DA and behavior literature to extraversion, suggesting that the role of DA is one of switching between sources of neural information. We are not in disagreement with Oades suggestion. He is merely addressing the function of DA at a different level than was done in the target article. But switching could be applied to our discussion as well: for instance, the establishment and selection of stimulus contexts in the NAS, which we suggest above is modulated by DA's role in heterosynaptic plasticity and salience encoding, could be viewed as DA's contribution to switching from one informational input to the NAS (context ensemble A) to another (context ensemble B). The benefit of Oades conceptualization is that it helps to explain several of the *non*affective manifestations of extraverted behavior, including deployment and rapidity of attentional focus, sensory discrimination, and perhaps cognitive switching (highly activated extroverts can switch rapidly between ideas). We have even suggested that such a switching process may account for the highly labile behavior and mood in mania and in histrionic personality disorder (Depue 1996; Depue & Iacono 1989).

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Letters "a" and "r" appearing before authors' initials refer to target article and response, respectively.

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