an exogenous virus as an aetiological agent, but there is no substantive evidence for any other environmental precipitant (e.g., Crow 1995a; 2000a). Only when this is apparent is one forced to consider an evolutionary explanation. But Burns does not exclude an environmental influence. In his abstract he refers to schizophrenia as "multifactorial but highly genetic" and writes "sequential hypermorphosis . . . rendered the hominid brain vulnerable to genetic and environmental insults." He nowhere tells us what these "multifactors," other than genetic, or "environmental insults," are, and he thereby fails to constrain his thinking about the nature of the brain changes and their genetic basis.

I missed reference to Huxley et al. (1964), who drew attention to the paradox that schizophrenia is apparently genetic but associated with a fecundity disadvantage. The first two authors, Huxley and Mayr, are distinguished "architects of the modern evolutionary synthesis." But the answer they gave – that the disadvantage of schizophrenia is balanced by an advantage to the affected individual of resistance to wound shock or stress – is obviously in error, as Kuttner et al. (1967) were quick to point out. It makes more sense to suppose that the advantage of the gene, whether to close relatives or to the population as a whole, relates to a human psychological characteristic. Kuttner et al. listed three – intelligence, the capacity for complex social interactions, and language – and opted for the second, as does Burns in his use of the theory of mind concept.

I have discussed the concepts of "Machiavellian intelligence" and the "social brain" as precursors in primate evolution relevant to psychosis (Crow 1991; 1993b) but particularly since 1995 I have believed that Kuttner et al.'s third option – that the balancing advantage is language – generates a more precise and heuristic evolutionary theory (Crow 1993a; 1995d; 1996a). From this perspective I see Burns' theory as deficient in three areas:

1. It provides no explanation of the cortical changes. According to the language/asymmetry concept these are anomalies of development of the sapiens-specific "torque" from right frontal to left occipital (Crow 1990a; 1997b; 2004d; Crow et al. 1989; Esiri & Crow 2002). Burns writes of "dysconnectivity"; but dysconnectivity of what, and why? His Table 1 lists 19 putative neuropathological features of schizophrenia. I suspect that many are not robust (for a review of post-mortem findings see Esiri & Crow 2002). Which does Burns regard as primary?

2. It provides no explanation of the nuclear symptoms. According to the language/asymmetry hypothesis, thoughts spoken aloud and running commentary voices are activated neural engrams misidentified as the phonemes of perceived speech (i.e., relating to Wernicke's area and its nondominant homologue), while thought insertion, withdrawal, and broadcast are anomalies of the transition from thought to speech production (relating to neural transmission from right to left frontal, including Broca's area [Crow 1997a; 1998b; 2004c]).

3. It generates no genetic predictions. In section 9.2, Burns lists ten genes that either "cannot be excluded" or "might be implicated" (para. 2), but nowhere discusses how abnormal structure or function of any one of these genes follows from his theory, or how any such prediction (were it to be made) is to be tested.

By contrast, the language/asymmetry theory is based on the premise that the torque is the characteristic that defines the human brain (the Broca-Annett axiom – for a critique of the evidence for directional asymmetry in other primates which Burns relies on, see Crow 1998c; 2003; 2004a; 2004b) and predicts that the genetic variation relating to psychosis accounts for the variations in cortical structure. From evidence relating to sex chromosome aneuploidies, I predicted (Crow 1994) a gene for asymmetry in a region of homology between the X and Y chromosomes, and an association within families between sex and handedness (Corballis et al. 1996). The Xq21.3/Yp region of homology created by a duplicative transposition at 3mya (a candidate for the Australopithecus-*Homo* transition) from the long arm of the X to the short arm of the Y generated genetic change relevant to human characteristics, and this region has been subject to subsequent change eg an undated paracentric inversion. Within the region a gene pair (Protocadherin X and Y – PCDHX and PCDHY) is expressed in both forms in the human brain, including (at least for PCDHX) the germinal cell layer of the cerebral cortex (Priddle et al. 2002). The gene pair codes for cell surface adhesion (transmembrane) molecules that may act as axonal guidance signals. In comparisons with the sequence of the X linked gene (Pcdhx) in the great apes, the ectodomain of PCDHX and the cytodomain of PCDHY have been shown to be under positive selection – that is, selection for change – in hominid evolution (Crow & Williams 2004). These genes are in a new situation with respect to protection from X inactivation, and thus, gene expression (Crow 2002a). The PCDHX/Y gene pair is a candidate mechanism for the evolution of cerebral dominance and the origins of language, itself a problem for the classical gradualist account of speciation (Crow 2002b; Maynard-Smith & Szathmary 1995). My argument, therefore, is that the language/asymmetry theory of the origins of psychosis raises questions for evolutionary theory and generates predictions testable in brain structure and function, and their relationship to chromosomal and genetic changes that are known to have taken place in the hominid lineage. Unless it is more precisely formulated, the theory that schizophrenia is a disorder of the social brain leads to no such predictions.

Threat, safeness, and schizophrenia: Hidden issues in an evolutionary story

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Abstract: There is evidence that people with schizophrenia have difficulties in some (recently evolved) competencies for processing social information. However, a case can be made that vulnerabilities can also lie in (previously evolved) threat and safeness processing systems. Evolutionary models may need to consider interactions between genetic sensitivities, early experiences of threat/safeness, and later cognitive vulnerabilities. Psychological treatments must address issues of experienced threat and safeness before working on more cognitive competencies.

Burns has provided a breathtaking overview of a vast literature. He attempts to identify the evolved origins and phenotypes for dispositions to schizophrenia, and their linkage to specific functional brain circuits and psychological symptoms. There are, of course, concerns with the concept itself, being highly heterogeneous in presentation, course, and treatment response (Bental 2003). Linking genes to phenotypic outcomes is also difficult and many researchers hold to some model of stress-vulnerability or protection interaction. For example, monkeys with the short version of the 5-HT transport gene are highly reactive to early stresses and vulnerable to anxiety, depression, and aggression. However, Suomi (1997; 1999) has shown that if "at risk" infants are cross-fostered to highly responsive mothers, their developmental outcomes can be significantly altered; these monkeys can do exceptionally well in their groups. Early developed phenotypes can influence a variety of processes, such as sensitivity to specific stressors, creating social stressors, (e.g., relational breakup due to poor bonding skills), symptom formation, coping responses, and treatment response. Burns navigates around these difficulties and focuses on evolved, genetically mediated processes (such as changes in neuronal interconnectivity, the emergence of the frontal cortex, and the organisation/interaction of cortical and limbic systems) that have given rise to our complex abilities for "self and other" cognitions.

While Burns does a good job in illuminating how these (top-down) social-cognitive competencies may be involved in schizophrenia, it may also be useful to consider bottom-up processes that can have multiple effects on the subsequent development of

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cognitive-affective competencies. There is now good evidence that humans process information through at least two pathways; one is the route that Burns focuses on. It is relatively slow and cortically focused, and it involves symbolic processing. The other route is far older. It operates through thalamic and amygdala tracts (LeDoux 1998), is preconscious and is the basis for automatic processing (Bargh & Chartland 1999) and emotional reasoning (Haidt 2001). This limbic-based system is key to rapid judgments of threat versus safeness, and can then recruit cognitive processes "to fit" and explain an emotion (Gilbert 1989; 1992; Haidt 2001). One cannot rule out the possibility therefore that (gene-linked) problems in these systems (e.g., people are shifted to threat- rather than safeness-processing in early life and have difficulties in feeling safe when with others) have effects on subsequent maturation of frontal cortical processing systems. There is increasing evidence that early experience does influence cortical maturation and the regulating pathways between cortex and limbic system (Saplosky 2000; Schore 2001), with genes also influencing the specific, emergent choreographies of experience with neuronal networking. Early vulnerability may emerge from a lack of felt safeness, marked by low positive affect, poor sooth-ability, and social disengagement; and later, low social confidence and fear of others. Threat processing systems (rather than safeness creation and affiliation) seem to dominate signal interpretation and role formation (Gilbert 1993). This is supported in Burns' review on the link between amygdala processing and frontal cortex regulation. Phenotypic variations in threat sensitivity (related partly to sensitivities in the amydala), may exist within the general population, but such sensitivities may become more extreme because of the further impact of traum, threat, and lack of safeness. Our abilities to learn about others, mature a theory of mind, and be able to explore our own minds, may depend on at least some modicum of safeness, that allows (affiliative) interactions for learning.

There is increasing evidence that a sizable subgroup of people suffering from this disorder have been traumatised in various ways and suffer from posttraumatic stress disorder (Neria et al. 2002; Resnick et al. 2003). While major traumas, including various forms of abuse, may interact with genetic vulnerabilities, there are a host of other ways that children can grow up in a climate of high threat and low safeness. Birchwood and Chadwick (1997) have shown that voice-hearers usually experience their voices as omnipotent, powerful, and dominating. Moreover, the more subordinate a person feels to others in general in their every day lives, the more subordinate does the person feel to their voice(s) (Birchwood et al. 2000), and of course malevolent voices are also repetitive threat signals (Gilbert et al. 2001).

People may generate hostile voices using similar processing systems for simulating and predicting the social behaviour of others, and for simulating, thinking about, and understanding self-generated thoughts and intentions (Gilbert 2000). Thus, for example, when people feel ashamed, they are self-critical and engage in the same type of self-talk (e.g., I am useless, ugly, a pervert) as would another person who sought to shame them might (e.g., you are useless, ugly, a pervert). They may cue emotional memories of others who have shamed them and where they have internalised these judgements of the self (e.g., "they think I am useless therefore I am useless"; Gilbert 2003).

Many forms of cognitive therapy focus on threat-filled cognitions related to evaluations of other people's intentions, or the source, power, and origins of internal voices (Byrne et al. 2003; Morrison 2002). Helping people with feelings of shame or stigma for this disorder itself, fear of the disorder, and grief, can be major interventions. Any coherent model of psychosis and psychotic phenomena must therefore direct attention not only to various social cognitive processing difficulties but also to the origins and organisation of threat and safeness processing located in old brain systems. Trying to build relationships in which a person can feel safe may be one of the most salient of interventions for people with this distressing disorder.

Schizophrenia: A benign trait

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Abstract: While schizophrenia may be genetically determined up to a point, neither it nor its nearest relatives offer any sort of reproductive advantage to its sufferers. Instead, from an evolutionary point of view, schizophrenia is benign – it neither promotes nor inhibits survival to reproduction. Because it is benign, its rate of occurrence should remain fairly constant over time.

Let us assume that everything Burns said about the evolution of the human brain being one of progressive demodularization is correct. Further, let us assume that demodularization coupled with increased neural complexity and connectivity produces an organ more vulnerable to insult, injury, and disease. Finally, let us assume that developmental diseases can have a cascading effect across the human brain, so that one rather minor glitch has the potential to wreak devastation across many regions. All of these are points that Burns skillfully and persuasively argues for in the text. The question I want to examine is whether these claims are enough to support the conclusion that schizophrenia is a heritable trait that has been maintained at a relatively constant level in our population for centuries because it is linked to other genes that offer a selective advantage. I believe that they are not.

I am willing to concede that schizophrenia has a genetic component, though environment certainly plays a large role in its etiology. How are we to explain the fact that approximately 1% of the human population, across cultures and time, is schizophrenic? If schizophrenia were just an overwhelming and ruinous mental disorder, than surely it would have been weeded out over evolutionary history, for many schizophrenics are incapable of caring for themselves, much less reproducing successfully. The conclusion that Burns draws is that there must be something about schizophrenia – or something about what schizophrenia is tied to – that confers an evolutionary advantage.

Burns argues that (1) our social brain is advantageous; (2) genes for schizophrenia predate our evolution into hominids (though they likely weren't expressed as such before our cortex developed such complexity); and (3) genes for schizophrenia are closely tied to the neuroregulatory genes that facilitate our brain development. Therefore, he concludes, genes for schizophrenia piggyback on the neuroregulatory genes such that if both are present, then both are inherited.

Let me suggest that there is a problem with this argument, even if we agree to all of Burns' premises. Consider two obvious facts. First, not everyone has genes for schizophrenia – or even some sort of schizotypal trait. Second, according to Burns, those with schizophrenia are less likely to reproduce than those without. If these premises are true, and Burns seems to believe that they are, then, over time, the carriers of the schizophrenia genes would reproduce less than those who don't carry the gene. Hence, over time, the incidence of schizophrenia should decrease and ultimately disappear altogether.

The only way that rates of schizophrenia could remain constant is if schizophrenia or one of its neighboring traits offered some sort of evolutionary advantage that offsets the reproductive disadvantage of full-blown schizophrenia. In this case, schizophrenia would be something like sickle-cell anemia: carriers of the partial disease would be fitter than normals, which could compensate for the decreased fitness of those with the disease proper.

But, as Burns points out, we have no way of making that argument, for there doesn't seem to be any reproductive advantage given to schizoptypal individuals.

So, then, how are we to explain schizophrenia's constancy across time and cultures? If it does not convey a reproductive advantage, then why didn't natural selection weed it out long ago? Let me suggest an alternative analogy in explanation. Schizophrenia is not

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