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**Annotation**

# A Model of Brain Function: Its Implications for Psychiatric Research

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Much current research in psychiatry proceeds in the absence of an integrated model of brain function. It is based instead on the effort to relate clinical syndromes to single, localised abnormalities in the brain. Such an approach is inconsistent with existing data, inadequate for linking research findings with clinical practice, and, probably, fundamentally misdirected. A model of brain function is presented that is based on Luria's notion of cerebral functional systems and on the proposition that the neural substrates of emotion are those processes that integrate different brain regions. Some of the implications of this model for research are discussed.

Three fundamental assumptions form the basis of much current research in psychiatry. Firstly, that the behavioural abnormalities of psychotic illnesses are associated with, and in some cases caused by, brain dysfunctions, as yet unspecified in nature. Secondly, that psychotic patients comprise a group with a variety of different brain dysfunctions. Thirdly, that even patients with similar clinical symptoms may have different illnesses and pathological processes. These assumptions are supported by the efficacy of somatic therapies, by genetic studies showing inheritable risk factors, and by the growing body of literature providing evidence of alterations in brain function and anatomy in psychosis. The situation has been compared to that faced by physicians treating dropsy or pneumonia a century ago, before it was possible to differentiate among the multiple causal and pathophysical processes that led to apparently similar clinical syndromes. Psychiatry can be seen as engaged in a struggle to follow the other branches of medicine and replace a nosology based on the apparent similarity of symptoms with one based on understanding disease processes and their effects on normal physiology (Foucault, 1973).

Despite this effort and these assumptions, however, most current research proceeds in the absence of any integrated model of brain function. Instead, most researchers search for single localised abnormalities, anatomical or neurochemical, to equate with different clinical syndromes. Such an approach fits well with concepts of disease which result from a specific external agent or genetic defect. It is, however, inconsistent with existing data; inadequate for linking research findings with clinical practice; and, probably, fundamentally misdirected. These three shortcomings of an approach focused on identification of a single pathological locus will be discussed more fully below. The remainder of the paper will offer a preliminary sketch of an integrated model of brain function, and discuss some of the implications of this model for experimental studies.

## Shortcomings of single pathogenic site models of psychosis

A single-focus anatomical model is inconsistent with existing data on regional brain function in psychosis, initial studies of which were based on the assumption that single localised dysfunctions characterised distinct clinical syndromes. The most common hypotheses tested and conclusions drawn linked schizophrenia with an overactive and dysfunctional left hemisphere, and depression with an overactive right hemisphere. Indeed, there is much data from studies, both of perceptual asymmetry and of surface electrical activity, suggesting the presence of such pathological processes (reviewed by Flor-Henry, 1979; Wexler, 1980; Newlin *et al*, 1981; Riederer, 1981; Merrin, 1982; Gruzelier, 1983). However, it is equally clear from more recent data that brain dysfunctions in both schizophrenia and depression are multiple and distributed. Studies of regional blood flow (Franzen & Ingvar, 1975) and regional metabolic activity (Buchsbaum *et al*, 1982) both indicate bifrontal alterations in schizophrenia. Computerised axial tomograms indicate, in at least some patients, bilateral dilatation of the ventricles (Luchins *et al*, 1982). One postmortem study of schizophrenic brains found abnormally large corpora callosa (Rosenthal & Bigelow, 1972), while several perceptual asymmetry studies suggest impaired inter-hemisphere information transfer (Green, 1978; Carr, 1980; Dimond & Scammel, 1980). Replicated studies of depressed patients, using techniques with demonstrated reliability,



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have reported statistically highly significant data consistent with alterations of left hemisphere (d'Elia & Perris, 1973; Perris, 1975), right hemisphere (Yozawitz *et al*, 1979; Bruder *et al*, 1981) and inter-hemisphere function (Wexler & Heninger, 1979; Johnson & Crockett, 1982). In retrospect, considering the multiple alterations in behaviour, in gastro-intestinal and immune system functions, and in the corticosteroid and thyroid systems, it should be little surprise that both hemispheres would be affected—if not early in the evolution of a psychotic state then certainly in the countless cycles and cascades of secondary and tertiary effects and compensatory and homeostatic efforts. What is impressive is that this conclusion should have been so long in coming.

A single pathogenic site model is incomplete because it lacks physiological elaboration. Without recourse to physiological processes it is impossible to predict, understand, or order the multiple manifestations of disease. This makes it very difficult to distinguish primary disturbances, should they exist, from secondary and tertiary disturbances. Such distinctions enhance our understanding, and are also of use in research. Moreover, experience in other branches of medicine indicates that important treatments can be based on models of the relationship of symptoms to disturbances in physiological processes, without identification of a primary anatomical cause.

A single-focus anatomical model may be misdirected because it localises pathogenesis on the anatomical level of organisation, rather than the physiological, psychological, or social levels. Pathological processes at higher levels of organisation may be associated with absent or variable changes in individual anatomical components. Classifications based on anatomical alterations would therefore be very difficult and, at least at times, misleading. Moreover, in psychiatry, assumption of a single-focus anatomical model is tantamount to assumption of a strict localisationist position on the mind-body problem: it implies that even if normal behaviour cannot be linked by such a tight phrenology to the brain, abnormal behaviour can be. Even if there is no specific site for happiness, there is one for depression. By relying heavily on a concept of disease, it may be possible to maintain that the relationship between the brain and abnormal behaviour is qualitatively different from that between the brain and normal behaviour. While a possible way to proceed, however, this is not the only, nor necessarily the best, one. For example, to do so makes the extant literature on the relationship between the brain and normal behaviour of limited use in psychiatry. Moreover, it flies in the face of the facts that no known anatomical lesions capable of causing major affective disorders or schizophrenia have been discovered, and that the rewards of this approach in neurochemical studies have not materialised as rapidly as predicted.

Taken together, then, these considerations indicate the potential value of alternative models of psychiatric disease: one such is offered here.

## Key concepts in the proposed model

There are two key assumptions or definitions in the proposed model. The first is that physiological processes organise local brain regions and relate them to each other; from a systems perspective, physiological processes emerge from the organisation and relationships among the regions. These processes are intermediary constructs between anatomy and cellular physiology on one hand, and subjective experience and behaviour on the other. The second key assumption is that emotional experiences and disturbances are closely linked with these physiological processes. Hence, physiological processes are critical in understanding the generation of the mind from the brain. These basic components of the model will now be explained in the context of ideas on the relationship of the brain to normal cognition and behaviour, to emotion, and to psychopathological states.

## Brain aspects of cognition and action

After prolonged study of brain-injured patients, A. R. Luria decided that the neural substrate of a particular behaviour or function is to be found in a series of brain regions, in the relationships among these regions, and in the processes that link them, rather than in a specific anatomical location. The brain processes and regions that together are associated with a particular cognitive process or behaviour constitute a cerebral functional system. Such a system is defined by "the presence of a constant (invariant) task, performed by variable mechanisms, bringing the process to a constant (invariant) result (Luria, 1973)."

The same function may be subserved by different combinations of neural components at different times; breathing is an example, where the invariant task is exchange of gases in the lungs, but the particular muscles used may vary considerably as a function of body position, respiratory illness, painful rib injuries, or pregnancy. Thus, the particular behaviour of breathing cannot be localised in a single centre, but is represented by an integrated array of

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regions and local processes, that itself has variable components over time. Similar systems subserve other behavioural and cognitive acts. Many of these functional systems develop during infancy and childhood. Luria thought this development was influenced by interpersonal contact, and through this contact by social and historical forces. The brain systems of attention, to take an example particularly relevant to psychiatry, develop in response to interactions with primary care-givers.

This is not to say that particular cells, cell clusters, or brain regions do not have specifiable and specialised functional characteristics. They do. Specialised characteristics of local cell groups appear to develop both phylogenetically and ontogenetically. Moreover, such specialisation is probably essential for the human behavioural repertoire. These loci, however, are not the sites of specific behaviours, which are represented by an integrated ensemble of such regions, as words are represented by composites of letters. Such a system is much more powerful and versatile than one in which specific behaviours are located in specific specialised regions, just as a phonetic alphabet in which a relatively small number of letters can be arranged in a large number of different words is more powerful and versatile than a pictographic language with the same number of characters, each representing a specific word.

The notion of cerebral functional systems relates cognition and behaviour to the integrated action of a fluid system of brain regions and processes. Furthermore, it allows a role for interpersonal and social processes in brain development. It does not, however, define the processes of integration and organisation within the system, or the process of interaction and regulation among different systems. It does suggest that the second of these will be complicated by the fact that specific regions may be part of multiple systems.

Little is known about the neural processes integrating functional systems. Cybernetic models involving feedback and feedforward mechanisms have been offered, but they say little more about physiology than to suggest combinations of inhibitory and excitatory processes. Something more is known about the interaction of functional systems, thanks to the work of Kinsbourne *et al* in mapping 'cerebral functional space' (Kinsbourne & Hicks, 1978); this has developed a functional distance principle, that activation of functional systems which share many components will affect one another, while activation of independent systems will not. Activation of overlapping systems may facilitate or interfere with one another, depending on the nature and degree of overlap. It is possible experimentally to map many functions according to this principle: in one particularly elegant experiment, Kinsbourne & Cook (1971) showed that while dextrals could ordinarily balance dowels longer on their right index fingers than on the left, when requested to speak while balancing, the left was better than the right. Work in this area thus far suggests that interference or competition be added to activation and inhibition in the catalogue of physiological processes.

## Emotion

I propose that the processes which integrate different brain regions are the neural substrate or brain correlates of emotion. In this model, the neural substrates of emotions differ from the functional systems associated with specific motor or cognitive activities: they are integrated and integrating states of multiple brain regions, including potentially the entire brain. They also differ in that rather than carry out a specific and invariant task, they define or limit the functional states of the brain regions of which they are composed, and that themselves compose the functional systems of cognition and action. The neural systems of emotion are not specific and distinct from those of cognition and behaviour, but are composed of the units of these systems, and link these units in emotional states that influence the functional systems of which these units are also part. In this, emotion is both fundamental (foundational) and superordinate to cognition and behaviour. Functional systems operate only and always in an emotional milieu. An analogy can be made to the team spirit and team work that are present in varying degree on sports teams; these are not the property of any particular individual, but rather refer to and arise from the interactions among individual members. They can facilitate or impair the performance of individual members and can be more decisive in outcome of sports contests than the relative quality of the individual players on the respective teams.

The emotional states experienced as surprise and fear can be taken as examples. With both emotions, according to the proposed model, certain functional systems are facilitated and others disrupted or inhibited. One might postulate that in surprise, neural processes in general are actively disorganised in such a way that makes possible a subsequent and potentially different reorganisation, so that autoplastic processes would be facilitated. In a state of fear, in contrast, integrative processes may be conservative, with particular facilitation of alloplastic systems. In the extreme, the conservative and

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alloplastic processes would correspond to flight or fight. Examination of these two emotions suggests that disorganisation and conservation be added to activation, inhibition, and competition in the catalogue of potential integrative processes. Analyses of the experience of other emotions may provide clues to the nature of other integrative processes, but such clues, of course, need to be evaluated experimentally.

Emotional states in this model may differ in power or intensity as a function of both the number of brain regions involved and the degree of their integration; they may differ in quality as a function of the nature of the integrating processes, the specific brain components linked by these processes, and the state of the individual components. The number of integrating processes and the common interregional linkages (neural axes), are both limited. These limitations define the set of primary emotional states. In the state of surprise, for example, some right-hemisphere systems may be particularly active, while in some states of fear, left-hemisphere systems may be the major components. As more systems are integrated and the intensity of an emotion increases, the effect on particular systems may change—e.g. the well-documented biphasic effect of anxiety (or fear) on performance. Further variation in these and other emotional states can be produced according to the proposed model, by differences in the functional development or state of individual components. If certain cognitive systems are active, for example, behaviour and experience associated with the emotional state may be more highly focused and differentiated. If certain cognitive systems are highly developed and chronically active, as in an intellectualising individual, many emotional states will reflect this activity. These speculations, as with those earlier, await experimental investigation.

## Psychopathological states

The model being developed here predicts that most psychopathological states are associated with multiple alterations in brain function. If we start with a specific anatomically defined locus, perhaps from an external disease agent, the model suggests mechanisms of pathophysiological elaboration. Firstly, since there are such rich interconnections between every brain region and at least some others, dysfunction of an area would effect the function of others, with these in turn effecting still others. Secondly, in addition to such secondary and tertiary effects, compensatory changes in other regions that are part of the same functional systems as the effected area would alter these regions, as well as other functional systems of which they are part. Such changes should be consistent with the functional distance principle. Thirdly, specific defects present during periods of neuropsychological development would alter developmental processes and sequences, and thereby affect multiple regions and systems. Fourthly, dysfunction of a specific area would affect the nature and intensity of the emotional systems of which it is part, which in turn would affect many other functional systems.

Perhaps of more importance, the proposed model allows for social pathogenesis of brain dysfunction: here, the neural correlates of emotion are the processes and states of integration of multiple differentiated brain regions. Luria has suggested that development of the functional systems of cognition and behaviour during infancy and childhood is influenced by interpersonal contact. If it is true that the neural systems of emotion, as defined here, are similarly influenced by interpersonal processes and socially mediated learning, then the potential influence of such processes on emotion and aspects of brain function secondary to it are both readily imagineable and available for experimental investigation. The great attention paid by one individual to another's emotional state, the effects of one person's behaviour on another's emotion, and the fact that one person's emotional state often leads to a similar or complimentary emotional state in another, make it likely that the development of neural systems of emotions is influenced by social processes. The model thus makes it possible to think of major psychiatric disorders as emotional disturbances and functional disorders, and at the same time to relate them to the brain and neural processes.

Clinical observation and reports of subjective disturbances indicate that there are disturbances in both cognition and emotion in all major psychiatric disorders, but the nature of each and the relationship between the two are variable. In individuals with primary affective disorders, the characteristic abnormalities are global and widely distributed, with dysfunction of specific systems present, but variable and less prominent. In schizophrenics, cognitive dysfunctions are at times more prominent and perhaps characteristic, but the emotional disturbances are significant, and often equally characteristic and essential. The general lack of emotion often noted in schizophrenia may both reflect and contribute to the lack of integration of cortical, psychological, and social functions. Furthermore, disturbances in neural systems of emotion may differentiate sub-types of this disorder: lack of emotion is particularly true of the chronic undifferentiated sub-type whereas in the hebephrenic, a

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constant state of wonder, novelty, and surprise is associated with pronounced cognitive disorganisation. Anger and fear in the paranoid are associated with rigid internal organisation and an extreme alloplastic orientation. Further study of the relationships between affect and cognition in psychopathological states may provide information about the physiological relationship between the two as well.

## Experimental tasks and methods

The experimental task at hand is investigation of the integrative processes of the brain—those that define the relationships among different brain regions, those that regulate and maintain individual functional systems, and those that define the interactions between and among different functional systems. In the model outlined here, the first group of these processes—between and among individual differentiated brain regions—falls under the general heading of neural systems of emotion. These processes may include the integrated activation or inhibition of multiple regions or functional systems, patterned competition among regions or systems, or the integrated disorganisation or conservation of the states of multiple regions or systems. To investigate them is to study the relationship between structure and function, or in short, to study the physiology of the brain as an organ.

Two experimental approaches have been developed, although neither has yet been much used in studies of clinical populations. The first, developed by Kinsbourne *et al*, uses the nature and degree of interaction between concurrent tasks (thus far only two at once) to begin mapping cerebral functional space. My collaborators and I have further developed a specific part of this approach in studies of the effects of concurrent tasks on perceptual asymmetry, which appears to be more easily altered than overall performance, and in this sense is more sensitive (Wexler & Halwes, 1985). The effect of a single concurrent task on a series of perceptual asymmetry tests, differing only in specific aspects of the test stimuli, can be recorded to map the functional significance of the alterations in the test stimuli. In a more recent (Wexler *et al*, in press) study, we studied the effects of emotional state on perceptual asymmetry, which served as an index of function of a series of specifiable brain regions and pathways. In general, this approach uses task interaction to assess dynamic aspects of brain function. It can be used to compare groups of patients with different constellations or severity of symptoms, or patients to themselves as they recover from acute illnesses.

The second approach is to administer multiple tests of brain function in close proximity to one another, but not concurrently; many tests can be used in this paradigm and they need not be all of the same type. The goal is to define a pattern of function (or dysfunction) with which to characterise a brain state and the integrating processes. Patterns in different groups can be compared, changes in patterns with sick/well repeated measures studied, and correlations between particular patterns and intensity of symptoms evaluated. The conceptual and statistical analysis of such patterns is difficult, but seems to be necessary, given the object of study. Simpler approaches leave investigators in the position of the proverbial blind man attempting to describe an elephant.

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