Parallel Distributed Processing and the Emergence of Schizophrenic Symptoms

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Abstract

Computer simulations of parallel distributed processing (PDP) neural networks have increased our understanding of brain functioning. This article reviews how PDP concepts can contribute to our understanding of schizophrenic symptoms. Psychotic states induced by phencyclidine and the adult form of metachromatic leukodystrophy, as well as neurometabolic studies, suggest that schizophrenia reflects a breakdown in communication between cortical areas. A computer simulation of this type of brain pathology has suggested two neurocognitive consequences: some cortical circuits will become functionally autonomous, and a subset of these circuits will yield "parasitic foci" that slavishly reproduce the same cognitive output. Delusions of control, paranoid delusions of the idee fixe type, thought broadcasting, "voices," and certain deficit symptoms are postulated outcomes of parasitic foci located at different levels of language processing. A neurodevelopmental model of impaired corticocortical communication is described, and this model's implications for further study are outlined.

Schizophrenia can alter a wide range of cognitive abilities, ranging from attention (Nuechterlein and Dawson 1984; Cornblatt et al. 1989) to memory (Gruzelier et al. 1988; Braff et al. 1991; McKenna et al. 1991) to language processing (Hoffman et al. 1986). Schizophrenia has been associated with functional and anatomic disturbances in many different brain regions: frontal (Buchsbaum et al. 1984, 1990; Weinberger et al. 1986, 1988; Pettegrew et al. 1991), hippocampal (Bogerts et al. 1990; Kerwin et al. 1988; Harrison et al. 1991), cingulate (Benes et al. 1987), subcortical (Volkow et al. 1986; Jernigan et al. 1991), and superior temporal areas (Barta et al. 1990). If there is any conclusion to be drawn, it is that there may be no single cognitive ability or brain area that somehow holds the key to understanding schizophrenia. What then is the alternative?

One possibility is that schizophrenia originates from pathological interactions of brain areas and cognitive potentials. The set of concepts that will be the focus of this article—collectively referred to as parallel distributed processing (PDP)—highlights the importance of this interactive perspective in understanding brain functioning. The necessity of this perspective stems from the fact that the human mind's extraordinary capabilities spring from vast arrays of neurons which individually are relatively dumb. PDP concepts provide tools for understanding how neurons form microcircuits and how microcircuits form complex networks. This information, in turn, suggests how microprocessing of neurally coded information can yield cognition. Information-processing capabilities are achieved by neuronal interactions that surpass the capabilities of their modular components. The whole must exceed greatly the sum of its parts.

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PDP Concepts and Brain Functioning

Suggestive Empirical Findings. Regional cerebral blood flow studies of mental exercises and language processing in normal individuals have established that activation of many different cortical areas is required for even simple cognitive tasks (Roland 1984; Petersen et al. 1988). More surprising is that information does not flow in a simple sequence from posterior sensory receptive areas to frontal executive and output areas. Instead, simultaneous bidirectional exchange of information is the rule.

Functional reciprocity is reflected anatomically in the fact that projections from posterior association cortex to frontal areas are inevitably accompanied by projections in the opposite direction (Goldman-Rakic 1988; Mesulam 1990). Intracranial recordings in humans provide a similar lesson: neuronal activation in the language output or Broca's area occurs simultaneously with (not after) neuronal activation in semantic association or Wernicke's area during language production tasks (Fried et al. 1981), suggesting reciprocal coupling of these cortical areas (Mesulam 1990). Reciprocal exchange of information has even been observed within posterior cortical regions: von der Heydt and coworkers (1984) demonstrated that visual illusions can induce firing of visual cortical neurons in monkeys when receptive fields are not directly stimulated (see figure 1). These observations demonstrate back-projections from visual object detection microcircuits to "primary" visual neurons. The process by which more abstract information-processing modules influence the functioning of lower order sensory input neurons is called top-down processing. In general, neural information does not flow in a single direction; there is no specific brain area that is the final arbiter during information-processing tasks (Dennett 1991). Instead, cognition emerges as the parallel output of neurons or groups of neurons in spatially distinct brain areas that act in concert (Goldman-Rakic 1988; Mesulam 1990).

Cortical Decoupling and the Induction of Positive Symptoms. What if those neurons or neuronal groups belonging to networks that usually produce higher order mentation (such as language and beliefs) communicate less effectively with each other? The following three sets of clinical observations suggest that this decrease in communication may relate to brain pathology in schizophrenia.

1. Phencyclidine (PCP) is currently the best psychotomimetic drug for inducing symptoms that approximate those of schizophrenia. PCP psychosis generally is accompanied by delusions, paranoid ideation, auditory hallucinations, and disorganized speech (Allen and Young 1978). Moreover "PCP, but not LSD, amobarbital or amphetamine, induce[s] abnormalities in tests of abstract reasoning, cognitive processing, attention, motor function and proprioception in normal volunteers that closely resemble those seen in patients with chronic schizophrenia" (Javitt and Zukin 1991, p. 13). PCP's effect derives from potent inhibition of a class of excitatory synapses that uses the amino acid glutamate as its neurotransmitter. There are at least three classes of synapses that utilize glutamate (see Ulas and Cotman 1993, this issue); PCP specifically inhibits the N-methyl-D-aspartate (NMDA) glutamate receptor (Duchen et al. 1985; Olney 1989; Javitt and Zukin 1991).

The mammalian cerebral cortex seems to be organized in columns ranging from 50 μm to about 0.5 mm in diameter (Crick and...
Asasuma 1986). Neurotransmission within columns is both excitatory and inhibitory, while projections between columns, which can occur over many centimeters, are thought to be exclusively excitatory (Braitenberg 1978; Nunez 1981; Thatcher et al. 1986). On average, roughly 95 percent of projections to a particular cortical column actually derive from other cortical areas rather than subcortical centers such as the thalamus (Thatcher et al. 1986). Corticocortical projections are probably glutamatergic and, at least in part, act on receptors of the NMDA type (Conti et al. 1988; Iriki et al. 1991). Thus PCP, through its antagonism of NMDA synapses, may achieve its psychotogenic effects by interfering with corticocortical transmission of information. However, other mechanisms of action need to be considered.

Two studies suggest reduced synaptic glutamate in schizophrenia. Sherman and coworkers (1991) conducted a postmortem study of isolated synaptosomes sampled from temporal and prefrontal areas and found reduced glutamate release in tissue preparations of schizophrenic patients compared to those of normal subjects. In addition, an in vivo 1H magnetic resonance spectroscopy (MRS) study demonstrated marked reductions of glutamate in the left prefrontal cortex of schizophrenic patients compared to normal controls (Stanley et al. 1992). Although nonsynaptic (i.e., metabolic) sources of glutamate cannot be ruled out as contributors, these MRS findings are very consistent with the Sherman and coworkers (1991) postmortem data. If schizophrenic patients have less available synaptic glutamate in the cerebral cortex, reduced corticocortical exchange of information is likely to result.

2. A review of published case reports by Hyde and coworkers (1992) argues that the neurological illness that best mimics acute schizophrenia is metachromatic leukodystrophy. This disorder is caused by the accumulation of sulfatide in white matter. According to the authors, cases with symptom onset in late adolescence and early adulthood often presented with some combination of paranoid and grandiose delusions, "hearing voices," and cognitive disorganization. Central nervous system (CNS) lesions in these patients occurred primarily in frontal white matter, with relative sparing of gray matter. In comparison, white matter disorders such as multiple sclerosis produce lesions that are more discrete and limited in size. It is likely that the bulk of myelinated fibers in frontal white matter derive from corticocortical projections (Braitenberg 1978). Thus, psychotic symptoms observed in adult metachromatic leukodystrophy may result from communication failures between different cortical modules (Hyde et al. 1992).

3. There is some empirical evidence that brain regions in schizophrenic patients are partially uncoupled. Using positron emission tomography, Clark and coworkers (1984) and Volkow and coworkers (1988) found reduced correlation of metabolic rates between multiple diverse brain regions in schizophrenic patients relative to normal controls. These findings could reflect impaired interactions between brain regions in this disorder.

**Computer Simulations of PDP Networks**

What are the functional consequences of reduced exchange of information between cortical neurons? Computer simulations of PDP information-processing systems may provide an answer to this question (McClelland and Elman 1986). These artificial systems are composed of large numbers of very simple computing units, generally referred to as neurons, which are densely interconnected via synapses. There is no single "command" unit; the network's effectiveness results from the cooperative interactions of its parts. Each neuron simultaneously receives information from many other neurons and computes its response to these inputs in parallel with the computations of the other neurons in the system.

**Attractor Networks.** Of special relevance to this discussion are artificial PDP systems that work on the basis of attractor dynamics (Hopfield 1982; Smolensky 1986; Amit 1989; Hinton and Shallice 1991) and on reciprocal connectivity. Their information-processing capabilities derive from the fact that they are attracted to particular activation patterns that are the low-energy states of the system. Here "energy" does not equate to the metabolic activation of the neural network, but derives from a branch of physics known as statistical mechanics. Statistical energy corresponds to the degree of disorder in the system. Attractor networks always seek to minimize their own statistical energy.

Energy minima "attract" the system; insofar as they reproduce themselves, they are the memories...
of the system. It follows that there is no one-to-one correspondence between a memory or energy minimum and the activation of a particular neuron. Instead, a memory corresponds to a pattern of activation involving many neurons of the network. Learning occurs when the system acquires new attractors or energy minima by adjusting the synaptic strength between neurons.

Content-Addressable Memory. In simulated PDP networks, attractor/memories are content-addressable, this is, if part of a system enters an activation pattern that matches that of an attractor, the remainder of the system will flow into an activation pattern that fleshes out the attractor as a whole. Different portions of the system coding different components of a memory can each be “seeded” with input information that will reproduce the memory in its entirety.

As content-addressable memory systems, these simulations have an intuitive appeal for actual human memory storage and access. Different small “chunks” of information—a facial profile, the sound of a voice, a name—can trigger the memory of a whole person, including myriad details (appearance, manner, recollections of past interactions such as conversations, etc.). People can identify a particular symphony or rock song from any one of a number of bars of music. Content-addressable memory is required for tasks ranging from spatial pattern recognition to complex problem-solving. In the latter, new problems are matched with old ones having known solutions. Mental flexibility is guaranteed by different pathways to the same memory. Artificial PDP systems also demonstrate this flexibility. A specific memory can be “precipitated out” by seeding these systems with any one of the different portions of the memory.

Speech Perception. Variations in these simulations can demonstrate more specialized functions such as speech perception. Speech produced under ordinary circumstances and at normal rates is acoustically ambiguous, although it is very hard to appreciate this fact. When we listen to another person speaking, the words seem clear, but acoustic analysis of speech sounds tells a very different story. An example of acoustic information contained in a typical utterance, “total budget,” is displayed in figure 2. The figure shows that there is a particularly high degree of uncertainty regarding the identification of consonants. For instance, the second “t” in “total” was not clearly articulated. This can be appreciated if you repeat the phrase in a larger sentence at a normal conversational rate, for example, “Economic pressure is reducing our total budget.” Listen carefully to how you say “total.” Generally, adult speakers do not create a second full “t” sound, but produce an ambiguous interruption between the two vowels, “o” and “a.” Yet we “hear” the second “t” as part of the word total.

Similar ambiguity can be noted for later consonants, especially the middle consonant complex in “budget,” which has acoustic features suggesting a broad range of phonemes. Further phonetic ambiguity derives from the fact that breaks between words within phrases and sentences are generally absent during the normal flow of speech: for instance, there is no break between “el,” the terminal

Figure 2. Illustration of the phonetic ambiguity of speech

Acoustic Analysis of Stream of Speech

| Time | T | OW | F.L | EL | B.V | B | AO | JH.N | V.O.B.S | D.H | I.X | P.K |
|------|---|----|-----|----|-----|---|    |      |        |     |     |     |
| 0.0 sec |
| 0.5 sec |

Phonetic Input

Perceived As

" T - O - T - A L - B - U - DG - E - T "

Note.—Acoustic decomposition of an utterance expressing “total budget” is illustrated (adapted from Woods 1982). The second “t” in “total” is poorly formed, yielding instead phonetic features reflecting three different consonants—“l,” “l,” and “p”—as well as the vowel, “a,” but nothing specifically suggesting a “t.”
phonetic segment of total, and the initial consonant complex for "budget."

Clarification of the speaker's intent occurs via top-down processing, which has been explored with PDP simulations (McClelland and Elman 1986). Hypotheses regarding alternative words are evaluated neurally on the basis of available phonetic information. A typical (though oversimplified) PDP simulation consists of the following: Neurons whose activation corresponds to particular words or concepts share reciprocal, excitatory projections with neurons whose activation corresponds to the appropriate phonemes. Reciprocal inhibitory projections are exchanged among competing words or concepts. This neuronal network is shown in figure 3.

Figure 4 illustrates the activity within such a network resulting from an acoustic stimulus halfway between the word "plug" and the nonword "blug." Initially both "b" and "p" are partially activated, as shown in the bottom left panel where the two letters are superimposed at an activation level of 0.2. At this point no word or concept neuron is activated. The next column of panels demonstrates what happens when acoustic information regarding the next two phonemes are received by the system. As in the total budget example, these acoustic features are ambiguous on their own. For instance, "r" has been activated as well as "i." A large number of alternative word or concept neurons are activated at a very low level.

The third set of panels reflects the state of the system just after all the acoustic information has been received. The neuron corresponding to the word or concept

![Figure 3. Simplified artificial neural network for perceiving words based on phonetic information](https://academic.oup.com/schizophreniabulletin/article-abstract/19/1/119/1895731/1895731)
“plug” is activated somewhat in excess of the two alternative words or concepts, “blood” and “bliss.” At a somewhat later time, “plug” becomes the clear winner. Thus, the neural network relaxes into an activation pattern that reflects the best match between alternative phonetic combinations and acceptable words.

Psycholinguistic data clearly demonstrate that the speech perception apparatus must use topdown processing: when phonemes embedded in words are completely masked by noise, phonemic illusions are perceived by listeners (Warren and Warren 1970). A more powerful PDP speech simulation might utilize additional expectations based on syntactic processing to narrow the number of lexical alternatives. For instance, suppose an intermediate stage of processing has produced the two lexical alternatives “plug” and “blood” in response to the speech stimulus (see the third set of panels, figure 4). If this segment of acoustic information was preceded by speech that had already been decoded as “he saw,” a processor with a syntactic component would tend to choose “blood” over “plug.” This is because the former, but not the latter, can be generated in the absence of an article like “a” or “the.”

Interactional Pathology in PDP Networks

Artificial PDP systems can provide insights into what would happen to biological PDP systems if information exchange between neurons or neuronal modules were reduced. A previous Schizophrenia Bulletin article describes a computer simulation of this type of pathology (Hoffman and Dobscha 1989). Briefly, the simulation used PDP attractor networks that operated as pattern-recognition devices. The networks received ambiguous input information and, as content-addressable memory systems, flowed into the memory that was the best fit. These systems were then tested when increasing numbers of neuronal connections were removed. This test was undertaken using a “pruning rules” based on the notion of “neural Darwinism,” in which neurons competed with each other for connections to other neurons. There is evidence that neural connectivity in brains is shaped by these competitive processes during neurodevelopment (Edelman 1987; Nelson et al. 1990). If a strong connection was not established in a connection that needed to traverse a long distance between a dendrite and an axon, the projection was pruned away. Another way to think about the pruning rule is that the cost of maintaining long neuronal projec-
tions was weighed against the benefits of the amount of information they carried. If the cost was too great, the connection was eliminated. It turned out that these systems could function with large reductions in neuronal connectivity. However, after a certain point the system became dysfunctional.

One consequence of excessive synaptic pruning was that the outputs associated with input information became bizarre. Inputs would cause the system to flow into fragments of unrelated memories that were amalgamated. A second consequence of excessive pruning was that subpopulations of neurons within the network became functionally autonomous with respect to the larger system. A third consequence was that some neural modules locked into a certain cognitive output independent of information received from other parts of the system (Hoffman and Dobbscha 1989). Moreover, these outputs arose de novo, that is, they did not reflect any particular memory previously stored in the system, and they relentlessly strove to reproduce themselves. The emergence of this form of network pathology was referred to as a parasitic focus.

If these functional transformations actually occurred in the brains of humans, how might they be experienced? First, the amalgamation of multiple disparate memory fragments could model the induction of actual loose associations in schizophrenia. There is some evidence that this disturbance, manifested in the speech productions of these patients, indeed reflects the blending of multiple gestalts that are represented simultaneously during the generation of speech intentions (Hoffman 1986; Hoffman et al. 1986). Along these lines, schizophrenic patients often report that their associations contain an overabundance of idiosyncratically clustered ideas that reduce their ability to remain focused (Freedman 1974).

How might autonomously functioning circuits expressing parasitic foci be experienced? To appreciate the phenomenology generated by this type of brain pathology, we need to introduce an additional concept.

Intentional Stance. One predilection of the normal human mind has been referred to as the intentional stance (Dennett 1991). We all tend to interpret events that occur around us as being intended by some willful agent. Since many of the important things that happen to us are indeed caused by other human beings, this is a useful perceptual bias. On the other hand, this bias can also alter our experience of many things. A now-classic example is playing against a chess-playing calculator (Dennett 1971). The calculator, composed of mindless printed circuits, nonetheless produces organized behavior, and the human opponent tends to regard the calculator as if it were a willful being, not a tangle of wires. A more common experience is our impulse to kick the car when it doesn’t start on successive days. We do this to vent anger but also because, momentarily, we believe that the car is intentionally not starting.

The intentional stance can yield certain forms of pathology. Consider, for example, a group of patients with lesions in the supplementary motor area (SMA) of the frontal cortex (Goldberg 1985). SMA lesions can cause repetitive, involuntary movements of the extremities, which seem to have their own purposefulness. For instance, one patient developed a “wandering hand” that repeatedly attempted to unbutton her clothing. With no evidence of a preexisting psychiatric disorder, these patients can develop the circumscribed delusion that their extremity is controlled by an alien, nonself being (Goldberg, personal communication 1987). The intentional stance represents a particular type of top-down processing: orderly events outside our control are experienced as if they are willed by another agent.

The following are models of positive symptom formation commonly observed in schizophrenia that suggest cortical parasitic foci operating in human cognitive systems. These explanations assume that parasitic foci elicit their pathological effects by altering speech perception or speech production processes by either influence or, episodically, complete control.

Thought insertion and delusions of control: A parasitic focus altering speech production. Our thoughts are often composed of internally generated word images. We talk to ourselves all the time to guide, reprimand, and encourage ourselves (Vygotsky 1978; Dennett 1991); these verbal images seem to be derived from the same speech production processes that underlie overt speech (Sokolov 1972). Suppose these speech production centers come to be dominated by a parasitic focus. If this pathology did not activate general motor initiation circuits such as the SMA, overt speech would not result, and a form of inner speech might be experienced instead. Actions (in this case mental actions) would be generated independent of cortical initiation.
centers and therefore would be experienced as unintended. This situation is analogous to that of the patient with an SMA lesion. Moreover, because these mental actions derive from a parasitic focal focus, they would be expected to be orderly or stereotyped in nature. The intentional stance predicts that the normal predilection to interpret orderly nonrandom events occurring outside a patient’s control as intended by a nonself agent would induce the patient to conclude that a particular alien nonself force is putting thoughts into his or her head. It is noteworthy that these delusions are generally attributed to agents whose presence cannot be directly confirmed or disconfirmed, such as the CIA, Satan, or God. This further suggests that the content of such delusions reflects the response of an intact rational system to data of which it must make sense: recurrent actions occurring in the absence of an observable agent.1

**Auditory/verbal hallucinations:**

A parasitic focus that episodically co-opts speech perception. If, on the other hand, a parasitic focus emerges in neural circuitry responsible for speech perception, factitious speech percepts or “voices” could result. The experience of nonself intentionality of these imagistic experiences would be enhanced if, as predicted, the parasitic focus produces words and phrases in a stereotyped fashion. Once again, the orderliness of these verbal messages would lead the afflicted person to believe that another agent is responsible for these experiences because they are not simple random events (Hoffman 1991). Moreover, a parasitic focus could, in theory, reproduce very complex outputs, coding not only for verbal content but also for sensory qualities of an acoustic image (soft vs. loud, male vs. female, etc.). The character, voice, and message expressed might not be recognizable as belonging to any individual in the person’s past, including the person himself, thereby reinforcing the alien nature of the experience.

Getting messages from the radio and ideas of reference: A parasitic focus producing top-down perceptual distortions. A parasitic focus involving speech perception, even when it does not directly produce a factitious voice percept, could influence speech perception in a top-down fashion. As indicated above, speech sounds are inherently ambiguous, especially if clarity is reduced or ambient noise is present. These conditions occur, for instance, in urban areas with multiple persons speaking or in speech electronically reproduced by television or radio. Speech heard in these circumstances is a setup for misperceptions induced by top-down perceptual processing. A parasitic focus could wreak havoc by molding ambiguous acoustic stimuli into its own verbal output. Returning to the example illustrated by figures 3 and 4, a parasitic focus might activate neurons that code for the word or concept “blood” when listening to speech with less than perfect clarity. Thus, in general, parasitic foci could cause a person to repeatedly hear the same word or phrase when listening to songs on the radio or to a television announcer with rapid speech, or when in public places where indistinct conversations can be overheard. The result in the first two cases would be experienced as getting messages from the radio (or TV). The last scenario would be experienced as hearing a similar spoken message from multiple, seemingly unrelated people producing an uncanny pattern of experience that could easily be interpreted as evidence that one is the center of some unknown plot—that the repeated word or phrase is intended for the person suffering from the parasitic focus. Why else would the same message be repeated by different individuals?

**Thought broadcasting:** A parasitic focus that influences but does not control both speech production and speech perception. Recall again that PDP language circuitry seems to involve a dynamic interplay of speech production and speech perception processes. Assume that a parasitic focus is functionally located, in essence, midway between these two systems. This pathology might then influence, but not dominate, internal language production and perception processes. The result would be periodic shaping of thoughts (i.e., inner speech), which are experienced as self-derived but whose content is somewhat stereotyped because it is influenced by the parasitic focus. At the same time, a parasitic focus of this type could influence speech perception in a top-down fashion (see previous section). The result is the episodic re-creation of thoughts (or inner speech) whose content reflects auditory misperceptions shaped by parasitically driven top-down processing. In short, this result could be the maddening experience of hearing another person produce words or phrases that one

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1The intrinsic rationality of assigning parasitically driven nonself intentions to agents who are “invisible” (such as the CIA or Satan) was first suggested to us by Jonathan Cohen.
is simultaneously thinking. If this experience recurs, it could lead the person to conclude that others can read his or her mind.

** Paranoid delusions of the idee fixe type: A parasitic focus altering narrative memory.** In theory a parasitic focus could also emerge in systems responsible for another aspect of cognition: retaining and recreating narratives. Cognitive studies have demonstrated that stories play a critical role in human intelligence (Bower and Morrow 1990; Schank 1990). In addition to enlivening our conversations, the stories we remember, those we have lived, heard, or witnessed, have critical adaptive value. They help us to predict the behavior of others and thereby provide indicators of how we should act and react. This is because stories assign intentions to their characters and, as content-addressable memories, allow us to use their plots (i.e., the interactions of the individuals in the story based on their surmised intentions) to interpret new situations. Moreover, experimental data indicate that story memories are stored self-referentially: during storage processes, we identify with one of the characters and attribute positive attributes to him or her while also attributing negative attributes to another character (Bower and Morrow 1990); these normal distortions can be detected by tests of story recall.

Suppose a parasitic focus occupies the memory system responsible for remembering and recalling stories. These belief systems might tend to retain the me versus them plot organization which seems to be a preconscious template for narrative memory in general. However, specific elements of plot could emerge de novo from the brain rather than reflect the integration of historically accurate experience. Insofar as these belief systems are parasitically organized, they would be highly resistant to disconfirming evidence and would be persistently relived; very small reminders could trigger the story in its entirety. For instance, assume that the parasitic focus expressed a narrative whose major plot element was that the person was about to be discovered to be the true king of England, but others were trying to prevent this. In summary, particular positive symptoms suggest that parasitic foci could refer, with varying degrees of specificity, to different language processes involving speech production and speech perception, as well as narrative memory. More complex positive symptom patterns could reflect a parasitic focus that bridges multiple processes. For instance, the parasitic focus that produces the “I will be king” delusional narrative might also co-opt the speech perception apparatus to yield a voice that repeats “Seek the crown.”

**Deficit Symptoms.** The above formulations all assume that the parasitic focus reproduces an output that can be registered as meaningful in consciousness. Computer simulations suggest that this may not always be the case. At times the parasitic focus yielded outputs that were very distinct from any meaningful stored memory. Pathology of this sort, in theory, can bring about many negative or deficit symptoms. One such deficit symptom is thought withdrawal. A parasitic focus yielding cognitive outputs that are not translatable as conscious experience or are extremely incoherent would result in having one’s thoughts involuntarily emptied out or experiencing thoughts that cannot be understood or communicated. Verbal hallucinations of unintelligible strings of words or phonemes are also theoretically possible. These different experiences, alone or in combination, could present as thought blocking or alogia. Furthermore, the loss of intentionality that constitutes an integral part of most positive symptoms can be negatively expressed as avolition or passivity. As such, negative or deficit symptoms may reflect not psychopathology that is ultimately distinct from positive symptoms, but rather a more severe disruption of cognitive coherence that is profoundly inexpressible and uncanny.

**Empirical Evidence for Parasitic Foci in Schizophrenia.** An ongoing study has provided support for the hypothesis that words composing the voices heard by psychotic patients can alter speech perceptual processing via top-down processing (Hoffman and Rapaport, in press). Patients with schizophrenia and manic episodes were instructed to repeat speech in which acoustic clarity was experimentally masked with superimposed multispeaker babble. Approximately half the patients re-
ported hearing voices and half reported not hearing voices as part of their symptom picture. A perceptual illusion was induced in approximately 60 percent of the patients who reported voices; certain words were misheard in ways that reflected the content of the hallucinated voices. For instance, one patient, hospitalized because she began hearing a voice threatening to kill her, misheard the word “beheaded” while listening to a masked speech segment that was otherwise incomprehensible to her. Another schizophrenic patient, whose voice said the word “masturbation” would periodically hear this same word when listening to the babble stimulus. It is important to note that these misperceptions were not experienced as hallucinations but rather as external speech deriving from the headphones. Moreover, the same external speech stimulus tended to reproduce the same voice-related misperception. These findings suggest that these misperceptions did not simply reflect the occurrence of voices during the experimental period, but actually reflected the coercive effects of a parasitic focus operating in speech perception systems via top-down processing.

**Neurodevelopmental Pathology and Corticocortical Interactions**

What might cause impaired corticocortical communication? Our model posits that this interactional pathology may have two components. The first reflects neurodevelopmental processes occurring before the onset of active illness, while the second reflects pathological effects of parasitic foci on the highly plastic circuitry of the brain.

**Cortical Pruning of Synapses and Adolescent Brain Development.**

Why is the most frequent time of onset of schizophrenia in late adolescence and young adulthood? One explanation is an abnormality in brain development (Feinberg 1982/1983; Weinberger 1987; Hoffman and Dobscha 1989). There is now considerable evidence in humans and other primates that following birth an overproduction of corticocortical connections occurs over time; these connections are then selectively pruned and shaped during later developmental periods (Hüttenlocher 1979; Rakic et al. 1986). Actual number of neurons is much less affected by this developmental process than is the number of synapses per neuron. In humans, pruning of cortical synapses for connections in frontal areas seems to extend well into adolescence (Hüttenlocher 1979). Although there is a net reduction in frontal synapses during this developmental period, it is likely that this phenomenon reflects a dynamic interaction between the growth of new connections and the elimination of others. The continued molding of corticocortical connections probably continues, albeit at a much slower rate, throughout adulthood (Buell and Coleman 1979; Petit and Markus 1987). Electron microscopic (EM) studies of monkey cortex show that postnatal elimination of synapses primarily involves the asymmetric type (Rakic et al. 1986): these synapses are probably excitatory and utilize amino acids such as glutamate as their neurotransmitter (Storm-Mathisen and Ottersen 1990).

**Cortical Pruning of Synapses and the Induction of Schizophrenia.**

Reduced corticocortical connectivity could reflect pathology involving postnatal pruning of cortical synapses. A simple model of this pruning process—and the neurocognitive pathology that could arise if this process runs amok—was the goal of the computer simulation, described above, that produced parasitic foci (Hoffman and Dobscha 1989). A reason for the characteristic age of onset in schizophrenia was provided, that is, modification of cortical circuits supporting a large number of “higher” cognitive processes occurs during adolescence (Feinberg 1982/1983). Excessive developmental pruning could yield parasitic foci.

A developmental model of schizophrenia is supported by magnetic resonance spectroscopy (MRS) studies. Pettegrew and co-workers (1991) compared drug-naive schizophrenic and age-matched normal subjects by examining neural membrane phospholipid turnover using $^{31}$P MRS (see also Pettegrew et al. 1993, this issue). The schizophrenic subjects showed reductions in phosphomonoester (PME) resonance and enhancements in phosphodiester (PDE) resonance in prefrontal areas compared with the age-matched controls. Developmental studies in animals suggest that increases in PME resonance reflect outgrowth of dendrites and axons, while increases in PDE resonances reflect elimination of these processes (Pettegrew et al. 1993, this issue). The authors therefore suggest that PDE increases in schizophrenic subjects may reflect exaggerated developmental pruning of frontal neuronal processes (synapses, axons, dendrites, and perhaps neurons themselves) occurring simultaneously with reduced outgrowth of new connections. Of
special interest was a case report of a subject in the normal group who demonstrated marked elevations in prefrontal PDE and went on to develop acute schizophrenia (Keshavan et al. 1991). This case suggests that excessive cortical pruning may precede and therefore be causally linked to acute schizophrenia.

Williamson and coworkers (1992) demonstrated reductions in prefrontal PME in chronic schizophrenic patients but elevations in PDE only in never-treated patients. These data suggest that reduced production of new dendritic-axonal connections may be typical of many schizophrenic patients during both acute and chronic phases of the illness. On the other hand, excessive pruning of dendritic-axonal connections may be specifically associated with earlier or acute phases of the disorder, or both.

In addition, Goldman-Rakic (1991) found large increases in the packing density of neurons and glial cells in the prefrontal cortex of schizophrenic patients compared to age-matched normal controls. Although the sample was relatively small, these results are statistically significant. Goldman-Rakic proposed that these neuroanatomic findings are secondary to a loss of surrounding neuropil, the dense intertwining of axons and dendrites surrounding neurons and glial cell bodies. This finding is consistent with the previously mentioned report of Sherman and coworkers (1991) that demonstrated reduced synaptic glutamate in prefrontal areas in schizophrenia. It is important to note that this study also demonstrated marked reduction in synaptic gamma-aminobutyric acid (GABA, the primary inhibitory neurotransmitter) in the schizophrenic group. Neuronal reductions and reduced synaptic pools of neurotransmitter are expected to result from excessive reductions in cortical synapses. These reductions could arise from either diminished outgrowth of axons and dendrites or excessive pruning of axonal-dendritic connections.

Cortical Pruning and Pathways to Schizophrenia. There are a variety of neurodevelopmental pathways that can yield reduced synaptic density during adolescence and young adulthood. They suggest a particular scheme of developmental subtypes of schizophrenia. While this scheme is undoubtedly an oversimplification, it may have heuristic value (see figure 5). The top graph reflects normal peaking and subsequent reductions of cortical synapses in frontal areas. The next graph represents conditions where peak elaboration of axonal-dendritic connection achieves normal levels, but excessive pruning results in functional fragmentation of cortical circuits and the expression of parasitic foci (Hoffman and Dobscha 1989). We refer to these patients as having type A schizophrenia and predict that they will have relatively good premorbid functioning and a relatively rapid illness onset. These features are reflected by the steepness of the synaptic density line as it crosses the psychotogenic threshold.

Patients with type B schizophrenia have a normal developmental curve reflecting peaks and declines in synaptic density that parallel those of the top graph. The difference is that the synaptic

![Figure 5. Cortical pruning and different pathways to a hypothesized psychotogenic threshold](https://academic.oup.com/schizophreniabulletin/article-abstract/19/1/119/1895731)
density of these patients has a lower baseline at birth. A paradigmatic model for this type of pathology is second trimester exposure to viral illness that interferes with the elaboration of neurons or axonal projections required for corticocortical connections (see Mednick et al. 1988 and discussion in Goldman-Rakic 1987). These patients will demonstrate childhood developmental difficulties, but may have a relatively acute onset of illness.

Patients with type C schizophrenia are those who have normal cortical synaptic densities at birth but fail to achieve a sufficiently high peak during postnatal development. Normal amounts of pruning result in a gradual convergence of the synaptic density curve with the psychotogenic threshold at a younger age. This convergence will be reflected in childhood developmental difficulties and an earlier, more insidious onset of illness.

Secondary Effects of Parasitic Foci

The brain is a highly plastic system, not only during immature states, but also during adulthood. The expression of parasitic foci within such plastic systems could have different long-term clinical effects, including the development of negative symptoms, increased relapse vulnerability, and functional deterioration.

Hippocampal Kindling, Volumetric Changes, and Lowered Threshold for Relapse. Most salient conscious experiences are stored as memories. If a parasitic focus repeatedly produces a consciously experienced belief or series of images, these experiences are likely to be repeatedly stored as memories.

The hippocampus is a relatively small portion of the limbic system that has diverse, reciprocal connections with multiple cortical areas. These connections play an essential role in the gestation of long-term memories (Rolls 1990); current thinking is that the hippocampus coordinates the storage of these memories in cortical systems (Mesulam 1990).

It is thus likely that the hippocampus would be repeatedly stimulated by the cortical output of a parasitic focus. This process may be akin to experimentally induced kindling. In this case, repetitive electrical stimulation of the hippocampus yields progressively larger physiological responses in experimental animals (Geinisman et al. 1988). Kindled hippocampal circuits can remain hyperresponsive for many months. Moreover, experimentally induced kindling induces a generalized loss of synaptic contacts in the hippocampus (Geinisman et al. 1988). These neuroanatomic changes probably augment the potency of remaining synaptic contacts and amplify responsiveness to selective input.

A parasitic focus that reproduces conscious experiences could also induce a kind of hippocampal kindling. In this case the hippocampus could become hyperresponsive to stimuli that resemble information coded for by the parasitic focus (see also the discussion by Haracz 1985, p. 199). The consequences of parasitically driven hippocampal kindling could be complex. First, the hippocampal cortical system's threshold for excitation of the parasitic focus could be lowered and more active or floridly symptomatic states could be triggered. These effects are consistent with clinical observations that patients are most vulnerable to relapse immediately following an acute episode (Strauss et al. 1985; McGlashan 1986). Second, kindled relapses would tend to repeat the symptoms and content of the earlier episode. Recent followup data have confirmed the relative stability of certain positive schizophrenic symptoms from one episode to another (Chaturvedi and Sinha 1990).

Finally, hippocampal kindling could lead to the regressive anatomic changes demonstrated with animal models (Geinisman et al. 1988). These changes would be consistent with a postmortem study of hippocampi schizophrenic patients demonstrating reductions in messenger ribonucleic acid (RNA) that encodes a glutamate receptor (Harrison et al. 1991) and also with multiple studies indicating reduced hippocampal volume (Bogerts et al. 1985, 1990; Jeste and Lohr 1989). Along these lines, Bremner and coworkers (1992) demonstrated that patients with post-traumatic stress disorder (PTSD) also have reduced hippocampal volume compared to controls. PTSD is another disorder characterized by repetitive reliving of certain memories or images that may result in regressive changes in hippocampal regions. This formulation could also account for impaired hippocampal functions (e.g., working memory) in schizophrenic patients (Gruzelier et al. 1988; Saykin et al. 1991). The fact that volumetric reductions have been noted most consistently on the left side in schizophrenia (Bogerts et al. 1990; Crow 1990; Rossi et al. 1990; DeLisi et al. 1991) may be consistent with the hypothesis that parasitic foci are...
frequently, if not primarily, language oriented.

Schizophrenic Deterioration. Although neural plasticity has been studied most extensively in the hippocampus (Barrionuevo and Brown 1983; Larson and Lynch 1989), there is now strong evidence that the functional connectivity of neuronal cortical systems in frontal, parietal, and temporal areas is subject to experience-dependent modifications well into adulthood (Cotman and Nieto-Sampedro 1984; Haracz 1985; Cotman et al. 1987; Petit and Markus 1987; Benowitz et al. 1989). This is not surprising because these brain areas provide long-term information storage, which is mediated by changes in synaptic connectivity between neurons (Mesulam 1990; Rolls 1990). Plasticity of anatomic connections has provided the basis for the neural Darwinism models of neural learning in which neuronal groups coding for particular memories compete with other neuronal groups for functional and anatomic dominance (Edelman 1987). Synaptic connections that are not used are eliminated (Beart and Lodge 1990).

Along with excessive developmentally induced synaptic pruning, neural Darwinism may contribute to long-term deterioration of cortical function in schizophrenic patients. This hypothesis is supported by studies demonstrating that adult mammals placed in environments where sensory stimulation is impoverished quickly show significant reductions in cortical tissue reflecting curtailing in dendritic size and number of synapses per neuron (Haracz 1985; Greenough and Bailey 1988). As described above, top-down effects of parasitic foci can pathologically constrain which sensory inputs are registered and processed. For instance, the delusional schizophrenic patient often ignores information that fails to confirm his or her delusions, thus reducing the range of input. This could result in functional sensory deprivation or experiential impoverishment. Moreover, repeated adaptive failures are likely to push schizophrenic patients into lives that are simpler, less stressful, more institutional, and less stimulating. If the effects of curtailing the range of experience on cortical integrity in animals are comparable to those in humans, a kind of disuse atrophy of cortical circuits could occur in the brains of schizophrenic patients.

At a neurobiological level, parasitic foci will tend to dominate competing activation patterns, which could directly induce disuse atrophy. Progressive loss of functional capacity or schizophrenic deterioration seems to be concentrated in the 5 years after onset (see McGlashan and Fenton 1993, this issue). Moreover, lengthy duration of active psychosis seems to have its own deleterious effects on long-term outcome even after patients go into remission (Wyatt 1991). These two observations are consistent with the hypothesis that the induction of parasitic foci can induce secondary functional impairments and perhaps even neuroanatomic changes in cortical systems. This may also account for the large number of reports suggesting mild, diffuse loss of cerebral tissue in many schizophrenic patients and the induction of negative or deficit symptoms that seem, at least in part, to be associated with such tissue loss. (For a review, see Bachneff [1991]; see also McGlashan and Fenton [1993, this issue] for a description of progression from positive to negative symptoms in schizophrenia.)

Limitations of the Model. There are several challenges to this model of schizophrenic pathophysiology.

1. MK-801 is an experimental anticonvulsant with a very high affinity for the PCP binding site at the NMDA receptor (Javitt and Zukin 1991). MK-801 might therefore be useful in assessing the density of NMDA receptors. Although an overpruning hypothesis would predict decreases in MK-801 binding, a recent postmortem study demonstrated nonsignificant increases in MK-801 binding in cortical and limbic areas of schizophrenic brains compared to normal brains (Kornhuber et al. 1989). Along these same lines, a binding study using $^{3} \text{H}$ aspartate and $^{3} \text{H}$ kainate suggested increased excitatory amino acid receptors in the orbital frontal areas of postmortem brains of schizophrenic subjects compared to those of normals (Deakin et al. 1989). This is consistent with an earlier postmortem Golgi study demonstrating increased dendritic branching in the orbital cortex of brains of schizophrenic subjects relative to normals (Senitz and Winkelmann 1981).

These results, however, are difficult to interpret. Nonsynaptic NMDA receptors which are known to occur during development (Blanton et al. 1990), may indicate neurons in search of new axonal connections. A denervation hypersensitivity with elaboration of nonsynaptic glutamate receptors could result from excessive pruning of cortical synapses occurring simultaneously with elevations in excitatory amino acid and MK-801 binding. Another possibility is that
the brains of schizophrenic subjects are characterized by a maldistribution of connectivity with an excess in connections between certain cortical regions and a pathological reduction in others. This possibility is suggested by another morphological study by Benes and coworkers (1987) indicating increased collateral projections in cingulate cortex of schizophrenic patients’ brains.

2. Actual cortical pruning of synapses and dendritic-axonal connections during normal adolescence has been demonstrated best in prefrontal areas (Hüttenlocher 1979). On the other hand, parasitic foci postulated to cause positive symptoms may primarily infect language processes that could involve both anterior speech production and posterior speech reception systems; the locus of such pathology is primarily the dominant hemisphere. There is no literature to support the idea that the dominant hemisphere is more specifically involved in adolescent brain development, cortical pruning, and so on.

This question of the relative involvement of different hemispheres is important for the model. Three points can be reasonably argued, albeit speculatively. First, it is likely that prefrontal neurons actively participate in both speech production and speech perception (Mesulam 1990). Thus, pruning of prefrontal synapses could result in pathological functioning at distant regions interacting with the prefrontal region, for example, the posterior speech perception region. Second, the prediction that language processes produce characteristic positive symptoms of schizophrenia does not rule out the possibility that neuroanatomic pathology in this disorder may also involve the nondominant hemisphere. It may simply be that this pathology is more likely to be expressed by the dominant hemisphere, which is more specifically coupled with language processes and consciousness (Gazzaniga 1985).

Third, there is some reason to believe that the dominant hemisphere is more vulnerable to corticocortical uncoupling and the induction of parasitic foci. This possibility is suggested by a study of electroencephalographic (EEG) coherence recordings at different locations showing more diffuse intrahemispheric exchange of information on the right side, which indicates less differentiated modular coupling compared to the left side in normal adults ( Thatcher et al. 1986). Also consistent with this perspective are magnetic resonance imaging (MRI) data indicating that in healthy adults brain volume is greater on the right side than on the left (Gur et al. 1991). This would be expected if corticocortical pruning and modular differentiation of cortical tissue are somewhat greater on the left than on the right.

3. A study by Benes and coworkers (1991) demonstrated reductions in small interneurons in prefrontal and cingulate cortex in schizophrenia, but such findings are not consistent with the model presented here. One explanation consistent with our model is that these cell losses could result from the reductions in neurotrophic drive caused by excessive pruning of excitatory corticocortical projections.

**Implications for Future Research**

**Microanatomy.** The model presented here calls for direct study of synaptic density in the cerebral cortex of schizophrenic patients. Frontal regions are of special interest because pruning in these areas is most prolonged in normal adolescents; however, other regions (e.g., medial temporal cortex) are also of considerable interest. Studies could use direct electron microscopic counts or Golgi staining of individual cells to determine size of dendritic trees or spine densities. Reductions in number of synapses and dendritic spines would be consistent with schizophrenia types A, B, and C, while reduced dendritic stalk outgrowth would be particularly suggestive of a type C mechanism (see figure 5 and table 1).

**Nuclear Magnetic Resonance (NMR) Spectroscopy.** 31P magnetic resonance spectroscopy is a tool that holds considerable promise in future studies of schizophrenia. Careful study of high-risk groups are critical to determine if excessive elimination of synapses precede the illness or are consequences of the illness. On the basis of our developmental model, type A schizophrenia would be presaged by elevations in PDE, while type C preschizophrenic patients would have abnormally low PDE levels (see figure 5 and table 1). During the psychotic and immediate postpsychotic phase, secondary regressive changes, reflected by elevations of PDE, would occur for all three types of schizophrenia (see table 1) and involve both association cortex and hippocampus. These changes are predicted to be secondary to the dominance of parasitic foci over competing circuits or modules with secondary disuse atrophy of corticocortical connections and the in-
Table 1. Specific predictions for the three neurodevelopmental types of schizophrenia

<table>
<thead>
<tr>
<th>Type</th>
<th>Early adolescent</th>
<th>Prodromal</th>
<th>Onset (acute)</th>
<th>Post-episode (subacute)</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G</td>
<td>E</td>
<td>G</td>
<td>E</td>
<td>G</td>
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<tr>
<td>A</td>
<td>nl</td>
<td>nl</td>
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<td>↑</td>
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<td>nl</td>
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<td>nl</td>
<td>nl</td>
<td>↑</td>
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<tr>
<td>C</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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</tr>
</tbody>
</table>

Note.—G = growth of new axonal-dendritic connections; E = elimination of synapses; nl = normal; ↑ = increase; ↓ = decrease; ↑↑ = robust increases.

1 Increases in the rate of formation of new synapses may occur in response to excessive pruning of synapses before or during the psychotic phase.
2 Reduced synaptic elimination is predicted during the chronic phases because there are fewer synapses to eliminate.

duction of a type of kindling in hippocampal areas. These predictions are consistent with a study by Barta and coworkers (1990), who found left superior temporal atrophy in hallucinating patients. Barta and colleagues' findings could reflect a burnout of cortical tissue caused by repetitive activation of stereotypic auditory and speech perceptions driven by parasitic attractors and disuse atrophy of competing circuits.

Proton NMR spectroscopy also has the potential to assay glutamate levels in the living brain (Frahm et al. 1989). Although serious technical difficulties remain (e.g., distinguishing synaptic and nonsynaptic pools of glutamate), this process could provide a useful in vivo probe for mapping excitatory synaptic density. Such tools have been applied in a preliminary way to studying glutamate levels in the cortex of schizophrenic patients (Stanley et al. 1992).

Molecular Studies. Central nervous system (CNS) proteins that modulate postnatal neurodevelopment should be considered potential etiologic factors in the development of schizophrenia. These factors include growth-associated phosphoprotein (GAP)-43 (Benoit et al. 1989) and brain-derived growth factor, a protein related to nerve growth factor that operates in the CNS (Thoenen et al. 1987). Genetic variations in either of these proteins could cause reduced neuronal outgrowth that could yield a type C pathophysiology. Excesses in growth factors, such as those reported in schizophrenia by Schwartz and Stevens (1988), could reflect compensatory responses to excessive cortical pruning in response to a type A pathophysiology. These factors are potential targets for postmortem studies and linkage studies in families with a high penetrance for schizophrenia. As mentioned above, other causes of type B schizophrenia would be various forms of prenatal insults: connectivity would begin at a lower baseline, although postnatal cortical development would unfold more or less normally.

Functional Studies. Precise methods are needed to detect the capacity of neural subsystems with reduced functional connectivity with other systems to uncouple and thereby create parasitic foci. The EEG, coupled with dynamic signal analysis techniques, holds some promise in identifying parasitically organized brain activity, although these data are limited by poor spatial resolution and artifactual signal contaminants. Hoffman and colleagues are currently pursuing this approach with mathemati-
nal analyses designed to detect time series attractors as defined by chaos theory (Grassberger and Procaccia 1983). Magnetoencephalography is a potentially promising tool because of its relatively high spatial resolution compared to the standard EEG (Tiihonen et al. 1992).

Cognitive studies that can detect the effects of parasitic processes are also indicated. Parasitic domination by particular words or phrases during speech processing is thought to occur among patients who hear voices (e.g., Hoffman and Rapaport, in press). Patients suffering from delusions of the idee fixe type are predicted to suffer from impairments in narrative memory, including mnemonic distortions of plot elements, and these distortions are predicted to approximate elements of the parasitic narrative.

Regional metabolic studies may be able to detect excessive activation of parasitic foci if they are spatially localized. For instance, a regional cerebral blood flow study by Uchino and coworkers (1986) demonstrated activation of left frontal regions in schizophrenic patients with thought insertion and thought broadcasting compared to those schizophrenic patients who did not experience these symptoms. Other groups, however, have not been successful in linking localized cerebral activation and specific positive symptom complexes (Mathew et al. 1982; Volkow et al. 1987). It is important to note that a parasitic focus need not be active at all times to induce significant symptoms, nor must it necessarily be spatially localized. The activation signal of a parasitic focus thus might be diluted over time and space and hidden amidst the background activity of other neural circuits.

Additional Neural Network Simulations. Our PDP model does not account for the proven usefulness of dopamine-blocking agents in reducing symptoms, especially positive symptoms, in schizophrenia. Cohen and Servan-Schreiber (1993, this issue) describe neurocognitive effects of down-regulation of cortical dopamine: their empirical and computer simulation findings suggest that dopamine regulates the gain or signal-to-noise discrimination abilities of individual neurons. It is possible that reduced neuronal gain could retard the expression of parasitic foci. Hoffman and Servan-Schreiber are currently exploring this possibility with computer models.

Closing Comments

Synaptic Slippage. Paul Meehl's theory postulates that vulnerability to schizophrenia is based on a genetically determined generalized reduction of neuronal selectivity to input signal patterns. This reduction results in synaptic "slippage" (Meehl 1989). Our model also suggests that brain aberration in schizophrenia is widespread, but we believe that these problems are caused by neuronal assemblies rather than the functioning of single neurons. Different organic disturbances in neuronal assemblies that produce functional disturbances are considered, including genetic influences (regulating, for instance, dendritic outgrowth in cortical areas and rate of cortical pruning) and prenatal disruptions in brain development. Moreover, our model considers the possibility that the infusion of information from parasitic foci into neuronal assemblies can result in further changes in brain architecture.

Other Neurodevelopmental Models of Schizophrenia. Weinberger postulates that schizophrenia is induced by prefrontal cortical dysfunction that goes "on line" during adolescence, and that a secondary induction of excessive mesolimbic dopamine drive produces positive symptoms (Weinberger 1987). The PDP model presented here predicts that schizophrenic symptoms are primarily the product of cortical-hippocampal neural circuits. This does not rule out the possibility that excessive limbic dopamine could be pathological; recent animal and human studies support the hypothesis that excessive limbic dopamine drive could result in disturbed cognition in schizophrenia, for example, excessive attention to extraneous stimuli (see Gray et al. 1991). The dopamine model does not account for the stereotypic content of many schizophrenic symptoms and their nonself aspects (Hoffman 1991). These aspects of schizophrenic phenomenology raise the possibility of functionally autonomous circuits that assume their own pathological self-organization and order.

PDP models of psychopathology operate at the mind-body interface. The ideas presented here are based on a still very limited understanding of mental and brain functioning and are, therefore, preliminary at best. PDP simulations in particular are still extremely primitive in terms of their cognitive abilities. They nonetheless yield novel, testable hypotheses.
linking phenomenology and neurobiology that may provide new insights into the nature of schizophrenia.

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**Schizophrenia: Questions and Answers**

What is schizophrenia? What causes it? How is it treated? How can other people help? What is the outlook? These are the questions addressed in a booklet prepared by the Schizophrenia Research Branch of the National Institute of Mental Health.

Directed to readers who may have little or no professional training in schizophrenia-related disciplines, the booklet provides answers and explanations for many commonly asked questions of the complex issues about schizophrenia. It also conveys something of the sense of unreality, fears, and loneliness that a schizophrenic individual often experiences.

The booklet describes "The World of the Schizophrenic Patient" through the use of analogy. It briefly describes what is known about causes—the influence of genetics, environment, and biochemistry. It also discusses common treatment techniques. The booklet closes with a discussion of the prospects for understanding schizophrenia in the coming decade and the outlook for individuals who are now victims of this severe and often chronic mental disorder.

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