The First Panic Attack: A Neurobiological Theory

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Abstract We extend a neurodevelopmental model of specific phobias to the etiology of an initial panic attack and its elaboration into panic disorder. An important difference between the initial panic attack and specific phobia is the developmental timing of critical emotional experience: Those occurring early in development lead to panic; those occurring later in development lead to specific phobia. By this account, sensory and emotional experiences that occur early in development are stored in a set of modules, each with a unique developmental trajectory. Reinstatement, which occurs during hormonal stress, produces an aggregate of sensory and emotional memories and the first experience of an unexplained panic attack. Panic disorder, which evolves from unexplained panic attacks, involves retrieval of a disaggregate set of sensory and emotional memory fragments supplemented by an inferential fitting of an explanatory context to this incomplete aggregate.

Introduction

Hebb's legacy includes many things, from an appreciation of the importance of synaptic plasticity in learning to the notion that we must pay attention to both behavior and biology if we are to make sense of complex psychological phenomena. In the spirit of this latter thesis we have, over the past decade, attempted to bring concepts of modern neurobiology to bear on some thorny clinical phenomena, including phobias and various anxiety disorders (e.g., Jacobs & Blackburn, 1995; Jacobs & Nadel, 1985, 1998; Jacobs, Nadel & Hayden, 1992; Metcalfe & Jacobs, 1996, 1998; Nadel & Jacobs, 1996; Nadel & Zola-Morgan, 1984). In the present chapter we focus on the problem of panic, and in particular the first panic attack. We will suggest the first panic attack has an etiology similar to that underlying the first phobic reaction, after which each takes its own developmental course. The kind of panic we have in mind is captured in the following description from Hawkrigg (1975):

"I was inside a very busy shopping precinct and all of a sudden it happened; in a matter of seconds I was like a mad woman. It was like a nightmare, only I was awake; everything went black and sweat poured out of me — my body, my hands, and even my hair got wet through. All of the blood seemed to drain out of me; I went white as a ghost. I felt as if I was going to collapse; it was as if I had no control over my limbs; my back and legs were very weak and I felt as though it were impossible to move. It was as if I had been taken over by some stronger force. I saw all of the people looking at me — just faces, no bodies, all merged into one. My heart started pounding in my head and my ears; I thought that my heart was going to stop. I could see black and yellow lights. I could hear the voices of the people but from a long way off. I could not think of anything except the way that I was feeling and that how I had to get out and run quickly or I would die. I must escape and get into fresh air. Outside it subsided a little but I felt limp and weak; my legs were like jelly as though I had run a race and lost; I had a lump in my throat like a golf ball. The incident seemed to me to have lasted hours. I was absolutely drained when I got home and I just broke down and cried; it took until the next day to feel normal again."

Students who participated in Hebb's Graduate Seminar came to understand a different kind of "panic," associated with the possibility that they might be called upon by Hebb to state their views on consciousness, free will, or just about anything that suited his fancy that day. This kind of panic was remarkably persistent, even in the face of repeated demonstrations that Hebb's bark was a good deal worse than his bite. Clinical panic also persists in the face of clear knowledge that harm is not probable. In that regard, and in many others, panic reactions closely resemble phobic reactions. The present paper, building upon these resemblances, extends our previously published model of specific phobias and traumatic memory (Jacobs & Nadel, 1985, 1998) to account for the first panic attack (see e.g., Barlow, 1988; Klein & Klein, 1989 for further distinctions).

Approaches to Panic

Three grand theoretical schemes dominate the analysis of panic. Biological theories anchor their accounts in anatomy, physiology, and endocrinology. Behavioural theories focus
on prior experiences and the current environment. Cognitive theories emphasize thought contents and cognitive processes occurring during a panic attack. Each of these approaches has its own framework, its own domain, its own data language, and its own database. Hebb would not be surprised to find that each of these schemes, taken on its own, is incomplete. Each has a range of phenomena that it can account for, and a range that it does not explain. For example, biological theories miss phenomenological characteristics of panic. Cognitive theories miss critical biological facts. Both are silent on the development of panic. Behavioural theories do address development, but miss both biology and cognition. Our concern is to take the best of these approaches and attempt a synthesis — a cognitive neuropsychological model of the development of panic that accounts for its existence and its particular properties.

We begin with a comparison between specific phobia and panic, which allows us to outline a behavioural model of the first panic attack. This behavioural model will then be situated within a particular approach to the neural organization of cognitive and behavioural processes — the “cognitive map theory” proposed by O’Keefe and Nadel some years ago (1978). Our argument rests upon data from biological, cognitive, and behavioural literatures. Although the facts we discuss are generally well known within their own domains, they are not necessarily appreciated outside that domain. We will argue that taken together they provide a coherent story regarding the phenomenological state known as panic.

Relationships Between Specific Phobia and Panic

Because the problems are so complex, there have been few attempts to provide integrated accounts of the anxiety disorders. In an ambitious theory, Barlow (1988) concentrated on relations among panic, agoraphobia, claustrophobia, social phobia, generalized anxiety disorder, post-traumatic stress disorder, and depression. Following Craske (1991) and McNally (1994), we will try to show that panic attacks and specific phobias share many phenomenological characteristics, and that these characteristics can provide powerful clues to an understanding of the development of panic and of specific phobias.

Compare Hawkridge’s (1975) description of a panic attack given at the outset with the following description:

Consider a man afflicted with a simple phobia — the fear of flying — but compelled by the nature of his business to undertake immediate travel. His secretary books a flight leaving within the hour. He rushes home, packs a bag, and drives to the airport. Although apprehensive, the full impact of his phobia does not strike until the plane leaves the starting gate. His mouth dries, he feels faint, dizzy, and vaguely ill. His hands begin to perspire and tremble, his breathing quickens, his heart pounds. With each passing moment, the reaction intensifies. As the physical reactions intensify, so do the psychological. The voices of others recede into the background, the words empty of meaning; the faces and objects around him seem to blend into a “booming, buzzing confusion”; he has little control over his limbs, as if it were impossible to move. He feels depersonalized and out of contact with reality. As the flight reaches the ground these feelings begin to abate. He disembarks limp, weak, sweat-soaked, and drained. Little of the flight remains in memory except his emotional reactions. He spends that afternoon recovering from the experience. The next day he books train passage for the return trip.

There is a remarkable similarity between the subjective experience of the individuals suffering from a panic attack and phobia reaction in these two descriptions. Though they captured their experience in different words, they might have been describing identical emotional experiences. Indeed, an examination of the panic attack and phobic reaction reveals remarkable similarities among features that characterize the development, maintenance, and subjective experience of each.

First, the onset of a specific phobia (e.g., Jacobs & Nadel, 1985; Shafar, 1976; Snaith, 1968; Solyom, Beck, Solyom, & Hugel, 1974) and the first panic attack often occur at a time of serious life-stress: Specifically, the onset of a specific phobia, or panic, occurs in the presence of prolonged discomfort, against a background of strained familial relationships, medical problems, death in the family, serious problems at work, pregnancy, extended labour, premature (or even term) birth, worry, or unhappiness (e.g., Asso & Beech, 1975; Buglass, Clarke, Henderson, Kreitman, & Presley, 1977; Burns & Thorpe, 1977; Faravelli, 1985; Freud, 1919; Goldstein & Chambless, 1978; Hallam, 1978; Marks, 1970; Roth, 1959; Westphal, 1871).

Second, only a minority of those who experience life stress develop specific phobias or panic attacks. They may have repeatedly been in circumstances eliciting their current fear, without previously developing any fear of it. It is only when these two are conjoint, that is, when the person experiences the feared object or place during a period of (otherwise induced) severe stress, that the reaction develops.

Third, a secondary phobia centred on the panic reaction may develop even though the individual may have experienced the same situation and the same sensations in the past and may be explicitly aware that no harm from the panic reaction is imminent. Although in this case fear of the panic attack (the secondary phobia) appears rational, the panic reactions are not. Such reactions often persist for years in the face of knowledge that they are irrational. Once triggered, both panic and specific phobic reactions are difficult or impossible to bring under rational control.

Finally, the onset of specific phobias and panic attacks often occurs without knowledge (or memory) of any specific experience that could have created the phobic/panic reaction.
Thus, panic attacks and phobic reactions share many characteristics, including development, strong persistence, felt experience, and resistance to cognitive or rational manipulation. The reactions share too many features to be classified as distinct phenomena (see Craske, 1991).

There are three characteristics that sharply differentiate a specific phobia from the first panic attack. (a) The victim of a phobic reaction can readily identify a proximal trigger of the fear; the victim of panic cannot. A phobic reaction is, by definition, tied to a known set of circumscribed environmental conditions; fear produced during panic is not. (b) Victims of phobic reactions can often control their fear by merely avoiding its trigger, but the victim of panic attacks cannot easily do the same. Consequently, as the condition develops, these individuals adopt other techniques to cope with panic. Dark sunglasses, the presence of a loved and trusted companion, staying at home, or even in bed, seem to help. Even when the panic attacks completely cease, these individuals quite sensibly retain the coping techniques. (c) The cognitive processes evoked by a phobic reaction and a panic attack are simultaneously identical and distinct. Human nature seems to demand that we generate hypotheses, models, and explanations for salient events that enter our awareness (Krull & Anderson, 1997; McArthur & Baron, 1983; Pennington & Hastie, 1991). When a person experiences a phobic reaction, a fully satisfying explanation is immediately apparent: The person is afraid of an identifiable trigger. A satisfying explanation brings the explanatory process to a halt. In contrast, when faced with a panic attack, no satisfying explanation is forthcoming. Although a host of (at best) flimsy explanations are available, none hold up under the experience of repeated attacks of panic.\(^1\) In such a case, attempts to explain the apparently inexplicable continue.

The fact that the fear trigger can be identified in specific phobias but not in panic is important to understanding the genesis of these two conditions, but we would argue that it is not a sufficient reason to see them as wholly distinct (Barlow, 1988; Craske, 1991; McNally, 1994).

A focus on the apparently spontaneous nature of the first panic attack has led some theoreticians to internalize its causes. Misattributions, physical sensations, anxiety sensitivity, and catastrophic cognition have been used as the basic explanatory tools in theories concerning panic. Although these models provide an account of how an already existing panic is provoked, they do not provide a good account for the development of the panic reaction. These theories do not explain why some panic attacks occur during sleep, why some people do not report catastrophic cognitions until after a panic attack or do not report them at all, and, most important to us, how anxiety sensitivity or the catastrophic misattributions that characterize well-developed panic attacks develop in the first place (Bootzin, Acocella, & Alloy, 1993).

Given this, Hebb might argue that the cognitive approach is incomplete. Indeed, he might argue that an adequate explanation of the genesis of panic attacks must include reference to the anatomy, physiology, experience, environment, and subjective state of the individual suffering the attacks (Jacobs & Nadel, 1998; Jacobs et al., 1992). Our approach to such an explanation starts with our already-proposed model to explain specific phobias (Jacobs & Nadel, 1985; Metcalfe & Jacobs, 1996, 1998), and with the many similarities between phobias and panic outlined above.

**Fears, Phobias and Panic**

Our original model for the genesis of specific phobias (Jacobs & Nadel, 1985) was couched within a particular view of the neural organization of learning and memory: the now well-accepted assertion that there are multiple learning systems (see Nadel, 1992, 1994; Schacter & Tulving, 1994), and that these are based to some extent in dissociable neural structures. We postulated two kinds of learning systems: the locale system concerned with spatial maps and contexts and centred in the hippocampus, and the non-hippocampal *taxon* systems concerned with emotions, categories, concepts, skills and habits (e.g., an emotional system centreing on the amygdala; e.g., LeDoux, 1994). These two kinds of systems have dramatically different properties, as detailed in Table 1, and differ as well in their developmental trajectories. Our model of the genesis of phobias, and the model we propose here for the genesis of the first panic attack, emphasizes the consequences of the pre-partum maturation of the amygdala and the post-partum maturation of the hippocampus. Most critical is the fact that emotional learning that occurs before maturation of the hippocampus reflects the characteristics and properties of the non-hippocampal *taxon* systems alone (Metcalfe & Jacobs, 1996, 1998; Nadel & Jacobs, 1996).\(^3\)

We proposed that an understanding of the perplexities of fears and phobias could emerge from a careful analysis of the characteristics of each of these learning systems on the one hand, and their developmental trajectories on the other. One central fact concerns the deleterious effects of damage to the hippocampus on autobiographical (explicit) memory.

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\(^1\) For example, many explain an initial panic attack as a heart attack and conclude they are in danger of immediate death. Both the explanation and the conclusion are soon disconfirmed, however, shortly after visiting the emergency room.

\(^2\) Barlow (1988) has done an admirable job using interoceptive stimuli as the stimuli critical for an explanation of panic disorder. We shall consider his model later.

\(^3\) Many versions of the "multiple learning systems" notion have been proposed in recent years (see Schacter & Tulving, 1994, for a sampling), but almost all of them share certain common features first spelled out by O'Keefe and Nadel (1978) in terms of the *locale* and *taxon* systems.
(e.g., Squire, 1992). Given that the hippocampus of a human is unlikely to be functionally mature until about 18 months of age (Mangan & Nadel, 1990; Seress, 1992), there are good reasons to assume that its delayed maturation accounts for at least some portion of what is usually termed "infantile amnesia" (Nadel & Zola-Morgan, 1984; Schacter & Moscovitch, 1984). Experiences critical to the development of a phobia, we proposed, occur before hippocampal maturation, under the veil of infantile amnesia, and exhibit features characteristic of the already-matured taxon systems such as context independence, generalization, and prolonged extinction. This learning proceeds in those areas of the brain functional at the earliest stages of life.

The unfettered behavioural control exerted by information acquired in these early-maturing systems disappears with maturation of the hippocampal system, which provides a basis for the conscious awareness typical of adult life. The early-acquired emotional information, however, remains. We postulated that the adult could undergo recovery of this information, complete with its unique properties, under certain conditions (Jacobs & Nadel, 1985) — most particularly excessive stress. This, we suggested, was due to a stress-related hormonal disruption of hippocampal function (e.g., de Kloet, Oitzle, & Joëls, 1993; Lupien & McEwen, 1997), which partially returns the individual to a neural state not unlike that of early life, with taxon-based systems controlling the organism’s behaviour. We pointed to the close correspondence between the features of phobias and the characteristics of learning early in life. This led us to suggest that reinstatement of stimulus control acquired early in infancy serves as the basis of specific phobic reactions. We now suggest that much the same is true of a first panic attack.

We hold that a critical difference between the first panic attack and phobic reactions resides in the stage of early development during which the critical learning events occur. This difference accounts for why a proximal trigger is identifiable in a phobic reaction but not in the first panic attack. To fully explicate this point we must turn our attention to an analysis of the nature of early brain and cognitive development, and the kind of learning that transpires before the hippocampal locale system has matured. This analysis must itself be embodied within a broader discussion of what learning is assumed to be all about in the first place.

The Nature of Learned Reactions

Those interested in the source of learned reactions (such as conditional responses, specific phobias, or overt behaviours) have typically sought to understand two aspects of learning: (a) how the features of one environmental stimulus are associated with the features of another; and (b) what determines the informational content of these associations.

To make these problems tractable, two theoretical assumptions have been common. First, it has been assumed that an organism represents stimuli in the central nervous system and then creates associations between the stimuli captured in these neural representations through neural connections. This first assumption defined two central tasks: (i) to delineate in some principled fashion the nature of the stimuli represented within the nervous system, that is, the features that compose them; and (ii) to uncover the means by which these features become associated. The second critical assumption asserts that there exists a 1:1 correspondence between environmental events — as psychologists/observers define them — and the underlying neural representations that enter into the associative learning captured by the first assumption. Thus, when an experimenter presents a tone or a light to experimental animals, and they learn that these stimuli “predict” some outcome such as food, or a shock, it is typically assumed that the animal represents these stimuli as integral entities — tones, lights, food and shock (see Jacobs & Blackburn, 1995 for details).

4 See Mullen (1994) for a careful analysis of some of the factors carrying infantile amnesia out to 3.4 years, well beyond the time when the hippocampus is likely to be functional.

5 The evidence concerning the effects of intense stress on hippocampal function is now a good deal more secure than when we first proposed this mechanism in 1985. Although it is beyond the scope of this paper to go into the details, those interested may consult Nadel and Jacobs (1996), Meech and Jacobs (1998), or Jacobs and Nadel (1998) for a brief introduction.

6 It is worth pointing out here that recent debates about the functions of the hippocampus turn on exactly this issue, and the ability to state what an animal, as compared to an experimenter, defines as a "stimulus." Configural theory (e.g., Sutherland & Rudy, 1989) and declarative/relational theory (e.g., Cohen & Eichenbaum, 1993; Squire, 1992) both depend on the view that animals’ nervous systems...
These two assumptions provide a basis for explaining how organisms represent various features of the available environmental information and form associations (and generalizations) among them in selective and complicated ways (see, e.g., Jacobs & Blackburn, 1995, for a review). These assumptions, however, leave untouched the critical problem of specifying relations among physical events, their neural representations, and subjective experience. That is, they beg the question of how to precisely characterize what an individual’s experiences actually feel like. We do not propose to provide answers to the riddle of subjective awareness; we want merely to make it clear that there is no fixed relation between external reality and inner subjective awareness. This relation is mediated by neural substrates, which in turn are dynamic across the life span (Jacobs & Blackburn, 1995).

Thus, we must reject any simple version of the correspondence assumption relating physical events and subjective experience. And this rejection provides a means by which we can explain the source of panic and phobic states. What organisms learn from environmentally based experience is not fixed solely by events that occur in the external world but also depends on the nature of the biological machinery available to process the information contained in those events. An interaction between these two factors determines the nature of the information available to an organism, and in consequence, what the organism both experiences subjectively, and what it learns.

The central postulate of our “stress-induced recovery” (SIR) model of phobias (Jacobs & Nadel, 1985) is that an experience critical to the subsequent development of specific phobias occurs when the neurological machinery of the infant/child is undergoing extensive maturation and physical change (Jacobs & Nadel, 1985; Jacobs et al., 1992; Nadel & Jacobs, 1996). To account for the contents of specific phobic/panic states we must understand the way in which the brain processes environmental information at various stages of life, and the nature of the neural representations of information that are formed. This knowledge is crucial to any model that seeks to explain the source (or associative content) of a learned reaction — especially one seeking to explain the inability of those suffering from panic attacks or phobic reactions to identify their source.

Therefore, we must consider the anatomical and physiological state of the systems devoted to the acquisition of information early in life. The questions that interest us directly — what information is available to the maturing organism, what its subjective experience is like, and what is the difference between the two — cannot be answered directly. Instead, we must approach these issues indirectly, through an analysis of various neurological syndromes that reveal the kinds of information that an individual can have without subjective awareness. Some of these syndromes create conditions similar to those in existence when the nervous system is immature, as in the developing infant. Others create conditions unlike anything observed in the normal course of events. All of them share the feature of revealing the distance between what our rational minds normally construct and what lies beneath the surface, typically but not always unknowable. Before turning to this analysis of what lies below subjective awareness, we briefly review some facts about brain maturation, to provide a basis for understanding why the mapping between the external world and subjective reality should be so dynamic during development.

The Maturing Nervous System and Information Processing

At birth, the human brain weighs about 300 g: Over the next two years its weight triples, reaching adult levels (about 1,350 g) by puberty. Most of the neurons, and some neural connections, that will exist in the brain are present at birth. In fact, there is at birth an overabundance of neurons, many of which will disappear with maturation. Similarly, many synapses formed during early maturation will disappear as the organism progresses through infancy (e.g., Changeux & Mikoshi, 1978; Garey, 1984; Hamburger, 1975; Huttenlocher, Courten, Garey, & Van der Loos, 1982; Innocenti, 1981a, 1981b; Ivy & Killackey, 1982; Lund, Boothe, & Lund, 1977; O’Leary, Stanfield, & Cowen, 1981).

The weight gained during the first two post-natal years partially reflects the growth of neurons, the extension of their total area, and an increase in the number of synaptic connections (Conel, 1939-63). As cortical neurons grow they show dramatic changes in the extent and complexity of their dendritic trees. In the cat, the number of synaptic connections formed by each cortical neuron increases from a few hundred in the first few weeks of life to about 13,000 after five weeks. Comparable increases occur in monkeys and humans, such that by 2-3 years of age there are roughly $10^{14}$ to $10^{13}$ synapses. In the human, the disappearance of synapses begins to predominate about the third year of life, continuing for the next 10-15 years until adult levels are

few of these sensory systems early in development, but accesses more as neurological development proceeds. Establishing a relationship between self-reportable awareness and associative processes over developmental time is crucial to our current account of panic, for it is necessary to establish that sensory information (stimuli) is available to the infantile (and adult) learning/emotional systems without necessarily being available to self report.
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finally reached (Huttenlocher, 1979).

The growth of dendrites and axons in the central nervous system is associated with concomitant growth of a variety of support and structural elements, including those that make up the myelin sheath. At the time of birth, areas such as the somaesthetic cortex, primary visual cortex, and primary auditory cortex are only partially myelinated (Flechsig, 1920; Langworthy, 1933; Yakovlev & Lacours, 1967; see Kolb & Fantie, 1988 for a review). Some regions of the human neocortex are not fully myelinated until the third decade of life (see Gibson & Petersen, 1991, Chapter 3; Goldman, 1971).

These neuroanatomical data make it clear that information processing in the maturing organism is likely to be different from that in adults. Regions of the brain critical for sophisticated analyses of experience are either unformed or unfinished. Subjective awareness during early development is, of course, hard to evaluate. Some insights may be gleaned from neuropsychological data concerned with the impact of neocortical dysfunction both in adults and children.

NEOCORTICAL FUNCTION IN CHILDHOOD

The use of neuropsychological tests with children, based on methods developed initially for adults, has provided some evidence on the mosaic nature of neocortical function during development. Children above the age of three, who can analyze various forms of information, also can be deficient at tests sensitive to frontal and posterior parietal lobe function, and to functions dependent upon interhemispheric communication (Kolb & Fantie, 1988). It does not follow, however, that neocortex is entirely non-functional during the earliest stages of life. Electrical activity can be recorded from the fetal brain (Bergstrom, 1969), visual evoked potentials similar (but not identical) to those of the mature brain can be detected in pre-term infants (Purpura, 1976, 1982), and cortically based epilepsy has been found in some newborns (Caviness, 1969). Further, glucose utilization has been detected in the sensorimotor cortex of infants about a month old, and throughout the cortex of infants beyond eight months. Perhaps the safest conclusion is that neocortical function is, during early life, unlike that observed in adults. One thing is clear: the experiences of early life play a crucial role in determining which among the vast oversupply of neocortical neurons and synapses will survive and which will die. Experience-dependent pruning of the cortical "tree" permits the creation of neural ensembles that can subsequently "represent" the kinds of external stimuli that the infant has been exposed to (see Edelman, 1987, 1989, for an interesting perspective on this process). Such a mechanism is clearly at play in the neocortical systems responsible for language, accounting for the survival of those neural ensembles representing the sounds of the language one hears early in life, and the concomitant loss of ensembles that might have represented the sounds of many languages not heard.

Thus, neocortical systems are partially functional early in life, and are themselves undergoing changes because of the kinds of stimulation to which the organism is exposed. This has implications for the learning these systems can manage during early development. Further, we have indicated that the hippocampus is not functional early in life, and that the contextual episode containing and organizing emotional memories cannot therefore be formed (e.g., Chen, Kim, Thompson, & Tonegawa, 1996; Phillips, & LeDoux, 1992, 1995; Rudy, 1993). Thus, much about learning in early life is bound to be different from what is seen in adulthood. There are, however, other neural systems, noncortical systems, that are functional from or before birth in most cases, and these can be responsible for extensive learning in the infant. Dramatic evidence comes from the study of human newborns suffering from disorders resulting in severely disturbed neocortical tissue: Microencephaly. In such cases, one can hope to come to an understanding of the capacities of those brain systems we know to be intact early in life.

One such case, described by Beritashvili and Dzidzishvili (1934), a microcephalic female admitted to hospital at about 10 years of age, was unable to speak or comprehend, was uncontrollably aggressive, and was unable to solve even simple abstract problems. Over the course of a year's training, however, she learned to find hidden food, to use sticks to retrieve food, and to respond to social overtures from others. Another case, presented by Jacobson, Bernal and Lopez (1972) was first seen at the age of 17. This microcephalic male could neither speak nor follow simple instructions. After five hours of motor-skills training he solved simple discrimination problems; toward the end of training he uttered his first words. This person could see, hear, touch, taste, and smell within normal range. He could maintain his posture, walk, reach, vocalize, learn, and remember.

Such cases suggest that even without functioning neocortical systems, the individual has a large range of behaviours, some of them quite complex. These indications that many critical human capacities can survive diminished neocortical function are confirmed by extensive research with nonhumans. Crawling, walking, maintaining posture, various motor patterns, rudimentary forms of learning, seeing, hearing, and sensing by touch have all been shown in animals suffering extensive cortical removals (e.g., Girden, Mettler, Finch, & Culler, 1936; LeDoux, Sakaguchi, & Reis, 1983; Oakley, 1983; Vanderwolf & Robinson, 1981).

Taking these data together, we must conclude that the subjective world of the infant is certainly unlike that of the

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1 It is worth noting that much recent data demonstrate the plasticity of neural representation even in fully mature adults (e.g., Merzenich & Sameshima, 1993).
adult. Most critically for our purposes, this almost certainly means that infants live in a simpler world, populated not with the familiar objects and events of conscious adult life (and dear to the hearts of experimenters), but with fragments and features, pieces and patches that will eventually contribute to their ability to recognize and remember in an adult-like fashion. This uncomfortable prospect implies that under the recognizable surface of our adult subjective awareness there must lie a veritable stew of impressions that we would scarcely recognize if they popped into conscious awareness. This, however, does not mean that they are incapable of influencing behaviour, a fact important in understanding the roots of phobic reactions and panic attacks.9

The idea that a potpourri of features and impressions lies beneath the objectified surface of subjective awareness receives considerable support from recent work on the organization of knowledge within adult cortical systems. This work includes the careful dissection of particular systems, such as vision (and visual recognition of objects and events), and attempts to characterize the structure of the organism’s learning and memory capacities. Converging evidence from these and other perspectives supports the view that the cortex is highly modularized, with separate areas responsible for specific pieces and particular patches.

How Is the World Represented in the Brain/Mind?
A commonly, though not universally, accepted view is that the brain creates internal representations of external realities, and that such mental models provide the foundations for much of our behaviour. The recent history of cognitive science, and the allied domain of cognitive neuroscience, reflects this view by focusing on the ways in which the brain structures information about objects and events in the world. For many, the brain can be viewed as a collection of systems, each representing certain kinds of information about the world. Recent work has made it clear that such distinct modules or channels exist, and has begun to shed light on the kinds of information they process. Although adults clearly possess systems representing the complexities of conscious life — tables, chairs, people, hopes, wants, needs, and the like (e.g., Lakoff, 1987) — it seems likely, as suggested above, that at least some representations in developing organisms are less complex.

The critical question then becomes: Of what simpler constituents are children’s systems composed? Evidence from clinical syndromes such as amnesia and prosopagnosia (a failure to recognize familiar faces) can help here. These kinds of syndromes confirm that underneath the consciously accessible level of recognizable representations — such things as faces, names, and places — there lie inaccessible representations that would be considerably less easy to recognize. These levels of representation, though inaccessible to awareness, are critically necessary for creating the representations of which we can be aware (e.g., Gorn, Jacobs, & Mana, 1987; Kihlstrom, 1987). Further, and essential to our understanding of phobic reactions and panic, some of these (inaccessible) representational systems are functional in the infant; they are being shaped by the infant’s experiences, and they provide the ground within which seeds can be sown for future fears.

REPRESENTATIONS IN THE VISUAL DOMAIN
Traditional views of information processing in the visual system have undergone considerable change recently. What was once conceived as a simple system, composed of a few parts, is now seen as a highly complex system composed of perhaps several dozen parts, each concerned with a specific step in (or aspect of) the process of constructing internal representations of visual information (see e.g., Felleman & Van Essen, 1991; Livingstone & Hubel, 1988, for reviews). Processing goes on largely in parallel in these systems, which are interconnected in complex, but regular ways. Most researchers would argue that, notwithstanding this parallelism, the visual system is organized such that some modules are concerned with primitive features or aspects of the visual world, while others are concerned with the objects/events comprised out of these primitives. It is, of course, only the product of these latter systems of which we are typically aware.

Support for these assertions comes both from the study of the basic neurophysiology of the visual system, and from the kinds of clinical syndromes that can result from focal damage in various parts of the system. Briefly, investigations of the response properties of nerve cells in various components of the visual system show that their activity patterns signal, in some complex way, the presence or absence of particular visual features at particular locations in the organism’s visual field.10 Neural elements at the periphery of

9 This would be as good a place as any to address the controversial issue of “recovered memory.” It should be clear to the reader that the conceptual framework we are spelling out, based on neurobiological analyses, leaves ample room for the possibility that “information” acquired early in life, and that remains for some time outside of awareness, can under some circumstances be “recovered.” However, and this is the critical point, the nature of this information is unlike anything one might legitimately attribute to one’s autobiographical storehouse. The point of our argument is that the subjective content of the “memories” formed early in life is not like what we would call an episode — it lacks spatiotemporal context — and it is likely composed of impressions and features that bear little relation to the stimuli and objects that populate our adult world. Thus, “recovery” is possible, but not recovery of fully articulated and veridical episodes. Transforming the sketchy impressions and features that our brains can form early in life into episodes later in life likely has a lot more to do with learning at that later time than it does with the “recovery” of events that might or might not have occurred (Jacobs & Nadel, 1998).

10 Traditionally, these visual neurons have been called “feature
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detectors," and the assumption has been made that one can usefully
decompose sensory/perceptual systems into these "atoms," out of
which ever-more-complex feature detectors can be assembled. This
positivistic approach has been questioned on both logical and
empirical grounds. Though forcing a re-evaluation of notions such as
feature detector and "receptive field," these critiques do not alter the
argument presented here. This is because the re-evaluations are about
the issue of underlying representation — local versus distributed, static
versus dynamic — and not about the issue of whether or not features
are being represented.

And could walk, run, climb, and maneuver around obstacles
using visual cues.

How can we evaluate the subjective nature of these visual
experiences, which proceed without the typical awareness
accompanying vision? A neuropsychologist who suffered
limited destruction of area 17 following migrainal occlusion
reports of lights in his blind spot: "I knew the light was on,
I just couldn’t see it." Other blind-sighted individuals
accomplish remarkable feats though they uniformly deny
having sight in the standard sense. They are subjectively
blind yet in possession of considerable visual information.
They cannot consciously perceive information that can be
shown — by behavioural means — to exist in their brains.
This syndrome reveals an aspect of what we suggest is the
situation early in infancy — the processing of sensory
information in terms of impressions and features that are
unlike what intact adults would experience in subjective
awareness. Exactly what the subjective experiences of infants
are like is of course impossible to say, but it is bound to
reflect "primitive" rather than fully structured aspects of the
external world.

Consider, as another example, the syndrome of
prosopagnosia, or the inability to recognize faces. This
syndrome confirms just how fragmented our visual world is
beneath the surface, even when it pertains to that most
salient of objects — the human face. Tranel, Damasio, and
Damasio (1988) report that prosopagnosics process information
about various aspects of the face below the level of
actual facial recognition — the age of the face, the gender
perhaps — but are not aware of this knowledge, nor are they
able to translate it into the recognition of a particular
person. They suggest that such findings point to a set of
(likely parallel) representational systems concerned with
different features contributing to our ability to detect such
things as age, gender, and identity in a face, all within a split
second. The very selective brain damage responsible for
prosopagnosia (focal bilateral lesions in portions of the
posterior parieto-occipital junction) apparently destroys
access to systems needed to identify a particular face, but
leaves intact those systems responsible for detection of
features like the wrinkled quality of the skin, and so on —
features that would permit differentiating young from old
faces. Again, this syndrome seems to recreate certain aspects
of infancy — presence in the system of information about
primitive features of the visual world, with minimal access
to more complex features (e.g., the age-limited indiscrimi-
nate smiling at facial features, independent of their spatial
arrangement).

CONCLUSIONS

The immature nature of the infant’s nervous system sets
certain constraints on the inner world of the child. Perception
of everyday scenes, understanding of parts, wholes,
relationships, and properties, and our ability to think about

The visual system are apparently concerned with primitive
features such as blotches of colour, or an edge, while
elements farther into the system can be selectively tuned to
faces, or even specific places in the world. The kinds of
incapacities resulting from focal damage to these regions
reflect this difference in the kinds of visual representations
in which they traffic. They also reflect the fact that organ-
isms can have information about various features of the
environment without conscious awareness of that knowl-
dge.

Consider, for example, the results of physical disruption
of neural connections in a restricted region of primary visual
cortex (area 17). Typically, a scotoma is produced and the
affected individual is subjectively blind in that area
(Weiskrantz, Warrington, Sanders, & Marshall, 1974,
described such a patient, D.B.). Remarkably, this patient
accurately discriminated vertical and horizontal bars and
pointed to the source of a spot of light within the blind area.
This occurred even though D.B. believed himself to be blind
in that field. Other individuals with similar lesions point
accurately to visual targets in their blind spot (Bridgeman &
Staggs, 1982; Pererin & Jeannerod, 1975, 1978), move their
eyes to stimuli (Poppel, Held, & Frost, 1973), distinguish
shapes such as circles and triangles (Weiskrantz et al., 1974),
and reach for objects — all with surprising accuracy. Ray-
mond and Leibowitz (1985) reported that individuals with
such injuries can use visual information in the blind spot to
mediate postural behaviours that are primarily under
reflexive control.

These data from the study of humans with damage to
primary visual processing regions are consistent with earlier
findings in nonhumans. Most mammals retain the ability to
orient toward diffuse light sources (Hore, Bettinger, Royce,
& Meyer, 1966; Klüver, 1941; Lashley, 1935), to detect
contours (Cowey & Weiskrantz, 1971; Dean, 1978), to
orient toward the location of specific forms, and to discrimi-
nate complex forms (Killackey, Snyder, & Diamond, 1971;
Pasik & Pasik, 1971; Spear, 1979) even after virtually
complete removal of primary visual cortex. Monkeys with
such complete ablations can use vision to avoid objects, pick
up berries, and catch live prey (Humphrey, 1974; see also
Humphrey, 1970; Klüver, 1941; Weiskrantz et al., 1974, for
exceptions). Weiskrantz and Cowey (1967) found that such
monkeys could still discriminate environmental patterns,
others and ourselves as actors in an intricately structured world all seem to depend in certain ways upon regions of the brain that may not be fully functional in early life. Much of what we, as adults, consider normal subjective experience could well be absent in the developing infant. Nevertheless, those parts of the brain that are functional early in life seem able to support some behaviour, even quite complex behaviour. Moreover, they support sight, hearing, touch, taste, and smell, but in ways that may be subjectively different from that for the adult. Further, and critical to our case, the early-maturing parts of the brain can support learning, and the formation of associations among those aspects of the organism’s environment that it can adequately represent. In other words, the associative learning that occurs in the earliest stages of human life frequently occurs among representations of primitive stimuli — features of objects rather than objects themselves, patches of an event rather than the event itself. This fact has cardinal implications for understanding cognitive development that we cannot explore here. It also has, we suggest, implications for an understanding of phobic and panic reactions.

Phobic and Panic Reactions Revisited

This analysis of the learning systems available early in life lays the groundwork for an understanding of specific phobias and the first panic attack. As we saw, learning that occurs early in life focuses on features in the environment, entirely ignoring the spatiotemporal context information processed by the late-maturing system. What is more, the features focused on are comparatively primitive, reflecting the narrow experience of the developing organism and its not-yet-fully-structured cortical representational systems. These will often be features of a sort unidentifiable to an adult. Reinstatement of behavioural (or emotional) control at the level of these features could create an environmental source of fear inaccessible to conscious awareness and verbal report.

In our view, reinstatement in adult life of affective and behavioural control based on early experiences is the central feature of phobic reactions and the first panic attack. The development of these syndromes depends upon: (1) the occurrence of particular experiences in infancy when learning occurs only in primitive systems, and without the involvement of the hippocampal locale system; (2) the occurrence of adequate stress during adulthood that suffices to shut down the hippocampus and simultaneously exposes the taxon memory systems; and, (3) the occurrence during stress of some reminder of an early experience, stored earlier in a primitive taxon system. Although many individuals may have had the appropriate early experiences (#1), and be in the appropriate state of stress (#2), triggering of a phobia or panic attack depends upon the precise experience of the individual during adult stress (#3).

According to this view, the first panic attack is formally identical to the first phobic reaction. Although the subjective content of panic differs dramatically from that of specific phobia, its source, developmental history, and abstract characteristics are no different from a specific phobia. A critical distinction between the two is their developmental trajectory. The critical experience leading to the first panic attack is assumed to have occurred at an earlier stage of development than that for specific phobia. At this earlier stage, associations are made between representations of quite primitive features, neither recognizable nor meaningful to the adult. By contrast, the critical experience leading to phobia occurs at a later stage in early life, when associations form between representations of object and event-like things in the environment, entities that can later be pointed to as the proximal source of the phobic reaction.

Thus, a panic attack and a panic caused by identifiable objects or events (specific phobias) are not distinct. There is little reason to suppose that any known characteristic of their development, or the individual’s subjective experience

awareness can affect cognitive processes, might anxiety itself not be instigated by unconsciously perceived cues? These data are congruent with the speculation that so-called spontaneous panic attacks may actually be attacks triggered by stimuli operating outside of conscious awareness” (p. 217).

11 More accurately, features of objects rather than objects as perceived by adults, patches of events rather than events as classified by human adults.

12 We do not have room here to fully explicate the idea that what serves as an unconditional stimulus for the human infant may be quite different than that for a human adult. Others have suggested that, “... physical and sexual abuse and/or severe episodes of rejection and abandonment ...” may serve as “... historical traumatic conditioning events ...” (Levis, 1987, p. 454). We see no reason that the fear expressed by a mother or a conspecific, properly detected by the infant, could not serve as an unconditional stimulus, thus providing a conditioning explanation (with appropriate constraints) of the "modeling" phenomenon found in monkeys (see, e.g., Hebb, 1946; Mineka & Cook, 1993; Mineka & Hamida, 1996).

13 Based upon a set of cognitive data (e.g., Matthews & MacLeod, 1986) and using a different theoretical approach to the problem, Chambless has arrived at a similar conclusion: “If danger cues outside of

awareness" (p. 35) argues, “... it seems that fear of strangers is but one example of specific fears that occurs to many stimuli at this point in time.” Before that time, we suspect, fears are associated with nameless stimuli or, more precisely, with only partially organized environmentally based features.

14 Rachman and his colleagues designated the first as “unexpected" and the second as "expected panic" (e.g., Rachman, Levitt, & Lopatka, 1987a,b).
of them, could serve to distinguish among them. It is, critically, the content of the phobia that separates it from panic, not the process that both produces it, and conveys its unique properties. The same sequence of events triggers both panic and phobias, distinguished only by the time in infancy during which the first step in the sequence is taken.

CONSEQUENCES: FROM THE FIRST PANIC ATTACK TO PANIC DISORDER

Few events could be more salient, unexpected, or puzzling than an initial, apparently uncaused, panic attack. Indeed, such an attack exhibits a range of characteristics described by Krull and Anderson (1997) as demanding a “problem based” explanation. The event is highly noticeable and appears potentially lethal. Under this and similar circumstances, human nature seems to demand that we generate hypotheses, models, and explanations (e.g., McArthur & Baron, 1983; Pennington & Hastie, 1991). We seem to do so by focusing on the salient, to-be-explained event (in this case, the panic attack), and then, using experientially based and culturally coloured memory, attribute cause to antecedent events. Most models generated in this way are adaptive; they help us predict and control critical aspects of our internal (e.g., emotional, cognitive) and external (e.g., social) worlds. Unfortunately, the method may be maladaptive. This is because it is logically flawed and subject to a multitude of cognitive biases. We must now attend to this flawed and biased process.

We view fully developed panic disorder as a part of a disregulated system. Ordinarily, the system involves adaptive perceptual, cognitive, behavioural, emotional, and physiological reactions (Jacobs et al., 1992). This is not true of a person who repeatedly experiences unexplained attacks of panic. Initially, a person who experiences a panic attack suffers much the same ordeal as does a person encountering a badly feared object or event. The difference, as we have noted, lies in the definition of object and event. In an initial panic attack, it is primitive features rather than objects such as insects or elevators, which serve as the basis for the conditioned reaction. This feature-based fear appears spontaneous because the features that trigger it, being primitive, might occur in a variety of environmental stimuli and settings. The victim cannot know what it is that is frightening. Thus, a critical issue in dealing with phobias and panic attacks concerns the delineation of the triggering stimuli. We expect that, when an individual experiences a psychological state such as fear, yet cannot identify any specific stimuli that precede it, that individual will embark on an intense search for the cause of the event—a search that will involve automatic perceptual principles, pre-existing knowledge structures, and a consuming, effortful, problem-based cognitive process based upon available perception and knowledge structures.

Krull and Anderson (1997) argue that such a process will be composed of two phases, each involving three steps. During the first stage (upon experiencing the first few unexpected panic attacks) we expect the person to notice the event, interpret it, and generate an initial explanation. It is difficult to miss a pounding heart, trembling limbs, sweating, and tingling extremities. Given that circumstance, immediate interpretations (e.g., I am having a heart attack!) and behavioural strategies (e.g., I must get to the emergency room now!) begin. Of course, if the individual “understands” that the pounding heart, shortened breath, sweating, and tingling extremities are due to ongoing exercise, then this catastrophic interpretation will not occur. If, however, these characteristics appear for unknown reasons, they are likely to be catastrophically interpreted as uncaused, internal, life threatening, and emotional (e.g., Clark, 1986, 1988). Moreover, these interpretations will depend at least in part upon experientially based, culturally constrained knowledge structures.

Suppose the person, as do many people experiencing an initial attack of panic, goes to an emergency room for diagnosis and treatment. Shortly after arriving in the emergency room evidence disconfirming the person’s original interpretation is forthcoming (e.g., the results of a series of not-inexpensive tests are negative). Because the initial explanation of the critical event is unsatisfactory, the process proceeds (e.g., Kruglanski, 1989). The person enters the second stage described by Krull and Anderson (1997), an effortful, deliberate, and cognitively expensive attempt to explain the target event.

A problem-based attempt to explain the target event consists of three components: Problem formulation, problem resolution, and satisfaction. People appear to formulate a problem using extant knowledge structures containing information about the target event and possible explanations for the event. Although for a person suffering unexplained attacks of panic, relevant knowledge and explanations may come from personal beliefs, attitudes, and memory, other primary sources of information (e.g., Anderson & Slusher, 1986) include professionals (e.g., those in the medical profession), acquaintances (e.g., “I had a friend who...”), and personal research (e.g., “self-help” literature). Indeed, some have noted that only after exhausting all these sources of information (and help), do individuals with panic disorder turn to mental health professionals for treatment (e.g., Jacobs et al., 1992). We expect this information, of course, to be subject to biases inherent in human information processing as it is incorporated into the problem formulation (e.g., Kahneman, Slovic, & Tversky, 1986).

When the person has formulated the problem he or she attempts to resolve it. People appear to integrate information collected during problem formation into a “best” explanation (Krull & Anderson, 1997). When a “best” explanation is found (using principles such as parsimony and
breadth coupled with ancillary information and estimates of the implications of these explanations, the explanation is accepted as satisfactory (e.g., Read & Miller, 1993). Unfortunately, as Krull and Anderson (1997, p. 4) note, "...the quality of an explanation is relative; people may be willing to accept a poor explanation if no better explanation is available."

Because there may be no satisfactory explanation for repeated unpredicted panic attacks, we suggest that a person attempting to explain the source of repeated panic attacks may never achieve the third and final portion of a problem-based explanation as described by Krull and Anderson (1997), that of satisfaction. According to their account, if an explanation is not satisfactory, then the explainer begins the process anew, seeking to reformulate and resolve the problem. Thus the person is caught in an effortful, deliberate, and cognitively expensive vicious cycle: Attempting to explain the target event. This cognitively expensive effort produces many of the characteristics now thought to be a part of the etiology of panic disorder.

McNally (1994) provides a comprehensive review of the best-known psychological aspects of panic disorder. Although each aspect has been implicated in the etiology of panic disorder, we shall make a slightly different claim. Staying close to our systemic orientation, we shall claim that although each of these factors are sufficient conditions for the maintenance and exacerbation of panic disorder, none are necessary components of its etiology or maintenance. Each of these factors, we shall claim, develop some time after and in response to, the initial set of panic attacks, panic attacks grounded in experience, governed by Pavlovian rules, and subject to characteristics produced by an anatomically and physiologically immature central nervous system.

Among the cognitive effects found to be disregulated in those diagnosed with panic disorder, McNally (1994) lists catastrophic misinterpretations of bodily sensations (e.g., Clark, 1986, 1988), persistence of catastrophic thinking (e.g., Seligman, 1988), anxiety sensitivity (e.g., Reiss & McNally, 1985), predictability and controllability (e.g., Mineka, 1985), sense of control (Barlow, 1988), expectancies (e.g., Barlow & Craske, 1988; Rachman, 1988), biases in information processing (e.g., McNally, 1990), interpretive biases (e.g., Mathews, 1990), attentional biases (e.g., Asmundson, Sandler, Wilson, & Walker, 1992), memory biases (e.g., McNally, Foa, & Donnell, 1989), and interoceptive acuity (e.g., Chambless, Capuco, Bright, & Gallagher, 1984). To his credit, McNally (1994, p. 135) asserts, "...it remains to be seen whether cognitive biases are causes or consequences of panic disorder. To determine whether they contribute to the etiology of panic disorder, researchers need to establish that biases precede the occurrence of panic." According to the present model, these well-researched cognitive factors are both cause and consequence of panic disorder; they are integral parts of a disregulated system that become sufficient eliciting conditions produced by a person's desperate attempts to explain a set of initial panic attacks.

This view helps us simultaneously understand why there is a high correlation between places or thought processes and panic attacks and why the cross correlation is far from unity. Hallmarks of the anxiety disorders are apprehension, worry, catastrophic thinking, and misperception even in the absence of panic (e.g., Beck, Emory, & Greenberg, 1985; Beck, Laude, & Bohnert, 1974; DSM IV; see Sokol, Beck, Greenberg, Wright, & Berchick, 1989, p. 712, for a different point of view). In addition, the content of catastrophic thoughts does not covary reliably with treatment success. Changes in catastrophic thinking may show marked fluctuations in content during therapy but show no detectable relationship to the progress of therapy. Catastrophic thinking may even continue unabated throughout successful cognitive therapy (e.g., Last, Barlow, & O'Brien, 1984, 1985; Last, O'Brien, & Barlow, 1985). The temporal relationship between negative cognitions and panic also show unusual characteristics with examples such as the following: "Cognitions continued to be negative following the panic attack, and only returned to a more neutral bias when the patient arrived back at the hospital" (Kenardy, Evans, & Oei, 1988, p. 477). The low cross correlation, the unreliable covariance, and the odd temporal arrangement between catastrophic thought and panic attack, of course, presents a major theoretical challenge to those who attempt to invoke apprehension, worry, catastrophic thinking, and misperception as primary causal agents in panic attacks (e.g., Argyle, 1988; Beck, 1988; Clark, 1986; McNally, 1990). In contrast, the present view incorporates these findings quite naturally.

It is our view that such cognitive activities are a part of, rather than a cause of, subsequent panic attacks. Thus, we would expect the victim first to notice the physical symptoms of an attack, and only then seek to account for its source. When the adult experiences a phobic reaction provoked by some unidentified stimuli, explanations will be sought, and found in some way. If panic regularly occurs in a particular context, (e.g., a shopping mall or on public transportation), a more serious misattribution may occur. Here, the victim might blame the place itself, the crowds, or the movement. If such misattribution does not occur, other candidates are present. For example, thoughts of impending doom are highly correlated with panic attacks (e.g., Rachman, Levitt, & Lopatka, 1987a, b). This can lead one to conclude that it was the thought itself that caused the panic. This is just the sequence of events that Wolpe and Rowan (1988), Hibbert (1984), and Ley (1985) reported. Although such attributions may enhance the panic attack, creating a vicious circle (Clark, 1986), they do not cause it.

Our systemic view encourages simultaneous interventions at the physiological, behavioral, emotional, and cognitive levels — without undue emphasis on any one. And
A FINAL COMMENT

We have, throughout this manuscript, emphasized the critical importance of taking neural development into account in thinking about the first panic attack. We have placed stress on the ways in which the brain is shaped during early life, the impact of this shaping on how an individual represents and experiences the environment, and the cognitive consequences of such representation. This too is part of Hebb’s legacy.

“How then does the earlier experience work? In the very first stages ... it operates to establish the perceptual elements ... These are the entities that make up more complex perceptions. Organizing such elements in the various sense modes would lay the foundation of all later responses to the environment. Secondly, there is a period of establishing simple associations, and with them conceptual sequences — the period in which meaning first begins to appear. Finally, the learning characteristic of the mature animal makes its appearance.” (Hebb, 1949, p. 117)

In this regard Hebb was, as usual, well ahead of his time. It is our view that a thorough exploration of the nature of early perceptual elements, and the simple associations they enter into, will help us to understand the genesis of a variety of psychopathological phenomena that have to date resisted such clarification. Inasmuch as the objects of our interest are quite obscure, this will not be easy. Hebb never said it would be easy.

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