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Summary

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These volumes record the deluge of facts concerning the hippocampus and related structures that has inundated the neurological and behavioral sciences in the past 25 years. Each reader can thus gather and organize for himself those data which are most relevant to his interests. We, as editors, felt that we would like to set an example and try to show how the book has enriched some of our formulations of hippocampal functions.

1. *Neuroanatomy Reconsidered*

There are aspects of the functional neuroanatomy of the hippocampal circuit which were either unknown to us or have become clarified by the evidence presented in this volume. In 1949 it became clear that the allocortex was surrounded by a belt of transitional tissue which was labeled "juxtallocortex" (Pribram and Kruger, 1954). These transitional areas had been given a variety of names: mesocortex, periallocortex, semicortex, etc. On the basis of the results of electrical and chemical neuronography (Pribram *et al.*, 1950; Pribram and MacLean, 1953), as well as the effects of resections of the transitional cortex on behavior (Pribram and Fulton, 1954; Pribram and Bagshaw, 1953; Pribram and Weiskrantz, 1957), the term "juxtallocortex" was chosen to emphasize the functional affinity of the transitional areas to the neighboring allocortical formations. This emphasis was necessary because some of these transitional areas were neocortical (relatively new in phylogeny) although *not* isocortical (ontogenetically true to the developmental sequence that characterizes the cortex of the convexity of the hemispheres). Until this evidence was obtained, it had been assumed that juxtallocortex should have functions akin to its neocortical neighbors covering the adjacent convexal surfaces.

In the opening chapter of Volume 1, Chronister and White review the anatomical facts regarding the juxtallocortical areas (they prefer the term

"periallocortex," which, however, was used in the earlier literature in a more restricted sense that did not include mesocortex and semicortex). Chronister and White now discern an additional surrounding region that they call "proisocortex," which is a novel formulation that warrants attention.

The intimate relationship between the juxtallocortical formations (cingulate gyrus, entorhinal cortex) and allocortex of the hippocampus is beautifully analyzed physiologically in the detailed and painstaking microelectrode studies by Vinogradova in Volume 2. The somewhat more remote relationship between the proisocortical formations and hippocampus is clarified by the equally prodigious and carefully analyzed experiments reported in Volume 1 by MacLean. Looking for inputs to the hippocampus from various senses, MacLean finds them to arrive reluctantly and by stages. He discovers that units are activated by sensory stimulation in juxtallocortex but *not* in the hippocampus—much to his disappointment, he states. However, taken together with Chronister and White's new delineation of the proisocortical ring surrounding juxtallocortex and allocortex, MacLean's findings fit the conceptualization that a cascade of systems degrades specific sensory input in stages until only some integral of sensory stimulation reaches the CA3 layer of the hippocampus. The nature of this integral is spelled out by Ranck in Volume 2.

MacLean's results can be related to yet another series of investigations. For many years neurophysiologists, led by Woolsey, were busy mapping sensory (and motor) projections onto the cortical surface. The functions of the mirror-image representations (somatosensory, auditory, and visual areas II and III) have until now remained a mystery, but they may be related to ways in which sensory signals are cascaded for future processing by the hippocampus.

2. *Computation in Fast Time*

How then does the hippocampus do its thing? Two additional facts are of interest before any formulation is attempted. One is a "wipeout" due to basket cell activity which occurs every few milliseconds—not just in the presence of input but even in its absence. Andersen, describing in Volume 1 his elegant intracellular recordings, points out that

> A remarkable finding of all investigators using intracellular recording in the hippocampal formation is the ubiquitous hyperpolarization associated with inhibition of cell discharge which follows excitation of the cell from *all* afferent sources studies so far. . . . This inhibition has a slightly longer latency than that of the excitation . . . and can be recorded as a baseline even with excitation.

These inhibitory phenomena are reminiscent of those described for the cerebellum, whose architecture is also of a rather simple nature relative to the complexities of isocortex. However—and this is the second fact of interest for us—differences in function are also manifest. Despite the immediate inhibition produced by the hippocampal basket cells, Vinogradova finds in the unanesthetized preparation long-lasting changes (lasting several seconds) in the firing patterns of hippocampal

neurons after afferent stimulation when measured extracellularly. Over half of these changes are in the direction of inhibition, but 40% of the cells show long-lasting excitation.

How can we reconcile these two apparently contradictory findings—the intracellularly recorded inhibition and the extracellular recording of long-lasting inhibitory *and* excitatory changes? Although quantitative data are not available, it is plausible that the basket cell hyperpolarization builds slowly over *successive* inputs to the granular cell layer of the dentate gyrus. This could account for the progressive decrementing (habituation) of both the inhibitory and excitatory outputs recorded extracellularly. In the cerebellum the inhibitory reaction is immediate and overwhelming. It quickly wipes the "slate" clean between successive inputs. In the hippocampus hyperpolarization builds more slowly, necessitating a succession of inputs before output becomes blocked. Andersen's observations of a prolonged baseline of hyperpolarization are consonant with this view. Further, because of the degradation of sensory specificity the hippocampal circuit appears to be processing primarily some general characteristic of the stimulus configurations as opposed to the differentiated sensorimotor patterns that distinguish the functions of the primary projection systems.

Something of the nature and functions of this processing is learned from the important contribution reported by Lindsley and Wilson in Volume 2. In their chapter, mechanisms are described which provide a means for the integration of the previously processed sensory signals arriving from juxtallocortical regions with those originating in the regulatory systems of the brain stem. Lindsley discerns two such major input systems. One arises in the anterior mesencephalon (locus coeruleus, nucleus reticularis pontis oralis, ventral portion of the mesencephalic tegmentum, and nucleus gigantocellularis), while the other originates more posteriorly (raphé nuclei and nucleus pontis caudalis). The anterior system traverses the medial hypothalamus by way of the dorsal longitudinal fasciculus (of Schütz), while the posterior system reaches the hippocampus by way of the lateral hypothalamic region and the medial forebrain bundle. The dorsal longitudinal fasciculus has been shown to carry noradrenergic tracts (Swanson and Hartman, in press), while the medial forebrain bundle is composed of serotonergic and dopaminergic tracts.

The dopaminergic fibers of the medial forebrain bundle, which probably include those originating in the substantia nigra, have been implicated in many different forms of behavioral change, including locomotor activity, stereotyped behaviors, and some appetitive behaviors, including feeding. Lindsley's studies have related stimulation of the dorsal longitudinal fasciculus (medial hypothalamus) to hippocampal θ rhythms (4–8 Hz) and stimulation of the medial forebrain bundle to the production of hippocampal desynchronization.

Further localization of the two hippocampal systems comes from Livesey's stimulation studies reported in Volume 2. Stimulation of the dentate layer (which receives cortical input) produces effects on behavior different from those produced by stimulation of the CA1 output layer. The differences in behavioral effects are attributed to Ranck's modulatory mechanisms, which lie between.

The classical contribution by Ranck in Volume 2 takes these systems into the

hippocampus proper by distinguishing with microelectrode recordings made in the awake moving animal, two groups of neurons. A small population (5%) fires if and only if regular θ rhythm is recorded. Another larger population (95%) of cells shows no simple relationship to θ and fires with complex spike trains when the hippocampal rhythms are desynchronized. The θ cells are distributed rather widely in the hippocampus and are probably short-axon Golgi type II (basket) cells, while the non-θ-related (complex spike) cells are seen mostly in the pyramidal and dentate granule cell layers. Ranck suggests that the θ cells are inhibitory interneurons.

The picture emerging from these studies is one in which the representation of sensory input arriving in the proisocortex is degraded in steps through juxtallocortical regions. This altered input reaches the hippocampus, where it is juxtaposed to at least two other inputs of brain stem origin. One of these systems produces synchronized electrical activities in the hippocampus in the θ range of frequencies, whereas the other acts to produce a desynchronized state. Both act on the inhibitory mechanism, one enhancing its activity, the other diminishing it. The inhibitory mechanism consists of the "θ cells," found by Ranck, which are scattered throughout the hippocampus and when activated impose a "pulsed" output on the complex spike cells that make up the vast majority of cells in the pyramidal cell layers of the hippocampus.

At the input layer (dentate and CA3), complex spike mechanisms are, according to Ranck's data, concerned with appetitive behaviors; at the output layer (CA1), they are concerned with "consummatory," "match–mismatch" processes. Ranck suggests that this difference results from a convergence at CA1 of (1) fibers from CA3 cells that are generally responsive in all appetitive situations with (2) fibers from other cells of CA3 that are active only when reinforcement occurs after an appropriate response. Neither appetitive nor consummatory behavior takes place when gross θ activity is being recorded. According to the reports that make up Part III of Volume 2, attentional (search) and intentional (nonhabitual "voluntary" motor) processes are correlated with the generation of θ rhythms. In general, these processes involve reorganization of current brain states. Since θ rhythms are also found during REM sleep, there is a suggestion that reorganization can also occur during sleep (Winson, Volume 2).

Pribram (1971) has distinguished the organization of appetitive–consummatory and other well-ingrained habitual behaviors which depend on the basal ganglia (and the nigrostriatal system) from attentional–intentional behaviors which depend on the hippocampal and cerebellar circuits for their controlling operations. Isaacson (1974) emphasized the same distinction by attributing instinctive and well-trained behaviors to the "reptilian complex" of the brain (as the term was used by MacLean, 1970), which includes the basal ganglia and associated brain stem systems. Appetitive–consummatory and habitual behaviors are regulated primarily by closed-loop, homeostatic, feedback mechanisms. Attentional and intentional behaviors are characterized by parallel processing, open-loop, feedforward control systems. Habituation can be conceived as a change from an "or" gate state (in which responses of complex spike cells are activated by any of a variety of inputs occurring at different

times) to an "and" gate state (in which a response depends on the convergent action of inputs). Essentially this means that in the presence of θ cell inhibitory activity, the complex spike channels are kept independent of each other. The system is maximally sensitive. Input systems can therefore act in parallel.

The suggestion emerges that the hippocampus functions to determine whether appetitive–consummatory processes should proceed in their habitual manner or whether novel, unfamiliar inputs have occurred which must be attended to. If they have occurred, behavior must become intentional—i.e., programmed to evaluate new conditions. In such cases, attention must be given to a variety of novel inputs which do not directly relate to familiar appetitive–consummatory processes.

The hippocampus can be conceived to compute in fast time—i.e., ahead of what occurs in real time –the likelihood that an appetitive–consummatory act can be carried to completion, given current environmental conditions. If that likelihood is high, the operation in the hippocampal desynchronized mode will continue, and the hippocampus will be relatively insensitive to new input since it is operating in the "or" gate state. If the likelihood is low because some novelty has been sensed, the activity of the hippocampus will be switched to the "and" gate mode, it will become sensitive to input, and attentional and intentional behavior will become manifest.

3. *On the Question of Response Inhibition*

How do we relate this knowledge to the results of damage to the hippocampal formation in animals and man?

First, as we shall see in the next section, any simple, long-term memory consolidation hypothesis of hippocampal function based on the initial findings with human subjects has become untenable in the light of subsequent analyses. Unfortunately, this hypothesis is still held by the majority of people not actively involved in hippocampal research.

Second, we must also note that any simple inhibition-of-response hypothesis of hippocampal function based on the initial findings with animal subjects has also become untenable in the light of subsequent analyses. Thus the intransigent irreconcilability of the human long-term memory loss with the animal disinhibition literature that has plagued understanding of hippocampal function need delay us no longer.

Instead, we are faced with a series of hypotheses covering some middle ground between consolidating long-term memory and the execution of behavior. In the electrophysiological chapters of this volume, these hypotheses become grouped under the rubrics of attention and intentional (or voluntary) behavior. Deficiencies in consolidation can become attributed to failures in attention; and disinhibition can be seen as the consequence of a loss of intentional capability. These changes may be viewed as merely semantic, but the new terminology is in fact derived from different data and enriches our understanding. Let us look more closely at this enrichment.

We first turn to the analyses of hippocampal function in terms of behavior *per se*. This analysis leads directly to intentional behavior. As Weiskrantz and Warrington note in Volume 2, the inhibition–disinhibition dimension in behavioral terminology is akin to the interference hypothesis in memory theory. They do not make clear, however, the steps by which such an identification occurs. These steps may be outlined as follows. The early disinhibition hypothesis foundered on the finding that, in animals, the capacity for go/no-go alternation and object reversal performance was preserved following hippocampal destruction despite severe impairment of right–left alternation and of spatial reversal performance (Pribram, unpublished data; Mahut, 1971; Mahut and Zola, 1973). Further, Douglas and Pribram (1969) showed that an instrumental response to distractors could be dissociated from the increased reaction times produced by distractors in a well-established response sequence. Hippocampectomized subjects continue to show the attentional effects of distractors even when their instrumental responses to those distractors are absent. This effect is obtained only when the animals are performing well-established behavior sequences (see Isaacson, 1974).

Further, Black reports in Volume 2 that the hippocampal θ rhythm is manifest in curarized, paralyzed subjects in situations where the rhythm was previously observed to be correlated with overt behavior: both results make it necessary to speak of hippocampal function in intentional terms rather than in terms of response disinhibition. Talking about such internal processes will produce outcries from behaviorists (such as Vanderwolf, Volume 2), but even they have had to resort to such terms as "voluntary" to cope with their data.

4. On the Question of Memory

The consolidation hypothesis for the formation of long-term memory was based on the inability of patients with medial temporal lobe lesions to remember events which had occurred subsequent to surgery (Milner, 1959). As Weiskrantz and Warrington point out, more recent evidence has shown that the deficit is not so simply described. Their analysis implicates defects in retrieval rather than storage mechanisms. They suggest that ordinarily recognition may depend on a relatively unconstrained (although not unorganized) retrieval process (e.g., Anderson and Bower, 1972) and that after medial temporal resections the process becomes inordinately constrained. This is borne out by an examination of H. M.—the most celebrated of patients with bilateral medial temporal resection (see Milner, 1959). The following hitherto unpublished utterance was recorded from H. M. by Marslen-Wilson in response to the question "What is it like to remember things?"

> You run through it, and you find out what's good, but you go through them all again and that, because you know which one is good . . . but you go through them all, to get the bad ones too . . . instead of get the good ones right off.

Note the repetitions, which David McNeil has analyzed as follows:

Concepts:	(Act) (Search)	3 times
	(Act) (Repetition)	2 times
	(Retrieval) (Target)	3 times
	(Search) (Memory)	3 times
	(Bad) or (Good) (Target)	5 times
	(Search) (Total)	2 times
Relations:	*not-prevent* or *prevent*	3 times
	has-extent	2 times
	has-appraisal	5 times
	has-number	3 times
	has-outcome	3 times

McNeil (personal communication) concludes that

> The impression H. M. gives is that he can manage a complex string of words perfectly well, but only by repeating configurations of concepts over and over. Such repetitiousness could reflect poor control of attention in that he apparently can't focus in an orderly manner on the concept within his field of attention; that, in fact, seems to be what H. M. himself is trying to say in this sentence.

In animals, an attention hypothesis was initially based on a series of experiments with hippocampectomized monkeys which showed deficiencies when previously reinforced and nonreinforced cues were matched against novel cues (Douglas and Pribram, 1966). Somewhat simpler versions of this experiment were later performed by Gaffan (1972, 1974) and have been discussed extensively by Weiskrantz and Warrington in Volume 2. Gaffan's results are stated in the language of memory theorists: e.g., certain aspects of recognition are impaired but not recall. Douglas and Pribram's results are discussed in the language of mathematical learning theory, and attention to previously reinforced and currently nonreinforced events is deficient. Yet both discussions emphasize a disturbance of reactions in a novelty-familiarity dimension.

Insensitivity to the novelty–familiarity dimension can confer a crippling constraint on recognition. Ulrich Neisser (1974, personal communication) and Vinogradova (Volume 2) have independently suggested that a match–mismatch comparison and a report thereof must be processed separately in order for an input to be recognized as familiar. The amnesic patient who can instrumentally correctly respond to prior experience while reporting complete unfamiliarity appears to furnish proof that the two processes (matching and appreciation of familiarity) can be dissociated.

Matching and familiarity are usually discussed by memory theorists in terms of encoding and association. Weiskrantz and Warrington in their chapter detail the evidence that encoding is relatively intact in amnesic patients and that the associative processes interfered with by hippocampal lesions are *contextual* in nature. When the appropriate context is provided, patients with hippocampal damage remember remarkably well. Piercy and Huppert (1972) have confirmed and extended this finding to a large range of variables determining context memory. Pribram (1971), on

the basis of his animal brain extirpation experiments, distinguished context-free and context-dependent processes. Context dependency is defined by behaviors which must be based on (recurring) changing events in a particular situation rather than on invariant events, which determine context-free processes. Alternation and reversal tasks are examples of situations demanding context-dependent behaviors. The hippocampal circuit, together with the remainder of the frontolimbic brain, was identified as the neural substrate for context-dependent processes.

Successful context-dependent behavior depends on loosening the constraints that operate at the moment the behavior becomes required. Flexibility rather than perseveration becomes critical. Attention must be given to a wide range of spatial (cognitive maps) and temporal (plans) factors. In the rat and the cat, with their large dorsal hippocampus subjacent to and intimately connected with the somatosensory mechanisms of the brain, such loosening of constraints could free them from the overuse of spatial cues ("maps" in the terminology of O'Keefe and Nadel, in press). In most primates, the dorsal hippocampus becomes less significant, and the hippocampal circuit becomes more closely associated with the visual and auditory modalities. Thus in the primate literature there is less emphasis on the relationship of hippocampal function to spatial maps, the preferred cues of rodents, and a greater concern with a loss of visual imagery and semantic encoding. Nevertheless, the special hippocampal contribution to behavior which allows the interruption of predominant plans and strategies would still apply. The differences in results obtained between laboratories (New England vs. Old England, as represented in the last two chapters of Volume 2) may, in fact, depend on differential pathological involvement—or, more likely, by the testing procedures—on the imagery (right) or semantic (left) hemisphere of the human brains being tested.

In short, as concepts become more precisely defined, one can discern a considerable convergence between the analyses of hippocampal function in terms of memory and in terms of attention. This convergence also applies, as noted in the last section and by Weiskrantz and Warrington, to the analysis of the human defect in terms of hypothesis formation (Isaacson and Kimble, 1972) and the execution of intentions or plans (Miller *et al.*, 1960; Talland, 1965).

5. *Intention, Attention, and Effort*

What is the relationship between intention and attention as it is influenced by hippocampal function? The key to answering this question lies in the observation that the effects of hippocampal lesions in animals show up most clearly when shifts in behavior are necessary because the environment has become uncertain. Thus animals with hippocampal lesions tend to persist in strategies of maze learning (Kimble and Kimble, 1970) and discrimination problems (Isaacson and Kimble, 1972) and have difficulty in shifting choices (Kimble, Volume 2). This difficulty in shifting choices has been related quantitatively to the hippocampectomized animals' insensitivity to errors reported by Pribram and Douglas and also by Douglas *et al.* (1969).

The processes underlying any shift in behavior have been shown to involve both

attention and response factors. Sutherland and Mackintosh (1971), as did Lawrence (1950), have produced an analysis of discrimination learning which involves both sensory "analyzers" and "response attachments." The "analyzer" has aspects which are related to attentional and motivational processes, and could be interpreted to include hypotheses held by the animals about their environments. The "response attachments" refer, in part, to associations formed between responses and particular aspects of the environment as coded (decoded?) by the analyzers. The analysis of discrimination learning and reversal has been extended further by Olton and his associates (Olton, 1973; Olton and Samuelson, 1974). They point out the need to have at least two types of response modification mechanisms: a response-suppression mechanism and a response-shift mechanism. They indicate that response suppression always precedes response shifts but that under conditions of stress or of frustration in intact animals (Maier, 1961), or after hippocampal destruction (Olton, 1972), animals can give clear evidence of response suppression without exhibiting a subsequent shift in the manner of responding.

Olton's conclusions that response suppression is intact but the response-shift mechanisms are deficient after hippocampal destruction help explain another difficult problem in regard to human memory. The results of Weiskrantz and Warrington show that amnesic patients, like H. M., do have the information available but do not respond appropriately because of proactive interference. The correct response cannot be made unless appropriately prompted. When asked, the patients report that they remember *nothing* pertinent to the test items. Neither the test items nor the items causing the interference are remembered. The patients have intact response suppression, but faulty response shift mechanisms.

This line of analysis leads to the suggestion that whenever a shift in strategies is required in order to execute an intention (i.e., to make a choice) the hippocampal circuit becomes most important. Attention theorists have performed a number of experiments relating the "paying" of attention to performance. They speak of the "effort" involved in attentional shifts (see, for example, the volumes on attention and performance: Kornblum, 1970–1973; Kahneman, 1973). Pribram and McGuinness (1975) in an extensive review relate this body of evidence to that concerning hippocampal function.

Their analysis discerns the following neural systems to be involved in intentional and attentional processes. First, there is an "arousal system" which deals with *phasic* reactions to input and centers on the amygdala. Second, there is an activation system concerned with *tonic* readiness to respond that centers on the basal ganglia. Finally, arousal and activation must become coordinated. Pribram and McGuinness argue that the hippocampus plays an important role in this coordination.

When considering the possible roles of the hippocampus in regard to behavior, we must consider what the coordination of arousal and activation means and what neural mechanisms are involved. If a tonic readiness to respond is associated with the mechanisms of the basal ganglia and perhaps with its associated catecholaminergic and cholinergic systems, then we must ask how the hippocampus influences these systems. Furthermore, if phasic reactions are mediated by serotonergic (and other) systems, we again must ask "how?"

In regard to the tonic activation of behavior, drugs like amphetamine which enhance the activity in catecholaminergic systems increase locomotor activity while at the same time reducing the exploration of novel objects in the environment (Robbins and Iversen, 1973). As the amount of amphetamine given the animals is increased, locomotor activity becomes less and gives way to stereotyped reactions of various sorts. Schiorring (1971) indicates that fewer and fewer types of behaviors become facilitated as the dose of amphetamine becomes larger and larger. There are reasons to believe that the elicitation of stereotyped behaviors by amphetamine is due to its effect on dopaminergic systems.

This suggests an association of the activation system with dopamine projections (basal ganglia) and the association of activation with readiness to perform well-established acts while limiting responsiveness to nonsalient input.

The role of serotonin systems in the regulation of arousal is somewhat more difficult to establish. There is, however, evidence that there is a monosynaptic projection from cells of the raphé to the amygdala which contacts cells in the amygdala whose activity is inversely related to phasic arousal (Jacobs, 1973). Administration of the precursor of serotonin affects these amygdala cells in the same way as stimulation applied to the raphe. Furthermore, depletion of serotonin by *p*-chlorophenylalanine (PCPA) does not greatly affect locomotor activities (see review by Weissman, 1973) nor does intracisternal administration of 5,6-dihydroxytryptamine in young animals (Lanier, Schneiderman, and Isaacson, unpublished observations). It is of interest, moreover, that serotonin depletion by PCPA has been reported to retard the acquisition of a passive avoidance response despite the drugs's well-known ability to produce an increased sensitivity to painful stimulation (Stevens *et al.*, 1969). Finally, there is some evidence that reactivity to novel environmental objects is enhanced by the serotonergic depletion produced by PCPA administration (Tenen, 1967; Brody, 1970). In general, therefore, the serotonin system can be thought of as serving arousal as defined above: a role reciprocal to that of activation of the readiness system.

In some ways, the effect of bilateral hippocampal destruction is to produce behavioral changes similar to those found after the enhancement of the catecholaminergic systems and the reduction of effectiveness of the serotonergic systems. Yet this is an inadequate summary of the changes. While studying behavior in a DRL_{20} task, Schneiderman and Isaacson (in preparation) have found that animals with hippocampal damage are *less* subject to improvements produced in intact animals by drugs which reduce catecholamine activity and by drugs which enhance cholinergic activity (physostigmine). In related studies, animals with hippocampal lesions exhibit an altered sensitivity to *d*-amphetamine on an FR6 operant schedule (Woodruff and Isaacson, in preparation).

These observations suggest that among the effects produced by destruction of the hippocampus are alterations in the reactions of the animals to changes both in the monoamine systems and in cholinergic systems. As noted earlier, the shift from well-established feedback-controlled appetitive–consummatory behavior to the development of new ways of responding may depend on the alteration of hippocampal func-

tion. This shift has a dual character. It has an attentional aspect in that a greater range of stimuli can be sampled and a motoric aspect in that new responses can be undertaken. These changes require "effort."

6. *Conclusion*

There is, of course, much more to be learned from the chapters in these volumes. Each in its own right brings together a wealth of data and displays the inconsistencies and unexplained effects which determine the direction that new research must take. In this final summary only the ruminations of a consistent sort have been dwelt on and these can be summarized succinctly: It is proposed that the hippocampal circuit is sensitive to the likelihood that a currently familiar situation will remain familiar. This is accomplished by sets of (complex spike) cells which compute correlations between the outcomes of recurring situations. When there is an absence of correlation, θ cells become active and the then-operating constraints on attention (arousal) and intention (readiness) are loosened, making possible their reorganization. Such reorganization takes effort to accomplish, the effort of coordinating arousal and readiness. Lack of coordination becomes manifest in the disabilities of attention, intention, and memory now described in such detail by researchers on hippocampal dysfunction.

New problems immediately surface while the older ones are hardly solved. How does one test for a loosening of constraints? And how does one measure cognitive effort? What *is* the relationship between familiarity, recognition, and recall? Just what brain mechanism makes it possible for instrumental skills to become isolated from the larger awareness that leads to the recognition of familiarity? Does this mechanism produce a critical difference in brain connectivity which then characterizes such feedforward operations as attention and intention? How, we may ask, does the hippocampal circuit, one of the oldest in the vertebrate forebrain, become involved in producing this critical difference, if it occurs? Thus the enigma of hippocampal function, although slowly yielding its wrappings, as yet has lost none of its appeal or challenge.

7. *References*

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