SPACE-TIME, ORDER, and HIERARCHY

in FRONTO-HIPPOCAMPAL SYSTEM:

A NEURAL BASIS OF PERSONALITY

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ABSTRACT

We present a model of hippocampal and frontal functions based on neuropsychology, brain imaging and neurophysiology. The type of memory register supporting the functions of these two systems and their relations is fundamental to the understanding of the nature of information processing they perform. In particular, a clear delineation must be drawn between active and "dormant" forms of memory respectively supported by post synaptic potentiation and synaptic facilitation. Nevertheless, there is a continuous transition and a mutual modulation between these two forms of memory. Further, the classical assimilation in particular in Neural Networks modelling of active form to short term memory and dormant form to long term memory is not tenable anymore. There is in particular a significant overlap between the two forms in the intermediate time range: the active form can be in different ways extended beyong the very short range. Symmetrically, the synaptic facilitation supporting the dormant form can take place very rapidly in particular in the Hippocampus system (Hs). Some aspects of the extension of the active form into the intermediate range is thought to be at the basis of temporo-spatial processing such as sequence learning in Working Memory (WM). Further, the interplay between the two forms as well as between the two systems Hs and Prefrontal cortex (Pc) helps to explain both WM operations and Long Term Memory (LTM) consolidation. In the paper, we try to compare and contrast the respective functions of Pc and Hs in particular in WM functions, mainly during temporo-spatial processing. We present a model that integrates in the same architecture a single mechanism for places learning and recognition and also for timing and ordering of sequences of events.

1 INTRODUCTION

Personality is to a large extent a characteristic of human primates, in the same way that language is. It results indeed from a unique combination of higher order brain functions including an explicit historical memory of the past, and at the same time, the ability to make plans, to change goals, to adapt strategies and therefore to project into the future. Both functions are based on the perception of a temporal dimension, or at least of an ordering of sequences of past or future events, in the field of consciousness. This field of consciousness itself, or its extension in working memory (WM), can be considered, from a neurophysiological point of view, as the embodiment of the present. In the past decades, the anatomical and structural bases of these functions have been more and more precisely delineated. In particular, hippocampal system (Hs) has been established as the support for the acquisition of explicit or declarative historical memory. Prefrontal cortex (Pc) could bring this temporal function one step further. Indeed, it is not so much the specific repository of learned past sequences of events, a function it could share with other cortical structures such as temporal and parietal cortices. More specifically, it emerges as the elective site for planification, intentionality, motivation and goal propagation, and therefore the structure where the hierarchical ordering of the sequences of cognitive or motor events takes place. More importantly, this planification is not limited to externally-elicited behaviors, but includes self-initiated endeavours founded on internal motivations or "willed" actions. These higher order brain functions can be considered as the highest expression of creativity and personality, in so far as they truly express field independence in behavior, the neurophysiological counterpart of the controversial philosophical construct of freedom. In "physical" time, present is an elusive reality caught between time-gone and time-to-be. Yet, in the time experienced by the mind, this present supports the field of consciousness, and forms the building blocks of our personality. The more elaborated the building blocks, the more sophisticated will be the whole construction. The brain has evolved a solution to this elusiveness of the present, that we could name working memory (WM). WM can be defined as an unique capacity to maintain information for an extended duration, and at the same time to process this information at any order of complexity during task performance. As such, it can be considered as an extension of the present. This WM is the brain function which makes the junction between past and future. Indeed, by its capacity to extend the duration of instantaneous events, it operates to link sequences of events together. Most investigations have emphasized the controlled aspect of WM. Not surprisingly, the volitional support of this function has been located in the prefrontal and temporal cortices. In this paper we provide neuropsychological and physiological evidence for a dual aspect of this function, which has been overlooked, namely an automatic uncontrolled face of WM, presented as one of the slave systems of the frontal executive. The main support of this automatic WM could be the hippocampal system. The integration and novelty detection capacities of the hippocampus (Carpenter & Grossberg, 1993; Denham, et al 1996) are twin functions which help both to create a stable state and to delineate transitions between states. They allow the construction of a stable representation of the environment and also the linking together of sequences of events. Symmetrically, by its capacity to reactivate and reenact memories, Hs provides the cortex with the capacity to maintain together in the field of consciousness, clusters of logically related events, and therefore, gives to Pc in particular the possibility for an hierarchical ordering and linking of full sequences of motor or cognitive actions to come.

The importance of prefrontal cortex as a support of personality is evident from the symptomatology of patients with a prefrontal syndrome. It is largely a consequence of perturbation of most of the higher integrative cortical functions such as judgement, reasoning and motivation, and degradation of some part of the LTM stores and the controlled aspect of working memory. These perturbations together put familial, professional and social life in jeopardy. Conversely, it is not obvious on the basis of superficial observation, that hippocampal lesions induce a deep disturbance of personality. In particular, there is no dramatic extended retrograde amnesia. Nevertheless, three decades of neuropsychological observation have made patent that personality disturbance is hardly less than after a frontal lesion, at least in cases presenting a total loss of Hs functions. Anterograde amnesia (the incapacity to acquire new declarative or explicit memories) was emphasized in the exploration of these patients. From these results was inferred the fundamental function of the hippocampus in the process of LTM consolidation, but not in LTM storage. These last functions were instead devoted to the cortices. From there, a logical step was to explore the hippocampus-cortical relations. Hippocampus receives information from and sends it back to the totality of the cortical mantle.

Nevertheless, a specially close relationship is established with the prefrontal cortex. The cooperation of the two systems in such diverse functions as working memory, rule formation, temporo-spatial processing is so intricate that it is often difficult to disentangle the specific contributions of the two systems. In this article we make the assumption that some of the most elaborated functions classically attributed to the prefrontal cortex, such as working memory (WM), sequence ordering, timing, novelty detection, are in fact based on a strong memory and computational support of the hippocampus, and then further elaborated in the prefrontal cortex. From this perspective, we do not consider the relations between the two systems as symmetrical. We rather think that the prefrontal cortex function is more dependent upon the integrity of the hippocampal system rather than the reverse. Accordingly, we first explore the hippocampal contribution to WM. We exclude the function of LTM consolidation. We consider this WM function of the hippocampus, on the basis of neuropsychological evidence, as the foundation of some of the higher order functions attributed to the prefrontal cortex.

In both Pc and Hs WM capacity is supposed to be responsible for the processing of order and time, and some aspects of spatial processing such as the building of maps and plans. In spite of this apparent communality of function, in particular for time and space processing, we emphasize the functional specialization and complementarity of the two structures:

- 1-Transient intermediate memory registers in Hs compute auto-and hetero- correlation and are suited for fusion of data on an intermediate range (of the order of minutes or more), and therefore allow for match-mismatch comparison on a window of time of this order of magnitude. Further, fast learning takes place in the hippocampal synapses, at the limit in one trial. These capacities together make the Hs ideal for the fast and transient learning of temporal sequences (Banquet and Contreras-Vidal, 1992a, b; 1993a, b;1994) or the multiple views of a global scene (Gaussier & Zrehen 1994, 1995, Gaussier et al 1996, Gaussier et al 1997a,b).
- 2- Complementarily, the activation and the propagation of goals at Pc level, under the influence of sub-cortical structures like the amygdala, in particular, endows Pc with the control power to design goal-oriented, hierarchically ordered sequences of actions (Zrehen & Gaussier 1997). The links of the Pc structures with different subcortical structures give Pc the possibility for both changing goals as a function of the context (link to Hs) and selecting the appropriate programs for these goal implementations (links to the basal ganglia). Learning there is slower than in Hs, and therefore needs either repetition, or the mediation of Hs. Symmetrically, just as Hs input-output is in direct relation with perception and cognition, the Pc input-output is directly connected to cognition and action. Due to this orientation to action, and also to its LTM capacity for storing sequences, Pc is the most plausible site for recombination of novel sequences of events on the basis of previous learning and present context, and, therefore, the seat of creativity.

2 HIPPOCAMPAL FUNCTION: An EXTENDED VIEW

Combined neuropsychological and biological evidence suggests a fundamental but selective role of the hippocampal system (Hs) in some forms of learning. Hs is necessary for rapidly (one exposure at the limit) forming declarative, explicit long- term memories (Banquet et al. 1997) while it appears to be unnecessary for the progressive acquisition of procedural, implicit memories. Recall of previously acquired declarative memories becomes gradually independent of Hs itself, suggesting a graded process of consolidation of traces which would be stored in another structure, plausibly cerebral and/or cerebellar cortices.

In the study of declarative explicit memory and WM, and particularly of the role of Hs in this type of memory, human neuropsychology leads animal neurophysiology. This unusual state of affairs raises the problem of the transposition to the animal domain of concepts specifically coined for human cognitive functions. Integrating in one single model concepts from neuropsychology and animal neurophysiology implies the implicit assumption of a continuity or even similarity (but certainly not identity) between memory processes taking place both in human and nonhuman primates or even lower order species.

o Anterograde/Retrograde Amnesia:

With this caveat, most authors agree that a major milestone in memory research was the report by Scoville and Milner (1957) of a dramatic but selective impairment in memory consecutive to a bilateral ablation of hippocampus and related structures in medial temporal lobe for the sake of an otherwise untractable epilepsy. This type of memory impairment in the patient HM contrasted with the preservation of skill learning and priming effects, and more broadly all the capacities labelled as procedural, implicit memory (Schacter et al., 1993). Most authors draw two conclusions from these results: First, some (declarative) forms of memory are initially stored in Hs, and then gradually transferred from there to other more permanent sites of storage, as neocortex. Second, other (procedural) forms of memory are directly stored in cortical areas. These theories grossly capture the gist of neuropsychological results. But in some sense they are partially wrong. Progress mostly in neurophysiology, but also in neural imaging and modelling, allows for more precise statements about the locus and the nature of stored information, in spite of the fact that the precise modalities of consolidation of these types of memory still remain a mystery.

o Hippocampus: a Link-operator Store and a Multirange Buffer

In particular, despite the contention of many neurophysiologists (O'Keefe and Nadel, 1978; Burgess, Recce & O'Keefe, 1994; Horel, 1994) and also some modellers we will argue that Hs does not " play a central role in the primitive storage and recall of the content of specific episodes and events...". Only the connectivity or "link operators" between compressed hippocampal representation of cortical activation patterns are transiently stored in Hs, and secondarily transferred and developed in the cortex under Hs control. Place cells in the rat and view cells in the monkey are a typical illustration of these processes of temporo-spatial correlation- integration that take place in Hs and lead to a highly symbolic representation of the surrounding world. Yet, the full-fledged memory traces are initiated and finally stored at the cortical level. Cortex is the alpha and the omega of our souvenirs. There is no need and no capacity for transfer and storage of the full traces in Hs. Preliminary evidence also suggests that even if procedural memory does not rely on Hs for its consolidation, it nevertheless implies complex cortico- subcortical circuits involving in particular basal ganglia whenever motor responses are implicated in the learned processes.

Whatever the cortico-hippocampal mechanisms involved in long-term consolidation of declarative memories, experimental results suggest that the role of the Hs extends far beyond that of a transient LTM store, for the time required for cortical trace consolidation. It seems to be implicated even during the very first wave of cortical processing triggered by stimulus input.

Even in the simple role of witholding and buffering information there is neuropsychological evidence from amnesic patients that Hs is already necessary in the short-term range, as far as information exceeds the STM span. This should not be surprising since the activation lag of the Hs compared to primary cortical areas in response to an external input does not exceed one or a few hundred milliseconds. A strong conclusion, in consequence, is that both systems process in parallel and interactively. Similar type of evidence argues in favor of a crucial role of Hs in the intermediate range as a WM buffer.

o A Unitary Mechanism Supporting WM and LTM Consolidation

Its multirange temporal capacity makes the Hs act as a buffer that can reenact activation patterns of information at cortical levels, not only during the lengthy process of LTM consolidation, but also when functioning as an intermediate (minutes time-scale) register supporting WM, during the moment to moment operation of current tasks. This last hypothetical function is conceptualised in the model as an automatic working memory. These two proposed functions are -first complementary, the process of LTM consolidation being engaged only if WM processing has transformed a short-lived trace to a transient LTM trace; -second, they are based on identical, or at least similar physiological processes, namely reinstatement or reenactment of electrical patterns of cortical activity either spontaneously or in reaction to a cortical cue. This unique process allows the network activation, according to its locus of initiation, either to trigger buffering and rapid learning of information in hippocampal subsystems (if the focus of activation is first cortical) or to reactivate cortical patterns, and therefore reinstate recent memories (if the initial focus of activation is endogenous in the hippocampus).

These processes of reactivation of cortical activity patterns, or reenactment of recent memories, directly derive from the capacity of the Hs to function according to two distinct, complementary modes: -first in a read mode, when it registers and processes external, cortical information; -then in a print mode, when it "endogeneously" or reactively reinstates the corresponding patterns of activation either locally in the hippocampal subsystems, or in both the Hs and the cortex. These two modes correspond to two clearly defined electrophysiological patterns in some animal species, theta and sharp waves (Buzsacki, 1989). In primates only sharp waves have been consistently individualised. It is claimed that this peculiarity corresponds in fact to an extension of the read mode which takes place not only as a consequence of the physical exploration of the environment (theta phase), but also as a follow up to any endogenously generated "cognitive processing".

The reactivation function is related in the model to the internal "bursting" capacity of the CA3 pyramidal neurons, and their collective capacity to synchronize under the modulation of septal inputs.

o Hippocampus as a Temporo-spatial Processor

In relation plausibly with this transient buffer function, behavioral and neurophysiological results point to a more cognitive role of the Hs in learning the temporal order of serial sequences, at least at a low level of processing. This function could be illustrated in the process of place recognition in lower species. Yet, spatial learning is only one example (possibly the best in some species) of this multidimensional correlational processing. Further, conditioning literature points to an important role of some parts of the hippocampus in learning temporal intervals between events, and more generally durations or timing. Some of these functions seem to be based on very basic processes of differential synaptic plasticity (Granger et al. 1994) as a result of the correlational learning capacity attributed to most of the hippocampal subsystems, applied to successive events. Some others, such as timing, could result from population coding by cells endowed with different dynamics that we locate in the dentate gyrus in our model. In this view of the hippocampal function as combining and contrasting fusion-integration and match-discrimination, place recognition appears in many respects as a degraded by-product of the Hs capacity to register sequences of events.

The long-term declarative memory consolidation function attributed to LTP is the current focus of much investigation. But in the present paper, we compare and contrast the functions, in particular WM, of Hs and Pc. By neuropsychological and physiological arguments, we make a case for the automatic working memory function supported by ITM (intermediate-term memory), operating in parallel to and in relation with the cortical WM, as a particular slave system of the frontal executive. We sketch a comparison and a unification of the experimental results in both human and nonhuman primates. We contrast and relate this WM function with the more classical LTM consolidation function attributed to Hs. We also provide physiological and behavioral evidence for the implication of the Hs in temporal order sequence processing and timing, which are the basis for our neural network model implementation.

3 WORKING MEMORY as BOTH a CORTICAL and a HIPPOCAMPAL SYSTEM

The existence of a graded retrograde amnesia is a strong argument in favor of a transient LTM probably based on hippocampal LTP and involved in LTM consolidation. We make here a case for a shorter time constant type of memory, namely working memory (WM) being based on both a cortical system(s) and a hippocampal intermediate transient memory (ITM). Neuropsychological and brain imagery arguments in favor of STM and ITM functions of hippocampus are important for our model. Since there is a general agreement on the role of the associative cortex, either prefrontal or temporal, in WM function, we will mainly emphasize the arguments in favor of an hippocampal contribution to the WM function.

3.1 PSYCHOLOGICAL ARGUMENTS for a SLAVE AMODAL AUTOMATIC WORKING MEMORY

Baddeley (1986) proposed a multicomponent model of WM as a substitute for the shortcomings of the modal model of Atkinson and Shiffrin (1968), which implied a unique STM store as a necessary passage to LTM. A single STM store could not simultaneously function as an adequate WM, and was therefore evolved into a multicomponent model. Still, WM was viewed by Baddeley as a single common resource, with a limited capacity.

o Working Memory as Control and Slave Systems

INSERT FIGURE 1 ABOUT HERE

The definition of WM as a "temporary storage of information in connection with performing other, more complex tasks" is vague enough to allow for any possible extensions or modifications of the model. Baddeley assumes a limited- capacity attentional controller, the central executive, that supervises two slave modality-specific systems, the visuo-spatial sketchpad to hold and manipulate visual and spatial images, and the articulatory loop, to rehearse speech-based information. The articulatory loop manipulates memory for sounds. It comprises a memory store for holding phonological information for a period of one or two seconds, coupled with an articulatory control process (Baddeley, 1986). Overt or covert subvocal articulation allows both refreshing the auditory memory traces and also feeding the phonological store with phonologically translated visual information. The temporary storage of visual information in a visuo-spatial sketchpad, would imply an occipital system involved in the visual aspects and a parietal system involved in spatial coding, and also possibly a frontal lobe participation (Goldman-Rakic, 1988). A related but more comprehensive construct proposed by Fuster (1995) is that of active memory. This is a state rather than a system of memory, and includes a widely distributed and changing representational network in the awake organism. Active memory therefore includes WM, but does not presuppose any mental or cognitive operation.

Until recently, only vague reference was made by Baddeley to the underlying brain structures supporting either executive or slave systems, but implicitly WM function was under the control of conscious awareness and therefore had plausibly a cortical location. The same is also assumed for animal WM (Goldman-Rakic, 1988). Yet, a fundamental ambiguity concerning the precise definition of WM, and the explanation of the results derived from the paradigms designed to probe WM theory, remains unresolved if one does not refer to the brain structures that support WM :"There is clearly a danger that a concept such as the central executive may reflect nothing more than a convenient homunculus"... (Baddeley, 1995). Furthermore, the sole reference to cortical structures is not enough to account for all the experimental data.

INSERT FIGURE 2 ABOUT HERE

More recently, results of brain imagery and animal neurophysiology were incorporated into the theory (Baddeley, 1995). Unfortunately, most of the experiments to date, either with metabolic or electrical brain imaging with event-related potentials (ERPs), use paradigms that are specifically designed for the study of the components of the model of Baddeley (1986), rehearsal systems in particular (Paulesu, Frith & Frackowiak, 1993). Furthermore, the ERP approach (Ruchkin et al, 1991, 1992) is more adapted to the exploration of the cortical mantle, than of the deep structures. Therefore, these studies confirm the involvement of cortical structures in different WM paradigms. Yet, more classical recall paradigms, not formally requiring rehearsal, show joint cortical and hippocampal activation (Squire et al., 1992).

o Working Memory as a Hippocampal Automatic Slave System

Neuropsychology and imagery suggest an automatic component of WM, supported by an intermediate register located in Hs, along with the controlled, supposedly cortical, component of the WM system explored both in humans (Baddeley, 1986) and animals (Fuster & Alexander, 1971; Olton et al., 1979). Like the cortical controlled WM, this system is endowed with both storing and processing capacity. It is supposedly based upon several systems:

- First, a complementary set of intrahippocampal or hippocampo-cortical loops;
- Second, a battery of memory registers covering a large temporal spectrum;
- Finally, rapidly instantiated but transient synaptic facilitation demonstrated in different hippocampal subsystems (Buzsaki, 1988; Jones, 1993).

Moreover, the operation mode of this intermediate system supporting WM is supposed to be just a restriction to the intermediate range (minutes) of the more comprehensive process of LTM consolidation generally attributed to Hs. This general process consists of maintenance and/or reenactment of cortical patterns of activation by reverberant activity between reciprocally connected systems. This hypothesis extends to WM the dichotomy that already exists in LTM between declarative explicit memory and procedural implicit memory. Psychological arguments in favor of this hippocampal automatic component of WM are provided below.

Refreshing either the visuo-spatial sketchpad or the phonological store by rehearsal every second or so is a controlled process. So too is performance of the concurrent cognitive task, usually verbal, required from subjects in WM paradigms. Supposedly, the central executive responsible for planning, strategy selection, and coordination of information is monitoring both of these tasks. Thus, several controlled processes work in parallel. Shiffrin and Schneider (1977), demonstrated the very limited capacity for controlled processing in the human brain. They made a good case that only several automatic processes, or at best one controlled and one automatic process, could be performed in parallel. Yet, surprisingly, the usual paradigms testing WM are tractable without overwhelming difficulty even by patients or aging subjects (Brebion, 1994). There could be several reasons for that, not necessarily exclusive, and more or less implicated according to tasks and subjects. -The so called complex cognitive task may be largely automatized in spite of its complexity, in particular when it involves verbal comprehension. Thus attention would be relatively free to focus on active rehearsal of the to-be-memorized material. - Alternatively, the material to be memorized may be more or less related to the task to be performed, so there is not really competition and interference between withholding information and processing it, but a nice interleaving and integration between the two tasks. This type of paradigm (where the information to be remembered is related to the cognitive process in progress) is certainly close to actual WM operation in natural conditions.

Certainly, one cannot deny the reality of the rehearsal process. But we contend that this low level and rote strategy is expensive in terms of limited controlled processing capacity, and unnecessary in most everyday situations. Whenever possible, subjects resort to cognitive strategies aiming to create supraordinate chunks of items or events, in order to increase the limited capacity of STM. However, this is still a controlled process. We therefore suppose the existence of an automatic support to WM, an intermediate transient memory register (ITM), which does not need rehearsal. This register is in such a functional relationship with the various cortical areas, that it may readily refresh recent memories relevant for the task in progress, by simple maintenance and/or reenactment of the corresponding activation patterns in the cortical populations. This reactivation does not preclude a state of priming or subliminal activation of the cortical areas to-be-reactivated due to their recent activity. This function is exactly what Hs supposedly performs, in the different processes of long-term consolidation of the declarative episodic and factual semantic memory traces. Both WM and transient LTM refer in some sense to an episodic, context dependent, or a factual type of information to be memorized. Nevertheless, the only important distinction between the two is that the trace already "long- term potentiated" will certainly be transferred to LTM, while the trace (and eventually the activity pattern) in WM is just a candidate for LTP and undergoes a test of eligibility to permanent LTM store. It is therefore further hypothesized that the two processes of LTM consolidation on one hand, and of WM refreshing on the other, are roughly similar and complementary. Only the duration during which the two types of memory traces keep relevance for the subject differs. This is of the order of minutes for working memories, but weeks or months for memories that must be "permanently" consolidated in the long-term stores. They are also complementary because transformation into transient LTM can only be considered if the long-term relevance of the information to be stored has been confirmed by the processing performed either in the intermediate hippocampal store or in the cortical system of WM, or in both. The neurophysiological counterpart of this information selection for long-term storage would correspond to the transition from loop iterative and punctual activation or even more important short-term synaptic facilitation (based on short-term potentiation (STP)) to a transient long-term synaptic facilitation (based on LTP). Both types of learning are documented at different levels of hippocampal subsystems (Jones, 1993; Buzsaki, 1988).

o Personality correlates of Working Memory and Transient LTM

One of the main implications of our model is the augmentation of WM beyond the classical, cortical, rehearsal-expandable STM range, by a rehearsal-independent register mostly based on ITM in the hippocampus. This ITM itself is distinct from transient LTM based on LTP. It is noteworthy that personality traits seem to correlate differentially with these memory components. Both extraversion and neuroticism relate, in experimental studies, to performance on retention tasks. Howarth and Eysenck (1968) showed that, in retention of paired-associates, extraverts show superior recall over retention intervals up to 5 minutes or so (in the ITM range), but thereafter introverts show reminiscence and increasingly better performance than extraverts. These results are difficult for current WM theory to explain, because the advantage of extraverts persists beyond the typical durations associated with the short-term components of WM. The present analysis suggests extraverts may have superior STM/ITM. Plausibly, on the basis of different performance equilibria in neuromodulators (in particular noradrenergic, dopaminergic, or serotonergic), cortical STM is more stable, and the Hs tends to operate so as to refresh these memories in extraverts. Conversely, the LTM consolidation processes would be more powerful in introverts. It is already admitted that emotional charge associated with events (and supposed to be larger in introverts than extraverts) favours LTM consolidation. Could it be that this same emotional component is detrimental to the automatic (non-rehearsal based) maintenance of information in STM/ITM? Consistent with this hypothesis, extraverts tend to show superior recency in free recall, a function normally attributed to STM, but effects of extraversion on WM tasks requiring active processing are unreliable (Matthews, 1992).

It is well-established that trait anxiety and neuroticism are associated with impairment of STM (Eysenck, 1982). In this case, effects are stronger for active WM tasks than for passive storage (e.g. Darke, 1988), implying that this anxiety effect may relate preferentially to the controlled, cortical component of WM. This psychopathological result is also consistent with our interpretation for the effects relating to the introvert-extravert dimension.

3.2 NEUROPSYCHOLOGY, BRAIN IMAGING and WORKING MEMORY

Neuropsychological evidence in favor of an automatic component of WM based on hippocampal structures remain important. Indeed, brain imaging experiments performed during WM paradigms are still scarce, and for most of them oriented to testing the controlled aspect of WM according to Baddeley's theory of the executive controller.

First, Brown (1958) and Peterson and Peterson (1959) showed that witholding information in STM is dependent on rehearsal, and rapidly lost if active rehearsal was prevented. This fact lies at the basis of the distinction between immediate STM and primary memory (James, 1890) which results from STM extension due to the rehearsal process. Second, responses of normal subjects to different recall or recognition tests, show in the absence of rehearsal, a residual memory which the STM decay tends to asymptotically. This residual memory is suppressed after bilateral Hs lesion. Therefore, we attribute it to an hippocampal ITM component. Classically, in amnesia consecutive to a medial temporal lobe lesion, STM in the sense of immediate memory is fully intact, in contrast with the loss of new acquisitions in declarative LTM (Baddeley & Warrington, 1970; Cave & Squire, 1991). The picture sketched from the study of amnesic patients is much more subtle than this black and white portrayal, in particular when one takes into account the role of the extent of the lesions in determining the depth of the deficit.

The following neuropsychological arguments derive from recall and forgetting curves, or visual recognition obtained by classical tests of STM and LTM both in normals and amnesic patients. In spite of the thorough analysis of these results, some repeatedly confirmed evidence has been either overlooked or even not accounted for. The patients show a deficit of learning and recall for verbal as well as nonverbal material. In terms of our model, these tests explore in fact both STM and intermediate term memory (ITM), according to the variable delay of recall. Since the depth and nature of the memory deficit depends on the extent and location of the Hs lesions, these parameters are taken into account in the interpretation of the results. Bilateral extensive lesions with complete loss of hippocampal function will therefore be treated separately from unilateral lesions and/or partial loss of hippocampal function. But, for the purpose of separating hippocampal from cortical components of WM, the most important parameter is whether or not the subjects are allowed controlled rehearsal, as supposed by the articulatory loop in the WM model of Baddeley (1986).

o Rehearsal allowed

The results from subjects with complete loss of Hs function (like patient HM) will be emphasized since a normal or close to normal performance on tests of STM or ITM in this case would imply all the more a normal performance when hippocampal function is partially preserved. In this case, the only possibility will be to attribute the corresponding performance to STM or to the controlled, cortical component of WM, since rehearsal is allowed and Hs function is lost. This complete loss of Hs function results either from bilateral and extensive resection of the mesial temporal lobe, as in HM's case, or from unilateral resection associated either with a severe degeneration (post-mortem diagnosis) or with a severe dysfunction (EEG recording) of the spared mesial temporal hemilobe (respectively cases PB and HF).

- First, rehearsal is spontaneous, as with verbal material well within the memory span and made of consonant trigrams presented in a variable delay matching-to-sample task (Sidman et al., 1968). Then STM range can be extended theoretically at will in what William James (1890) has named a primary memory (Fig. 2d), even for patients with total loss of hippocampal function.
- Second, the material is easily verbalizable but at the limit of the memory span as in the short version of the visual maze (Milner et al., 1968). This test requires the memorization of a sequence of turns (8 choice points). The patients cannot learn the task even after many trials. There is complete disruption of the memory process. Thus these patients face an actual cognitive defect, related to the incapacity to simultaneously maintain and organize accessible information (type of turns to make), and to implement the task (topographical translation of the turns on the maze). This is a genuine definition of a WM task. In this situation, rehearsal is not sufficient due to the memory load at the limit of the STM span. Furthermore, practice does not improve performance. There is no evidence of learning over 125 trials, as if the subject was unable to devise a learning strategy in order to split a too difficult task into accessible subgoals.
- Third, if the material to be memorized is not naturally or easily verbalizable (elliptic geometric forms with one variable radius to compare to a sample after various delays), the extension of the STM range is not possible in patients (Fig. 2d). Even with very sensitive measures, a limited residual control of the sample stimulus on the performance is restricted to the 16-24 sec range, i.e. the classical decremental STM range. Remarkably, this is not the case with normal subjects or even 9- 12 year old children who demonstrate no evidence of performance deterioration at delays up to 40 msecs. Similar results of poor performance in the case of extensive bilateral lesions have been found in tests involving other types of geometrical items (Milner et al., 1968).

- Finally, these defects are further corroborated and extended to the immediate STM by the classical test of digit span. Digit sequences of various lengths are presented at a typical rate of one digit per second. Subjects speak out recalled digits at their own pace. The percentage of strings correctly recalled (Fig. 2c) demonstrates an inverse linear relation between the recall performance and the length of the string, similar in amnesic and controls. But, consistently (Drachman & Arbib, 1966; Baddeley & Warrington, 1970) amnesic subjects perform worse (in fact, are completely unable to recall) on sequences exceeding the normal memory span (7 items). These last results point to another critical factor in recall performance, besides the delay of retention, namely the memory load. As for the delay duration, medial temporal lobe seems to play an important role with regard to memory load. Furthermore, this very last result shows clearly that medial temporal lobe helps to buffer overflow of information out of the very limited capacity attended STM store. It can be argued in this case that rehearsal is not efficient anymore as a consequence of the overflow of the immediate memory span. Still, normal subjects demonstrate a residual mnemonic performance in spite of this overflow.

Taken together, these results confirm the integrity of immediate STM for material within the immediate STM span in amnesics. They also confirm the efficiency of the articulatory loop as a rehearsal device allowing the extension of the immediate STM span into a primary memory, either for verbal material or for material easily verbalizable. This articulatory loop is intact and efficient in patients. Nevertheless, the results also point to the fact that the possibility of rehearsal is not enough to guarantee recall or learning in patients. If the material is difficult to verbalize and/or exceeds or even is close to the immediate memory span, as in the short version of the visual maze (Milner et al., 1968), there is a complete disruption of the memory process. Therefore, for patients with Hs lesions, there is a clear difficulty in fractioning a too difficult task into accessible subgoals. Conversely, the results do not give a strong support for a corresponding rehearsal system which refreshes the visual sketchpad when material is not naturally verbalizable. Otherwise, the performance in geometric tasks should have been close to normal in patients.

o Rehearsal Prevented

The tests where rehearsal is prevented during the delay between learning and recall are similar to experiments designed by Baddeley to test WM. Indeed, they combine withholding information with an interfering task. However, they differ from genuine WM paradigms, in that the items to be remembered are not at all related to the interfering task, and also not related to each other. Conversely, in a WM paradigm, the task is not designed to interfere with item memorization. The items may even be related to the task, and task performance is quantitatively evaluated. Also, in a classical WM task, STM and ITM components cannot be dissociated while they can in the memory tests by monotonic variation of the delay of recall. The results of these tests critically depend on the extent of the lesion.

Bilateral Lesions of Hs

Subjects with bilateral extensive lesion of the mesial temporal lobe like patient HM are clinically evaluated as being in a severe even dramatic condition. They depend on continuous rehearsal of the information to be retained. Catastrophic forgetting is induced by distraction (Milner, 1966, 1968). The most dramatic illustration of this psychological condition is reported by Milner: The patient H.M. was able, by devising an elaborate mnemonic scheme, to remember a three-digit number for 15 minutes, but forgot it as soon as he was distracted. The question is then why a normal subject after maintaining for 15 minutes a three digit number in his field of awareness has no difficulty in remembering it, even after distraction. Even hypothesising that 15 minutes could represent enough exposure for a "permanent" LTM storage, this type of material does not represent any long-term relevance for the subject. There is little chance that the transient storage takes place at cortical level; otherwise patient HM could have learned this information, as he did learn from procedural memory paradigms. Since the main difference between normals and patients, in this case, is the presence or absence of the hippocampal system, it is logical to attribute the primary cause of the recall defect to the Hs and not the cortex. This does not provide a clue for the actual mechanisms responsible for the retrieval of information in normals. In normal subjects, continuous rehearsal or refreshing memories cannot be directly responsible for this retrieval which looks to us so natural. Indeed, the very definition of distraction implies an interruption of the controlled rehearsal process. The retrieval of information in normals (compared with the non-retrieval in patients with extensive Hs lesions) strongly suggests that the continuous process of rehearsal, or reactivation of memory has somehow succeeded in rapidly laying down a trace, not at the cortical level (otherwise both patients and normals would have been able to recall), but at the Hs level. The ITM hypothesis explains the retention of this information in normal subjects, in spite of its irrelevance for long-term storage (LTM consolidation was not involved), and in spite of the interruption of the rehearsal process (STM was not prolonged any more by rehearsal). Fifteen minutes is well within the WM range. This is therefore an argument in favor of an automatic component to WM. We will see how recent findings on the multiple-range memory registers operating in the hippocampal subsystems, in conjunction with the complex closed-loop system of the hippocampus, may provide a clue to the actual mechanisms responsible for these transient intermediate-range remembrances (so useful for our moment-to-moment processing of the continuous flow of information).

A more formal assessment of this type of patient was performed in a visual memory task, based on face recognition. Subjects had to select from an array of 25 faces the 12 faces that had been shown 90 secs earlier. Performance fell to chance level in patients when the test was performed with a distracting task interpolated between the presentation of the two sets of photographs (Milner, 1968). We have seen previously how excess in memory load, or difficult verbalization of the material to remember, is equivalent to a prevention of rehearsal.

Partial Lesion of Hs

The picture is apparently different when there is a partial preservation of the hippocampal function. This is the case for patients after unilateral temporal lobectomy, or alcoholic patients suffering a Korsakoff syndrome which present an identical pattern of results to the latter (Baddeley & Warrington, 1970). As we have seen, delayed recall tests with interfering tasks present some similarities with the WM paradigms even if they are not identical. The variable delay between item presentation and recall allows a quantitative separation between deficits in STM (20-30 secs), and intermediate memory, beyond this range. This is not the case in the WM paradigms, which represent a more natural situation, in the sense that the material to be memorized may be related to the associated processing task.

In the short-term forgetting task subjects are presented for a few seconds (e.g. 3 secs) with item sequences (3 words) well within the memory span. They are required to recall the item sequences, after delays varying according to trials (0, 5, 10, 15, 30, 60 secs). During these delays they perform a tightly controlled intervening task designed to prevent rehearsal. Manifestly, the forgetting curves present an exponential decay (Fig 2b), and reach asymptote within 30 msecs, which is the maximal range of STM. For this reason, the corresponding decay can be fully explained by a STM decay. Conversely, the residual information withheld beyond this short-term range is logically attributable to an intermediate store independent of either the articulatory loop, or any other aware controlled cognitive process, which are both prevented by the experimental design. Therefore the process responsible for this memory is automatic. That the two curves are almost similar in controls and unilateral temporal lobectomy or Korsakoff patients can be attributed in both cases to a close to normal cortical function sustaining the STM capacity, combined with a residual hippocampal function attributed to the spared side of the Hs, or to the diffuse and partial lesions of the Korsakoff syndrome, in a situation where item lists to be remembered are well within the STM span (3 items). This interpretation is strongly suggested by the catastrophic forgetting of patients with bilateral lesions, when faced with an interference situation. Further, there is also electrical brain imaging evidence that unilateral hippocampectomy alters little or not at all the cognitive ERP patterns (in particular P300) recorded on the scalp, with the possible exception of very limited areas of the temporal lobes where a trend towards asymmetry shows up (Johnson, 1995).

In the classical free recall two component task, lists of unrelated items exceeding the memory span (e.g. 10 words) are presented to the subjects at a pace similar to that of the previous experiment. At the end of the presentation, with a variable delay, during which subjects have to perform an intervening task, free recall in any order is performed. The main difference with the previous task is that the memory load here exceeds the memory span. In the zero delay, immediate recall condition, in spite of the absence of an intervening task rehearsal after each item presentation is prevented by the continuing presentation of to-be-recalled new stimuli. Very robustly, the recall curves (Fig. 1a) show in controls both a primacy and a recency effect (Glanzer & Amitz, 1966). The items delivered first and last in the list are better remembered than the ones in the middle. The recency effect is classically attributed to a persistence of items in STM. This interpretation is consistent with our model which differentiates STM (present both at cortical and hippocampal level) from ITM (which would be a more specific attribute of Hs). As such, the recency effect disappears both in patients and controls when a 30 sec. delay with performance of an intervening task is interpolated between presentation and recall. The primacy effect is also classically attributed to long-term memory. But in the context of our model, it is supposedly dependent on intermediate-term memory (ITM). This primacy effect greatly deteriorates at zero delay even in these patients with partial preservation of medial temporal lobe functions (Fig. 2a). It becomes completely abolished in the same patients after 30 sec. delays, while it still persist in normal controls. Thus when the memory load exceeds STM span, partial preservation of the medial temporal lobe function is not anymore sufficient to prevent intermediate memory deficiency, compared to controls, as was the case in the short-term forgetting task with a memory load within the STM span.

In summary, both patients with bilateral and unilateral lesions of the Hs present close to normal immediate STM for information well within the STM span (typically 3 items), and can further extend this temporal range when rehearsal is possible and natural (verbal material). Both types of patients present catastrophic loss of information and forgetting when there is overflow, beyond the strict STM span. This loss of information is much less systematic and dramatic with normal subjects. There are some indications that the STM span may be reduced in patients. When information is well within the memory span (and only then), patients with unilateral temporal lesions or Korsakoff syndrome, preserve close to normal intermediate range memory capacity, independent of rehearsal. This is not the case for bilateral temporal lesions. It must be further emphasized that the side of the unilateral temporal lobectomy is not neutral for the type of performance which is the most spared (verbal or visual). Thus, both the forgetting curves and the primacy-recency effect in partial lesions support the distinction between an immediate STM and an ITM, rather than an LTM, as was classically stated. Further, the distinctive behavior of patients with a bilateral extensive ablation or lesion of Hs corroborates this ITM as a possible automatic support (non rehearsal-based) of WM.

The development of brain imaging techniques based either on EEG, MEG, PET or functional MRI, raises the possibility of a simultaneous and direct investigation of anatomy and function of memory, both in normal subjects and patients. The few results obtained by these techniques vary according to the experimental paradigms. They lend support to both cortical and hippocampal components of WM.

o Electrical Brain Imaging

Electrical brain imaging can be used to record event-related potentials (ERPs). These ERPs can be defined as scalp potentials reflecting different cognitive processing operations or steps performed by the brain. There are different ERP responses discriminated on the basis of their latency and topography. Some reflect automatic identification of the stimulus, like N200 (negativity at 200 msecs) Mismatch Negativity; others like Processing Negativity (N”a”at”anen, 1982) reflect attended stimulus processing (Banquet, Smith & Renault, 1990; and still others like P300 (positivity at 300 msecs) reflect context processing or updating. The ERP investigation of WM confirms the involvement of various modality specific or associative cortical regions, for components later than P300, like P600 and over (Ruchkin et al., 1991, 1992). Surprisingly, P300 related to context updating and in particular probability processing (Banquet, Renault & Les‘evre, 1981; Johnson & Donchin, 1982) does not reflect the cortical ”explicit” component of WM. These results do not allow the exclusion of the participation in a typical WM paradigm, or in other types of paradigms, of a deeper structure like the Hs. Indeed, scalp electrical recording as in EEG is known to explore predominantly, if not exclusively, the cortical mantle of the brain. Furthermore, a P300-like activity has been recorded in the hippocampus (Halgreen et al., 1980). But this P300 hippocampal source is not the generator of cortical P300s. Further, it has little influence on cortical P300 generators, since right or left hippocampectomy does not induce any significant cortical asymmetry. There are however two notable exceptions. First, far-lateral temporal electrodes (T5-T6) in oddball paradigms present a reduced P300 on the side of Hs removal. Second, left hippocampectomy induces a change in P300 behavior rather than P300 asymmetry, along with a performance deficit in the number of correctly recognized items in recognition paradigms involving stimulus familiarity (Johnson, 1995).

o Positron Emission Tomography

PET or functional MRI studies, still contribute very little to the solution of the problem of hippocampal involvement in intermediate term memory, despite their long-term promise.

INSERT FIGURE 3 ABOUT HERE

Neural correlates of verbal WM involving the articulatory loop were explored by PET measures of regional cerebral blood flow in a task engaging both components of the articulatory loop, the phonological store and the subvocal rehearsal system, compared to a simpler condition engaging only the subvocal rehearsal system (Paulesu et al. 1993). This paradigm allowed localization of the phonological store to the left supramarginal gyrus whereas the subvocal rehearsal system was associated with Broca's area. These results are a strong support for the cortical component of WM, and more specifically of the articulatory loop. Nevertheless, since subjects were explicitly instructed to rehearse the consonants to be recognized after a 2 minutes delay period, the absence of significant engagement of Hs cannot be considered as an argument against the implication of Hs in WM, in as far as a specific memorisation strategy was forced upon subjects. It must also be noticed that the task involved recognition and not recall.

One of the most salient items of evidence in favor of a combined involvement of cortex and hippocampus in Intermediate Transient Memory (ITM) comes from Squire et al. (1992). In a delayed (3 minutes) cued recall paradigm without any interfering task subjects learned visually presented word lists (15 words). During cued recall, PET scan found significant activation, compared to baseline conditions, of right hippocampus and parahippocampal gyrus, plus right (and to a lesser degree left) frontal lobes (Fig. 3). Left hippocampal region and amygdala did not change their activation level during cued recall. In our model this task corresponds to a test of ITM supporting WM, because of both the delay of recall and the memory load, which far exceeds the STM span. The absence of any interfering task during the delay may have favored rehearsal strategies and a bias towards cortical activation. But this bias may have been limited by the length of the item list. Nevertheless, the activation of Hs along with the frontal lobes provides strong support for a WM with two components, cortical and hippocampal, combined in a closed- loop system. The selective activation of the right Hs can be explained as a processing bias introduced by the cued recall (visually presented stem completion) towards processing the visual characteristics of the word-forms.

The dual involvement of Hs in both priming condition and cued recall (Fig. 3) contrasts with the selective involvement of the frontal lobes in cued recall. This suggests that the declarative aspect of memory involved in recall (in contrast to the automaticity of stem-completion priming) is a cortical, possibly frontal cortical characteristic. At the same time, it justifies the term of automatic component of WM for ITM. The interpretation of these results is biased by Squire in order to support his theory of the role of Hs in the declarative aspect of memory. Thus Hs activation in the simple priming task is accounted for by a covert implication of explicit memory during the priming condition (Squire et al, 1992). But this explanation is not parsimonious and is to some extent tailored to fit his hypothesis. Conversely, we attribute the involvement of Hs in stem-completion priming to the implicit- procedural characteristic of this task which matches the automatic aspect of ITM support to WM. Further, if we make the plausible assumptions, -that the declarative character of memory is independent of the process of consolidation itself, and that the final repository of memories is cortical, in particular frontal, the interpretation of Squire is not supported by the decrease of prefrontal activation to a level close to that of the baseline condition during the priming task.

3.3 NEUROPHYSIOLOGY: HUMAN versus ANIMAL WORKING MEMORY

At variance with some neurophysiologists (Goldman-Rakic, 1994), we do not believe that the criterion "relevant only transiently" is the unique characteristic of WM. As previously stated, WM, at least in humans, could be characterized by combining temporary storage of information and a capacity for more complex cognitive processing. Among tests designed to explore WM in animals, these two functions are obvious in radial maze performance, but not so much in delayed response tasks, where the emphasis is on temporary information storage.

The emergence of the construct of WM occurred almost simultaneously in animal and human research. In parallel with human neuropsychological studies of WM (Baddeley & Hitch, 1974), the same concept was developed independently in animal learning to refer to the capacity to retain information across trials within a test session (Olton, Becker, & Handelmann, 1979). These authors were among the first (and perhaps the only ones so explicitly) to propose that the hippocampal system could be necessary for animal WM (memory for recent information of current and specific relevance). At variance with this passive witholding function of relevant information, we think that hippocampus is also equipped for an active information selection and processing, more in the line with human models of WM. In Olton' s radial maze, each arm is baited with food. Typically, on a series of trials, in the same session, the animal will avoid revisiting an arm from which it has already taken food, suggesting a retention of behavioral events associated with entering each arm. This WM could involve the encoding of specific episodes associated with specific maze arms. As such it could represent the ITM equivalent of episodic memory. But performance could also be guided by the stronger relative familiarity of cues related to arms more recently visited.

In the seventies, recordings performed on awake monkeys trained on delayed response tasks allowed for an extension of the concept of WM. These recordings showed that some prefrontal cortex neurons were activated during the delay period between stimulus and response (Fuster & Alexander, 1971; Fuster, 1980; Niki, 1974). From the very beginning, these activities were supposed to reflect the cellular expression of mnemonic processes. The evidence in favor of a mnemonic process rather than a motor set or any other activity has grown more convincing by the discovery of some specificity in the response. In particular, in an oculomotor delayed response paradigm, neurons alter their discharge rate only for one or a few target locations, thereby demonstrating a kind of memory field (Funahashi, Bruce & Goldman-Rakic, 1989). This result has been extended to other brain areas, inferotemporal cortex in particular during DMS tasks (Fuster & Jervey, 1981; Myashita & Chang, 1988).

This form of activity has been qualified as active by some authors, in contrast to a passive form (Eichenbaum et al., 1994). Passive memory is characterized by a reduced response to familiar or repeated stimuli. Some neurons in inferotemporal cortex fired much less in response to an immediately repeated stimulus in a serial recognition task (Baylis & Rolls, 1987; Rolls et al., 1989). Item specificity of the neuronal response was also demonstrated (Baylis & Rolls, 1987; Miller et al., 1993). This paradoxical response has been interpreted as a rapid form of habituation. The decrement in stimulus-elicited firing would reflect a decreased responsiveness of cortical neurons to familiar stimuli. At variance with the active memory this passive response could be interference-resistant and may persist through the presentation of intervening mismatch choice cues within the same trial (Miller et al. 1993). Yet, both active and passive memory representations disappear between trials, suggesting a system reset when the information is no longer relevant (Miller et al. 1993). Nevertheless, a gradual cumulative decrement of response across testing sessions to multiple repetitions of items confirms our hypothesis of a graded transition between ITM supporting WM, and transient LTM based on LTP supporting permanent LTM consolidation. It should be noted that this decrement in response to stimulus repetition is dependent on an automatic, passive type of processing. When the sample stimulus has to be actively maintained in awareness for comparison with several test stimuli, stimulus repetition does not induce a decreased response, but an increased one (Miller et al., 1994).

There are striking similarities between electrophysiological recordings in monkey and brain imagery in man, either electrical recording of ERPs on the scalp, or metabolic PET imaging. We have previously mentioned the functional significance of specific ERP components. In particular, N200 or Mismatch Negativity reflects automatic identification of the stimulus in an iconic or echoic memory; others like Processing Negativity represent attended stimulus processing; and still others like P300 reflect context processing or updating. When two types of stimuli are sequentially presented with different probabilities (rare and frequent), the P300 and N200 response to rare and frequent stimuli is at first very similar, but becomes smaller for frequent and larger for rare types of stimuli. This evolution in response amplitude takes place after only a few stimuli (less than 10) for P300, but needs more stimuli presentations for N200 (Banquet & Grossberg, 1987). This kind of probability processing is fully automatic, and in fact better reflected by P300 amplitude when the subject is not aware of it (Johnson & Donchin, 1982). The decrease in amplitude of response to frequent stimuli can therefore be compared to the decrease in neuronal response to stimulus repetition in monkey. Conversely, the Processing Negativity, corresponding to an attended, selective filtering of only some preselected type of stimulus, remains insensitive to event probability and presents an increased amplitude in response to a match (i.e. repetition) condition. The same results hold for PET imaging. A decreased activation was found in the occipital cortical areas in response to items that had been recently presented (Squire et al., 1992). This result was interpreted by Squire as a reduction in neural computations required for the processing of recently presented information. The similarities between human and animal electrophysiological activities extend to preparatory set. A contingent negative variation (CNV) paradigm in humans is a formal analog to experiments used in monkey to explore WM (Fuster, 1980; Niki, 1974). After a warning stimulus S1 and a delay, an imperative stimulus S2 commands the subject to emit an (usually motor) response. Cellular recording experiments in the monkey show that in the S1-S2 interval the CNV presents two distinct components, an early one which has been related to the processing of S1, and a late frontocentral component with a ramp-like activity preceding S2. This late component does not just correspond to a motor-set, but reflects also timing and perceptual-cognitive set (Ruchkin et al., 1986).

4 SPATIO-TEMPORAL PROCESSING in HIPPOCAMPUS and PREFRONTAL CORTEX

Most of the specific functions attributed to Hs and Pc, mainly in the domain of temporospatial processing can be related if not reduced to the global WM capacity proper to these two systems. In fact some of the paradigms used to probe the WM capacities of these two systems, and already mentioned in the previous paragraph, presented strong explicit or implicit spatial or temporal factors. Nevertheless, in this section we aim at a specific parametric exploration of spatial or temporal functions, and also other related functions such as rule formation, planification etc.. Here also we make a distinction between neuropsychological or brain imaging arguments and neurophysiology of the monkey in particular, since both approaches make a specific contribution to the problem.

4.1 NEUROPSYCHOLOGY and IMAGING of SPATIO-TEMPORAL FUNCTIONS in PREFRONTAL CORTEX and HIPPOCAMPUS

Neuropsychology has provided evidence that important lesions of prefrontal cortex (Pc) are compatible with the performance of conventional linguistic, memory or even intelligence tests, which can be sensitive indicators of damage to the temporal lobe. The portraying of the Pc as the "seat of intelligence" was therefore discarded. At the same time, less conventional paradigms brought to light less basic, but no less critical, perturbations of cognitive and relational adaptations following important lesions of the Pc. These patients completely lost the ability to make choices, although sensory and motor sequences remained intact. Reduced flexibility and inventiveness on the approach to new problems, poor adjustment to everyday life and disturbances of personality were among the most common signs of prefrontal dysfunction. These disturbances of personality are diverse, but could find some of their common denominators in a disinhibition of basic drives, combined with lack of motivation and purposeful behavior. For these reasons these personality changes are most obvious in family, professional and social life, all spheres which require a high degree of instinctual sublimation, not to speak of motivation. Since these familial, professional and social components of a person are the more distinctive ones, the patient loses his singularity to become common if not vulgar: "Gage is no more Gage". In spite of their limitations, these neuropsychological explorations uncovered the structural and functional diversity of Pc, and sketched a "functional topology" that is presently demonstrated by brain imagery.

Since Hs seems to contribute to the computation of the learning of places and sequences and amygdala participates in the integration of external and internal drive signals, one can wonder why motivation, based on this drives, seems to be integrated not at this subcortical level, but in the Pc. Several reflections along these directions can be proposed:

- First, goal formation supposes a precise representation of the target form and location, which can only be precisely defined at cortical level;

- Second, goal implementation supposes comparison with LTM, precisely located in cortex and particularly in Pc, but not in Hs;
- Third, goal enactment supposes a direct and bidirectional relation with premotor and motor structures which is a property of Pc, but not of Hs;
- Finally, goal execution needs control and willed action, which depends on the executive function of Pc.

All these reasons seem to make the prefrontal stage necessary. But the most compelling argument in favor of the necessity of a prefrontal stage for behavior integration comes perhaps from computational constraints. If drives were integrated at subcortical level such as Hs for subsequent planning, there would be confusion between perceptual and "executive" representations of sequences of events (Gaussier & Zrehen 1994b; Zrehen 1995). Veridical reproductions of learned sequences could still be possible. Indeed, short cut relations between Hs and motor programming systems such as basal ganglia do exist through subiculum and nucleus accumbens. This anatomical connection permits the possibility of short- circuiting prefrontal cortex through the subcortical implementation of overlearned automatic programs. But there would be lacking the extra degree of freedom provided by a representation which is directly dependent neither on perceptual units nor from motor units, but lies in fact at the junction of the two (Fig. 9). This extra degree of freedom results in a giant evolutionary step because it allows for adaptation and creation of new behavioral sequences as needed by specific circumstances.

o Spatial Working Memory, Principal Sulcus and hippocampus

The brain imaging results from tasks inspired by delayed spatial tasks in monkey locate spatial working memory in man either in Brodmann's area 46 which corresponds to principal sulcus in monkey (McCarthy et al., 1994) or in area 47 of the inferior convexity (Jonides et al., 1993). Recent results from PET paradigms manipulating spatial working memory factors (Owen et al., 1996; Petrides et al., 1993) or simply simulating this spatial information (Recce & O'Keefe, 1997) have shown the involvement of the hippocampal formation in man during these tasks.

o Temporal Ordering and Dorsolateral Prefrontal Cortex

Frontal lobe lesions present a specific memory deficit. In delayed comparison tasks, they induce an impairment of temporal ordering of recent events (Milner, 1982). The subjects have no problem in making the distinction between new and previously presented items. This could be a function of the hippocampus, or even modality specific cortical areas. But they present a specific impairment in judging the relative recency of items suggesting an incapacity to keep successive trials apart. Considering the pace of presentation of the item sequences this recency judgement cannot be based on the rehearsal of temporal order or the organization of material, but rather on the relative salience of items in memory. This result is congruent with a defect in STM (maximum 30 secs) whereas the distinction between new and old items is better accounted for by a dysfunction of Hs-based ITM. A symmetrical pattern of deficit in medial temporal lobe lesions, with no impairment on recency discrimination but a deficit in recognition memory confirms this interpretation. This distinction could be related to the dichotomy in experimental psychology between recency effects (attributed to STM) and primacy effects related to LTM. As previously mentioned, in the framework of our hypothesis this LTM would correspond to ITM. STM would be cortical, and prefrontal in particular, whereas ITM would have an hippocampal support.

The left frontal lobes make a special contribution to the organization and planning of responses a few moves ahead. Therefore, the poor performance of patients with unilateral lesion of dorsolateral (DSL) Pc on memory tasks could rather result from a failure in control processes of memory rather than a deficit in retention per se. The perturbation in the temporal ordering of events after DSL lesions is congruent with several interpretations. Pc is either the site of processing of such information, or the site of storage, or both. The processing of this order information in other structures such as Hs in particular, and the subsequent storage in Pc cannot be excluded. We will discuss in the model how this ordering or sequencing function could be dependent on the WM function of both Pc and Hs.

o Other Cognitive Functions

Feedback Regulation of Behavior and Superior Pc

Patients with a superior Pc lesion present an incapacity to extract information from environmental cues elicited by their own responses in order to regulate behavior, in the sense of formulating or altering rules of their behavior. This inability to overcome previously established response tendencies is manifested by the generation of fewer hypotheses, and perseveration. While superior, mostly left, frontal cortex lesions produce persistent impairment, unilateral, orbital, or inferior frontal lesions produce no deficit of this type. This defect is independent of the valence of the feedback signal, of the nature, verbal or spatial, of the material. This "rule breaking" behavior does not only concern the identification or formulation of the rule. It extends to a specific failure to comply with task instructions and a tendency to error perseveration. As such, it could be viewed as a special "cognitive" instance of loss of inhibition otherwise encountered in the everyday life of these patients. These attitudes of perseveration contrast with the hyperflexibility in adaptation to rule changes of the patients presenting mediotemporal lesions. In this latter case a defect in ITM and the consequent impairment in extracting consistent perceptual or motor schemes for a sufficiently protracted period of time could be responsible for this inconsistent behavior.

Conditional Associative Learning and Periarcuate Cortex

In contrast with patients presenting lesions of the anterior temporal cortex, who have normal learning, there is an impairment in learning conditional tasks, either spatial or not, after lesions of the frontal lobes. Lesions producing such deficits are more specifically located in the posterior part of the DSL frontal cortex and the periarcuate cortex (areas 6, 8).

Even at a plain neuropsychological level, prefrontal cortex demonstrates neither structural nor functional homogeneity. Nevertheless, the diversity of these functions is more an expression of the nature of its cortical or subcortical connections, than the result of structural variations.

In parallel with this compartmentalization of prefrontal cortex according to sensory modality other authors isolate regions according to processing hierarchies. According to this criterion, upper and mid-dorsolateral parts of Pc (Brodmann's areas 9) could be devoted to the most executive, high monitoring level of nonspatial WM. Conversely, low- monitoring requirements (such as those of delayed matching-to- sample) would be processed by inferior convexity.

4.2 NEUROPHYSIOLOGY of SPATIO-TEMPORAL FUNCTION in ANIMALS

Rats and monkeys have been the main subjects of investigation, especially for the learning of space rather than for the learning of sequences.

o Hippocampus: Rat place cells versus monkey view cells

It is not the point of this article to make a review of the vast experimental literature concerning place cells and more generally the learning of space in living beings. We just will point to some inter or intra-species experimental disparities that do not find a satisfying issue in experimental accounts, and yet can be integrated in a single unified mechanism by our model.

Experimental results on spatial integration seem, at least at first look, to differ significantly from one species to the other, or even in the same species from one experimental condition to the other. One of the most striking interspecies difference, between the rat and the monkey in particular comes from the quasi-absence of place cells in the monkey. Instead, electrophysiological recordings (Rolls et O'Mara, 1995) demonstrate the existence of "view cells" that react not so much to the position of the animal in space, but to where the monkey was looking in the environment. From such facts some authors have inferred that the hippocampus, at least for some species, could be the site of the construction of an allocentric frame of reference for space representation. Our model and its robotic implementation (Gaussier et al., 1996, 1997a,b) demonstrate that a unique mechanism based on a realistic simulation of the CA3 network explains both the emergence of CA1 place cell-like activity when the robot camera pans 270 degrees around the room (Fig. 4). Conversely, when the "visual field" of the robot is restricted to less than 180 degrees (similar restriction of the visual field takes place in the monkey compared to rats), the robot becomes unable to develop cells that generalize a place and rather develops analogs of directional view cells.

INSERT FIGURE 4 ABOUT HERE

Another important intraspecies critical factor for the development of place cells concerns the position of the landmarks in the arena. In their usual standard position the landmarks are located at the periphery of the arena, and more or less uniformly disposed around the circle. Nevertheless, a few experiments have placed the same landmarks at the center of the arena (Cressant et al., 1997). In this new experimental paradigm it becomes very difficult to record a place cell type of activity. In most of the cases, place cell coding was not stable. In a very few cases where stability could be found, this happened after a prolonged stay in the arena. In the same vein, the model gives a mathematical account of the absence or at least difficulty of constitution of stable spatial attractor basins corresponding to the learning of a place when the referent is a landmark and not an absolute direction (Gaussier & Zrehen 1995).

o Spatio-temporal function of the frontal lobe in monkey: Location versus Form in DSL

Several functionally distinct regions have been delineated in monkey. There is some agreement with neuropsychological results in human. In particular, a dissociation exists between the representation of external space, for a stimulus which has been removed from the field of vision (spatial form of delayed matching to sample or delayed alternation), and representation of the form of the visual objects.

Electrophysiological recordings and lesions studies have localised the memory for space in dorsolateral prefrontal region, principal sulcus in particular. The inferior prefrontal convexity ventrolateral to the principal sulcus processes color and form, since lesions in these areas induce deficits in tasks requiring memory for the identity of objects (Goldman-Rakic et al., 1994). Specific stimulus identity neurons there, are particularly responsive to pattern delayed response tasks. The reverse is true for neurons in the dorsolateral prefrontal cortex, and sulcus principalis coding for location. Neurons hold "on line" these distinct types of information when the stimulus is no longer present, and are clearly distinct from neurons coding for the direction of limb or eye movements that can also be found in the same areas. Degeneration studies have confirmed the anatomical links between sulcus principalis and posterior parietal cortex (area 7), and between inferior convexity and inferotemporal cortex (area TE) which respectively process spatial and pattern visual information. As yet, it is not clear if spatial information recording takes place in either allocentric or egocentric coordinates or in both. The possibility remains of both, since at least in primates hippocampus could be the locus of processing for space in an allocentric (not necessarily cartesian) frame of reference.

o Response Pattern and Motor Control in Inferior and Arcuate Convexity

Inferior convexity has also been attributed diverse other functions. According to the unlearning hypothesis, these may include inhibition or unlearning of response patterns which do not maximize the probability of reinforcement, and therefore induce a change of a predominant response mode. Finally, inferior convexity could be involved in motor control for interrelating the stimulus-reinforcement associations with behavior, in order to promote motivated behaviors and to prevent indiscriminate motor choices.

o Autonomic and Motivational control in Orbital Frontal Cortex

Another, uncontroversial functional focus is located in the medial orbital cortex and endowed with autonomic and emotional control. It could be involved in motivational evaluation of reward and continuous modulation of ongoing behavior by competing drives.

Nevertheless, in monkeys as in human, there are arguments against a functional compartmentalization that would be uniquely based on perceptual modality. Reversible lesions of the dorsolateral Pc during a cross-modal version of delayed matching-to-sample task produce deficits in somasthesic, spatial or nonspatial WM demonstrating the amodal or supramodal processing taking place in these areas. This could result from a partial convergence of inputs from posterior cortical areas to the Pc.

As in man, at this neurophysiological level, there is evidence both for functional uniformity of the prefrontal cortex, in particular with regard to WM function and neurotransmitter modulation such as dopamine, and also for diversity, as shown by lesion and degeneration studies in animal.

5 FUNCTIONAL MODEL

We present first a global model of Pc-Hs functional relations which specifies the contribution of Hs in LTM consolidation and transient WM operation. Then we compare and contrast the respective roles of both structures in spatio-temporal processing. In particular we give an integrated view of the different experimental results concerning place cells, view cells and the experimental conditions leading to the emergence (or not) of such abstract representation of space as place cells, and also the plausibility of more elaborated cognitive maps. We suggest one plausible mechanism (retropropagation of goals) and its cortical implementation which controls selection and hierarchical ordering of a sequence of elementary step-actions in order to lead to subgoals and final goal. In this endeavor we not only take into account cognitive processes but also drives and motivations. The mathematical model has been simulated. It is also the object of an algorithmic implementation for the control of robot navigation either in open space, or maze environment.

5.1 CORTICO-HIPPOCAMPAL RELATIONS

There are many common points between functions of Hs and Pc. And one of the major problems of research on the functional relations between these two structures is rather to find what are the specific contributions of each of the two systems to this apparent functional overlap. In particular both systems seem to participate in different aspects of WM. And the capacity for a WM function can be expected to contribute a major step to encephalization. On anatomical grounds, the localization of these functions in Hs and mostly in Pc (the development of which is the most pre-eminent anatomical correlate of primate evolution), supports the functional importance of a "protracted present" for humanization and personification. WM provides the animal with the possibility to escape from a purely reflexive behavior, by taking into account its more or less immediate past and simulating the consequences of planned actions into the future, so the animal's behavior can be grounded not only upon external stimuli, but also on internal representations.

A direct consequence of this WM capacity is the possibility to learn and to plan long temporo-spatial sequences of events or actions hierarchically subordinated to a global but not physically accessible goal through intermediate subgoals. This capacity seems to constitute one of the distinctive properties of Pc. This temporo- spatial property is crucial for the orientation and situation of the animal in its environment. Nevertheless, even in this domain of sequence learning and spatio-temporal integration, several levels of analysis must be delineated. At the level of the hippocampus in particular, in rodents, there is evidence of theta and gamma rhythms possibly generated by inhibitory feedback circuits. These rhythms can be related to a basic oscillation of postsynaptic potentials under the influence of this inhibitory modulation. The gamma rhythms in particular, overriding the theta activity have been viewed as the encoding support of discrete event sequences during exploratory behavior. These sequences would be partially repeated, proceeding further as a travelling window of activity, at each theta cycle. The hippocampal NMDA receptors are endowed with slower time constants (circa 200 msecs) than the short time constants of the cortical NMDA receptors (circa 20 msecs). Therefore, they will allow for the learning of correlations between successive events occurring less than 200 msecs apart, that is about a full single theta cycle, and approximately 7 event-coding gamma cycles. This possibility remains quite plausible for rodents that would thus be able to separate events about 20-30 msecs apart. In confirmation that learning this type of sequences of elementary events could take place at Hs level, a primacy gradient of LTP has been found at the synapses between Schaffer collaterals and CA1 cells during the presentation of a sequence of stimuli (Granger et al., 1994). By virtue of this primacy gradient the earlier the event in the sequence, the larger the corresponding synaptic facilitation. Therefore at the presentation of a stimulus of the sequence the playback of the sequence in the correct order is favored.

INSERT FIGURE 5 ABOUT HERE

Despite the interest of this mechanism, our model does not operates at this low elementary level of resolution. It rather tries to emulate events reaching awareness in the human field of attention and consciousness. At this level individual mental states have an approximate duration of the order of the second. This does not certainly preclude the possibility, even in humans, of automatic subconscious temporal discriminations of sensory events in particular, of the order of a few tenths of millisecs. Increasing in duration, our activation states gain also in flexibility and control, and become closer to the brain states that actually control behavior. In the course of the chapter, arguments from neuropsychology and brain imaging have been provided in favor of an involvement of Hs at every phase of information processing, from the very short-term to the transient long- term. There are also some arguments against the implication of Hs as a "permanent" LTM store, although opinions diverge on this issue. Thus, we have been led to contrast hippocampal function devoted more specifically to information selection, consolidation, and basic temporo-spatial correlation from cortical function supporting a direct dialectic confrontation between STM and LTM during recall and recognition.

o Cortex-Hippocampus complementarity

The first claim concerns the complementarity between cortical and hippocampal memory systems. Cortex is mostly endowed with short-term and long-term permanent memory capacity, even though there exist range variations from primary, to secondary, and association areas (L"u et al, 1992). And it has more specifically, but probably not solely, a capacity for slow learning. Hippocampus is richly endowed with a full spectrum of temporal ranges, from the short- term to the transient long-term, possibly to the exclusion of the permanent long-term. More specifically, this combination of a large variety of memory registers, with just as much diversity of close loops of different sizes, including one to at least five synaptic relays, seems unique in the brain. It is probably responsible for the property of one-exposure learning proper to hippocampus. On the basis of logical arguments yet to be experimentally confirmed, we suggest that fast, transient learning should take place not only inside the hippocampus itself but also at the interface of the convergent cortico- hippocampal pathway (either entorhinal cortex or dentate gyrus), and similarly at the interface of the divergent hippocampo-cortical pathway (possibly in the cortex superficial layers). Conversely, experimentally confirmed slow-permanent learning in the neocortex could be restricted to the level of polysynaptic cortico-cortical connections.

o Two Types of Transient Memories

The second claim concerns the complementarity of the two aspects of hippocampal transient memory, intermediate transient memory (ITM) supporting a WM function and transient LTM supporting the process of WM consolidation. These complementary functions cooperate to fulfill the contradictory constraints of storing as much relevant information as possible in a large but limited capacity system. The WM function thought to operate both at cortical and hippocampal level is devoted to this segregation between information worthy to be "permanently" stored because of its relevance for survival, or its human social relevance for the personal history of the subject, and information which can be forgotten without major damage. For this purpose several hardwired devices implement different functions in various subsystems of the hippocampus:

- Severe filtering on the basis of stimulus intensity, duration, or repetition, mostly at the level of entorhinal cortex;
- Orthogonalization of noncorrelated patterns of information, along with lumping correlated information and/or suppression of redundant patterns, possibly in the dentate gyrus;
- Correlation of these orthogonal patterns on the basis of spatio-temporal criteria of either co-occurrence or sequential ordering.

The CA3 subsystem is specifically equipped for these processes of autocorrelation. There is some evidence of temporal order processing of the events at the level of CA1 (Granger et al., 1994). All these functions argue in favor of a specific processing capacity devoted to the Hs, based on ITM. This may be possibly more devoted to temporal aspects of information (like temporal order and timing), than spatial learning, which is the focus of current investigation. More exactly, spatial learning itself would include a strong temporal dimension (in the sequential recording of snapshots), where temporal order is not relevant. Correlational processing could be the hallmark of Hs, and could account for many aspects of its cognitive processing, including temporal processing. But it is certainly not the only form of processing performed in the hippocampus. On the basis of CA3 autoassociative architecture, artificial systems can be designed such that simultaneous pattern correlation processing becomes a special case of successive pattern temporal order processing. The main difference is that events occur simultaneously instead of taking place in sequence.

The other class of transient memory is transient LTM based on LTP, and a support for permanent LTM consolidation. The most prominent sites of LTP in the hippocampus are at CA1 level, but also in the entorhinal cortex, dentate gyrus and CA3. LTP is not specific to the hippocampus. Different cortical areas, in particular, are also prone to LTP. What seems more specific, if not exclusive, to the Hs is the conjunction of systems susceptible to LTP along with shorter versions of synaptic facilitation, in the framework of an architecture adapted to facilitate a smooth transition between short-term and long-term facilitation, without the need to resort to externally dependent repetitions of activation. These two functions of ITM and transient LTM are therefore complementary. Indeed, information or events have to proceed through the cortical and/or hippocampal WM process in order to get a "certification" as being worth passing to the history of the individual. This certificate could correspond to the transition from ITM supported by short duration synaptic facilitation (STP), to transient LTM supported by LTP.

o A Unique Mechanism for LTM and WM

The third claim concerns the unique mechanism supporting WM operation and LTM consolidation. This unique process takes advantage of the reciprocal, topographically organized connections between cortex and hippocampus, combined with the endogenous property of pyramidal neurons, mostly in the CA3 region, to discharge by bursts (Buzsaki, 1989), and synchronise within populations connected by previously facilitated synapses. Endogenously generated bursts of activity have been documented in the CA3 region, and are manifest at CA1 level as sharp waves. In contrast with theta rhythm which have been consistently recorded mostly in rodents, sharp waves have been also found in primates and humans. They could form the basis for reactivation of recently facilitated neuronal populations either at hippocampal level or at cortical level or both. They would correspond to what we call the print mode of the Hs, by contrast to the read mode. In episodic learning, this print mode would subserve the function, attributed to the repetition or practice process during the formation of procedural memories.

Two general mechanisms will cooperate in the reactivation of cortical patterns, starting either from these endogenous hippocampal bursting and synchronization capacities, or from hippocampal reactions to cortical activation of cue patterns. First, there is resonant or reverberating activity between reciprocally connected networks. It has been used in neural network modelling as a mechanism for synaptic weight modification leading to class learning (Grossberg, 1976a and b). Second, neural population synchrony, a consequence of the reverberant activity has been presented as a plausible temporal coding used locally by the brain for the coalescence of features into a unified percept (Singer, 1983; Gray et al., 1989). The main contention of the model is that the central location of the hippocampus as a site for both convergence from, and divergence towards the different cortical areas allows the Hs to act as an information selective pacemaker (Banquet, 1983; Banquet & Contreras-Vidal, 1994). As such it can selectively synchronize distant cortical areas that have been previously coactivated. This mechanism provides for both the refreshing of memories during WM operation, and the reactivation of cortical patterns during the more lengthy process of LTM consolidation. In this last case it will create the conditions for the slow facilitation of distant polysynaptic cortico-cortical connections, which eventually will make recall or recognition independent of hippocampal function.

o Transient Storage by the Hippocampus

The last claim is largely but not universally accepted. The information processed through the hippocampus is not bound to be permanently stored there, at least in humans. Beside anatomical arguments, like the relatively limited capacity of the system, the strongest support for this contention comes from the limited range of the retrograde amnesia in hippocampal lesions. Most of the memories from the distant past are spared. This raises the issue of the necessary transfer of the information to cortical and/or cerebellar areas, which are supposed to be among the most pre-eminent sites of permanent storage.

5.2 MODEL of DENTATE-CA3 FUNCTION

The experimental sources for the inspiration of our mathematical model are of two different types. First, the learning of space by animals as demonstrated by rat place cells or monkey view cells, and eventually the formation of cognitive maps in an allocentric frame of reference, more plausibly in primates. In our model this structuring of space is considered as a degraded form of sequence learning. Second, in trace conditioning with a motor response there is evidence of adaptive timing of the behavioral response as we shall see in the dentate gyrus model.

INSERT FIGURE 6 ABOUT HERE

In our model these two subsystems of Hs dentate gyrus (DG) and CA3 are endowed with specific functions which go beyond the classical attributes of pattern orthogonalization (dentate gyrus) and autocorrelation (CA3) which are the usual characteristics of these subsystems in neural network modeling. These two classical functions are in fact implemented in such a way as to add a temporal dimension to both of them, on the basis of experimental evidence. The addition of this temporal characteristic to these networks is globally justified by the temporal properties of the hippocampal registers which are capable of fast transient short-term or long- term learning thanks to the synaptic properties of short-term and long-term potentiation particularly developed in Hs. To this propensity for rapid transient learning must be added the loop-like organization of the different circuits which allows for a few repetitions or iterations of patterns of activation even though they have been externally triggered only once (Buzsaki, 1989). Thus, these loops endow Hs with the potential to maintain for some limited duration, or rather to punctually reactivate, a recently activated pattern that has been transiently learned in the synaptic connections of the recruited populations.

As a consequence of these temporal properties, the model implements two different temporal functions:

- First, a function of timing, i.e. a flexible evaluation of time intervals or durations, at the level of granule cells of the dentate gyrus.
- Second, the corresponding temporal or order function of the CA3 network consists of linking together successive similar or different events of a sequence. This chaining process results from a combination of autocorrelation and crosscorrelation as we will see in the paragraph on the CA3 model.

o Factorization of Time and Pattern in the Dentate Gyrus

The model presented here is based on the same principles of population learning and coding of time by a limited assembly of neurons whose dynamic range of activation varies along a biologically plausible continuum. This timing function has been attributed to the dentate gyrus on the basis of results derived from the paradigm of trace conditioning of the nictitating membrane response in the rabbit (Berger & Thompson, 1978; Solomon, 1980). The evidence of first monitoring and then anticipation of the behavioral response, by firing patterns of pyramidal cells shows up first at the level of CA3 neurons. This lets us suppose that processing the duration of time intervals takes place upstream to the CA3 system. Dentate gyrus is the immediately preceding stage (Fig. 5). Granule cell population there is sufficiently important to present variations in size and time constants which could support different dynamics of activation. There are several lines of evidence for neural dynamics in the brain varying according to a continuum, in particular in spinal motoneurons and there is also evidence of spectral decomposition of space in the visual cortex. This hypothesis forms the basis for a population coding of time by cells endowed with these different dynamics. Similar neural mechanisms underlying the hippocampal adaptive timing function during conditioning were proposed by Grossberg and Merrill (1992), among others. We have already proposed a model including a timing system which gates or modulates the flow of information in a categorization system (Banquet & Contreras-Vidal, 1993a, b; 1994). The main difference between this last model and the present one, is, first, that the onset of the input stimulus is not held on by an hypothetical external device but the STM is directly implemented through the positive feedback from the GC to MC and their return to the GC (see Fig. 7 for the DG architecture and Fig. 8 for a simulation of its temporal dynamics). A second difference is that the same populations of cells process, or register, both pattern and time, thus realizing a "factorization" of the two parameters. This basic computational competence may also be shared by cerebellum which is more suited for the motor response (Ivry & Keele, 1989; Bullock et al, 1994). There is at present no decisive argument against the fact that the cerebellum, could support the upstream system forwarding timing information to CA3. Nevertheless, the plausibility of multiple local timing systems dedicated either to perceptual, motor, or even cognitive processes argues in favor of an hippocampally based local system for the timing of perceptual events.

INSERT FIGURE 7 ABOUT HERE

The figure 8) shows how a particular punctual event can be extended in time by a battery of cells endowed with randomly varying time constants, until the subsequent significant event takes place. The two events could be the CS and the US of a trace conditioning sequence. But more generally, our system deals with any arbitrary sequence of either distinct or repetitive events or both, occurring at variable time intervals. As thus, it can account for the learning of any pair, and therefore sequence, of events independently of the presence or not of a reinforcer. reinforcement learning and conditioning becomes a particular case of this more general associative learning. As thus, it can account for the learning of any pair, and therefore sequence, of events independently of the presence or not of a reinforcer. reinforcement learning and conditioning becomes a particular case of this more general associative learning.

It cannot be excluded, on the basis of the presently available experimental evidence, that the function of maintaining a pattern of information in STM or ITM could not be performed by CA3 itself. There is indeed evidence of such a maintenance of information under a "dormant" form of short-term (STP) or long-term (LTP) synaptic facilitation. In order to be used by the system for purposes of information processing (match-mismatch, filtering, correlation...) this dormant form needs to be reactivated or reenacted as a coherent pattern of activation. In a sequence of dissimilar events, this reenactment is not possible from one event to the next. Therefore the pattern of activation must be maintained in an active form in order to be compared or associated to the next one. The circulation of information in a loop could in theory also perform this function of maintaining a pattern of information in an active state. Also, event-locked theta activity could be another mean used by Hs to protract in time an active pattern. Our system of population coding by a battery of cells seems parsimonious, flexible and therefore plausible. but it does not exclude these other possibilities.

In our model, relations of Hs with other structures in particular frontal cortex for temporal order processing, and cerebellum for timing are viewed as special cases, in the temporal domain, of the more global function of Hs as a rehearsal system for the rapid acquisition of any kind of information. This interpretation seems to be confirmed by the fact that learning this type of information, time intervals in particular, is not really suppressed by hippocampal lesion. It just requires more trials to be learned.

o A Temporal Order Network in CA3-CA1

Different models of temporal order processing have been designed. The most recent models aim in particular to emulate temporal processing attributed to prefrontal cortex. Guigon, Dorizzi, Burnod and Schultz (1994) have designed a model directly inspired from the electrophysiological studies performed in monkeys. The implementation of processing units which can commute between two stable states of activity (bistable units) in response to synaptic activations allows the learning of temporal sequences. After learning, the sustained activation of a given neuron represents the selective memorisation of a past event, selective anticipation of a future event, or the prediction of a reinforcement. Thus, the model reproduces the functions of delay neurons encountered in frontal cortex. Bapi and Levine (1990, 1994), Levine and Park (1992) designed network models of frontal cortex function. In these models, sequence learning is secured by storing in LTM (synaptic weights) the transitions between the events of a sequence. The different types of learned sequence are encoded in a compressed form, and then categorized. It presents some similarities with our own model of WM for temporal order and probability coding (Banquet & Contreras-Vidal, 1992a, b; 1993a, b; 1994). Both are in particular inspired from the same design principles of Grossberg (1978). Dehaene, Changeux and Nadal (1987) implemented a network that can learn temporal sequences based on biological properties of allosteric receptors.

INSERT FIGURE 8 ABOUT HERE

In our model, the dentate gyrus performs simultaneously the double coding of time and pattern. This output of the dentate gyrus can then be used by the CA3 stage. This stage represents a multimodal event or state as a correlation pattern of activation. It performs then for each event a double correlation:

- First, a zero-delay "auto-correlation" of the event with itself thanks to the temporal conjunction of the direct pathway input to CA3 and the fast spectral component of the indirect input transiting by the trisynaptic loop of the dentate gyrus (Fig. 5).
- Second, a delayed auto- (stimulus repetition) or "cross- correlation" (successive stimuli different) between the present direct input to CA3 and the previous indirect input which has been maintained in an active state thanks to the slow spectral components of the dentate gyrus granule cell population (Fig. 8). CA3 learns this cross-correlation between successive events. This last process results in the recording of transition states between events. These transition states allow at any points in the sequence prediction, priming or playback of the subsequent event according to the functional mode of the system (i.e. learning, recognition or reenactment of a sequence). The transition from a functional mode to the next is endogenously determined by the type of neuromodulation (ACh in particular; Hasselmo et al., 1994) and the biological rhythms.

For the purpose of linking a specific behavior to a particular view of the environment, as in a PerAc (Perception- Action) architecture (Gaussier & Zrehen, 1995), linking of these transitional states to elementary motor actions has been found to better support the planning and implementation of specific sequences, rather than the mere relation of perceptual states to actions (Fig. 10; Gaussier et al 1997a,b). These transition states do not differ in their coding from simple states since they are also encoded as correlation patterns in CA3 network. Their meaning is different since they correspond to the correlation between patterns which do not occur simultaneously in time. The timing system of the dentate gyrus is set in derivation on the main flow of information that transits through CA3, and thus modulates or even gates and controls the activity of CA3. This property makes the system very flexible with respect to the nature and variable timing of successive significant events.

The learning not only of autocorrelations between simultaneous patterns of activation, but also of "cross-correlations" between successive patterns can subserve several functions. First, during the learning process of a repetitive sequence, the predictive activity of the system results in priming the next event in the sequence when the present pattern of activation acts as a trigger for the transition pattern. This priming is critical for the implementation of the match-mismatch process that operates to recognize the successive events of a sequence at CA3 level. There, the previous pattern maintained in DG and reaching CA3 by the mossy fibers is matched with the present pattern of activation forwarded by the direct connections from EC to CA3 pyramides distal dendrites. Therefore, the learning process is modulated according to the degree of predictedness or novelty of the events. Hasselmo et al. (1994) has shown how ACh septal modulation of the Hs activity could provide for an automatic control of the learning process, as a function of novelty or familiarity of the events. One can suppose that a match inducing familiarity preempts the learning of a new transition and sequence. The resulting "resonance" between learned and input patterns provides for both the transient stability of a state and the reinforcement of previous learning. Conversely, mismatch between the expected or primed pattern and the input pattern fosters, by means of a high Ach modulation, the prevalence of input over the stored pattern and therefore the recording of a new transition pattern. Second, in sequences of events that occur only once or a few times, the Hs provides the unique facility for fast transient learning, thanks to its capacity for reenactment of recent patterns of coherent activation. This reenactment correspond to a synchronous discharge of CA3 neurons which activates CA1 pyramidal cells. The activity of CA1 cells manifests as sharp waves (Buzsaki 1989). These sharp waves present some of the characteristics, in particular in amplitude and frequency, of the stimuli capable of inducing LTP. They could therefore participate in the reactivation of cortical patterns necessary for the LTM storage at cortical level. The linkage between successive events constituting transitional states would result in a playback not of single events but of sub-sequences of events.

5.3 From HIPPOCAMPUS to PREFRONTAL CORTEX

INSERT FIGURE 10 ABOUT HERE

This memory of states and transitions forming a sequence of events is, in the model, further integrated at CA1 level, with a possible partial restitution there of the "cortical" topology thanks to the direct pathways from entorhinal cortex third layer to CA1. From CA1 there are direct as well as indirect connections to prefrontal cortex. At this prefrontal site the long-term registration of a sequence can be considerd as a result of the successive activation of nodes which can be assimilated to cortical columns. By the very orderly nature of a sequence encoded by a spatial pattern of activation, one could assume that the best neurophysiological support for such a storage would be a unidirectional facilitation of the synaptic weights of a specific path in a network architecture, as it has been implemented in Bapi and Levine (1994). It is plausible that such an oriented unidirectional facilitation takes place in primary or secondary cortical areas. Nevertheless, the prefrontal cortex is the most plausible site for the linkage between sensory and motor sequences at least at a high level of controlled processes (Fig. 9). This does not preclude the possibility of sensory-motor links at subcortical or even lower levels as schematized by figure 9. At cortical level, the execution of a sensory-motor sequence is necessarily linked, at least implicitly, to the completion of a goal selected by motivation. A goal in the model corresponds in fact to a secondary goal, i.e. a situation which allows the satisfaction of a basic drive or of a sublimation of this basic drive. At the executive controlled level of the prefrontal cortex there is clear, even if only subjective, evidence that the goal is usually present and therefore activated at the very onset of the sequence. Thus it can influence the choices of subgoals and the hierarchical unfolding of specific endeavors to reach them. The most parsimonious implementation of this psychophysical reality requires the instantiation of a bidirectional facilitation of the different pathways leading from the starting point to the goal of a sensory-motor sequence. In this way, the activation of a goal induces a retropropagation of activity, similar to a priming by top-down activation from the categorial nodes in an ART architecture (Grossberg, 1976a, b). Yet, here the priming process concerns an entire sequence of events, and accordingly, is implemented according to a gradient. This subliminal backward priming of a sequence in conjunction with a bottom-up activation from subcortical structures such as the hippocampus helps the selection of the best sequence of actions to reach a specific goal. This process of goal retropropagation is not solely efficient for selecting the optimal way for goal attainment. It also operates in deciding the order of goal satisfaction, when several goals are simultaneously active or in competition. As such, it implements aspects of hierarchy setting performed by Pc. Similar disambiguation between several possible sequences takes place at Hs level during the playback of the sequence if the prediction of the future event is based on several previous events instead of just the immediate preceding one.

When such a neural network is used for the control of a mobile robot, different types of behavior in order to select and reach a goal are exhibited by the robot. These choices are dependent on three parameters of the system: the relative strength of the different drives, the weights of the connections implicated in the different paths, and the required match level between perceived and memorized steps towards the goal. Any node of the cognitive map learns transitions between pairs of learned places. The level of activation of these nodes results from the addition of bottom-up (match- related) and top-down (drive and path length-related) activations. These combined activations of the nodes can lead to a variety of behaviors of the system which have counterparts in real life. If the top-down influences are too weak, the system is unable to follow a specific path for the attainment of a specific goal. It is susceptible to distraction by any new input previously associated with a different behavior. Conversely, if the saliency of the top-down input is too strong, the recognition of a situation could be biased in the direction of a situation corresponding to the satisfaction of its goal. The initiation of such erroneous recognitions can be self-reinforcing. All these situations correspond to pathologies of frontal lobe.

6 FRONTO-HIPPOCAMPAL FUNCTION and PERSONALITY

Personality in humans presents three key "primitives":

- First a temporal function which seems to obey some principle of symmetry of past and future, memory and prospective, with respect to the present. This temporal memory function is mostly based on the capacity to evaluate and record the order of occurrence of event sequences (a kind of segmentation lost in frontal patients), and complementarily the capacity to recognize new from familiar events (a kind of fusion of events lost in hippocampal patients). We have seen the importance of the Hs in the recording of "one exposure" events. The consequence of the suppression of this memory function is illustrated by anterograde amnesia, i.e. the incapacity starting at a period of life, corresponding to some time prior to the lesion, to build up a continuing history, just as if the factual life of a person had stopped at this moment. Yet, the Pc is also involved in this historical function, as one of the favoured cortical sites for the permanent recording of these event memories. Symmetrically, the prospective function supposes the capacity to project in the future an orderly sequence of planned events in order to either actually perform them or merely simulate them. This planing capacity is also an hallmark of personality. This function is as important as the previous one, and in fact intimately linked to it. Our capacity to make plans, i.e. to project our actions in the future, is narrowly dependent on a library of past behavioral schemes and of their consequences. As our personal history goes back in time as far as our early childhood, our ability to project our life in the future concerns more or less remote time. The range of this prospective capability is closely linked to the strength and integration of our personality, and supports our motivation. Mostly from neuropsychological studies, the role of the Pc in this function is well documented. Pc is essential not only for the strict and logical ordering of events or actions. Furthermore, it operates in the determination of an hierarchy of subgoals and actions to reach a predetermined goal. The incapacity to forecast the consequences of actions could be responsible, along with the neutralisation of affective life, for the incoherent and self-destructive behavior eventually encountered in prefrontal patients.

- Working memory can still be considered as a part of the temporal function. Nevertheless its unifying role, and its implication in practically every other function related to personality deserves a separate account. The historical and prospective function, in particular, could not exist without the support of an "extended present", i.e. a working memory. The capacity to link successive, logically related events oriented towards the performance of a task, or the accomplishment of a goal, is essential to the development of personality. WM is not present in early childhood and this absence explains the non-permanence of hidden objects in the field of consciousness as internal representation, and therefore the incapacity to perform delayed tasks. This capacity progressively develops during infancy, and probably supports the unfolding of logical reasoning. This logical function is a prototypical illustration of the characteristic of WM defined as both maintenance and manipulation of information over an extended period of time. Classically, Pc is endowed with WM capacity, but so also are temporal and plausibly other cortical or subcortical structures. Our contention is that Hs also partakes of an automatic aspect of WM, even though delay neurons have not been recorded there, as in different cortices. We have proposed at least three subsidiary mechanisms that could support this function at Hs level.

- Emotions and motivations are another important facet of personality. One could hardly contend that a robot is a person even though by its previous experience it can have a semblance of history. Emotions could be viewed as resulting from sublimation, but certainly not a suppression, of basic drives including the instinct for survival and even the instinct of death. Motivation could result from an integration and a trade-off between the need for drive satisfaction, emotions, and social constraints. Motivation is usually dependent on the degree of satisfaction of these needs. Here also limbic system and Pc act conjointly. Amygdala is as important for emotional life as hippocampus proper is important for correlational and WM functions. Similarly, orbito-frontal and medial Pc are essential for the integration of drives, emotions and motivations while more cognitive information processed in dorso-lateral Pc. The suppression of any type of affective colour, positive or negative, in the life of severely damaged prefrontal patients, as after lobotomy, induces a disengagement from real life. This underlies the importance of the integrative function of Pc, in particular, between cognition and emotion. These different functions are not compartmentalized. In particular emotional charge of events, as previously mentioned, modulates the process of memory consolidation in the hippocampo-cortical system. The cooperation of these different functions is perhaps best perceived in the mechanism of attainment of goals.

- Attainment of goals can be considered as the uttermost expression of the cooperation between Pc and limbic system. This function presents: -a sensory aspects which consist of recognition of goals and evaluation of the outcomes of action; -a motor aspect made of the setting and execution of motor programs. In the classical learning theory, such as proposed by Skinner (1953), the necessary chaining of sequences of sensory- motor events results from associative (or operant) conditioning of a neutral stimulus by a reinforcer. And cascades of secondary, and higher order, conditioning could account for linking sequences of events together. Obviously, this process can be and has been accounted for without the extensive implication of prefrontal cortex as in our model (Gray et al., 1991). The main structures concerned are hippocampus, amygdala and basal ganglia. They certainly correspond to a kind of automatic operation mode for the attainment of goals. Nevertheless, several problems arise if the basic components of sequences, plans, or chained actions remain limited to stimulus-response conditional associations. In particular, latent learning (Tolman, 1948) does not obey any clearly defined drive satisfaction, motivation or goal attainment. The conditioning process seems to work correctly for simple sequences of actions. But, taking into account simply the present states in the recognition or reproduction of long sequences of actions leads to a combinatorial explosion of possible paths, which can only be avoided by an active representation of more than one pair of events. Furthermore, the strength of secondary or higher order reinforcers seems to sharply decrease with the distance to the unconditional stimulus. Significant progress has been achieved by the identification of latent learning useful to build cognitive maps, even if these maps are used independently of any prespecified goal. We think that the definition of goals based on the satisfaction of basic (or not so basic) needs conjointly with the learning of more or less complex maps is a further step required to account for complex behaviors. The possibility for diffusion, and in particular retropropagation of goals allows the discovery of solutions that have never been experienced during learning, and thus are created from new by the system. This is an actual illustration of creativity. This functioning mode requires a supplementary degree of freedom in the system, independent from both sensory and motor processing, but still bridging the two systems. This extra degree of freedom is provided by Pc. The efficacy of an algorithmic version of the model for the parsimonious solution of several problems of robotic learning and navigation either in free space or maze constraint does not automatically deliver a certificate of biological plausibility for the system. Nevertheless, the fact that this efficacy has been obtained thanks to a stringent taking into account of essential neurobiological constraints, makes us confident that the model is oriented in a relevant direction.

7 CONCLUSION

Two different forms of memory, "active" and "dormant" , supported respectively by post synaptic potentials (PSPs) and synaptic potentiation are present everywhere in the brain. The interplay between the two forms of memory and in particular the transition and/or the modulation of one form by the other are at the bases of the different processing modes and memory capacities of the brain. Variations in the implementation modalities and in the ranges of these two types of memory along with variation of connectivity give functional specificities to the different systems. This is specially true for Hs and Pc.

Cortical processing depends essentially on two memory registers, STM and permanent LTM. The transition from the long-term to the short-term seems to be direct and normally encounters few problems. Plausibly, at a gross level of analysis the anatomical substrates are topographically identical (STM representing active forms of LTM). Nevertheless, at a fine grained level, the neurophysiological supporting mechanisms must be necessarily different as previously mentioned, involving respectively either electrical or durable structural-chemical changes. Conversely, the transition from STM to LTM store follows a more intricate path, probably for the sake of optimizing the amount of information stored, but also for securing the storage of unique events which built up the unique history of each living being. Between these two extreme ranges (STM and LTM), only minor variations from primary to associative areas can be recorded at the sole cortical level, with a tendency to an increase in the temporal range of memory with the increasing level of complexity in processing performed by these areas (L"u et al., 1992). Prefrontal and temporal cortices are endowed with delay neurons that can bridge a gap between two sensory or sensori-motor events. Nevertheless, the temporal range in the usual experimental tests of this property remains largely in the domain attributed to STM, i.e. less than 30 secs.

The specificity and vantage point of Hs concerns both topographical and temporal facets. The topographical aspect of Hs specificity as a unique compact site of input convergence and output divergence has been extensively emphasized. It has been credited with the correlational function of Hs which implies some loss of the cortical topology. This functional characteristic is corrected and complemented by a loose topological correspondence between cortical and hippocampal system in the longitudinal direction. This loose correspondence could be transformed into a dynamic learning-dependent precise mapping between hippocampal and cortical neuronal populations in order to implement the topologically specific consolidation function. This function could be implemented thanks to the fast-transient learning capacities present both within the hippocampus itself, and also at the interfaces between cortex and hippocampus. The emphasis placed on the spatial aspects of Hs function was detrimental to the exploration of the no less important temporal function. This function results from the capacity of Hs to interact very flexibly with a whole spectrum of registers from the short-term to the long-term, and also possibly to be detached from permanent LTM. The unique characteristic of Hs would be the conjunction of this array of registers with a wide variety of loops of various sizes providing for an easy transition between dormant-inactive and re-activated forms of memory.

Beyond these range differences between cortex and Hs memory registers, some more subtle differences could exist in the implementation modalities of active memory. Extensive research has been conducted on delay cells in Pc or temporal cortex, as a support for WM. Indeed, this type of activity can bridge the gap between two sensory or sensory-motor events. Up to now, delay cells have not been located at the level of the Hs. Nevertheless, the equivalent function in Hs could be performed by different mechanisms subserving slightly different functions.

First, loop iterative activation could operate the punctual reenactment of recorded patterns of activation either during information processing in WM, or during the more lengthy process of LTM consolidation.

Second, spectral timing as performed in our model by DG could also operate the function equivalent to that of the cortical delay neurons. This function consists of maintaining significant information in an active state, while waiting for correlation with a new significant event. This process creates the chaining of basic components of the sequence. The Hs functional specificity would be in multimodal fusion and correlations.

Finally, event locked and modulated theta activity could constitute, at least for some species, a basic mechanism for the maintenance of a pattern in an active state, thus making possible a cross correlation with forthcoming significant patterns.

These types of complementary "hardware" constraints in the implementation of active memory and in the range of "dormant" registers determine the type of cooperation established between the two structures Hs and cortex. Further complementarity results from the direct contact of the cortex with environment, favoring externally triggered activation. Conversely, Hs is the only brain structure so easily prone to autoactivation. That property leads, in the pathological domain, to seizure activity. The specific import of Pc to this processing chain seems to result from its unique position at the top of the hierarchy of sensory-motor and motivational streams of information (Fig. 9). Both, its independence from and its close contact with multisensory and complex motor representations or codes provides the entire system with an extra degree of freedom. This feature gives to the brain the capacity for:

- recording and simulating both sensory and motor sequences independently of their actual implementation, in relation with planning and adaptation
- motivated hierarchical selection of goals and subgoals, and goal attainment
- finally invention and creativity

These properties can be considered as the highest expression of all these capacities.

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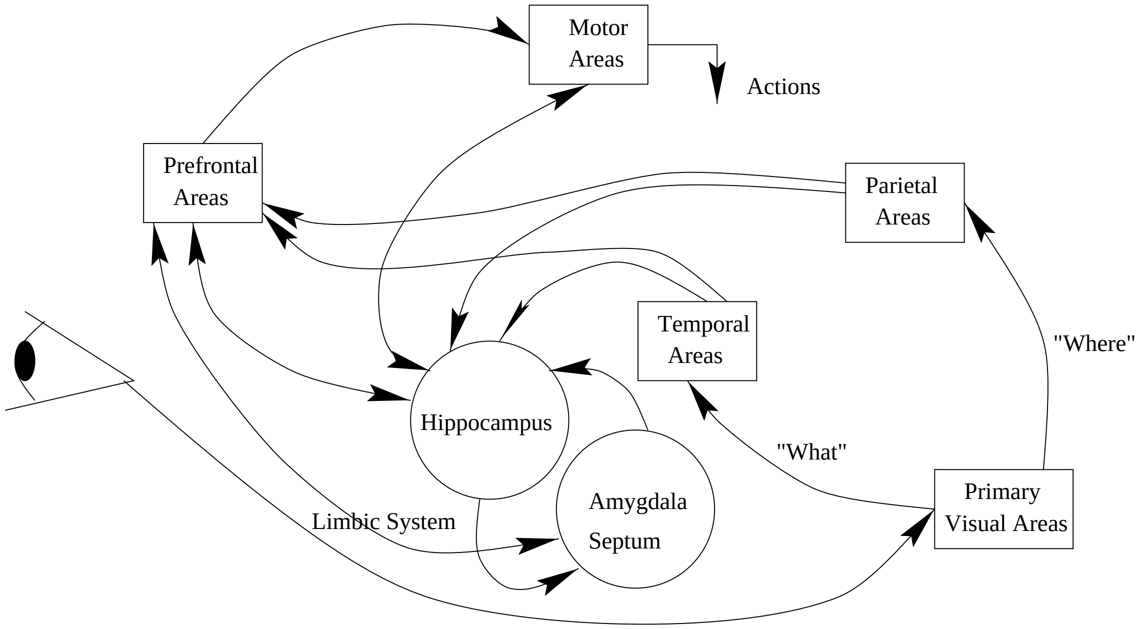

Figure 1: A global view of the cortico-hippocampal relations. In the model, the hippocampus is used as a plastic fusion operator and Working Memory (WM). It allows through its connection with the limbic system to regulate vigilance and learning levels.

Figure 2: -A: Two component free recall task. Mean percentage correct recall (immediate recall) as a function of order of presentation for subjects presenting partial lesions of the hippocampus or Korsakoff syndrome (amnesic) and controls. - B: Short-term forgetting. Short-term retention of word triads for amnesic and normal controls. -C: Digit span: Immediate memory for digits in amnesic patients and normal controls. Mean percentage of sequences correct as a function of sequence length. (Adapted from Baddeley and Warrington, 1970, with permission). -D: Adjusting delay procedure of the delayed matching-to-sample task. Delay periods on consecutive trials of the adjusting delay series allow a quick check on the limits of the subject's ability to remember the sample. On combination of three consonants trigrams, HM had no difficulty in remembering the trigrams for as long as 40 secs. On the set of geometrical stimuli (eight different ellipses) progression was reduced to steps of 1 sec with best performance at 5 sec delay, achieved once.

Figure 3: Behavior of the right hippocampal (left), right occipital (middle), and right prefrontal (right) regions, in comparison to the fixation-point control condition, for four task conditions (i: no response; ii: baseline stem completion by first word to come to mind, no stem could form words presented; iii: priming: stem completion by first word to come to mind, half the stems could form words already presented; iv: stems had to be used to recall words from the list presented, half of the stems could be completed to form these words). The right hippocampal response observed in memory minus baseline subtraction (fig 2A, table 1, Squire et al. 1992) did not arise simply as a result of a reduced hippocampal activity in the baseline condition. A right hippocampal response was observed both in the priming-minus baseline subtraction and in the memory-minus priming subtraction. Conversely, the right prefrontal response was more specific to the memory task. (Adapted from Squire et al. 1992, with permission).

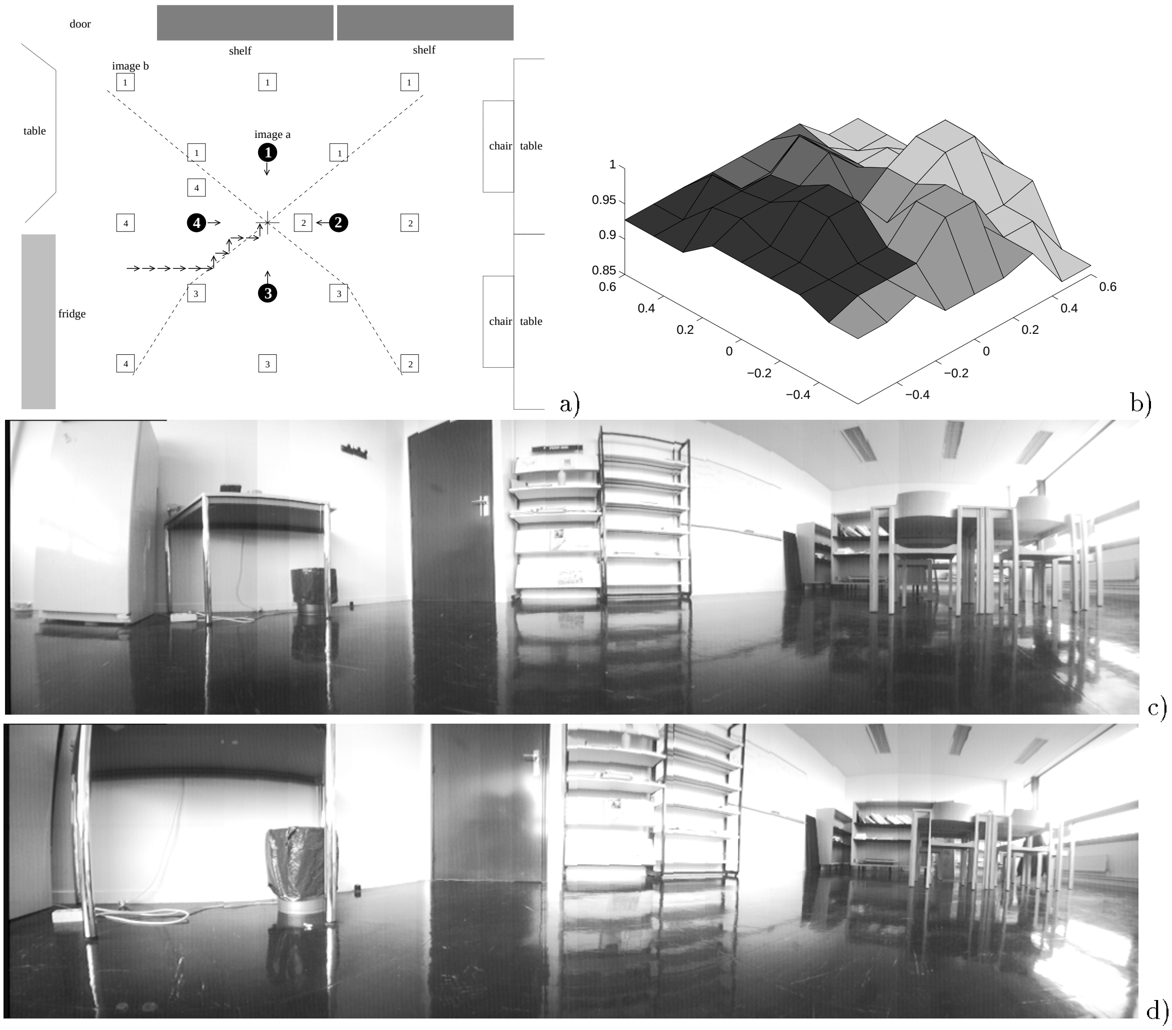

Figure 4: Place cell-like segregation of space in a robotic experiment. a) Four views are learned (circles), others are associated with one of those learned (boxes). As we can see, if the robot learn to reach the cross from each learned view it can reach the cross from all the views (generalization). The set of arrows represents a possible path. The views are in a 1:2m x 1:2m area, the learned views are at 30 cm from the center. The scale is not respected for the position of the different furniture (in fact they are about 1.5 m from the center). b) The different learned view cell activities for several positions in the same environment (unit is meter). c) and d) Panoramic images referenced in a).

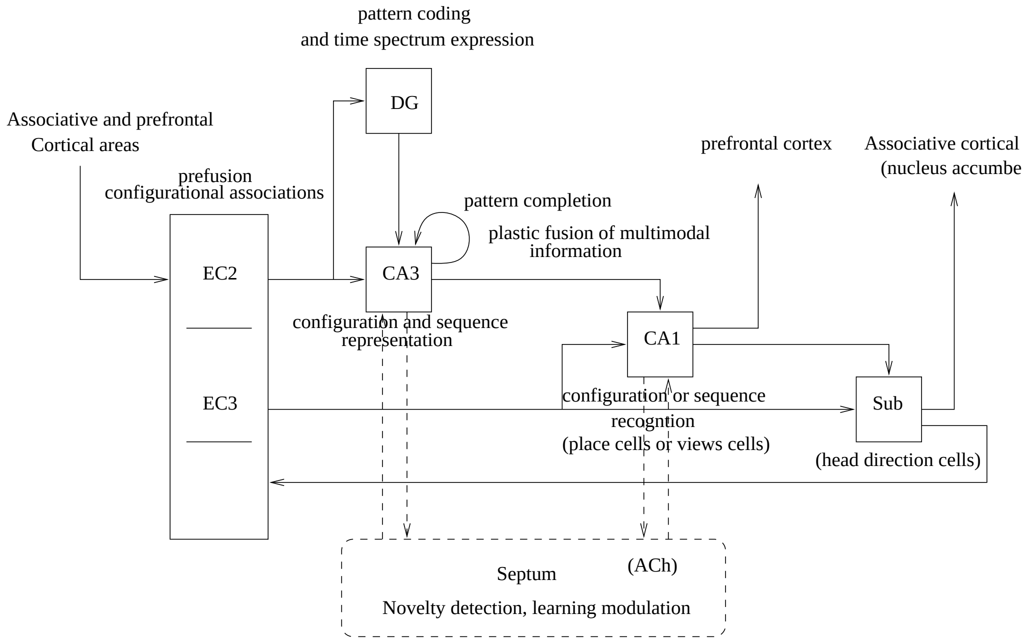

Figure 5: Schematic representation of the hippocampus. Entorhinal Cortex (EC) receives information from the associative cortical areas. Highly filtered information form the EC layer 2 is transmitted to the Dentate gyrus (DG) and to the CA3 pyramidal cells. In the model, the DG recognizes activity pattern from EC2 and develops a temporal activity spectrum (factorization of time and pattern). CA3 recurrent links allow pattern completion and association between an incoming pattern and a previous pattern recognized and maintained in DG granular cells. CA3 allows a "plastic" fusion of multi-modality information. Integrated recognition of the CA3 representation is performed on CA1 pyramidal cells. It can be either place recognition (i.e. rat experiments) or view recognition (i.e. primates) and more generally sequence recognition. Information from CA1 is then treated by the Subiculum (Sub). This information could become invariant to animal orientation due to this structure (i.e. head direction cells).

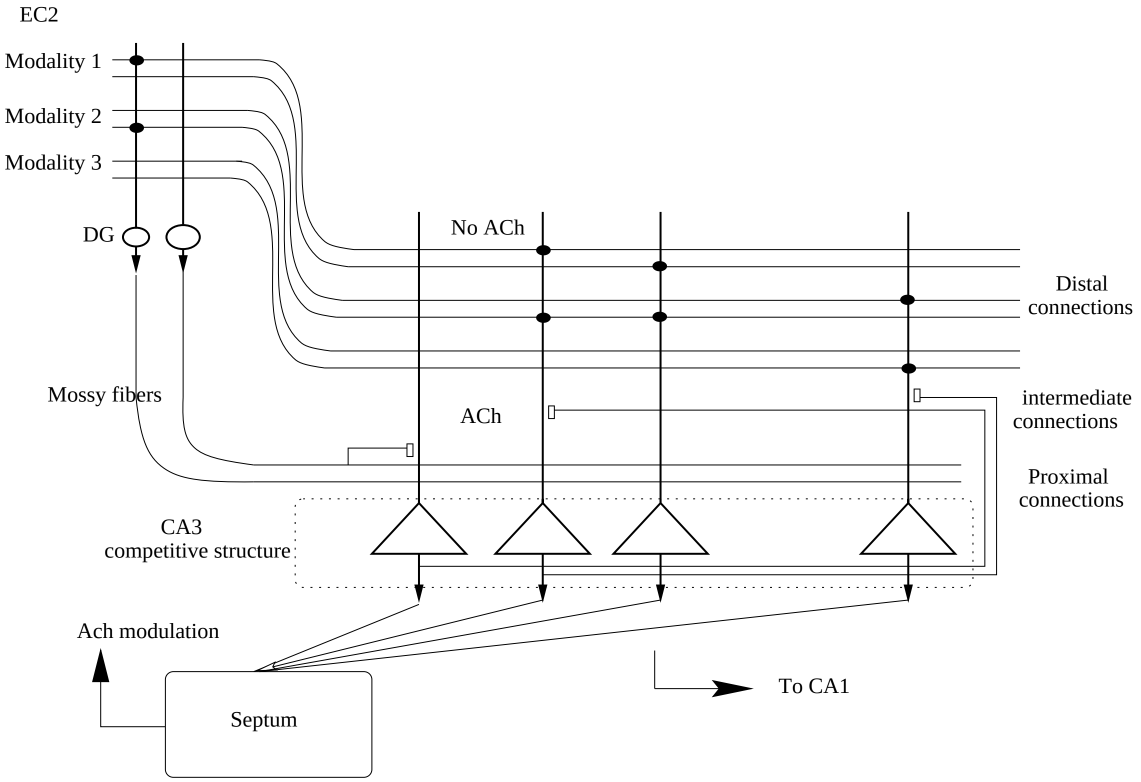

Figure 6: Detailed model of the CA3 connections Figure 7: Detailed representation of the different neurons and connections in DG used in our simulations. Instantaneous information coming from EC2 is learned by the Granule Cells (GC). We suppose activity spectrum of GC depends on their size. GC are linked together in a functional cluster through a particular Mossy Cell (MC). This recurrent connection allows GC to develop time spectrum activity while EC2 stimulation is over. Basket Cells (BC) allow choice of a winner cluster of GC: pattern recognition of EC2 information. Another MC and BC subset allow the reset of the active GC cluster at the onset of new significant input from EC2 to avoid pattern recognition problems.

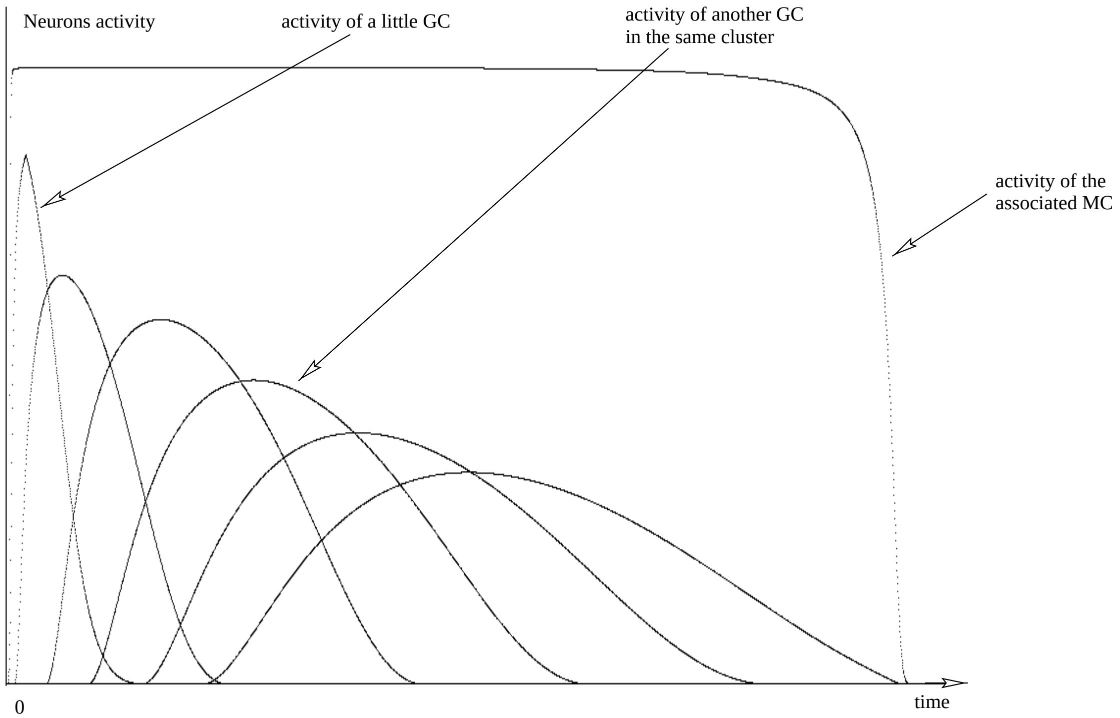

Figure 7: Simulation of a cluster of "spectral" Cells (GC) randomly selected in the Dentate Gyrus (DG). A pattern is presented just at time 0. As a result, the GC develop a time spectrum activity depending on their size. Activity of the GC is maintaining due to recurrent connection through a MC cell. The decrease of GC activity is due to an habituation term at the synaptic level (between MC and GC).

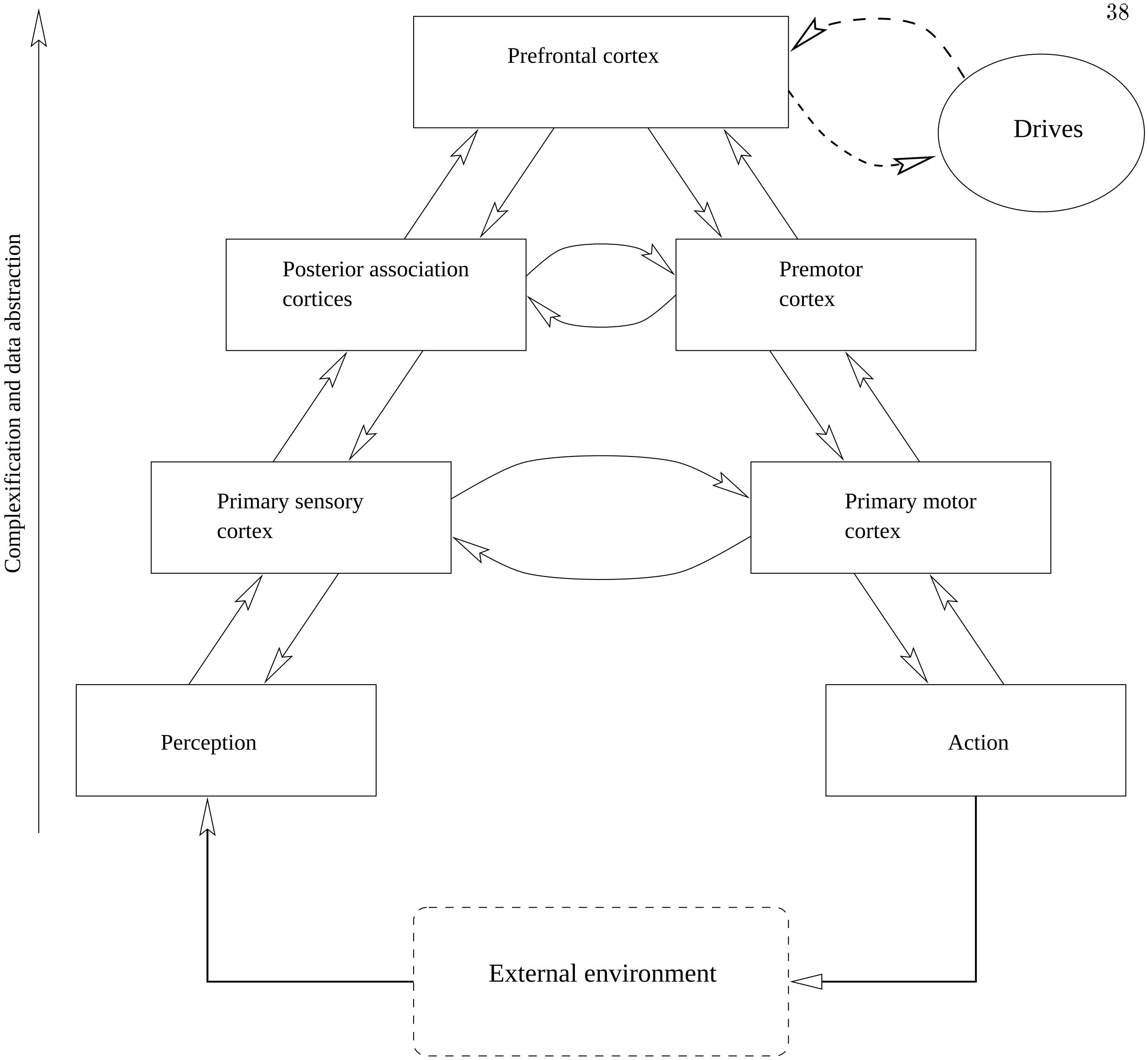

Figure 8: Flowchart of multilevel information transfers: 1) between sensory and motor areas (horizontal connections) 2) between sensory (or motor) and associative areas of increasing complexity (vertical connections) 3) between internal drives and planification capabilities (prefrontal cortex)

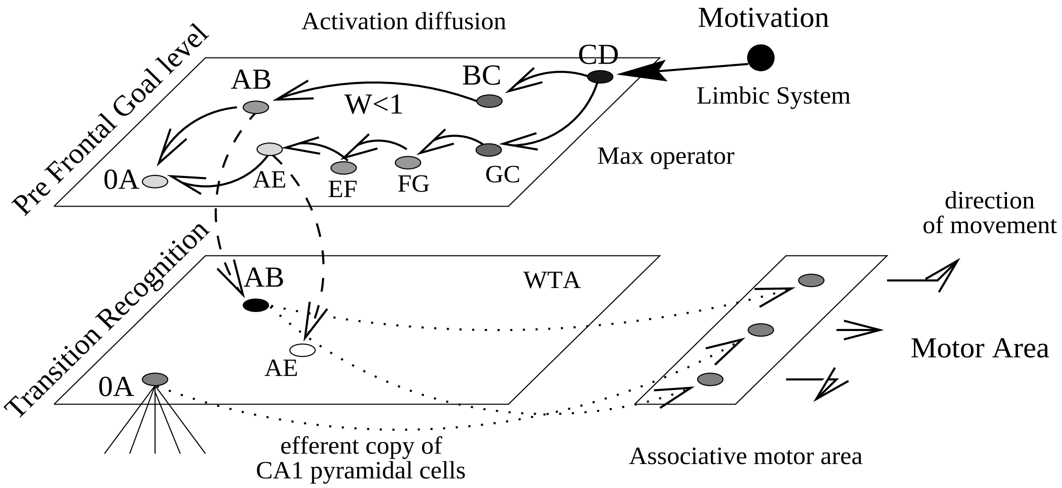

Figure 9: Goal backpropagation: The model is used to learn transitions between stable states such as to go from A to B (AB) and next from B to C (BC)... on CA1 neurons. CA3 neurons are used to merge the recognition of the current state coming directly from the entorhinal cortex EC2 and delayed information about the previous state that we suppose comes from the Dentate Gyrus and more precisely from the Granular Cells (the GC developing a time spectrum expression of the information coming from EC2). The CA3 representation of the state transition is then learned on CA1 neurons and copied on prefrontal cortical neurons which learn the "anti causal" (backpropagated) links between pairs of transition states. These prefrontal neurons also learn associative links with motivation nodes if they are activated simultaneously with them. Assuming the activation of a motivation coming from the limbic system (the will to eat for instance), the model explains the propagation of the goal to subsequent subgoals on the prefrontal cortex. When a subgoal transition can be achieved because the robot state corresponds to the first part of the transition, the associated learned action is the trigger and allows the robot to reach a new state which is the starting point for triggering the recognition of a new transition. When several transitions are possible from a current state (like BC or BD) the level of activation of the prefrontal neurons associated with the different possible transitions allows the choice of taking the shorter or the most interesting pathway from the current state to the final goal.

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