TEMPORAL DYNAMICS OF ATTENTION AND MEMORY: NORMATIVE AND CLINICAL STUDIES

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Recent invasive primate studies of attention generally agree that attention acts to enhance the mean firing rate of individual neurons and that effects of attention can be demonstrated at many levels within the visual system, including primary visual cortex (e.g., Ito and Gilbert, 1999; Mehta et al., 2000). The monkey studies also suggest that the initial feedforward flow of information establishes the neuron's classical receptive field and its basic tuning properties typically associated with *pre-attentive* processes (Lamme and Roelfsema, 2000; Worgotter and Eysel, 2000); this feedforward sweep through the ventral stream is complete within 100 ms poststimulus. Maunsell (1995) points out that the difference between early and later stages of visual processing include not only changes in the complexity of the stimulus attributes that they represent but also a transition from veridical representations of the visual image to representations which emphasize the viewer's interest; that is, vision is an active process. Our laboratory has attempted to profile feedforward versus feedback activity in the occipital cortex of humans (Aine et al., 2003) and has examined when and where effects associated with attention/memory occur during direct tests of attention/working memory (i.e., the subject/patient is instructed that they need to remember the items for later recall or recognition). This talk will review results from our laboratory and others to examine whether or not some pathological conditions result from the ability or inability to modulate early sensory activity. For example, significant abnormalities in early sensory processing have been shown to exist in schizophrenia patients (sensory gating deficit) which suggest abnormal responses to the second stimulus of sequentially presented paired stimuli, relative to normal controls (e.g., Freedman et al., 1996). Our pilot data in schizophrenic patients also reveal earlier maximum peak latencies in the timecourses localized to medial occipital cortex, compared to normal controls. In contrast, early visual activity in patients diagnosed as being mildly cognitively impaired (MCI), appear delayed and reduced in amplitude compared to elderly controls (see Figure 1).

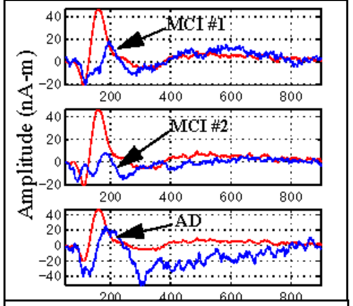

Fig. 1. Response profiles from 6 healthy elderly were localized to medial occipital cortex during a delayed-match-to-sample task and were then averaged together (see the large amplitude tracings). Tracings marked by an arrow represent timecourses from 2 MCI patients and one patient with Alzheimer's disease.

The preceding discussion deals with direct tasks. However, we have also been examining data acquired from an indirect auditory task. That is, subjects engage in semantic decision tasks (e.g., Is the word heard larger than a television set?) and are not told to remember the items for later recall/recognition, although their recognition memory for these items is tested later. This type of task has been used frequently to examine repetition priming effects (e.g., Tulving and Schacter, 1990). In perceptual priming, a non-conscious form of memory (implicit or nondeclarative memory), individuals tend to have lower perceptual identification thresholds for repeated stimuli (i.e., faster and more accurate) with concomitant reduction in activity in posterior regions upon repetition (Squire et al., 1992; Buckner et al. 1995). Several investigators have demonstrated that this type of primitive memory is distinct from explicit episodic memory; it is preserved in amnesia for example (Schacter and Buckner, 1998; Wiggs and Martin, 1998). Repetition priming is often linked to the physiological findings of repetition suppression effects noted in monkeys which have typically been documented in posterior association and inferior temporal regions (e.g., Desimone, 1996). Stimulus repetition in monkeys leads to a smaller population of activated cells in posterior cortex, or smaller stimulus representations in posterior cortex (Desimone, 1996; Rolls et al., 1989). In our indirect task, two groups of healthy normal subjects (20-40 and $\geq$ 65 years) listened to a list of 105 words representing common objects, 3 times. The subjects' task differed upon each presentation: 1) is the object larger than a television set; 2) is the object used in daily living; and 3) after 20 minutes, the original list of words was embedded within a new list of words and subjects had to decide if each word was one they heard previously. Our results suggest that differences between the 1st and 3rd trials were significantly different for young subjects only in the superior temporal gyrus (see Figure 2) and that dorsal lateral prefrontal and anterior cingulate (bottom portion of Figure 2) did not reveal significant differences between the 1st and 3rd trials at all.

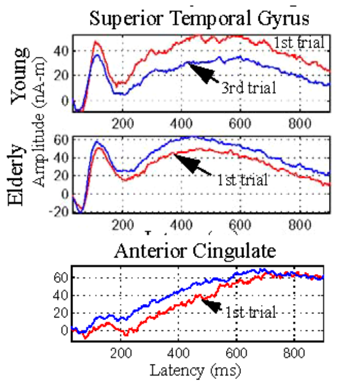

Fig 2. Response profiles from 10 young and 10 elderly subjects were localized to the superior temporal gyrus during the indirect verbal memory study. Response profiles from the young were averaged together (top row) and response profiles from the elderly were averaged together (middle row). Each plot shows averaged profiles when the words were heard the first time and third time. Anterior cingulate responses did not reveal significant differences (bottom row).

In conclusion, although many studies have been conducted in the past suggesting the existence of many different forms of attention and memory, recent reviews of the functional neuroimaging literature reveal few qualitative differences in neural patterns associated with attention, learning, and memory, including short-term versus long-term memory and encoding versus retrieval processes (e.g., Cabeza and Nyberg, 2000; Duncan and Owen, 2000; Ranganath et al., 2003; Andreasen et al., 1995; Fuster, 2001; Schacter and Wagner, 1999). Similarly, investigators of attention and memory in monkeys generally conclude that many of the psychological constructs encountered in cognitive psychology are likely to be indistinguishable at the level of cortex (Desimone et al., 1995; Fuster, 1997). However, one distinction between memory systems has garnered support from both the animal and human literature. Implicit or nondeclarative memory (automatic) versus explicit or declarative memory (controlled processing) appears to be distinguishable at the cortical level in rats and monkeys and by neuroimaging studies in humans (Desimone, 1996; Schacter and Buckner, 1998). It is our working premise that pathological processes can to some extent be understood by how early in time feedforward activity interacts with feedback influences. These two types of tasks allow us to examine the temporal dynamics of several different aspects of automatic versus controlled processes. If an interaction between controlled and pre-attentive processing occurs too early, it may be difficult to discern fact from fiction (e.g., reality versus hallucinations). This investigation should be considered exploratory.

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