The Effect of Memory Load on the Relationship Between the Dorsal Hippocampus and the Prefrontal Cortex in Spatial Working Memory

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A number of pathological disorders including schizophrenia, bipolar disorder, depression, and obsessive compulsive disorder appear to have in common impairments of the prefrontal cortex and hippocampus. A common symptom of these disorders is a deficit in spatial working memory. Not surprisingly, accumulating evidence strongly supports the prefrontal cortex and hippocampus as key brain regions associated with the spatial working memory system. However, it is unclear what the specific roles of each are in regard to spatial working memory as a function of time or memory load.

The purpose of the present study was to determine the roles of the dorsal hippocampus and prefrontal cortex in short- versus intermediate- versus long-term spatial working memory, under the effects of increased memory load. Animals were initially trained on a radial eight-arm maze using a delayed nonmatching-to-place (DNMP) paradigm. During the training phase, animals visited 4 randomly selected arms serially. This was followed by a 10-second delay, after which animals were given access to all 8 arms and had to select the 4 arms that had not already been visited. After reaching criteria of 95% choice accuracy, animals were randomly assigned to receive one of 4 surgery conditions: bilateral lesions of the dorsal hippocampus (dHPC), bilateral lesions of the infralimbic/predlimbic region of the prefrontal cortex (IL/PL), or sham lesions of either the IL/PL or dHPC.

Following a 1-week recovery, animals were retested, with no deficits observed across all groups on the 10-second delay. The animals were then tested with 5-minute delays intermixed with 10-second delays. When the delays were intermixed, all groups continued to perform well on the 10-second delays. However, the results showed that on the 5-minute delay IL/PL lesioned animals and dHPC lesioned animals were impaired, i.e., made more errors, in comparison to controls. This implies that both the IL/PL and dHPC are necessary to perform well on an increased memory load on 5-minute delays. Previous research has shown that if only one arm needs to be remembered on an 8 arm maze, IL/PL lesioned animals are not impaired, whereas dHPC lesioned animals are impaired at the 5-minute delay. In comparison, it appears that the dorsal hippocampus plays a role whether it is 1 or 4 arms to be remembered, but the infralimbic/predlimbic prefrontal cortex seems to become important when 4 arms need to be remembered, i.e., when memory load is increased.