Nature 401:699--703, 1999 (October 14)

Top-Down Signal From Prefrontal Cortex in Executive Control of Memory Retrieval

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Knowledge or experience is voluntarily recalled from memory by reactivation of the neural representations in the cerebral association cortex. In inferior temporal cortex, which serves as the storehouse of visual long-term memory, activation of mnemonic engrams through electric stimulation results in imagery recall in humans, and neurons can be dynamically activated by the necessity for memory recall in monkeys. Neuropsychological studies and previous split-brain experiments predicted that prefrontal cortex exerts executive control upon inferior temporal cortex in memory retrieval; however, no neuronal correlate of this process has ever been detected. Here we show evidence of the top-down signal from prefrontal cortex. In the absence of bottom-up visual inputs, single inferior temporal neurons were activated by the top-down signal, which conveyed information on semantic categorization imposed by visual stimulus-stimulus association. Behavioural performance was severely impaired with loss of the top-down signal. Control experiments confirmed that the signal was transmitted not through a subcortical but through a fronto-temporal cortical pathway. Thus, feedback projections from prefrontal cortex to the posterior association cortex appear to serve the executive control of voluntary recall.

PMID: 10537108, UI: 20005500

Comments:

This is a fascinating and ingenious study that may have significant clinical implications. Our perceptions of our outside world result from an interaction between the hard input from our primary sensory systems ("bottom-up" signals) and processing from higher centers that is a function of our experience and stored knowledge ("top-down" signals). In the normal brain our perceptions and cortical activity result from a linkage of these signaling processes. In the present study the authors offer insight into the role that the prefrontal cortex plays in this top-down signaling function.

The prefrontal region of the brain is a likely candidate region for this top-down signaling function, because it is greatly enlarged in primates. With its interconnections with all of the main systems in the forebrain, the prefrontal cortex has long been thought to be involved in synthesizing data needed for executive control of behavior.[1,2] In the intact brain, there is a functional connection between the prefrontal cortex and the inferior temporal cortices, where visual memory is stored. Information is also shared between the inferior temporal cortices; the authors severed the connection between the inferior temporal cortices by selectively sectioning the posterior corpus callosum and anterior commissure (that

is, the inferior temporal cortex could only receive bottom-up input from the opposite visual field), whereas the anterior callosal fibers connecting the prefrontal cortices in the two hemispheres were left intact. When the authors presented activity to the visual field cortex that could not see the cue, this cortex nonetheless reflected the recalled object, although with a long latency. The information was passed to the "blinded" temporal cortex via the intact prefrontal connections in a long circuitous route. They subsequently confirmed the pathway by disconnecting the prefrontal interhemispheric connections, and the monkeys did not receive the activity to the inferior temporal cortex and could not complete the executive function task.

From the surgeon's perspective, these results indicate that the prefrontal cortex is an important regulator of brain function, which exerts executive control over a variety of functions and, in part, explains why damage to this region may produce wide-ranging defects in memory and behavior. Studies such as this should prompt renewed respect for performing surgical interventions in this region.

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2. Nauta WJ: The problem of the frontal lobe: a reinterpretation. **J Psychiatr Res** **8**:167--187, 1971

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