Japan Academy Prize to:

Yasushi Miyashita

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for "The Discovery of Associative Memory Neurons in the Cerebral Cortex and Studies of the Cognitive Memory System"

Outline of the work:

Dr. Yasushi Miyashita discovered the neuronal basis of our long-term memory by experimentation using non-human primates. His discovery is best understood by remembering that our knowledge and experience are voluntarily recalled from memory by the reactivation of their neural representations in the cerebral association cortex. To answer how our brain can do it, Miyashita made two major contributions that have a strong impact on cognitive neuroscience. First, Miyashita discovered memory neurons that encode associative long-term memory in the temporal cortex, elucidating the neuronal basis of memory storage and knowledge representation. Second, he identified the top-down signal from the prefrontal cortex to memory neurons in the temporal cortex. Psychologists long presumed the existence of this signal as a substrate with which a higher brain region sends operational commands to lower brain regions. His finding not only provided a direct proof for this presumption, but also opened a new approach that enables the direct analysis of signal contents and functional roles of the top-down signal. These discoveries, together with his other recent contributions, clarified where and how mnemonic representations are organized in the primate brain, and what the mechanism underlying the reactivation of representations on demand of voluntary recall is.

Background: To investigate these issues, Miyashita utilized the visual memory system as a model, because of the enormous accumulation of our knowledge on visual perception. This choice was important because neuropsychological studies of humans suggested that long-term declarative memory is likely stored in the neocortical association area, which is also engaged in sensory perception. Miyashita's experiments were also inspired by another controversial clinical report: when the temporal lobe of epileptic patients was electrically stimulated using cortical macro-electrodes, the patients sometimes reported recollection of past perceptual experiences, called the 'experiential response'. This recollection suggests that an artificial electrical input to the putative memory storehouse might reactivate the 'brain's record of auditory and visual experiences'. This interpretation as well as the reproducibility of the experiential response had been debated. Miyashita's experimental studies of monkeys moved beyond these classical clinical observations and revealed a clear solid view of memory representation in the temporal cortex and its activation mechanisms.

Achievements: Miyashita found the neuronal correlates of associative long-term memory in the anterior inferior temporal (IT) cortex. The IT cortex of monkeys is located at the final stage of the ventral processing stream devoted to object vision. He devised a memory paradigm that requires the monkey to create a link of associative memory between mathematically designed pictures. His single-unit recording experiments revealed the existence of a class of memory neurons in the IT cortex that exhibit significantly correlated visual responses to arbitrarily assigned picture pairs ('pair-coding neurons') and three mnemonic properties of these neurons. First, the stimulus-selectivity of IT neurons can be acquired through learning in adulthood. Second, the activity of the memory neurons can link the representations of physically or geometrically unrelated stimuli when the stimuli have cognitively meaningful associative relationships. Third, the basic mechanism underlying this cognitive association relies on the temporal correlation of neuronal firing as originally conjectured by D. O. Hebb.

Then Miyashita found the neuronal correlates of memory reactivation as 'pair-recall neurons', which are located in the same cortical area as 'pair-coding neurons'. He clarified the nature of pair-recall neurons by devising a new modified pair-association task in which the necessity for memory retrieval and its initiation time are controlled by a color switch, independent of the cue stimulus presentation. Single-unit recordings in monkeys performing this task revealed that IT neurons selective to a memorized object are dynamically activated at the time of memory retrieval of that object, and suppressed at the time of retrieval of other objects.

Then the next critical step was to determine the brain-wide global structure of the neural network that drives the memory retrieval machinery in the IT cortex. One key candidate is the top-down activation from the prefrontal cortex. The prefrontal cortex has been implicated in various executive processes, and its contribution to mnemonic functions, particularly in episodic memory and working memory, is repeatedly demonstrated in human neuroimaging studies. Miyashita first behaviorally examined the contribution of the top-down signal to memory retrieval on the basis of the capacity for interhemispheric transfer of mnemonic signal through the anterior corpus callosum, the structure interconnecting prefrontal cortices. He introduced a novel split-brain paradigm ('posterior-split-brain preparation') into the associative memory task in monkeys, which proved that long-term memory acquired through pair-association learning does not interhemispherically transfer via the anterior corpus callosum. Nonetheless, when a visual cue is presented to one hemisphere, the anterior callosum could instruct the other hemisphere to retrieve the correct stimulus specified by the cue. Therefore, although visual long-term memory is stored in the temporal cortex, memory retrieval is under the executive control of the prefrontal cortex.

Miyashita then provided direct evidence of the existence of the top-down signal by conducting single-unit recordings of this posterior-split-brain monkey preparation. In the absence of bottom-up visual inputs, single IT neurons are robustly activated by the top-down signal, which conveys information on semantic categorization imposed by visual stimulus-stimulus association. Behavioral performance was shown to be severely impaired concomitantly with the loss of the top-down signal.

Summary: Dr. Miyashita discovered the memory neurons that encode associative long-term memory in the temporal cortex and also the top-down signal from the prefrontal cortex to the memory neurons. These discoveries, together with his other recent contributions, clarified where and how mnemonic representations are organized in the primate brain, and what the mechanism underlying the reactivation of the representation on demand of voluntary recall is, which made a strong impact on cognitive neuroscience.