

The Hierarchical Organization of Prefrontal Cortex of Working Memory

Huanyan Zheng^{1,*}

¹Keystone Academy, Beijing, China, 101318

*Corresponding author. Email: huanyan.zheng@student.keystoneacademy.cn

ABSTRACT

Working memory is a dominant topic in neurobiology that has been investigated frequently. The hypothesis related to the mechanisms of working memory leads to high controversy among scientists. More specifically, how working memory is organized to allow short-term retention of information without the information present in the environment is the core of the debate. The hierarchical organization of working memory is a widely accepted system that describes the organization of the memory as a hierarchy that has different levels of complexity and abstractness. The development of the system has encountered several major leaps of accomplishment that eventually led to the mature model of the hierarchical organization over the past decades. The enhancement of the system encounters different stages, including the proposal of working memory framework, the discovery of persistent firing of the neurons during the delay period, the proposal of hierarchical organization of the neurons, and the discovery of the architectural arrangement of the organization of neurons in the prefrontal cortex. The research subject is human, more specifically, the reaction of the human brain towards temporal information and to remember the short-term information without it present in the environment. The research method involves synthesizing articles and experimental results from history that have contributed significantly to the proposal of hierarchical organization. The review presents several major developments and experimental accomplishments that is monumental to the process of hierarchical organization of prefrontal cortex development.

Keywords: *Working Memory, Hierarchical organization, prefrontal cortex, systems of working memory, top-down control*

1. INTRODUCTION

The fact that humans can remember things is related to our ability to memorize things. Normally, people consider memorization as long-term, achieved through repetitive stimulus, which is described as long-term memory, or LTM. This kind of memory, by stimulating frequently, creates new synapses between neurons [1]. However, another type of memory, the working memory is also important to daily life. There are different definitions of working memory, which relates to different hypothesized mechanisms of it. Typically, in a more general sense, the definition of working memory is a system that holds a limited amount of information for temporary availability in an ongoing process, which is consisted of several components [2]. More specifically, working memory is the ability to hold information that is no longer available in the environment temporarily. Working memory is thought to be important to the

behavior of an organism because it is highly likely to direct a variety of decision-making of cognitive tasks. It allows for more complicated tasks involving planning, reasoning, and cognitive control. Therefore, working memory is a highly investigated subject in cognitive neuroscience that directs studies relating to its mechanism of it [3]. The prefrontal cortex is an important region in the brain to direct cognitive control. This review aims to briefly investigate the different monumental development and studies that grounds the proposal of the mechanism – hierarchical organization in the prefrontal cortex and its potential implication towards other relating mechanisms. By unfolding the review on this aspect, readers can have a systematic recognition and understanding of an important aspect of working memory and connect them with real-life situations. It is important to understand and provide a clear line of progression in scientific research underlying the hierarchical organization of working memory.

2. MAJOR WORKING MEMORY FRAMEWORK

Based on the behaviors and neuronal activity that have been recorded and investigated, two major models of working memory are constructed. From roughly 1985 to 2005, the neuroscience study of working memory has been based on the multi-component model, which established the dominant theoretical framework of the field. It describes a central executive that is contributed by three subcomponents: the visuospatial sketchpad (visuospatial information), the episodic buffer, and the phonological loop (verbal information). As an advancement of the past, this model can explain how an individual can maintain and carry out several behavioral goals simultaneously. The proposal of parallel subcomponents explains when multiple stimuli have to be processed, why is it possible for no interference to occur between tasks using different kinds of information codes, and interference between tasks with the same information codes. The episodic buffer is added to include the interaction between the other three components and the LTM [1]. However, the state-based models are gaining increasing attention due to the increasing emphasis on the allocation of attention to internal representations, which allows the short-term retention of specific information. Cowan's embedded-process model changed the understanding of the working memory framework significantly, which utilizes the focus of attention as the core idea. In this model, the relationship of LTM and WM is typically a three concentric model. The smallest one, which is the Focus of Attention (FoA), is embedded in the middle one. The middle one, which is the activated LM, is embedded in the largest circle. The largest circle represents the common LTM. Cowan believes that the FoA only has a limited capacity with four regions dealing with information of different codes with top-down control, and that the activated portion of LTM has an expansive state. There is a different variant based on the different capacity limits of FoA and activated LTM, but the essence is the same [4].

3. GROUNDING STUDIES FOR THE DEVELOPMENT AND PROPOSAL OF THE HIERARCHICAL ORGANIZATION MODEL

The hierarchical organization of WM was gradually developed across decades and concepts are proposed consecutively along with technical development that allows different ways of providing or rejecting a hypothesis. Here, the article presents the mainstream of discovery with experiments associated with it.

3.1 Persistent neural activity during the delay period

The study of WM has different stages, and the study of WM achieved a significant improvement in 1971 with the discovery of persistent neural activity during the delay period. In Fuster and Alexander's work, they performed an extracellular recording of nerve cells in Monkey's prefrontal cortex and nucleus medialis dorsalis of the thalamus. During the cur presentation period, the firing rate of the majority of the cells increases and is slightly higher at the beginning of the delay period. More importantly, the spikes continue to discharge throughout the delay period. The monkeys retain the information that is not available in the environment but was relevant to the assigned task. This opened a significant entry for discovering the underlying systematic structure of WM [5]. Moreover, Kubota and Niki presented similar persistent neural activity during delay alternatives in the area of midprincipalis of the dorsolateral prefrontal cortex in a monkey. They recorded the single-unit activity of 502 units in both hemispheres. Together, these two landmark studies suggest that neurons fire during the delay period. With the development of fMRI technology in the late nineteenth century and different studies, the notion that the PEC maintains representational information that directs behavior. This is because the firing of the neural is maintained throughout the delay period until it can be used for guiding behavior [6].

However, with the application of MVPA to fMRI and EEG data, objection to this notion is raised. In a study of short-term recognition tasks, the participants, staying in a scanner, are presented with English words, pronounceable pseudowords, and line segments. In every trial, two stimuli are selected from separate trials, and in a probe, one randomly selected stimulus will be cued. Following a delay period, the participant is asked to recognize the stimuli presented and respond to the cue. After responding to the first, the participants are immediately asked to do the second probe, in which another stimulus is presented, and the participants are asked to respond to it. It means that the participants need to maintain the memory of both items until the beginning of the second cue for successful indication of stimuli. After analyzing the neural activity scanned, it was discovered that in response to the retro-cue (the second cue), the MVPA study shows that the unintended memory is dropped below the baseline. This explicitly shows it is possible that the neural activity may not be essential for maintaining representations in WM as thought before [7]. The significant change of the basic understanding acts as the foundation for the discovery of the hierarchical organization of information.

3.2. Systematic organization

The WM is closely related to the prefrontal cortex, which is responsible for high function tasks. Some have analyzed how the maintenance of information in PFC is related to the sensory feature of information of the working memory information. From a neurobiology level, because the prefrontal cortex is a major target of dopamine coming from the brainstem which forms symmetrical synapses on the spines of pyramidal neurons, and normally it is in touch with an asymmetrical bouton characteristic of axons which likely to perform excitatory firing. As the pyramidal cells face sensory input, direct control of dopamine is reached, to ultimately manipulate the output via axonal projection to different cerebral regions [8].

Although this idea is influential when it is proposed, the following studies presented another convincing notion of WM having selectivity on the information that it retains. Working memory is said to exhibit high-dimensionality, which means the seemingly heterogeneous and disordered data is involving multiple task-related variables. More specifically, dimensionality, in the case of an experiment, is the minimum number of axes needed to categorize and define data. This property of neural representations gives the foundation of performing dynamic and complex tasks by allowing the implementation of a large number of input-output relations. Although there isn't a definitive mutually embracive relationship between high dimensionality and complex dynamic tasks, the high dimensionality can make the design of local neural circuits simpler. It is also shown that utilizing dimensionality is possible to predict animal performance [9].

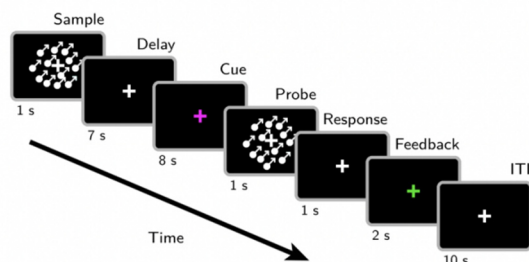


Figure 1 Time extent and steps of the fMRI study

More empirical data have gradually built upon this. A human fMRI study investigated the essence of the representation in PEC. In the study, participants have presented dots that have both direction and speed of moving. In the middle of the delay period, the participant is told whether they are tested on the direction or speed of the dots and the person needs to respond to the probe [10]. The team used different analysis methods to test it. With a general linear model (GLM) the team failed to clearly define a specific pattern or stimulus information, although it can show that during the delay period, the neurons are firing. The team also used the multivoxel

pattern analysis (MVPA), which has successfully identified patterns and trial-specific stimulus information, specifically from frontal and parietal areas. This means that the PFC seems to have a different dimension of preserving and presenting information, in this scenario, from direction and speed. Along with it, there are different fMRI testing having analogical results and all support the notion of high dimensionality and oppose to the idea of PFC typically functions like storage or WM and turned the discussion more to activation-based system modeling [10].

Moreover, an EEG study shows a more apparent hierarchical organization of memory. Paul and his colleagues performed a task involving human electrophysiology and pattern analysis and cognitive modeling. They examined the data of over 50 subjects, presenting them with a picture of different colors representing high and low tones and having different directions, and asking them to respond to the cues of one of the two cues [3]. They discovered typically two states. One is related to the selected memory which is encoded in functionally active states which is related to the persistent brain firing during the delay period. In contrast, simultaneously held memory is coded in a functionally latent state, in which information will be elicited only when the stimulus has evoked brain activity but does not involve in the persistent decision dynamics. It is maintained on a longer-time scale and is not related to the individual trial decision on the response. These two states are highly flexible, meaning that information can shift between two states without affecting the precision of memory, but still the information in the separate states is coded with dissociable neural patterns. This suggested a clearer hierarchical structure of working memory, in which latent memories are maintained throughout the period and can be transformed into an active decision process to direct cognitive behaviors. Overall, their study suggested a hierarchical model that has a single item stored in a format that is qualitatively different from concurrently maintained items. This item is in the prioritized format in which it is directly related to the task-relevant transformation of tasks and guidance of behavior and decision, while the latent information is not interfering with the ongoing processing. More studies are done in supporting this hierarchical organization [3].

3.3 The Architecture of Hierarchical Organization in Prefrontal Cortex

The overall system of how WM is organized in PFC is relatively clear, but PFC is a large and heterogeneous region having a variety of functions. The question How is the hierarchical structure lies in the PFC is the next stair of investigation. Some have proposed new findings defining the architecture of executive control in the lateral prefrontal cortex [11]. They outlined a cascade model that depicts the hierarchical organization of the

WM executive system along the anterior to posterior axis of the lateral PFC. This model suggests that the interference between different representations, associating with sensorimotor, contextual, and episodic control, is resolved by the mutual information with control signals. This idea is supported by their fMRI scanning of the anterior and posterior PEC, showing connectivity between the regions responsible for the different representations. Their early work also supported this model by demonstrating an increase in the abstraction of contextual information required to respond to the cues and relevance over a long interval, having fMRI detected activation increasing from caudal to the rostral region of PFC [11].

From an anatomy and physiology aspect of the cerebral analysis, the rostro-caudal axis also has a hierarchical organization. The neurons in the PFC face multiple sources of input and can still behave in line with the action rules depending on whether the stimuli are relevant or not to the specific goal, with facing a variety of distractions. Neurons in the rostral region seem to show the distinguishment of the level of abstractness of representation and the complexity of rule that they can maintain [12]. There is evidence discovered that neurons in the rostral region have more ability to influence the caudal regions relatively to such influencing the rostral region. This rostral-to-caudal flow of control is confirmed by experiments demonstrating the region being activated and used is depends on the kinds of representation of the information is. Results are showing a coherent functional network on the rostro-caudal gradient, also from the parietal to lateral temporal cortex. However, the consensus is not reached among scientists regarding more details of the system of WM [12].

However, how can it be demonstrated that it is a hierarchical structure with top-to-bottom influencing power but in which the bottom cannot influence the top? Barbas and Pandya's research shows that the neurons in the rostral areas with less laminar differentiation tend to have extensive connection with other regions, while the neurons in the caudal areas with mature laminar differentiation have limited connection to other regions. The high connectivity to other regions, typically area 10, in the rostral area, allows it to have the direction to more portion of the brain in performing tasks. The low connectivity of caudal PEC, such as area 9/46 and 8, to other regions, make it suitable for the lower part of the hierarchy. This shows one direct influence of the hierarchical organization of the WM, but not a mutual effect [13].

4. DISCUSSION

The hierarchical representation of information has an advantage on the abstractness of categorizing rules and goals, which makes it possible to perform top-down signals that direct behavior and goal-directed control.

This advantage makes the further implication of the development of a top-down control system logical and possible. It has been argued that the PEC has top-down control capability to suppress useless information and target relevant information. When receiving incoming sensory input from a particular modality, the PFC can prove it and provide a direct signal to the posterior cortical regions to have specific action performed. The PFC would maintain the representation of the goal which is termed biased signal to depress the irrelevant information and enhance the relevant information. As suggested by the top-down control system, the hierarchical structure makes it ideal to control the bottom brain regions and guide behaviors [1].

Working memory is an important aspect of our life. When calculating, it is important for working memory to keep the previous calculating in mind when continuing with the last. When calling someone, working memory keeps the dial of number in the brain for several minutes and leave it away when finished the specific task. The development of working memory applies to a different field and is important to our understanding of the particular aspect. When brain-computer interface becomes natural in the future, the use of working memory cannot be overlooked. In the future, when the concept of metaverse becomes applicable with BCI, working memory is going to further help people construct a world with only mindset.

5. CONCLUSION

The development of the hierarchical organization of the prefrontal cortex of working memory have gone through several stages, from the initial proposal of the state-based model to the discovery of consistent neuron activity during the delay period to the proposal of hierarchical organization in the PFC to different empirical evidence supporting the hypothesis, then to the architecture of the organization in PFC, lastly to the application of the model on other systems. The hierarchical system is proven by different studies and has shown that the sensory input that neurons receive is organized in an order of level that facilitated the direction of cognitive behavior from top regions to other cerebral regions. It is also investigated that within the large region of PFC, there is a cascade model of how information is organized from caudal to more rostral region. In conclusion, working memory has a different level based on the complexity and abstractness of information. The top part of the hierarchy, typically related to the caudal region of PFC, have extensive relation to other regions of the brain, while the bottom part is more related to rostral, relating to limited regions but maintaining information over longer intervals. This explains the different regions of brain activity shown by fMRI and EEG when the target is asked to respond to a specific cue.

This property of organization makes it possible to perform top-down control using biased signals.

The development of the system is a cumulative process of different scientists working in psychology and neurobiology to perform a variety of experiments to test the proposed hypothesis. The review mainly investigated the major leap of the development and experiments relating to it. There is more investigation done to enhance the notion proposed. The article can include more of the unmentioned important studies by briefly mentioning them, indicating the wide support that a specific hypothesis has made. For future research and experimental studies, the focus can be on the categorization of seemingly heterogeneous information, which may lead to the discovery of the organization of received information.

ACKNOWLEDGMENT

During the process of writing, special thanks to my parents for supporting me to investigate my specific interest in this field. Thanks to the professor and teachers of neuroscience helping me to gain more subject-related information. Thanks to the partner in our study group who has discussed the topic with me. This paper may be difficult to complete without the assistance of these individuals. Their effort in helping me is appreciated and I'm very thankful for their expectation of me and trust in me to complete the first formal review in my study process.

REFERENCE

- [1] D'Esposito, Mark, and Bradley R Postle. "The cognitive neuroscience of working memory." *Annual review of psychology* vol. 66 (2015): 115-42. doi:10.1146/annurev-psych-010814-015031
- [2] Adams EJ, Nguyen AT, Cowan N. Theories of Working Memory: Differences in Definition, Degree of Modularity, Role of Attention, and Purpose. *Lang Speech Hear Serv Sch*. 2018 Jul 5;49(3):340-355. doi: 10.1044/2018_LSHSS-17-0114. PMID: 29978205; PMCID: PMC6105130.
- [3] Muhle-Karbe PS, Myers NE, Stokes MG. A Hierarchy of Functional States in Working Memory. *J Neurosci*. 2021 May 19;41(20):4461-4475. doi: 10.1523/JNEUROSCI.3104-20.2021. Epub 2021 Apr 22. PMID: 33888611; PMCID: PMC8152603.
- [4] Bablekou, Zoe. (2009). *Nous: Cognitive Models of Working Memory*. 10.4018/978-1-60566-392-0.ch006.
- [5] Fuster JM, Alexander GE. 1971. Neuron activity related to short-term memory. *Science* 173:652–54
- [6] Kubota K, Niki H. 1971. Prefrontal cortical unit activity and delayed alternation performance in monkeys. *J. Neurophysiol.* 34:337–47
- [7] Lewis-Peacock JA, Drysdale AT, Oberauer K, Postle BR. 2012. Neural evidence for a distinction between short-term memory and the focus of attention. *J. Cogn. Neurosci.* 24:61–79
- [8] Sawaguchi T, Goldman-Rakic PS. 1991. D1 dopamine receptors in prefrontal cortex: involvement in working memory. *Science* 251:947–50
- [9] Rigotti M, Barak O, Warden MR, Wang X-J, Daw ND, et al. 2013. The importance of mixed selectivity in complex cognitive tasks. *Nature* 497:585–90
- [10] Riggall AC, Postle BR. 2012. The relationship between working memory storage and elevated activity as measured with functional magnetic resonance imaging. *J. Neurosci.* 32:12990–98
- [11] Koechlin E, Summerfield C. 2007. An information theoretical approach to prefrontal executive function. *Trends Cogn. Sci.* 11:229–35
- [12] Badre D. 2008. Cognitive control, hierarchy, and the rostro-caudal organization of the frontal lobes. *Trends Cogn. Sci.* 12:193–200
- [13] Barbas H, Pandya DN. 1991. Patterns of connections of the prefrontal cortex in the rhesus monkey associated with cortical architecture. In *Frontal Lobe Function and Dysfunction*, ed. HS Levin, H Eisenberg, AL Benton, pp. 35–58. Oxford, UK: Oxford Univ. Press