Working Memory: How It Works and Why It Is Important

By Kelsey O'Neill

What is Working Memory?

Have you ever wondered how you were able to hold a conversation with someone? Have you ever thought about how you can listen to what someone else is saying and think of how that relates to something you've experienced? In addition, have you ever wondered why it is that you can recall what someone is saying during the conversation but have a hard time remembering it afterwards? You probably haven't thought about it much as most brains perform these tasks seamlessly. This process of remembering information in an active setting is called working memory and is so called in reference to the short-term store of memory in computers.

Working memory consists of the short-term memory required to carry out intricate tasks such as learning, reasoning, and understanding. It is essential to our ability to hold conversations with people. It enables us to change our plans last minute. Working memory is worth studying due to its many applications, as well as the main brain area involved: the medial prefrontal cortex (mPFC), and one of the main neurotransmitters (dopamine). The mPFC is a brain area that is thought to play a role in working memory function and to be involved in reward-related mechanisms (Tzschentke, 2000). Specifically, the mPFC is a part of the brain reward system (Tzschentke, 2000). Dopamine (DA) is a neurotransmitter in the brain reward system. Thus, dopamine is experimentally correlated to working memory in the prefrontal cortex (D'Ardenne et al., 2012). Therefore, the presence of dopamine in the mPFC supposedly is correlated to the function of the working memory in the brain, but what are some studies that have proof of that?

A study was performed where specific dopamine receptors (D1), units that receive dopamine from outside the cell, were activated in the mPFC, meaning that nerve cells in the mPFC were more sensitive to dopamine (Seamans et al., 1998). The results were that the activation of specific receptors in the mPFC improved accurate foraging behavior in rats that already had prior knowledge of the location of food on the maze (Seamans et al., 1998). In rats, this working memory is tested using mazes with radial arms. The foraging behavior in rats requires recognition of the environment and the ability to associate that environment to a food source. In the maze, food is put in one arm of the maze and the rats are trained so that they associate that arm with the food. Their ability to go directly to the arm with the food demonstrates the functionality of their working memory. If a rat enters each arm only once, they have exemplary working memory. If they enter the same arm multiple times, it shows that there is working memory error because they don't remember how to find the food (Phillips et al., 2008). A secondary study was performed where the specific dopamine receptor (D1) was blocked in the mPFC so that dopamine could not be received by the receptor and the working memory was impaired (Seamans et al., 1998). In other words, when dopamine was stopped from entering the cell and the working memory didn't work as well, it proved that the presence of dopamine in the mPFC is essential to working memory function.

Several studies were conducted in freely behaving rats and it became apparent that the prefrontal cortex is positively correlated with high performance in behavior guided by working memory and that this activity is regulated by D1 receptors (Williams and Goldman-Rakic, 1994). The blockage of these receptors in the prefrontal cortex disturbs choice behavior guided by working memory after a small time delay (meaning that the memory is tested not long after training, Williams and Goldman-Rakic, 1994) and after a long time delay (meaning that the memory is tested a long time after training, Seamans et al., 1998). It has thus been proposed that working memory is optimized when the D1 receptor has an ideal amount of dopamine or equilibrium, of sorts. A study also examined the changes in dopamine release in the mPFC while performing a radial maze task with a delay period that was significantly longer than what had been previously studied. The results were that the dopamine output in the mPFC increased during the training phase of the task, but returned to normal levels during the delay period (Phillips et al., 2004). What does all of this tell us about the impact of dopamine release on working memory in the mPFC? These studies show that one particular dopamine receptor manages the amount of dopamine in the mPFC and that the function of the working memory is dependent on the having the right amount of dopamine in the mPFC at the right time.

But how does dopamine work? As stated earlier, dopamine is a neurotransmitter in the brain, meaning it is a chemical that is released by nerve cells to transmit signals to other nerve cells. There are several unique dopamine systems, one of which is the mesolimbic dopaminergic system or the brain reward system. As shown in the previously mentioned studies, dopamine released is linked to the function of the working memory in the mPFC. Dopamine release is also associated with reward, motor control, and controlling the release of other hormones. This process is all for naught if there are no dopamine receptors (such as D1) to receive the dopamine and facilitate its transmission to the next cell. Some sort of stimulus triggers dopamine release, which in this case could be a need to remember something. There are several types of receptors that could receive the dopamine on the postsynaptic cleft, but the most prominent excitatory one (meaning it triggers an increase in dopamine in the next cell) is D1 (Grace, 1991).

How does it have such an impact on the working memory? There unfortunately is no concrete answer to that question, but some of the surrounding questions have fairly solid answers. For instance, there was an issue of whether dopamine promotes or impedes the sustained activity of the neurons seen in working memory tasks. An experiment showed that dopamine reduces the active elongation of the time that the postsynaptic cleft is excitatory or the postsynaptic potential that increases the likelihood of the neuron firing an action potential (EPSP) (Rotaru et al., 2007). The derivation of these results in terms of working memory is that shortening the length of the excitatory postsynaptic potential (EPSP) narrows the requirements for efficient summation or totaling of signals and induced spiking (Surmeier, 2007). This added information could be the next step to discovering the mechanism of dopamine in working memory.

What is so important about understanding the role of dopamine in the mPFC and its correlation to working memory? Memory in general is still a major topic of study, not just because there is so little known about it, but also because of its role in many crippling disorders such Alzheimer's disease and Schizophrenia. Memories also build the foundation for who we are and distinguish us from others. Working memory dysfunction is involved in both Alzheimer's disease and Schizophrenia and is implicated in a host of other neurological disorders. In fact, D1 receptor deficiency in schizophrenic patients has been linked to impairments in working memory in those patients (Abi-Dargham et al., 2002). Another cause of working memory issues is traumatic brain injury. Since the prefrontal cortex is extremely vulnerable to trauma, damage to it gives rise to impairments in working memory (Kobori et al., 2011). Damage to the prefrontal cortex and in conjunction its dopaminergic pathways thus influences the function of working memory.

But why is working memory so important? As stated in the opening paragraph, working memory consists of the short-term memory required to carry out intricate tasks such as learning, reasoning, and understanding. It is essential to normal functions such as conversing with other people. When we hear a question and seek to respond, our working memory allows us to keep that question in our minds so we can respond. It allows us to reprioritize when things don't go as planned. It enables us to divert our attention to the thing that requires our attention. It helps us view our surroundings in a way that we can navigate without every new environment being completely foreign to us. In conclusion, working memory is worth studying due to its many applications, as well as the main brain area involved (the mPFC) and one of the main neurotransmitters (dopamine).

References:

Phillips, A., Vacca, G., & Ahn, S. (2008). A top-down perspective on dopamine, motivation and memory.Pharmacology Biochemistry and Behavior, 236-249.

Tzschentke, T. (2000). The medial prefrontal cortex as a part of the brain reward system. Amino Acids, 211-219.

D'ardenne, K., Eshel, N., Luka, J., Lenartowicz, A., Nystrom, L., & Cohen, J. (2012). Role of prefrontal cortex and the midbrain dopamine system in working memory updating. Proceedings of the National Academy of Sciences, 19900-19909.

Phillips, A. (2004). Magnitude of Dopamine Release in Medial Prefrontal Cortex Predicts Accuracy of Memory on a Delayed Response Task. Journal of Neuroscience, 547-553.

Kobori, N., Hu, B., & Dash, P. (2011). Altered Adrenergic Receptor Signaling Following Traumatic Brain Injury Contributes To Working Memory Dysfunction. Neuroscience, 172, 293-302.

Williams GV, Goldman-Rakic PS (1995) Modulation of memory fields by dopamine D1 receptors in prefrontal cortex. Nature 376:572–575.

Cohen, J. D., and Servan-Schrieber, D. (1992). Context, cortex and dopamine: A connectionist approach to behavior and biology in schizophrenia. Psychological Review, 99, 45-77.

Grace AA (1991). "Phasic versus tonic dopamine release and the modulation of dopamine system responsivity: A hypothesis for the eitiology of schizophrenia".*Neuroscience* 41 (1): 1–24.

Rotaru DC, Lewis DA & Gonzalez-Burgos G (2007). J Physiol 581, 981–1000.

Surmeier, J. (2007). Dopamine and working memory mechanisms in prefrontal cortex. J Physiol 581.3: 885.

Abi-Dargham, A., Mawlawi, O., Lombardo, I., Gil, R., Martinez, D., Huang, Y., Hwang, D., Keilp, J., Kochan, L., Van Heertum, R., Gorman, J. M., and Laruelle, M. (2002). Prefrontal Dopamine D1 Receptors and Working Memory in Schizophrenia. The Journal of Neuroscience 22.9: 3708-3719.