WHAT IS THE PROFILE OF MEMORY CONSOLIDATION IN POPULATIONS WITH DEVELOPMENTAL DISABILITY?

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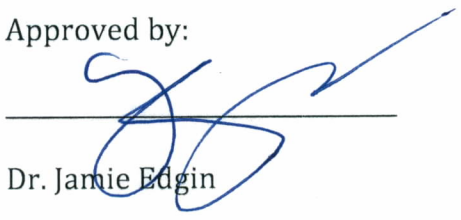

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Neuroscience and Cognitive Science Honors Thesis Abstract: What is the profile of memory consolidation in populations with developmental disability?

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The aim of the literature review is to explore the trajectories of hippocampal-dependent memories in typical and atypical populations. Memory is linked to the development of neural circuitry within the brain. The development of synaptic connections aid in the ability to process and consolidate memories. At the system level, the hippocampus plays a crucial role in memory processing and hippocampus-dependent memory has a protracted development. A memory system stores "features and attributes" of concepts so that retrieval of information is efficient and able to be produced through language. This allows for features to be placed into representations, forming congruent memories, that are then able to be retrieved and later expressed. In conclusion, Hippocampal dysfunctions result in memory deficits. These deficits are specific to different memory profiles. For example, the Down syndrome population has issues with associating an object with a location; William syndrome population has issues with inhibition and recall; lastly, the Autism Spectrum Disorder population has issues with projecting themselves into an fictional scenario and complex-information processing.

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Memory is encompasses a large facet of information storage and processing. Consequently, differing developmental disorders are affected differently in their overall memory trajectories. The issue stems back to the initial question of memory and its own transformation throughout the lifetime. Ebbinghaus looked into the concept of memory and ultimately how a memory was learned and forgotten. The "forgetting curve," took note on the aspects of how there is a loss of memory or information as a function of time. He found that there is an exponential loss of information within the first 20 minutes of learning it, and a significant about of information lost in one hour (Ebbinghaus, 1913). He also looked into what he called the "learning curve," or how fast someone can learn new information. He found that most information is retained on the first try, but with repetition, less and less new information is learned. Therefore, the idea is that the memory of the information has been formed (Ebbinghaus, 1913). This shows that there is some time dependency that affects a memory's development and consolidation. This time constraint may also affect how an overall trajectory of memory develops. Knowing the typical developmental process of a memory can be used in comparison to those with a developmental disability to better learn how memory is different between the populations and how memory changes throughout the typically developing populations lifetime.

Although memory has been extensively explored, it is still unclear what is the effect of time on memory. Memories are thought to be fragile during the consolidation time, and it is only when they are integrated with previous memories in the long-term store, that they reach a more stable form. Another temporal aspect of memory is when a specific memory system comes online and how it changes over time. Do memory systems change as a result of brain maturation? Or does the trajectory of a memory depend on the type of

memory and its overall vulnerability? It is known that the brain develops at the fairly same rate for most healthy individuals with the similar progression from conception to birth (Jarrold et. al., 1999). However, this is not congruent with after birth. How does time component play a role in this developmental process?

In this paper I will review the development of memory, while trying to answer the question of time and its importance to memory. This exploration has two parts: the first looking at how time can affect memory consolidation and its transformation. In the second part I will explore how memory systems develop across typical and atypical populations. In particular, I will focus in neurodevelopmental disorders such as individuals with Down syndrome, Williams's syndrome, and autism spectrum disorders. These developmental disorders have been shown to have a different cognitive profile compared to typically developing peers, including impairment in the development and recall of specific memories.

I. What is Memory?

There are several different, yet interconnected sub-groups of memory that categorize the different types of memories and their consolidation. It is estimated that there are over 25 different types of memories that serve the purpose of dividing information from a large memory domain into smaller sections (Tulving, 1972). For example, there is short-term memory and long-term memory. Within the short-term memory we can distinguish between the auditory and visual memory. Within long-term memory, there is the declarative memory system, which can be divided into episodic and semantic. Semantic memory included a lexical component, in which language is

represented and "can serve as a basis for processing information in memory tasks." On the other hand, episodic memory receives and stories information about episodes and events. Both systems show a large number of similarities in processing of information, but have distinct differences as well. Their similarities include: selectively receiving information, retaining a wide range of informational attributes, and transmission of specified information to other systems, including behavior and consciousness. They differ, however, in the way information is stored, whether the information is considered autobiographical or reference, what conditions are needed for retrieval, and the vulnerability to be edited based on transformation.

Episodic memory falls under the umbrella of declarative memory, in which events are consolidated and ultimately, stored for later use. According to Tulving, episodic memory is an active, conscious effort in which events and situations are remembered from the past, present, and future (2002). It is an autobiographical reference, which is most susceptible to transformation and memory loss (Tulving, 1972). It is considered a memory system that is late developing and early deteriorating, and most vulnerable to dysfunction (Tulving, 2002). Episodic memory has substantial qualitative changes specifically between infancy and early adulthood (Ofen, 2012). The developmental trajectory for memory is linear until late childhood and early adolescence; this is when there is a burst of growth, maturity, and ultimately a change in function within the brain.]

Recognition and recall are two areas within episodic memory that require further explanation. When dealing with recognition type memory, there is less time needed to make a decision and more focus on deciding whether or not a stimulus has been seen before; consequently this calls for a different application of strategies (Ofen, 2012). For

memories that are recalled, a longer amount of time is needed to respond and participants are challenged to not only remember the stimulus but also the location and time of when the stimulus was presented. Recall requires more strategic planning and places a strong demand on executive components of the working memory, particularly those associated with the frontal cortices.

Semantic memory, on the other hand, is the other piece to the puzzle that completes declarative memory. It is defined, by Martin and Chao, as a memory system that stores "features and attributes" of concepts so that retrieval of information is efficient and able to be produced through language (2001). Semantic memory organizes the knowledge a person possesses about words and symbols, including their relationships, rules, and formulas for manipulation (Tulving, 1972, p. 385-390). Since this memory system is based on reference, the retrieval is not always a direct route, but rather allows for the information to be extracted just as it was stored, being less susceptible to change and transformation (Tulving, 1972, p. 385-390).

The last type of memory that will be discussed is implicit memory. This is a non-declarative memory system, which is sometimes also encompasses procedural memory. It is hypothesized that implicit memory will appear earlier in development and may have an overall different growth pattern than that of explicit memory (Hayes & Hennessy, 1996). Various experiments with habituation have confirmed that the encoding of memories starts at a very young age and the ability to encode and retain is present at birth. As the child grows and develops, so will their memory improve with complexity and durability. Overall, implicit memory is thought to play a part in procedural memory and emotional memory.

II. Neural Substrates and Neurophysiology

Researchers have looked into better understanding brain regions, their functions, and specifically the mechanisms to explain behaviors and other neurological phenomena. In this section I intend to review research on current hypotheses concerning memory substrates and their effects on memory properties. What we know about the underlying neural mechanism of memory has been extensively influence by the animal literature. For instance, Menzel and Muller (1996) explored learning and memory within honeybees. In this approach, the authors were able to examine the pathways, at the neural level, that were used for coding; as wells as explore the effects of Nitric Oxide (NO) at the cellular level. It was found that honeybees have long-term memory lasting for several months, and the encoding is similar to that of humans. Memory is considered to be "sensitive to extinction" and multiple trials aid in the solidifying of memories. Like humans, honeybees take in the stimuli into their short-term memory, and then consolidate it in their "middle term memory." Honeybees' short-term memory is vulnerable to change and interference, once a memory is within the middle-term memory it is much more protected and stable; after multiple trials, the information is moved into the long-term memory. An interesting aspect of the experiment showed that all three types of memory were found to be time and event dependent. This would mean that there was some time needed for a memory to be consolidated and available for the brain to later retrieve. It also means that depending on how the memory was received – whether that be initial retrieval, with repetition, or possibly repeated – its consolidation process would be slightly different than another memory.

On a cellular level, the presence of NO was a key factor for Long-Term Potentiation (LTP) and Long-Term Depression (LTD) within honeybees and humans (Menzel & Muller, 1996). It is hypothesized that NO plays a role in the "regeneration of the nervous system" during both LTP and LTD. Unlike other neurotransmitters, NO is not bound in a vesicle and can easily diffuse through the plasma membrane, therefore easily interacting with nearby targets. Consequently, if NO synthase is removed or inhibited, there is an issue with the production of NO and subsequently an issue with the ability to solidify sensory memories in the long-term memory. Along the concept of long-term memory, it was found that the formation of memories was dependent on the BDNF levels and the "de novo" protein within the hippocampus (Bekinschtein et. al., 2007). Having both the "de novo" protein and BDNF present during acquisition or shortly after, was a key component in determining whether or not a memory was to be retained). Interestingly, memory retention improved in relation to the increase in BDNF protein, suggesting that this protein allowed memories to become more stable. This modification was also time sensitive, the BDNF needed to be synthesized during the first hours of the acquisition of the memory. Although this strategy of modification of addition BDNF protein present at the synapses helped with the pace of consolidation, it was not necessary; meaning a memory would be consolidated eventually but at a slower pace and with the increased potential to be vulnerable to change (Bekinschtein et. al., 2007).

Another mechanism for strengthening memory mechanisms was the presence of dopamine. Dopaminergic systems play a crucial role in memory regulation and synaptic plasticity (Jay, 2003). Areas of the brain that seem to be most plastic, or undergo considerable progressive growth, show a difference of their ability to be affected by

dopaminergic systems. On the other hand, dopamine can also cause an increase in long-term depression (LTD). LTD, mechanism by which a memory a synapse is weakened, occurs when the dopamine interacts with receptors of a synapse within the CA1 region of the hippocampus (Jay, 2003). With an influx in dopamine, this allows for the receptors within the CA1 region to increase LTD by having and increase in glutamate, an inhibitory neurotransmitter, on other regions within the hippocampus.

Recently, several studies have detected which receptors within a neuron play a crucial role in the memory process. One of these receptors is the NMDA receptor, which has particular structure and biological advantages for which it aids neurons in the memory process. NMDA receptors are properly known as N-methyl-D-aspartate, a receptor on the neuron that has been found to play a critical role in the memory process (Monyer et al., 1994). The NMDA receptor has many cation channels that are gated by excitatory neurotransmitters, such as glutamate, and also mediate signal transductions. What is most interesting is that the receptor is highly permeable to Calcium, yet blocked by a Magnesium ion, and has slow gating kinematics. This all adds to the uniqueness of the receptor and allows it to be open for various amounts of time, yet being very selective initially. It has been found that the NMDA receptors are present and active since the beginning of the developmental process, and that their presence is key to the plasticity within the central nervous system (Monyer et al., 1994).

In addition to the uniqueness of the NMDA receptor, there are many combinations of subunits within the receptor. Monyer, et al., (1994) extensively explored two subunits, NR1 and NR2. It was found that there was a high amount of NR1 subunits present in the cortex, hippocampus, spinal cord, and other predominant areas such as a the cerebellum,

during the embryonic period of development and that there were monitor-able increases throughout the development process (Monyer et al., 1994). It is thought that the NR1 and NR2 subunits add to the unique combinations of the NMDA receptors, along with the high calcium permeability, voltage-dependent magnesium block and the slow gating behavior to affect the finality of the various combinations. There is a clear difference in the strength of the voltage-dependent block based on the different combinations of NR1 and NR2 subunits; while these combinations do not affect the reversal potential of the calcium permeability (Monyer et al., 1994). What is most intriguing is that the gating decay is highly affected by these combinations, so much in fact that the NR1 and NR2A combination is 3-4 times faster that any of the others; while the NR1 and NR2D have the longest offset time (Monyer et al., 1994). Cui et al., (2004), examined the NR1 subunit of the NMDA receptors and its crucial role in the preserving of remote memories. It was previously thought that NMDA receptors might be related to the plasticity of memory formation at the synapses of neurons. By using a knockout technique, they were able to assess how the NMDA receptors played a role in the storage of fear memories (Cui et al., 2004). Initially there was a significant decrease in expressed NR1 subunits in the cortex and the hippocampus when the knockout technique was administered. To test the role of the NR1 protein, fear conditioning was taught to the mice and there was a measurement of their freezing responses. They found that the memory consolidation of mice was unique in the fact that a lesion must be made in a crucial time of the consolidation process to effect the memory overall.

A lesion during a specific time during the memory consolidation process would hinder the memory trace. For the mice this happened to be during the first 1-7 days of the memory consolidation process; if a lesion occurred 28 days after the initial memory, there

was no effect on the memory. It was found that the knocking out of the NR1 subunit in the CA1 region of the hippocampus was most significant during the first two weeks of the memory consolidation process of the contextual fear conditioning. In the future the suppression of these NMDA receptors may be a strategy to help stabilize spatial memory within the hippocampus. This led to the hypothesis that the memory consolidation process was time sensitive and most stable when little interference or resistance occurred. In this case, memories that have been completed in their transition and consolidation are considered remote memories.

In conclusion, there are a variety of ways to explore the mechanisms of memory within the brain. By merely increasing the protein synthesis of BDNF, or increasing the presence of dopamine, the memory process was edited and its temporal speed increased. At the molecular level, NMDA is one receptor that plays a crucial role in memory consolidation process, and the various combinations of its subunits can vary the receptors delay time and sensitivity. Having a better understanding of the different mechanisms and their effects on the memory process is very important for increasing our understanding of time dependency of memories.

III. Neuroanatomy and Neuropsychology

Memory has been investigated with a variety of approaches including neuroimaging techniques. Within this section, I intend to explore the various parts of the memory processes of encoding, storage, and retrieval, and how these techniques have lead to greater understanding of memory process. One of the most crucial regions of the brain that has been associated with memory is the hippocampus. The hippocampus is a major

component of the memory system and necessary for the consolidation of multiple memory types. It is located beneath the cerebral cortex and the medial temporal lobe (Amaral & Lavenex, 2006). The hippocampus is broken into various regions including dentate gyrus, and CA subfields (CA1-CA4). Proper formation of the hippocampus will lead to the ability to process episodic memories and the ability to store and utilize spatiotemporal context (Lavenex, 2013). Even though development may be on track, there is an inability to form an episodic memory before the age of 2 years in typical development, which is referred to as infantile amnesia.

There has been research on the hippocampal dysfunction and its correlation to issues with memory and memory systems. Hippocampal dysfunction is ultimately considered to be the failure to learn new information (Aggleton, 2014). It was found that the recall of episodic memories strongly activates the hippocampus. It was found that when the hippocampal activity was balanced and regulated, that the overall learning process was enhanced as well. Aggleton also looked into various forms of lesions to the hippocampus. In particularly, the lack of oxygen to the brain would result in cell loss within the hippocampal region. This would consequently correlate to cognitive deficits and issues with memory. Aggleton & Brown (1999) also noted that lesions do not give one, absolute answer. Rather every lesion is different and affects a person differently. Different types of memory can be affected at different rates, and sometimes not all episodic memory and recognition are lost.

The temporal lobe patients who have damage or a lesion present show difficulty with object naming and information retrieval for "object-specific characteristics," which is predicted to be organized in a hierarchy that increases in complexity and necessity to integrate information (Martin and Chao, 2001). The posterior region of the temporal cortex

is believed to play a role in differentiating what type of information is to be retrieved, whether it is naming of an action related to an object or naming something within a perception domain, such as color (Martin and Chao, 2001). Interestingly enough, there is more posterior activation when a word is action related versus a visual or auditory stimulus (Martin and Chao, 2001). There is also an interaction between the frontal lobe and the temporal cortex when selecting from semantic features, like color and action object associations (Martin and Chao, 2001). It is thought that the semantic feature information is stored in the temporal cortex (Martin and Chao, 2001).

These are just a few of the highly activated regions of the brain related to memory consolidation and retrieval, and for different types of memories. Each one with a specific task and function but important to the overall process. With the removal of a specific, memory process dependent regions of the brain, it is obvious how important they are to consolidation and ultimate retrieval of memories. Without regions such as the hippocampus, medial-temporal lobe, and amygdala, a simple memory may never be encoded or able to be retrieved.

IV. Theories on Memory

As previously addressed, there are many parts to memory as a whole. Previously discussed was encoding and retrieval, but perhaps the most important part is storage, better known as consolidation of memory, where it is thought that memories become solidified and reinforced throughout various regions of the brain. In this section, various theories of memory consolidation will be explored. There are many theories but in this paper I will focus on the Standard Model of Memory Consolidation and the Multiple Trace

Theory. Both lay an important foundation in the understanding and background of the memory consolidation process.

A. Standard Model of Memory Consolidation

The hippocampus has been described as an intermediate memory storage system because its synapses change quickly; whereas the neocortex synapses are slower, allowing for less overall interference (Squire & Alvarez, 1995). The consolidation process occurs when there is repeated activation of the representation in the neocortex by the hippocampus. These representative connections are made stronger and result in less dependency on the hippocampus. Having memory storage in the neocortex is beneficial because it changes in a gradual way, slowly integrating in new representations. If it were to do this at a more rapid pace there would be a large amount of instability within the memory representation. Initially the memory is temporally stored in the hippocampus, where the fast synapses allow for change and modification, and then sent to the neocortex where the representations are solidified at a slow gradual pace. This is known as the Standard Model of Memory Consolidation. This initial binding of information, (e.g., cohesion), occurs in the short-term memory and is thought to be completed within seconds, and at most ten minutes. Later, the long-term consolidation occurs, starting with the hippocampus and other related structures, until the neocortex is able to sustain the memory alone (Nadel & Moscovitch, 1997).

B. Multiple Trace Theory

A theory that challenges the Standard model of memory consolidation is the Multiple Trace Theory (MTT). Nadel and Moscovitch argued that the hippocampus is involved in every type of memory storage and retrieval process (Nadel & Moscovitch, 1997). It is proposed that the MTT has distinct and unique strategies for which memories are recovered; four of which are consistent with the Standard Model. It begins with the hippocampus as being necessary for the encoding of all information and it does so at a rapid pace (e.g., cohesion). The second strategy of the MTT is that the information is distributed amongst multiple neurons within the hippocampus for the cohesion process. The third states that hippocampus acts as a director to the neocortex neurons that represent the desired information and representations and assists in the binding of those neurons to create a cohesive memory. The fourth, and last point that is similar to the Standard Model is that the hippocampus and the neocortex work together in coordination to trace a memory. This happens because the neocortex contains feature specific information of a memory, in which its spatial context is found in the hippocampus (Nadel & Moscovitch, 1997).

The fifth strategy is that there is re-activation of the memory when there is an alteration to the memory or the neuron. This means that when a memory is encoded incorrectly, or with incorrect facts, it can be altered and corrected but the entire trace of the memory is activated. This leads to the sixth strategy stating that the alteration of memory actually leads to the creation of a new hippocampal memory trace, which is distributed amongst various neurons. The seventh strategy is that these neocortex neurons all hold a piece of the initial memory and are all able to be activated based on the idea of an

index, as mentioned previously. The eighth strategy, may also be seen as a consequence, nonetheless the sematic and episodic pieces of the memory are stored separately and independently of each other. This allows for multiple facets to trigger the retrieval of the information and allows for semantic information to be integrated in to previous schemes. Lastly, the ninth strategy includes the continual need for the hippocampus and frontal cortex when needing spatial and temporal context. For example, when we have to recall the "when" and "where" a specific event occurred, the hippocampus is needed to retrieve the spatial context and the frontal cortex is needed for the temporal context (Nadel & Moscovitch, 1997).

There are, however, differences in the amount of hippocampal involvement based on whether the memory is semantic or episodic. There is a necessity for hippocampal activity memories to be retained and retrieved that are episodic; however semantic memories are less dependent on the hippocampus and need it primarily for the encoding of the memory. Although the hippocampus is initially needed for all memory consolidations, MTT is similar to the Standard Model in the fact that over time there is less need for the hippocampus as memories become established and strengthened, although within the MTT model this happens after several years. Another difference is that the older the memory is, the greater number of traces there are and the greater number of ways to access that memory are present. The newer the memory, the more vulnerable it is; but an older memory with multiple connections can withstand a great amount of stress on the hippocampus and/or loss of hippocampal tissue (Nadel & Moscovitch, 1997).

Based on these progressions and advancements in memory theories, it is clear to see there is no commonly agreed upon answer as to how memories are consolidated and

established in the brain. It is interesting to see how the theories have evolved off of each other and become more refined in their understanding of the overall process. It seems that memories consolidation is time dependent and needs specific regions of the brain, such as the hippocampus, for the solidification of a memory. It also seems to be that sleep can aid in that time-dependency. This is important to remember as there is much more information on the different types of memory and the differences between the typical and atypical populations.

V. Memory Development

It is universally agreed upon that memory changes, adapts, and grows throughout the human lifespan. It is unclear the specificity of a memory trajectory and how the developmental process affects its processes. To better understand how the memory changes over a lifetime, we must examine brain development and the different types of memory that can be affected.

Recently, Lavenex examined how the maturation of the hippocampal circuits was related to learning and memory development (2013). As previously mentioned, the hippocampus is crucial for the consolidation process of a memory trace, particularly for episodic memories (Lavenex, 2013). Before the age of two, children are unable to properly or adequately store and retrieve memories – this is known as infantile amnesia. This is thought to occur because of the hippocampus' rapid development between birth and two years of age (Newcombe et al., 2007). Then between the ages of three-five, there are considerably less recalled episodic memories (Newcombe et al., 2007). Infantile and childhood amnesia are the results of the different developmental and maturation speeds of

the different areas within the hippocampus (Lavenex, 2013). The dentate gyrus, as well as regions CA1 and CA3 of the hippocampus undergo a protracted development and lead to the theory of delayed hippocampal growth causing this form of amnesia from childhood (Feliciano and Bordey 2013).

Lavenex suggested that there was a hierarchy to the development of the memory system due to the development of the brain, and in particular the hippocampus (2013). A newborn sees the world largely from a spatial perspective, until they are able to appropriately use landmarks and environmental cues around nine months of age (Lavenex, 2013). This strategy is mastered and more similar to that of an adult when a child is in the age range of two-to-seven years old. The resulting hypothesis stated that the hippocampal maturation of various circuits was due to the gradual growth and emergence of neurons, which resulted in behavioral abilities at various ages. With age, there are better spatial memory capabilities, spatial resolution, and overall maturation, although gradual of the hippocampus and dentate gyrus. These changes are most significant between the ages of two and five; allowing the child to get better with location identification of objects near and far from each other. It is important to remember that although a specific region may not be required to consolidate a specific memory, it may be complementary to the process, and able to consolidate a particular aspect of the memory.

Based on behavior alone, it is clear that there are developmental changes over the life span. Children become better at retaining and recalling memories and making decisions with age (Ofen 2012). In contrast, adults are known to show declines in these fundamentals skills as they age. It is evident, that memory quality is age-related; meaning the details are much more enriched over time and with brain growth and maturity. To better understand

these changes, it is important to look at the different forms of memory and to investigate how they each uniquely develop.

Shing and Lindenberger looked into episodic memory trajectories in depth; by exploring the development over the lifespan and how different strategies could possibly aid in development There are two types of mechanisms that are at work within the realm of episodic memory: association and strategies. The first has to do with ability to make associations in memory; which means there is the ability to bind various elements of memory into a coherent representation (Shing and Lindenberger, 2011). This mechanism relies on the Medial Temporal Lobe (MTL) and the hippocampus, which develop at a fairly rapid rate. The association mechanisms are thought to be mature by the middle of childhood and decline in with old age, this is in congruency with the development and maturation of the lobes of the brain. The ability to bind details and features is thought to begin at a fairly young age and be fully developed at the ages of 5 and 6 years. It is argued that younger children, in particular preschoolers, have difficulty with binding because they have trouble identifying context specific information within a memory and judging whether an action was performed or imagined. When the MTL is damaged, there is a loss of the ability to form new declarative memories, or episodic memories (Ofen 2012). Activation within the MTL correlates to the explicit memory and the sub-categories being activated. For example, when predicting a novel stimulus activates the anterior MTL, but predicting a stimulus already seen activates the posterior MTL and hippocampus.

The second mechanism deals with strategies used by the brain. Strategies in this sense refer to the ability to cognitively control memory processes, particularly those that include encoding and retrieval (Shing and Lindenberger, 2011). Strategic mechanisms are

thought to mature much later in childhood development, but also decline around the same time as the associative mechanism. The temporal and frontal lobe undergo an overwhelming amount of maturation during childhood years and is related to the rather slow rate of memory development, which may conclude why children have a particularly challenging time remembering details. The theory is that the frontal and temporal lobes mature and develop with age, just as the functions of the episodic memory improve; therefore the two are age-related. Behaviorally, this maturation can be seen when older children have the ability to apply strategies within the encoding and retrieval processes, particularly the encoding of verbal information and the extraction of information, as well as its overall context. Once these strategies are practiced and learned, children are found to be more flexible with memory encoding and retrieval.

It was found that children had a more plastic episodic memory and that they could benefit from training strategies at a young age. In particular, when children have external resources and extensive practice with a certain skill, it can activate their cognitive resources and aid in their plasticity.

It is also important to remember that memory is not perfect at every age. There are pros and cons to the development of memory. Children have issues with strategic memory far into their late childhood years. Their attenuated performance may be due to the inability to better utilize multiple memory strategies and techniques compared to adults (Ofen 2012). The issues with memory recall could arise from a multitude of reasons including: not having information within the memory to pull from, the deterioration of a memory after consolidation, or possibly the inability to access information at all (Shing and Lindenberger, 2011). With age, children gain more knowledge and experience and can

improve on their ability to memorize, and strengthen the interactions between strategies and known knowledge (Ofen 2012). Interestingly enough, there are different locations and processes of semantic memory in the brain. Even though it is considered declarative memory, its function and purpose are separate from episodic memory.

Lastly, the fusiform gyrus is typically related to facial recognition, but is has also been activated during color-word association paradigms (Martin and Chao, 2001). The fusiform gyrus was found to have activation for words that were related to living things, such as humans and animals, as opposed to inanimate objects, such as tools. This paradigm showed activation in a large portion of the ventral cortex, not just limited regions as preciously hypothesized.

This is illustrated in the experiment done by Mitchell, where nonverbal implicit responses were found much earlier than those that were verbal (Hayes & Hennessy, 1996). These children showed "phylogenic and ontogenetic," individual and organized based, responses to stimuli, suggesting that these nonverbal responses allowed for the development and integration of memories before the ability to vocally express them.

It is also speculated that implicit memory is primitive in the development of memory because of its automatic response. The responses done by implicit memory are based more as a response to the environment, past experiences, and considered "automatic, without intention" (Glenberg, 1996). As explicit memory develops, so does the ability to practice habituation and suppress behavioral responses to the stimuli from the environment.

In conclusion, the development of the typical memory system is very complex with multiple routes within it. Not only is declarative memory a separate trajectory than implicit

memory, but episodic and semantic memories are unique as well. This confirms the fact that not all is known about the different types of memories, but there is a great deal of information that can allow for further research to be sought out.

VI. Memory Disorders During Development

a. Amnesic Patients

Another important case study is of Jon, a patient with developmental amnesia due to an underdeveloped hippocampus. What is interesting about his case is the fact that he was able to describe and create detailed fictitious scenarios without having the physical hippocampus to aid in this process (Cooper et. al., 2011). It is hypothesized that due to his ability to rely on other regions of the brain, he was able to strategically develop these scenes with the damage and limited hippocampal activity. This is interesting because of the idea that having the actual hippocampus for a portion of the lifetime, the connections with the brain are able to interact and strengthen. Once the hippocampus is damage, the surrounding regions are able to rely on those previously made connections to preserve some hippocampal function, but with the use of a different region.

Now, with the understanding of the consequences that come with the removal of the medial-temporal lobe, it is understood how lesions of this region to progressive impairment of memories and the removal can cause damage to the hippocampus (Scoville & Milner, 1957). The degree of memory loss is unique to each individual due to their age, the region of which the brain has been removed, and the amount that was removed (Scoville & Milner, 1957).

Neurodevelopmental Disorders

With a common understanding of the different trajectories of memory systems and how they change in typical development, we can better characterize memory profiles of atypical development, such as Down Syndrome (DS), Williams Syndrome (WS), and Autism Spectrum Disorders. Several studies have examined memory trajectories of these disorders and how the two relate to each other.

a. Down Syndrome

Down Syndrome is a genetic disorder due to a third copy of chromosome 21 (Patterson, 2009). The DS population has been associated with physical and mental growth delays, characteristic physical features, and some form of intellectual disability (Weijerman, 2010). Although there is a mental delay, the DS population commonly has a better language understanding and speech abilities. There is also a high percentage of the development of Alzheimer's at an early age (Schwartz, 2012).

Nadel (1999) illustrated how the there was significant volume reduction of the brain in the DS population, particularly the hippocampus, pre-frontal cortex, and cerebellum. Next he looked into figuring when this began. He found that there was a delay in myelination of the brain and the frontal lobes were considerably smaller that the typically developing population within the first months of birth (Nadel, 1999). The brain stem was considerably smaller than the typically developing population, as well as the cerebellum at this age as well (Nadel, 1999). The next question was whether this onset continued into adulthood. IQ is affected by the DS in the sense that it will continue to be

below the norm and eventually range between a score of 22-55 (Gibson, 1978). Because this trajectory is into and throughout adulthood, there is a higher risk of early Alzheimer's Disease and decline of their IQ happens much sooner (Epstein, 1989).

One of the first papers that examined memory from a cognitive neuroscience perspective was Pennington et al., (2003). Pennington looked into the comparison of mentally matched typically developing population and the DS population. The aim was to study neuropsychological development, in particular in comparison of hippocampal activity. There was a significant difference in hippocampal activity when comparing the typical and DS populations. There was also strong evidence supporting dissociation between the hippocampus and the working memory. The hippocampal dysfunction was not entirely specific, meaning there was a range of dysfunction and variances per each individual.

There was little cognitive decline across the age ranges tested, although there was a correlation between the increased hippocampal deficits with age. However, there is little evidence on how the hippocampus dysfunction progresses through the adolescent age range other than reduced hippocampal volumes (Pennington et. al., 2003). They also found difficulties with recognition and recall. The real question is during which specific process of memory consolidation does the dysfunction occur: the encoding, retrieval, or storage component?

Edgin et al., (2014) examined object memory in relation to context specific events. They looked into how development of object memory progressed, which was found to be nonlinear. The hippocampus is able to process configurations of objects in particular scenes around the age of 4.5 years. There are three hypotheses as to why there are errors

that occur within the DS population: 1 – there is a "binding" effect in which the object and the scene are bound together and are needed to be together to reactivate the memory; 2 – there is an issue with the flexibility with the object and a being placed in a different scene; 3 – lastly, there is a refinement in the skills to reemerge an object or context with age (Edgin et. al., 2014).

b. Williams Syndrome

Williams Syndrome is a neurodevelopmental disorder due to the deletion of the 26 gens on chromosome 7 (Francke, 1999). The WS population is associated with a characteristic appearance and decreased inhibition in social settings (Cozolino, 2006). Although there are developmental delays, their language and verbal skills are strong (Kaplan et al., 2001). Some more background in the Williams Syndrome: it is known that there is a reduction in overall grey matter throughout the brain, as well as the anterior region of the brain smaller in comparison to the typical population, yet larger that the DS population (Karmiloff-Smith, 1998). Although the frontal cortex appears proportional to the posterior region of the brain, both are significantly reduced in size. Abnormal layering, clusters, and orientations of neurons have been detected and there is an issue with overall inhibition.

Research has looked at how the memory trajectories of these two disorders differ but how they may be possibly linked with similar developmental schemas. Since both disorders are linked to cognitive development delay, it is common to assume that the two may possibly develop in the same pattern. Particularly, working memory has been extensively investigated in Williams Syndrome. Working memory is a cognitive process

that holds new information constant, while manipulating and processing it. In a study done by Jarrold, Baddeley, and Hewes (1999), working memory was examined in those with DS and WS. This study looked into the memory deficits and constraints that may be present in individuals with memory disorders; in particular verbal short-term memory and visuo-spatial short-term memory (Jarrold et. al., 1999). The study was broken up into two experiments: the first looked at verbal and visuo-spatial memory in DS, WS, and a typically developing (TD) group; while the second looked at non-verbal mentally matched WS participants and other groups matched based on short term abilities.

In the first part of the study, the WS group had a higher verbal mental age than those with Down syndrome (Jarrold et. al., 1999). The DS group showed difficulty with digit span, (e.g., participants keep certain numbers in mind and manipulate them, such as recalling them backwards). The second part of the experiment had conflicting results but was used to eliminate covariance and prove that mental age is an important factor to take into account when looking at memory differences between different groups; overall the short-term memory in DS is thought to be a consequence due to the learning difficulties associated with the disorder. A possible explanation for the poor performance on the digit span may be because of the poor verbal skills of those with DS and subsequently their inability to express their answer. WS participants are primarily non-verbal and that would play a role in their performance on the Corsi exercise (Jarrold et. al., 1999).

There is a noticeable deficiency in the visuo-spatial memory of the Williams syndrome population (Vicari et. al., 1996). This deficiency is also evident in the overall long-term and short-term memory. The WS population is, however, very strong in facial processing and

language (Bellugi, 2000). The typical IQ of the William Syndrome population is fairly mild although the cognitive abilities are hindered.

c. Autism Spectrum Disorders

In Autism Spectrum disorders (ASD), there is a great deal of variation, as it includes a wide range of developmental pathology and social impairments. This variation makes discussion of their trajectory complicated because of the great amount of variation. The Autistic population has been known to have abnormal and inconsistent brain growth throughout development (Kelleher and Bear, 2008.) There is an enlargement of the hippocampus and very excessive period of physical brain growth, leading to macrocephaly – also known as an enlargement of the brain. The Autistic Spectrum Disorder population (ASD) have been found to have consistently disrupted synaptic function - this can be either excessive or diminished excitatory synaptic connectivity.

In general, there is a significant difference in declarative memory (Boucher et. al., 2012). The neural substrates, in particular, have issues with processing and integrating information. This, consequently, interferes with consolidation and storage of memories. The level of deficit is dependent on the level of function. That is there is a strong relationship between hippocampal function and severity of autistic symptomology. However, individuals that show high and moderate levels of function show a lack of executive control and issues with working memory. This can be correlated with the lack of brain development in the hippocampus, frontal cortex, temporal cortex, and atypical neural connectivity. In individuals with ASD, Complex memories are the most difficult to process. These memories require high levels of organization, processing, and strategy. There is also

a significant dysfunction within the primary sensory systems, and with the neighboring association regions (Boucher et. al., 2012).

This overall issue in processing leads to dysfunction and can be found to be in the hippocampus, prefrontal cortex, and parietal lobe. These are similar to the disorders listed above and can be hypothesized to have similar deficits and issues. Although the memory profiles are somewhat similar for across the spectrum, particular impairments can differ depending on the severity of autistic symptoms. That is, individuals that are more severely impacted by autism have more memory impairments and abnormal connectivity (Boucher et. al., 2012).

There is a significant impairment of episodic memory throughout the lifetime within the ASD population (Lind et al., 2014). There is major difficulty generating a specific response about past experiences and recalling specific memory details. ASD participants had a significant decrease in event recall utterances. There is consistent difficulty for ASD patients to self-project into an alternative scenario and construct an imaginary sequence or story. There are considerably noticeable difficulties with processing representations, which are thought to stem from a difficulty to mentally stimulate. There is a hypothesis that complex information processing skills are impaired in the ASD population, while simple-information processing skills are not affected (Renner et al., 2000). The hippocampus' size and function are different per individual with ASD, which would play a role in the level of function. For example, high-functioning autistic children have an intact hippocampus, while low-functioning children have an imparted hippocampus.

So often the typically developing population forgets how important working memory is to every day processes. It allows for information to manipulated and moved

around, for vocabulary to move between the phonological-loop and then to other memory structures, and to work with spatial and visually stimulating objects. This leads to phonetically different observations of behavior and cognitive development. Exploration of the different cognitive profiles of individuals with developmental disorders not only provides great insight into the nature of the disorders themselves, but insight into typical development as well.

Discussion

Over the past several decades, much has been discovered and informed us about memory development and memory processes. .Time plays an important role in memory. This can be the actual seconds, minutes, hours, or days a memory needs to consolidate; or it can be the lifetime of a memory system, how it develops and it able to help us live efficient lives.

The first area of discussion is the time dependency of the memory consolidation process. There is discussion on how the subunits of the NMDA receptors are related to the speed of memory consolidation. This can be clause-able in two different ways, the first being if one were to knockout the NR1 subunit then memories need about 7-14 days to solidify (Cui et al. 2004). The other way the subunits affect memory is that the different combinations of subunits can admit for slow delays or quick delays, which in turn may affect the number of additional AMPA receptors to the membrane. This would then affect the consolidation efficiency and strength as well.

Not only do we examine neural development of memory processes at the cellular level, but the examination of neural structures that map onto memory is important to study

as well. Of particular interest are two structures that work in cooperation for the memories to be retained, the hippocampus and the neocortex. These two regions work together to solidify types of memories based on their vulnerability and type of representation. The neocortex slowly solidifies a memory gradually so that there is a precise and slow integration of representations. Memories can be recalled, and reconsolidated into a new memory, as well. The hippocampus, on the other hand, does this in a much more fast manner, therefore it is more vulnerable and unstable. This is interesting because the two structures work in unison to consolidate a memory based on its own properties and to maximize efficiency for an individual. This then leads to the question of how involved these structures are for a specific memory type. It has been suggested that the hippocampus is needed more in the consolidation and retrieval of episodic memories. This may be the case because of the high vulnerability of episodic memory and the ability to alter them each time they are recalled, as mentioned by the Multiple Trace Theory. Semantic memories, however, rely less on the hippocampus and this may be because of the need to incorporate a vast amount of representations that the neocortex is more apt to do. Based on these suggestions and hypotheses, there is still the underlying question of time and how much of it is needed for a specific memory to be created, and does this time dependency vary based on a memory type or its specific properties?

This leads to the interesting debate over the role of time in cognitive processes, particularly memory. For motor memories, the duration required to consolidate a memory generally lasts four to six hours and can occur while awake or asleep. On the other hand, consciousness tends to be necessary in the case of episodic memories. If episodic memories rely heavily on the hippocampus and have a necessity for conscious effort of consolidation,

then one could hypothesize that it is the fastest to be consolidated with the least amount of time needed to be stored. We must also be cautious of the development of the brain as a whole takes a while to develop (i.e., the most protracted development) and is important for episodic memory formation and retrieval. This may mean that, just like time, consciousness is a variable to consider in the memory consolidation process.

With respect to development, it was also found that as children aged, they were able to improve on recall and retrieval tasks, as well as make better decisions. These improvements are related to the development of the prefrontal and temporal cortex, strengthening the previous claim. But why does this peak in the mid-life, and then decline with age? Is this because of the natural deterioration of the body, or could it be that the structures within the brain are unable to keep up with the formation of new memories and the constant modifications of others?

The hippocampus works with as associative areas of the brain to enhance its memory capabilities, using different strategies to better encode details and features. When there is a dysfunction of the hippocampus, whether a case study or a neurological disorder, the effects are visible on may levels. With amnesia, or the removal of the hippocampus, there are instances that memories cannot be created or retrieved from the point of the lesion. In other cases, imagination and false memories are created because of the use of surrounding connections and regions to "act" as a hippocampus. Either way, there is no specific answer as to how memory will be affected due to a lesion-resection surgery.

Lastly, looking at the memory system as a whole, there is a temporal aspect relating to the hippocampus. By comparing typical and atypical groups there is a lot of knowledge to gain about each of these populations and how memory differs within each. The overall

trajectory of the WS group and the DS group were similar to each other but considerably different and delayed from the TD group. The delay may be in consequence to the late neural development of the atypical group or the fact that it is a slower process. Most interestingly, although the trajectories were different when looking at sequential steps, the overall trajectories were linear and showed the same progression of the memory system. This raises the question as to whether memory systems have a specific growth pattern and based on disorder type, whether that progression is either delayed or expedited.

By increasing the understanding of atypically developing populations, there is a better understanding of the typically developing population as well. From the information stated above one can infer that there is a linear trajectory of the development of memory systems within a TD individual. As the physical development of the brain becomes more refined, an individual is able to enhance their retrieval ability, as well as their application of past experiences towards making more appropriate and rewarding choices in decision making tasks. The DS, WS, and Autism Spectrum disorders all have some form of hippocampal dysfunction, yet its affects are specific to each disorder. Each disorder suffers from a lack of growth in the hippocampal region.

It is known that those with DS and WS show difficulty making decisions, as well as application of their past experiences. Difficulty with decision making can be attributed to the protracted development of the temporal and frontal lobes, and the inherent inability of the frontal lobe to effectively communicate with the hippocampus—also has a delay in development. If a memory is consolidated when these structures are strong and adequate, it could be consolidated fairly quickly and easily retrieved. This could also be used to explain that those with DS and WS have a particularly hard time with the consolidation

aspect and retrieval the information, along with the issues of "bounding" various details and features together of a memory.

Individuals with Autism Spectrum disorders show hippocampal dysfunction as well, yet the case is a little more complicated. Hippocampal function varies based on the level of impact that autism has on the individual's development (e.g., more severity is associated with poorer memory recall). However there is an overall, cohesive difficulty with the processing of complex stimuli, due to the high level of organization, processing, and strategy usage. It is apparent that these individuals have a harder time with memory consolidation and why their processing speed my take longer than that of the TD population because of reduction in hippocampal volume, which becomes burdened by the amount of information being processed.

It is important to ask if there are critical periods during the development of the hippocampus and how that will affect the memory process trajectory. When are these critical periods and what do they entail? Overall, the hippocampus is important in a number of developmental disorders. It is important to do more work to understand how it relates to development within these disorders, with specific attention to the variations in structure of the hippocampus, temporal and parietal lobe. From there, further analysis is needed to see how these differences relate to differences in outcomes, including patterns in structures, subfields, or connectivity.

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