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Impairments in the acquisition of new object-name associations after unilateral temporal lobectomy despite fast-mapping encoding

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IMPAIRMENTS IN THE ACQUISITION OF NEW OBJECT-NAME ASSOCIATIONS AFTER UNILATERAL TEMPORAL LOBECTOMY DESPITE FAST-MAPPING ENCODING

by

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CERTIFICATE OF APPROVAL

MASTER'S THESIS

This is to certify that the Master's thesis of

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has been approved by the Examining Committee for the thesis requirement for the Master of Arts degree in Speech Pathology and Audiology at the May 2013 graduation.

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ABSTRACT

Learning new object-name associations (i.e., word learning) is an ability crucial to normal development starting in early childhood and continuing through the lifespan. To learn a new word, an object must be associated with an arbitrary phonological (or orthographic) string representing a word. The declarative memory system formulates and encodes associations between two arbitrary stimuli and has been well established as playing a critical role for adult word learning. Research investigating the neural substrates of the declarative memory system and word learning has implicated the hippocampus and the surrounding medial temporal lobe (MTL) as crucial structures. A substantial literature on populations with damage to these particular structures (e.g., hippocampal amnesia, temporal lobectomy) has supports the view that without these structures, declarative learning, and word learning by extension, is grossly impaired. However, a recent study Sharon and colleagues (2011) suggested that non-MTL structures may be sufficient to support word learning under special study conditions (“fast mapping”) (Sharon, Moscovitch, & Gilboa, 2011). Fast mapping is a word-learning phenomenon described as the ability to acquire the name for a new word in a single exposure to an unknown word and unfamiliar referent alongside a known word with its referent (e.g., Carey & Bartlett, 1978; Carey, 2010).

This study evaluated the ability of patients with unilateral temporal lobectomy (TL) following early-onset temporal lobe epilepsy to learn new object-name associations in two different word learning conditions: fast mapping (FM) and explicit encoding (EE). The word learning performance was evaluated relative to a group of healthy normal comparison participants (NC). The goal of this study was to examine the role of the hippocampus in word learning to answer the question: does a FM condition promote word learning in participants with temporal lobe epilepsy who have had a left temporal lobectomy?

NC participants were able to acquire a rich representation of novel items (as evidenced by improved familiarity ratings and generalization of items) while TL participants had severely impaired performance on free recall, recognition testing, and generalization tasks. TL participants did not learn novel object-name associations despite a FM paradigm while the NC group performed significantly above chance on recognition testing. These findings in conjunction with broadly similar results obtained from hippocampal amnesic patients tested using the same paradigm (Warren & Duff, 2012), support the necessity of the hippocampus for rapid and flexible associations to be obtained via the declarative memory system.

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CHAPTER I

REVIEW OF THE LITERATURE

The ability to learn new words is often taken for granted. Across the course of development from childhood to adulthood, one is able to retain and express labels for a variety of people and things. In the word learning literature pertaining to children, the concept of fast mapping provides a framework for understanding how this remarkable feat occurs. By some accounts, the process of fast mapping is also available in adulthood as our mental lexicon expands and we continue to apply semantic knowledge to new experiences. The ability to learn words has been linked to specific neural correlates and cognitive mechanisms as theoretical and methodological advances have been made. Converging methods point to the hippocampal declarative memory system as a key neural/cognitive system for word learning. The declarative memory system is thought to formulate and encode associations between two arbitrary stimuli – such as a word and its meaning.

The role of the hippocampal system in word learning was recently challenged (Sharon, Moscovitch, & Gilboa, 2011). These authors suggested a fast mapping paradigm could “bypass” the hippocampal system and thus patients with hippocampal damage and profound memory impairments *could* learn new words rapidly. The current study is a partial replication and extension of the work by Sharon and colleagues. The goal of the study is to examine the role of the hippocampus in word learning during fast mapping. Participants with left temporal lobectomies (i.e., resected tissue of the left hippocampus and left medial temporal lobe) due to epilepsy and control participants underwent two word learning conditions: *fast mapping* (FM) and *explicit encoding* (EE). Before presenting the methods and results of this study, the present literature regarding word learning throughout the lifespan is broadly reviewed for both those with normal memory systems and those with damage to a variety of brain structures.

Word Learning

The average adult knows approximately *sixty thousand* words by the time she walks across the stage at a high school graduation ceremony (Aitchinson, 2012; Bloom, 2000; McGregor, Sheng, & Ball, 2007). How and over what time period is such an extraordinary lexicon accumulated? As it so happens, the ability for children to learn the meaning of words is a robust feat that starts at a remarkably young age. By the age of 12 months, children have learned their first words. By the age of two or three, children are able to rely upon a variety of sources to infer the reference of a new word. These include an understanding of the external world, an appreciation for syntactic cues, and the tendency to interpret a new word label a referent for a whole object (Bloom & Markson, 1998; Swingley, 2010).

Children grow to understand about 10,000 words by the time they reach their sixth birthday, on average learning to understand 9 new word *each day* (Templin, 1957; Anglin, 1993). At around the age of 8 years, children are learning words at a remarkable rate of 12 words per day on average (Fenson, Dale, Reznick, Bates,Thal, & Pethick, 1994; Bloom & Markson, 1998). The changes that occur throughout development influence the multifaceted task of word learning and add to the challenge of accounting for this ability (Bloom, 2000; Bloom, 2005; Brown, 2009; McGregor, Sheng, & Ball, 2007). How does such a robust learning process occur in children?

Three general proposals have been established in the developmental psychology literature as to how children learn word meanings (Brown, 2009): (1) children have innate capacities and biases that shape the language-specific inferences they make about word meaning (e.g., assumption of mutual exclusivity), (2) children collect statistical information regarding the presentation of a word and contexts and develop an associative pairing, (3) adults promote word learning by structuring the environment and interactions in a conducive way for children. While there is general agreement in that all three realms likely contribute to optimize word learning, the relative impact of each domain is largely unknown and widely debated.

The sheer quantity of words children acquire, as well as high accuracy in deducing meaning, suggests that children must be able to store meanings during the briefest of encounters with a novel word (Bloom & Markson, 1998; Swingley, 2010). The concept of fast mapping fulfills such a requirement. Fast mapping can be defined as the robust “process through which a new lexical entry is established and through which representations of the linguistic context of a newly heard word interacts with representations of its nonlinguistic context to fix an initial partial meaning” (Carey, 2010, p. 184). This rapid learning process involves a fragile initial memory trace of word form (e.g., number of syllables) to semantics (i.e., word meaning) with only minimal experience with a new label. Despite the limited exposure time, young children are able to construct and maintain these incomplete lexical representations (e.g., Swingley, 2010). The ability to maintain a large number of incomplete representations that get updated in memory over time would account for the remarkable word learning feat in early childhood (Dollaghan, 1985). According to Alt and Gutmann (2009), however, a new word can only be considered functionally learned if a person recognizes not only the label but also the semantic features associated with the newly learned label:

> “simply recognizing a whole object and its associated label (e.g., scissors) will not provide any clues about an object’s function. Semantic features may serve as indices to more in-depth information about an object. For instance, awareness of even simple visual semantic features of an object (e.g., scissors have sharp points and loops) can provide insights about purpose” (p. 13)

Fast mapping paradigms in research with children often consist of pairing a new word with its referent alongside a known word with its referent (Ramachandra, Rickenbach, Ruda, LeCureux, & Pope, 2010). In a classic study, conducted by Carey and Bartlett (1978), children were introduced to a single new color word (“chromium”) by a classroom teacher. The context for learning through fast mapping was set up by the teacher asking the children for one of two objects, identical in all aspects except for color. The non-target objects were a color familiar to the children (e.g., “Do not get the blue tray, bring the chromium one”). All of the children brought the correct tray and more than half indicated that “chromium” was added to their lexicon by showing retention of the word up to 6-10 weeks later. While only a singular contrast is created between a well-known item and a novel item, a wealth of information is provided about the meaning of the new item (Heibeck & Markman, 1987). Furthermore, children have a remarkable ability to apply a variety of available cues (semantic, syntactic, and/or social) to narrow down the hypotheses for what a novel word may mean in order accurately fast map new words (Wilkinson, Ross, & Diamond, 2003; Heibeck & Markman, 1987).

The question that still lingers, however, is whether children truly learn the words they fast map? A few studies in the literature have in fact shown that children do often retain mapped word-object pairings after initial learning (e.g., Carey & Bartlett, 1978; Golinkoff, Hirsh-Pasek, Bailey, & Wenger, 1992). Spiegel and Halberda (2011) demonstrated learning and retention of at least one novel word for two-year-old participants despite challenging test conditions (i.e., large number of competitors). Recent research has begun to suggest that while “fast mapping may be important for word learning, selecting a novel object in response to a novel name is not coextensive with learning the novel name” – a child may merely hold a simple representation in short-term memory of the recently presented trial (Horst, McMurray, & Samuelson, 2006, p. 339). A child does determine the most likely object of an unknown referent online during a fast mapping paradigm with great success, yet this moment does not necessarily translate to learning the name-object pairing. The processes that supported an initial ability to select a novel object did not lead to retention in a variety of other studies despite reduced numbers of novel names or total objects presented (Horst, McMurray, & Samuelson, 2006; Horst & Samuelson, 2008).

These various studies emphasize the importance of specificity regarding task requirements of participants and the type of stimuli utilized in research as to not conflate the process of fast-mapping specifically to childhood word learning. For the child, factors such as delay between learning and retrieval or distractions in the environment may disrupt certain elements of acquisition. In a similar vein, certain contexts (e.g., depth of semantic representation) may have a facilitative effect on word retrieval (e.g., Capone & McGregor, 2005). For those assessing the behavior, the exact definition of success will largely influence the amount of learning deemed to occur. Ultimately, complete knowledge of the mapped word meaning can only be obtained through increased exposure over time in a meaningful way for the child (Brown, 2009; Carey, 1978; Carey, 2010; Kucker & Samuelson, 2010; McGregor et al., 2007; Spiegel & Halberda, 2011). The process of establishing and elaborating a representation to fully capture the meaning of a novel referent can take weeks, months, or even years (McGregor, Friedman, Reilly, & Newman, 2002).

Despite the controversies outlined above, the fast mapping process itself has been instrumental to the research literature on word learning. As stated by Kucker and Samuelson (2010), "Fast-mapping…is perhaps the canonical example of young children's word learning prowess" (p. 2621). For example, a variety of studies maintain the notion that fast mapping supports the vocabulary "burst" observed for normally developing children between the ages of 1 and 2 years (Bloom, 1973; Wilkinson et al., 2003). Children must be able to rapidly store, recall, and expand upon the knowledge of words in order to show such a remarkable vocabulary expansion. The fast mapping paradigm has been extensively replicated and expanded, enhancing understanding of the dynamic and complex nature of word learning in childhood.

Overall, fast mapping studies provide evidence for a remarkably robust word learning process for normally developing children. For children with developmental disorders, however, the very same mechanisms supporting this ability are vulnerable. In a study conducted by Rice, Buhr, and Nemeth (1990), a group of 5-year-old language-impaired (LI) children were able to correctly recognize an average of 1.5 new words after a fast mapping paradigm task compared to 2.3 words 3-year-old controls matched for Mean Length of Utterance (MLU) and 4.22 new words for typically developing 5-year-old controls. Despite the fact that "very little is known about the lexicons of language-impaired children, the way in which they learn new words, and the manner in which their world knowledge influences other linguistic competencies," the majority of the research literature indicates that children with SLI exhibit deficits in fast mapping (Rice, Buhr, & Nemeth, 1990, p. 33; Oetting, Rice, & Swank, 1995; Ellis Weismer, Venker, Evans, & Moyle, 2011).

The clinical implications of a deficit in the ability to fast map are important. A child's poor performance at the fast mapping stage of exposure to a novel item is related to future success of word learning. For example, children with SLI who have difficulty acquiring new words may need to have *twice as much* exposure as a child with normal language skills in order to adequately map phonological, semantic, and syntactic information (Gray, 2003). Furthermore, there may be a quantitative difference in the initial ability to learn new words: children with SLI may have a limited capacity for verbal processing (e.g., Records, Tomblin, & Buckwalter, 1995).The graded nature of word acquisition in normal development (i.e., an initial exposure through fast mapping to a novel item only lays a foundation for future scaffolding of the entry) requires a clinician to be sensitive to these possibilities in assessment and treatment for children with or without language impairments (Capone & McGregor, 2005).

Word Learning into Adulthood

Of course, word learning is a language process that does not cease once childhood is over – it carries well into adulthood. Adults do not, however, learn several new words each day as they did during the robust vocabulary acquisition period during their childhoods. While this may be a product of declining abilities in word learning or the immediate environment being satisfied with words already known (Bloom & Markson, 1998), adults do encounter situations in which learning new words is critical. For example, adults may need to acquire jargon relevant to the workplace or for greater educational advancement and are constantly adding proper nouns to their repertoire; these are all arbitrary relationships between a word and its referent (Alt & Gutmann, 2009).

Fast mapping accounts of word learning are also prevalent in adult word learners. According to Ramachandra and colleagues (2010), "fast mapping is not only essential during childhood but also plays an important role in the expansion of mental lexicon in adults" (p. 214). The successful strategy of assigning a new label as the term for a novel object should not lose its efficiency over time, especially considering that the semantic knowledge base increase over time with more experiences (Golinkoff et al., 1992). The same abilities children use to choose the correct referent of a new word, as outlined earlier, do not disappear. Despite the fact that healthy adults can draw upon a vast knowledge system and are presumed to fast map at some level, little is known about the fast mapping process or their neural correlates (Alt & Gutmann, 2009; Shtyrov, 2011). In a study conducted by Golinkoff and colleagues, adult participants selected unknown objects as the referent for a new term 100% of the time and extended a newly learned term to a new token 100% of the time, showing evidence of generalized word learning through the process of fast mapping (Golinkoff et al., 1992).

The similarity in word learning between adults and children through the fast mapping process may point to similar cognitive and neural substrates. In the next section, I will first review the neural substrates implicated in word learning. Secondly, two populations with localized damage resulting in a profound detriment to learning, patients with amnesia and patients with temporal lobe epilepsy, will be presented. The literature regarding impairments or failures of word learning in these populations has been vital in refining our understanding of the cognitive mechanisms and neural substrates critical for word learning.

Word Learning: Cognitive Mechanisms and Neural Correlates and Structures

The ability to learn words has been linked to specific neural correlates and cognitive mechanisms. The two memory systems that comprise long-term memory include the declarative and the nondeclarative systems. The declarative memory system houses the ability to encode, store, and recall the meaning of a word. More broadly, declarative memory is memory "for facts, ideas, and events – for information that can be brought to conscious recollection" (Squire & Kandel, 1999, p. 15). The ability to consciously recall knowledge is a defining feature of declarative memory:

> "a hallmark of declarative memory is that it is accessible to conscious awareness and can be consciously brought to mind as a verbal proposition or nonverbally as an image, unlike procedural knowledge which is accessible only through reenacting the task in which the knowledge was learned" (O'Kane, Kensinger, & Corkin, 2004, p. 422)

Declarative memory has been associated with forming and encoding associations between two arbitrary stimuli, such as a novel word's phonological form and its meaning. For stimuli that have an arbitrary relationship, a learner cannot significantly rely on any semantic knowledge in order to build an association between the items (Weintrob, Saling, Berkovic, & Reutens, 2007).

The declarative memory system is critically dependent upon the hippocampal system in order to take the fragmented pieces of an experience and bind them together. The hippocampal system (i.e., hippocampus and surrounding neocortex) is located in the medial temporal lobe (MTL). For each event experienced, the hippocampal system represents information about a variety of elements (e.g., people, places, and things) along with co-occurring spatial, temporal, and interactional relations. These representations are subsequently stored among a variety of specialized cortical areas involved in the initial processing of the information (e.g., memory for visual elements is stored in visual-processing regions):

> “the hippocampus provides a mechanism for rapid acquisition but temporary storage of information…[the system] then mediates the creation of permanent memory representations in specific neocortical sites, maintaining a hippocampal-neocortical interaction for a considerable time after learning…[the interaction] over time produces richer and more interconnected representations within the neocortex” (Cohen & Banich, 2004, p. 353)

As detailed above, the hippocampal memory system is necessary for not only the moment of learning, but also for consolidation and cortical reorganization after the initial learning episode takes place (Squire & Kandel, 1999). By providing a record of experiences over time, the hippocampal system is able to support relationships *among* a variety of events that are encountered (Cohen & Banich, 2004). Therefore, the hippocampus is vital for initial episodic learning as well as the development of rich semantic knowledge. The interaction with multiple neocortical storage sites renders the hippocampal system necessary for encoding, maintaining, and retrieving many kinds of memories (O’Kane et al., 2004; Cohen & Banich, 2004).

According to a model proposed by Ullman (2004), the lexicon (consisting of memorized, word-specific knowledge) relies upon the MTL system for declarative memory. The non-declarative memory system, however, may also play a role in language learning. Aspects of language learning that are slow, systematic, and require multiple exposures (e.g., phonological form, grammar) are hypothesized to rely on the procedural memory system while arbitrary links, such as word meaning, are established rapidly through the declarative memory system (e.g., Gupta & Tisdale, 2009; Gupta & Cohen, 2002). Particular aspects of language that are either impaired or spared after focal brain injury seem to selectively depend upon declarative or non-declarative memory. For example, the ability for long-term memory storage and retrieval of vocabulary acquisition is lost or grossly impaired when the MTL is damaged (e.g., Squire & Kandel, 1999; Broadbent, N., Clark, R., Zola, S., & Squire, L., 2002; Mayes, 2002; Nyberg, L., 2002).

On the other hand, there is evidence that amnesics are able to learn artificial grammars via intact procedural memory structures in the brain (e.g., Knowlton & Squire, 1996). In the next section, the learning impairments associated with amnesia are explored. The research literature surrounding amnesia establishes the direct relationship between the declarative memory system and word learning.

Failures of Word Learning

The Case of Hippocampal Amnesia

Damage or dysfunction of the hippocampus (and/or related MTL components) causes amnesia. Patients with hippocampal amnesia have a severe and selective impairment in declarative memory while non-declarative memory is intact (Cohen & Squire, 1980). There is a substantial literature pointing to profound deficit in acquiring new words in patients with hippocampal damage and declarative memory impairment. Studies with H.M., a patient with anterograde amnesia after surgical resection of the hippocampi bilaterally (Scoville & Milner, 1957), provide a wealth of information. A series of experiments conducted by Gabrieli, Cohen, and Corkin (1988) showed that H.M. showed normal learning on several measures of premorbid semantic knowledge, moderately impaired learning on information from the 1950s, and severely impaired learning of semantic knowledge beyond the 1960s. As the authors eloquently stated, H.M.'s amnesia had "rendered him an alien in his own land and time" (p. 174.). Regarding acquisition of novel associations, the most striking outcome was H.M.'s complete failure to learn any new words.

The blanket statement that these participants cannot learn *any* new semantic knowledge is not true. Patients with amnesia can show learning and retention of new factual information, but this learning occurs through the non-declarative system. This learning should be considered far from normal: information is learned *remarkably* slowly, the new knowledge is highly inflexible, and learning requires a much larger number of exposures than for healthy participants (Bayley and Squire, 2002). For example, patient E.P., a participant with profound amnesia, required *48* trials to learn material that normal comparison participants were able to learn in just *4* (Bayley & Squire, 2005).Therefore, MTL structures are necessary components of the declarative memory system while neocortical structures support nondeclarative knowledge.

Despite the grossly impaired ability of amnesic patients to learn arbitrary relations, these same patients have been shown to have robust collaborative learning for similarly arbitrary referential labels (Duff, Hengst, Tranel, & Cohen, 2006). This barrier referencing task required generation of *meaningful* labels, rather than arbitrary associations, as a consensus label for a novel item was achieved between a participant with amnesia and a familiar communication partner. The learning and common ground acquired by the amnesic patients was independent of the hippocampus and encoded at a normal rate, which implied that other brain regions must have supported the acquisition of the new assocations. According to Duff and colleagues (2006), the learning "may be most consistent with tuning of cortical processors, including conceptual, semantic and visual processors" (p. 144). These same participants were later asked to learn a new set of materials through arbitrary association (i.e., experimenter generated labels) and the expected profound learning and memory impairments was observed.

The various studies of patients with amnesia presented above provide evidence that the hippocampal declarative memory system is critical for word learning. When asked to learn new words in a study-test format, patient HM failed miserably and was unable to learn a single new word. In other contexts, patients with amnesia have been able to slowly learn new semantic information. This is not to say that this learning is normal, however. Via nondeclarative cognitive processes, individuals with amnesia require a greatly increased number of exposures or are only able to learn a fraction of the amount retained by healthy individuals. In neither case would word learning be considered a normal or unimpaired.

The Case of Epilepsy

The primary focus of this project is on word learning in patients with epilepsy. Epilepsy is a “chronic seizure disease characterized by the risk of recurrent seizures” that affects approximately 0.5-1.0% of the population worldwide (Burneo & McLachlan, 2005, p. 1175). A seizure is an episode of abnormal electrical activity in the brain that is manifested by changes in behavior or other physical findings. There are many varieties of seizures that range in severity (e.g., generalized tonic clonic seizures, partial seizures, petit mal seizures). While all seizures are characterized by sudden electrical activity in the brain, the specific symptoms depend on which part of the brain is involved. There are a variety of causes for seizures which can be treated to variable success. If seizures continue repeatedly after the underlying cause is treated, the condition is referred to as epilepsy (A.D.A.M. Medical Encyclopedia, Seizures, 2012).

Approximately 40-60% of patients with seizure disorders have temporal lobe epilepsy (TLE). Localized epilepsies typically result in specific cognitive deficits that are traditionally associated with particular regions of the brain. Therefore, TLE is a notable locus for focal epilepsy due to its overall higher prevalence than other focal seizure disorders (e.g, frontal lobe) as well as the common disruptive effects on memory reported (Elger et al., 2004). While TLE patients have memory impairments, amnesia is unusual (Helmstaedter and Kurthen, 2001). TLE typically starts in childhood and produces seizures that vary in severity, patient awareness, and episode symptoms (e.g., olfactory, visual, or autonomic responses). Early onset epilepsy is typically defined as occurring before the age of 5 years old as normal lateralization of brain functions is established by that age (Lespinet et al., 2002). If seizures are unable to be controlled via mediation, diet, devices, and/or surgery, they may cause brain damage in young children that creates impairments in generalized cognition. Unfortunately, “it is not uncommon for people with epilepsy, especially children, to develop behavioral and emotional problems in conjunction with seizures” (N.I.N.D.S, 2012).

Early onset epilepsy can have adverse effects on overall cognition that are not limited to memory function (e.g., Hermann et al., 2002; Lespinet et al., 2002; Oyegbile, Dow, Jones, Bell, Rutecki, Sheth, Seidenberg, & Hermann, 2004). For those with early onset focal epilepsies or recurrent seizures intellectual functioning decreases within 3 to 4 years of onset and a significant association has been found between increased time in years of seizure exposure and degree of cognitive morbidity (Elger, 2004; Oyegbile et al., 2004). In a study conducted by Oyegbile and colleagues, participants with chronic temporal lobe epilepsy performed significantly lower on all cognitive measures (intelligence, naming, immediate and delayed verbal and visual memory, working memory, and executive function) compared to healthy control participants (Oyegbile et al., 2004). The degree of cognitive morbidity had a clear relationship with duration of epilepsy exposure. Similarly, Hermann and colleagues (2002) found that the neuropsychological performance of participants with childhood-onset temporal lobe epilepsy was significantly worse across all subtests compared to not only a control group but performance of late-onset participants. While the brain of those with chronic epilepsy may have a different functional organization and consequently behavioral compensation occurs via brain plasticity (Grabowski, Damasio, Tranel, Cooper, Boles Ponto, Watkins, & Hichwa, 2003; Elger, Helmstaedter, & Kurthen, 2004), the differences in brain structure and function seem to have an overall negative outcome on cognition. Whether cognitive performance is already affected and to what degree before the onset of seizures as well as a consequence of long-term seizures or anticonvulsant medication is still unclear (Elger, 2004).

While the impact this disorder has on cognition is complex and variable, the complaint most common for patients with TLE consistently lies in the cognitive domain of memory. TLE systematically affects the MTL and consequently impacts the memory system (e.g., Helmstaedter, 2002). The medial temporal lobe structures implicated in declarative long-term memory storage and retrieval of vocabulary are the vulnerable targets of neuronal discharge during a seizure. Consequently, individuals with left-sided TLE and a language-dominant left hemisphere of the brain have deficits in long-term consolidation and retrieval of words (Elger et al., 2004). Medial temporal sclerosis, a hallmark of TLE, is defined by hippocampal atrophy, medial temporal sclerosis, and loss of volume in the amygdala (Bortz, 2003). Furthermore, certain antiepileptic medications have an influence on attention processes and may further impact memory (Bortz, 2003).

Temporal Lobectomy

Advances in diagnosis and pharmacological treatment of focal epilepsy have improved seizure-free outcomes. However, 25-60% of people with localized-related epilepsy continue to have persistent seizures despite medical intervention (Helmstaedter, Kurthen, Lux, Reuber, & Elger, 2003). Individuals with uncontrolled epilepsy are at risk for higher levels of unemployment, mortality, and morbidity rates (Sperling, O'Connor, Saykin, & Plummer, 1996). Therefore, patients with medically intractable epilepsy (i.e., lack of control over seizures despite maximum drug doses of at least two antiepileptic medications and not resulting due to cortical malformation, tumors, or arteriovenous malformation) often seek surgical options with resection of focal areas of the cortex.

Surgery can be offered for safe and effective relief of these refractory seizures. Anterior temporal lobectomies are performed most often, proven to result in more effective control over seizures than mediation alone or other focal cortical surgeries (Yucus & Tranel, 2007). More than 100,000 people with epilepsy in the United States may qualify for epileptic surgery; however, only approximately 1,500 eligible patients undergo the procedure each year (Burneo & McLachlan, 2005; Sperling et al., 1996; Wiebe, Blume, Girvin, & Eliasziw, 2001). A standard resection includes up to 4.5 cm of the dominant temporal lobe and 6.5 cm of the nondominant temporal lobe including the amygdale, at least 1.0-3.0 cm of the hippocampus, the temporal tip, and anterior parts of the parahippocampal and inferior temporal gyri (Burneo & McLachlan, 2005; Yucus &

Tranel, 2007). Certain preoperative variables (e.g., early age of first risk for seizure ≤ five years of age) have been associated with a higher probability of seizure-free outcomes. For most patients, anterior temporal lobectomy results in a reduction or elimination of seizures without causing significant impairments in cognitive status (Sperling et al., 1996).

While overall pre-surgical cognitive status remains relatively unaltered following successful anterior temporal lobectomy, naming deficits are often found post-operatively and are likely to contribute to poorer neuropsychological outcomes (e.g., Elger et al., 2004; Grabwoski, Damasio, Tranel, Cooper, Boles Ponto, Watkins, & Hichwa, 2003; Saykin, Stafiniak, Robinson, Flannery, Gur, O’Connor, & Sperling, 1995). Verbal memory may be disrupted at the word retrieval or word activation level due to ATL and affects the ability to learn or retain different types of verbal information (Jones-Gotman, Zatorre, Olivier, Andermann, Cendes, Staunton, McMackin, Siegel, & Wieser, 1997; Ojemann, & Dodrill, 1985; Saykin et al., 1995). However, seizure-free patients tend to show “a long-term recovery of the verbal memory decline that is common immediately after left-sided temporal surgery” (Elger, 2004).

While there is considerable variability in cognitive outcomes following ATL, onset of seizures or other risk factors before the age of 5 is associated with reduced incidence of verbal memory decline after surgery (Saykin et al., 1971). Interestingly, a strong preoperative neuropsychological performance has been associated with poorer cognitive outcomes after surgery (Griffin & Tranel, 2007; Yucus & Tranel, 2007). This may be attributed to the fact that patients with the least hippocampal damage on the same side as the TL seizures have the least memory impairments preoperatively; postoperatively these patients have the greatest negative change in memory function (Golby, Poldrack, Illes, Chen, Desmond, & Gabrieli, 2002). Overall, patients who undergo ATL overwhelmingly report a significant decline in memory abilities affecting everyday functioning (e.g., Weintrob et. al., 2007). In a PET activation study conducted by Grabowski and colleagues (2003), subjects who had undergone left anterior temporal lobotomies did not have increased activity in the area surrounding the lesion or in the contralateral location during a proper noun naming task that activated the area of resection in normal controls. Instead, TL subjects had greater activation than controls in the visual cortex. In summary, there is strong evidence that hippocampal/MTL damage, whether in amnesia or TLE, is associated with poor word learning abilities. Next, recent challenges to the role of the hippocampal system in word learning will be discussed.

Recent Challenges to the Role of Hippocampal Declarative Memory System in Word Learning: Evidence from Fast Mapping

As previously presented, there is a rich research literature supporting the notion that hippocampal damage and subsequent memory impairments have been associated with profound impairments in acquiring new word associations. Given this assumption regarding the neural correlates of fast mapping, adults with damage to the MTL should perform with gross impairments on any task requiring rapid learning of new names.

In a recent study by Sharon, Moscovitch, and Gilboa (2011), four participants with profound amnesia due to bilateral lesions to the MTL system (without ATL damage) showed normal acquisition of arbitrary word-picture associations through a fast mapping paradigm. Even more surprising, subjects retained these labels after delay period of one week. This research study was the first to report *normal* rapid learning outcomes with arbitrary stimuli for participants with amnesia. In contrast, two patients with unilateral damage to the left polar temporal cortex were impaired on FM. One of these participants (A.A.) "had no tissue in his left temporal pole and also significant reduction in the left hippocampus and MTLC" without damage to right MTL structures (p. 1147). The other participant with impaired performance (K.S.) had significant loss of left temporal pole tissue as well as left MTL cortex reduction, but was reported by the authors to have a normal hippocampal volume. Unlike the four participants with amnesia, A.A. and K.S. showed impairments on the FM task and performed significantly worse than the controls, scoring essentially at chance on the immediate recognition test. The poor performance by those whose lesions incorporated the ATL was consistent with Sharon and colleagues belief that FM learning may be mediated by extrahippocampal structures.

In the fast mapping phase, participants were exposed to two pictures (from the category of animals, plants, fruit, or vegetable) consisting of one familiar and one unfamiliar item. In this condition, amnesic participants showed normal learning. When these same participants underwent an explicit encoding condition where only a single picture was presented, their performance on this task was significantly impaired compared to the normal controls. Therefore, new learning was only observed for the participants with amnesia after fast-mapping encoding specifically. These results suggested to the authors that learning by fast mapping may occur through an entirely different system than the traditionally established medial temporal lobe structures, implying that the hippocampal system may in fact *not* be necessary for learning arbitrary relationships if fast mapping is the method of learning. Recent imaging studies have pointed to a neural network of neocortical areas that are activated during word acquisition: the perisylvian structures of the left hemisphere, temporo-pareital, premotor, and prefrontal regions (eg., Shtyrov, 2011). This network may be a separate route of word learning that does not rely upon the traditional MTL system for declarative memory that is affected by conditions such as amnesia.

In order to further explore this surprising finding, Warren & Duff (2012) evaluated learning of new picture/word associations in patients with amnesia using a similar format and the identical stimuli from the Sharon and colleagues study (2011). The two learning conditions (EE and FM) were utilized and new learning was assessed via a variety of tasks: forced-choice recognition, generalized associated recall (uncued and cued), familiarity rating changes (post-test minus pre-test familiarity scores), and eye-movement data to assess covert expressions of the learning experience. Warren & Duff predicted that fast mapping may permit rapid learning of new associations with the hippocampus and that fast mapping without contribution of the hippocampus would *not* produce rich, flexible associations. The results of their study indicated that participants with amnesia did not remember new word/picture associations regardless of EE or FM condition.

Fast mapping did not yield robust associative learning: a remarkably different outcome from Sharon et al (2011). Some important differences in the methodology between the two studies may have influenced this outcome. For example, Warren and Duff created forced-choice recognition sets with homogenous categories of items (e.g., plant targets were matched with plant competitors). The heterogenous composition of test displays in Sharon and colleagues (e.g., plant targets were matched with animal and vegetable competitors) may have allowed for weak category associations alone to drive selection of the correct item: an incomplete semantic representation of an item does not indicate actual learning of a word. Furthermore, Warren and Duff utilized a multi-modal association presentation (auditorally presented name with visual picture) versus the unimodal presentation of Sharon and colleagues (visually presented name with visual picture). These changes were introduced in order to provide a more ecologically valid context reflecting how word learning often occurs in everyday life, and to examine how deeply a word and its meaning must be encoded to indicate true learning.[1]

These two studies resulted in entirely different outcomes for participants with bilateral hippocampal damage. The question remains if the experimental changes provided by Warren and Duff would produce different results in participants, like those in Sharon and colleagues, who have unilateral hippocampal damage. This raises an

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[1] A complete overview of design changes from Sharon and colleagues is provided in the design summary section of the methods chapter.

important issue as Warren and Duff would argue that their methodology more accurately represents what is required in word learning in the real world (e.g., multi-modal presentation of stimuli).

The Current Study

The goal of this study is to examine the role of the hippocampus in word learning to answer the question: does a FM condition promote word learning in participants with temporal lobe epilepsy who have had a left temporal lobectomy? In order to address this question a larger, well-characterized sample of individuals with left temporal lobectomy were included. Three predictions are possible based upon previous research:

1. Participant performance is intact on the FM condition only

Despite not having a functional left hippocampus, the TL group does not have significant memory impairments. Based on neuropsychological data, these participants do not have amnesia and have scores placing them in the normal range on a variety of standardized measures. Intact performance on the FM condition could be taken as evidence in support of Sharon and colleagues view that the hippocampus may not contribute to the rapid word learning process associated with the FM condition. However, this interpretation would not be conclusive given the presence of the intact right hippocampus. Because the hippocampus is assumed to contribute in the EE condition, dissociation between FM and EE performance could be expected.

2. Participant performance is intact on both the FM and EE conditions

The damage in the TL participants is relatively restricted to the left MTL. The intact right MTL could potentially enable normal word learning processes, especially if there was any cortical reorganization for word learning due to chronic early onset epilepsy. However, this result is highly unlikely given the characteristic word learning difficulties associated with this population

3. Participant performance is impaired on both conditions

The TL group has relatively localized damage to the left MTL, a region traditionally associated with language function. There is strong evidence that hippocampal damage, whether in amnesia (bilateral damage) or left temporal lobe epilepsy (unilateral damage), is associated with poor word learning abilities. The ability to learn a new word requires an association between two arbitrary stimuli; the declarative memory system formulates and encodes these associations. The hippocampus is necessary to bind those associations together and to use the newly acquired information in a new context. Impaired performance on a word learning task for this population, regardless of learning condition, would align with this area of research even if the severity of the impairment is not as great as that observed in patients with amnesia or bilateral hippocampal damage.

This study provided a larger, better characterized sample, more methodologically rigorous design, and additional overt behavioral measures in order to answer the research question. The results of this study, in conjunction with the findings by Warren and Duff (2012) provide an opportunity to determine if an alternative pathway for word learning may exist that bypasses the traditional hippocampal system. If the FM condition, but not the EE, enabled associative learning for populations with isolated left hippocampal damage, it may be a useful rehabilitation tool; “bypassing” the MTL route of declarative learning through a FM paradigm could improve learning for individuals with unilateral damage. Familiar items may support the modification of existing semantic knowledge in order to aid word acquisition and create durable associations. If the findings instead align with the traditional literature regarding word learning and MTL damage (i.e., both the amnesic and TL participants would be impaired in word learning regardless of FM or EE), it would provide further evidence for the rapid, flexible associations the hippocampal system supports and the inability to bypass the hippocampal system for successful word learning.

CHAPTER II

METHODS

Participants

Participants were five females with early onset epilepsy and subsequent unilateral temporal lobectomy ("TL"; N=5) and five female healthy comparison participants ("NC"; N=5). The TL participants were recruited from the Patient Registry from the University of Iowa Department of Neurology (henceforth, "the registry"). In accordance with their enrollment in the Patient Registry, the patients were free of histories of intellectual limitation, learning disability, psychiatric disease, and dementia, and they all had focal, stable lesions. Demographic and neuropsychological data were obtained from a database of the registry. NC participants were recruited from Iowa City and the surrounding communities. NCs were matched pairwise to the patients on age, sex, and education.

The mean age at epilepsy diagnosis for the group was 22.2 months (range 5-36 months) and the mean age at surgical resection was 43.2 years (range 31-61 years). At the time of this experiment, TL participants were on average, 53.8 years old (range 42-68; SD = 13.1) and had, on average, 14.6 years of education (range 12-20). TL participants had standard left hemisphere language dominance as determined by WADA testing. Handedness, measured with the Geshwind-Olfield Questionnaire, indicated 4 TL subjects as fully right-handed (+100) and one TL subject with majority right-handed preference (+15). Demographic information on the participants with TL is presented in Table 1.

All participants have an intelligence quotient in the normal range (mean = 102.0; SD = 9.0) as measured by the Wechsler Adult Intelligence Scale. The average verbal IQ was 95.2 (range 85-107; SD = 2.1) and average performance IQ was 101.8 (range 92-109, SD = 8.1). Memory performance was measured by the Wechsler Memory Scale-III General Memory Index (WMS GMI), trial 5 and delayed response from the Auditory Verbal Learning Test (AVLT 5/DR), and delayed response on the Complex Figure Test

(CFT). The mean score on the WMS GMI was 90.2 (range 88-93, SD = 2.2) and is in the low average range (mean = 100, SD = 10). Performance on the Auditory Verbal Learning Test (AVLT) trial 5 and Delayed Recall (DR) was in the normal range: 12.2 (range 11-13. SD = 1.1) and 8.4 (range 7-10, SD = 1.1) respectively. Performance on a measure of visual memory, the Complex Figure Test (CFT) was also in the normal range: 18.0 (range 12-25, SD = 5.4).

Participants do not have significant disruptions in language (i.e., they do not have aphasia) as a group performance on neuropsychological measures of language are within normal limits. Performance on the Wide Range Achievement Test was in the normal range (100.4; range 90-117, SD = 10.4). On the Boston Naming Test, participants were able to name an average of 52.8 items presented during confrontation naming (range 50-57; SD = 2.8). On a measure of auditory comprehension, the Token Test, the participants had an average score of 42.2 (range 38-44, SD = 2.7) (max score is 44). Participants verbal fluency, as measured by the COWA, was quite varied; scores ranged from 27-61 with an average performance of 42.9 (SD = 16.4).

On the Wisconsin Card Sorting Test, a measure of executive function, the average number of categories completed was 4.6 with 19 perseverative errors (range 3-6 categories; SD = 4.6; range 4-37 errors; SD = 3.2). Participants scored within normal limits on a visual-spatial perception task (Copy Figure Test) with an average performance of 31.0 (range 27-31; SD = 3.2). All of the neuropsychological data for the participants with TL is presented in Table 2.

In general, participants had relatively intact cognition, memory, and language skills. None had significant memory impairment, reflected in the fact that each participant scored similarly on normative tests of general intellectual ability and memory (i.e., <25 point difference between each patient’s WAIS full-scale IQ and WMS general memory index. That said, there were some individuals who had scores that approached deficient levels (i.e., 2 SDs below the means). Those scores are in italics in Table 2.

Neuroanatomically, TL participants had nearly uniform resections of the head and body of the left hippocampus as well as varying resection lengths of the left temporal pole and lateral/ventral temporal cortex with an average age at surgery of 43.2 years (range 30-61, SD = 13.6). As a group, participants had lesions relatively focal to the left MTL region. An image showcasing extent and overlap of lesions for the TL group is provided in Figure 1.

In addition to the TL and NC groups described above, an additional group of participants were recruited who completed an abridged version of the main task. In order to determine how much outside knowledge a participant may be able to rely on in order to successfully complete the naming task without actually learning new names, a healthy naïve comparison group of adults ages 40-70 was also included in this study (“NN”; N = 15). These participants did not complete either the FM or EE conditions, but rather were interviewed about their familiarity with the same words as the other groups and then immediately completed the three-alternative forced-choice phase of the task (i.e., without any study exposure). Their performance was compared with the TL and NC participants as a baseline measure.

Stimuli and Materials

The study design is a replication of Warren and Duff who adapted stimulus materials from those developed by Sharon and colleagues (2011). The original stimuli from Sharon et al. consisted of two image sets of uncommon plants, animals, fruits and vegetables with each set containing 16 items (i.e., 32 items total). These sets were expanded upon for this study, incorporating 16 additional uncommon items for a total of 48 novel animals, plants, fruits, and vegetables. Materials were divided into two separate sets of 24 items each and counterbalanced with 12 animals and 12 plants among the uncommon items in each set. One additional image of each uncommon item was obtained for the purpose of generalization (i.e., cued recall) testing (see Procedure below). In addition to the uncommon images, images of 60 *common* items were collected to use as competitors and filler items. All images were obtained with permission from Sharon et al. or from the World Wide Web under the principle of fair use.

Item names and accompanying carrier phrases were presented in the auditory modality rather than orthographically (as done in Sharon et al.) as eye movements are best recorded with as few visual competitors as possible. All auditory materials were recorded by a single female speaker in an English dialect common to the region. The speaker was compensated for her services. Recordings were divided into carrier phrases and objects in order to ensure that accurate timing information was available regarding playback.

Equipment

Visual stimuli were presented on a 21 inch LCD monitor which the participant observed from at a distance of 550 mm. Non-verbal responses (e.g., response selection) during the study and recognition phases of the task were issued by the subject using a computer mouse. During the study and recognition testing phases, subjects placed their head in a padded chinrest/headrest to maintain head placement for the entire length of the eye tracked phases. Eye movements were sampled at 1000 Hz using an EyeLink 1000 remote infrared camera system. Calibration and validation procedures for the study and recognition testing phases ensured that gaze position was accurate within 1 degree of visual angle.

Procedure

Participants were informed that they would be voluntarily participating in a project designed to investigate word learning. Informed consent was obtained from all participants prior to the first experimental session. Reimbursement was provided for participation in the study. All subjects completed both conditions (i.e., explicit encoding [EE] and fast mapping [FM]) in separate sessions. For the TL group, the sessions were typically administered on the same day in morning and afternoon sessions, respectively. For the NC group, the EE and FM sessions were separated by at least one month. This long between-session interval was utilized in order to minimize any risk of proactive interference and to reduce familiarity with the testing routine for the second condition. All subjects completed the FM condition first. Each of the eight phases, detailed below, was completed during a testing session in both conditions. For a broad overview of procedure, refer to Figure 2. Table 3 provides an overview of the protocol for each phase as well as brief description an approximation of duration for each phase.

Pre-Familiarity Rating Scale

Participants were asked to rate their familiarity with a list of words consisting of common and uncommon (i.e., presumably unfamiliar) items. Responses were recorded as each named item was rated for familiarity on a 1-6 scale, 1 being not familiar at all to 6 being very familiar. Any rating higher than 1 required participants to provide a brief description of the time. The uncommon items in the list were all later presented during the study phase, and any uncommon items (presumed unfamiliar) found to be familiar were removed from later analyses in order to remove the effects of familiarity. For an example of this scale, see Appendix A.

Study Phase

Immediately following the pre-familiarity rating, participants were introduced to the study format of their assigned condition (EE or FM) in a practice study phase. The practice study phase was included to familiarize the participants with the task requirements and incorporated two familiar items on each trial. After the practice phase, 64 total items were presented in the practiced study format, with each item repeated once in the main study phase (i.e., 24 uncommon words each presented twice for a total of 48 trials). The remaining trials (16) were “catch” trials of two familiar items presented with a familiar name. Catch trials were included to check task comprehension and compliance as well as to provide a basis for comparison with response time and eye movements in the fast mapping condition. Gaze position was calibrated and validated immediately prior to the main study phase, and central fixation was checked before each trial.

In the critical trials of the FM condition, pictures of two items were presented to the left and right of the screen and the carrier phrase “Click on the ___” (accompanied by the name of one of the items) was presented in the auditory modality. In these trials, one familiar and one unfamiliar item were presented along with an unfamiliar name. For any trial (catch or critical), participants were told to follow the auditory instructions and guess if necessary.

In the EE condition, a single picture was presented with the auditory carrier phrase “This is [a(n)] ____” (as appropriate) accompanied by the name of the item. During critical trials, the image was an unfamiliar item while during catch trials the item was familiar. For all trials, participants were told to listen to the phrase and name and then click on the picture. Displays were presented for up to 15 seconds after the auditory instructions were presented, after which a time-out response was recorded. An example of the difference in presentation for these two conditions is represented in Figure 2.

Free Recall

After all the trials of the study phase were completed, participants were asked to immediately recall as many of the presented items as possible (familiar and unfamiliar) with an emphasis on unfamiliar items. If any time remained, they were asked to share any impression of items they saw but could not provide the name for. The free recall was recorded for up to three minutes or until invitations from the examiner to recall further items were twice declined.

Thirty Minute Delay

Participants were offered a short break and then preformed non-verbal tasks testing visual working memory for any remaining time in the 30-minute delay. Data from these tasks are not reported for this thesis.

Free Recall

Recall for familiar and unfamiliar items from the study phase was tested again after delay in the same manner as reported above. Refer to Appendix B for an example of the free recall form used by the examiner.

Recognition Phase: Three-Alternative Forced-Choice

A three-alternative forced-choice (3AFC) test was administered following the delayed recall phase to test recognition memory for item-name associations. Gaze position was recalibrated and validated. Participants were told to follow the auditory instructions and use the mouse to click on the target item or guess if they were unsure of the answer. A short practice of the 3AFC format preceded the main phase, and used common items presumed to be familiar. Participants were presented with three responses alternatives (top-left, top-right, and bottom-center of the screen) and given auditory instructions by the computer using the carrier phrase “Click on the ____” followed by the name of the target. The position of the target was counterbalanced across the three response locations of the display. All 24 unfamiliar items were tested in this phase. Eight sets of 3 items each, from the same semantic category, were presented three times. Each set item was the target once, every set appeared once before any set was repeated, and all sets repeated once before a second (and final) repetition. Items were displayed for up to 15 seconds after the instructions were given, after which a time-out response was recorded. Refer to Figure 2 for an example of the 3AFC presentation.

Generalization Phase

In order to evaluate the participant's ability to generalize any knowledge recently acquired, novel exemplars of the same unfamiliar item were presented in two sessions of the generalization phase. First, participants were asked to try and produce the name of a previously-unfamiliar item when cued with a novel picture of the item with no prompting by the examiner (i.e., visual cue condition). In this session, participants viewed a randomized series of novel exemplars and were asked to name each item or pass to the next item if they could not. All responses were recorded and correct responses were verbally reinforced by the examiner as accurate. Near-miss responses were met with encouragement and an invitation to try again. The second generalization session included the same novel images, but the examiner additionally provided the first sounds of the name being prompted (e.g., "num" for target *numbat*) unless the participant had produced the name immediately and correctly (i.e., visual and verbal cue condition). Responses were also recorded in this condition. A scoring form for the Generalization Phase is provided in Appendix C.

Post-Familiarity Rating Scale

Lastly, each participant was asked to again rate familiarity with a list of words. The same list and procedure was used as in the pre-familiarity rating. After both the FM and EE conditions were completed, subjects were debriefed verbally.

Study Design Summary

This study was designed to explore word learning via two different conditions (FM or EE) with the explicit intent of extending the work in the literature by Sharon and colleagues (2011) and Warren and Duff (in preparation). Both of these studies were similar in the sense that the EE and FM conditions included the same materials. However, Warren and Duff differed from Sharon and colleagues in critical ways in order to increase the validity of the word learning research paradigm. The crucial differences and rationale are described below.

Warren and Duff included pre- and post-familiarity rating scales in their design. This measure verified that the unfamiliar stimuli were truly novel words and not already familiar words. Additionally, comparison between post- and pre-familiarity ratings (example, a novel word moving from a familiarity rating of "1" to "4") provided another index of learning. Furthermore, the depth of semantic information gleaned from short exposures to the stimuli is available for analysis from the descriptions participants provided in the post-rating phase.

Warren and Duff added a free recall immediately after the study phase as well as after a 30 minute delay. The free recall provided a first opportunity for participants to showcase any learning that may have occurred in a more demanding context than the 3-AFC recognition. This measure enables direct comparison in the number of items recalled between groups as well as between learning condition (FM or EE). The 3-AFC recognition task was also increased in difficulty. In Sharon and colleagues design, the 3 items presented sometimes belonged to different semantic categories (cf. Fig 1, Sharon et al., 2011). In Warren and Duff, the 3 choices were from the same semantic category (e.g., animal targets were matched with animal competitors), increasing the difficulty of the task and requiring a more complete semantic representation for the learned items. In Sharon and colleagues, even weak category associations may have sufficed for a "correct" response which does not indicate true learning of a word. The inclusion of the generalization phase added by Warren and Duff required participants to extend their knowledge regarding an item to an item that varied slightly from the learned item. The ability to generalize learning to slightly different variations of the same item indicates an ability to flexibly apply a label to various representations of the same item.

In Sharon and colleagues, items were presented in the visual modality (names were written and presented along the bottom of the screen) rather than the auditory presentation in Warren and Duff. While this change was made to decrease the amount of visual competitors for eye tracking, it also created a more ecologically valid design as new words are often encountered in the auditory modality in everyday life. However, the difference in types of associations drawn between these studies (i.e., multi-modal auditory-visual in Warren and Duff versus unimodal visual-visual in Sharon and colleagues) may have created differences in the regions of the brain necessary for creating associations. Lastly, Warren and Duff added eye-tracking in order to track covert expressions of learning experience.

Data Analysis

The dependent measures analyzed in this thesis include behavioral data summarizing proportion of correct responses and the total number of items recalled in various phases of the study. Eye movement data will not be included in this manuscript as indications from behavioral performance carry the greatest and clearest implications regarding overt learning outcomes from this task paradigm. Overt behavioral responses collected include familiarity ratings, free recall, referent selection in the FM study condition, 3 AFC referent selection in both conditions, and generalization recall. Data were aggregated using Matlab 2007b (Mathworks), Python 2.7, and Python's pandas module and subsequently analyzed and graphed utilizing R 2.15.1 employing R's base system and the nlme, multcomp, lattice, and Cairo libraries. Repeated-measures analyses were used for the majority of behavioral measures and are described in detail below for each type of data collected. In each case, the repeated-measures analyses were implemented as linear mixed effects (LME) models designating subjects as a random effect. Planned comparisons were conducted using linear contrasts applied to the appropriate LME model and were corrected for multiple comparisons (i.e., for the number of linear contrasts tested for a given model); for these planned comparisons, the Z value of the test statistic and the corresponding p value are reported.

Familiarity-rating data were measured twice for each participant in each condition. First, a mean per-participant rating for uncommon words was calculated for pre- and post-study phases separately for the FM and EE conditions. Changes in familiarity ratings were then investigated via a repeated-measures ANOVA. Participants were entered as a random effect and within-subjects fixed effects included study condition (levels: FM and EE) and time of testing (levels: pre- or post-study). Group membership (levels: TL or healthy comparison) was a between-subjects fixed effect. Similarly, number of uncommon items named during the free recall phase and the visual/visual and verbal cued generalization phase were analyzed using repeated-measures ANOVA, substituting a delay factors (levels: pre or post-delay) or a cue-type factor (levels: visual only or visual and auditory) for time of testing as appropriate. Each repeated-measures ANOVA test was accompanied by planned comparisons among groups (i.e., between-subjects, non-paired t-tests) and phases (within subjects, paired t-tests).

Referent selection performance in the study (FM condition only) and 3 AFC test (both FM and EE conditions) phases was first summarized per participant as a proportion correct (i.e., number of correct responses divided by the number of response opportunities). FM referent selection performance was examined only once per participant and was therefore analyzed using a simple ANOVA with group membership as the sole factor (levels: TL or comparison participant), supplemented with planned comparisons between groups. 3 AFC test performance analysis included an additional, within-subjects factor for study condition (levels: EE and FM), and an additional level in the group membership factor (i.e., naïve comparison), and planned comparisons were used to test for group-level differences (i.e., between subjects) and study condition differences (i.e., within subjects). The results of these measures are described in the next chapter.

Table 1: Demographic Information of Participants with TL

Participant	**Sex**	**Hand**	**Age at Testing (Years)**	**Education (Years)**	**Age of Epilepsy Diagnosis (Months)**	**Age at Surgery (Years)**
2246	F	R	68	20	10	53
2403	F	R	55	12	24	41
2555	F	R	42	12	5	30
3166	F	R	39	16	36	31
3472	F	R	65	13	36	61
Mean			53.80	14.60	22.20	43.20
SD			13.10	3.44	14.39	13.61

Note: F = female, Hand = handedness, R = right, SD = standard deviation

Table 2: Participant Neuropsychological Information

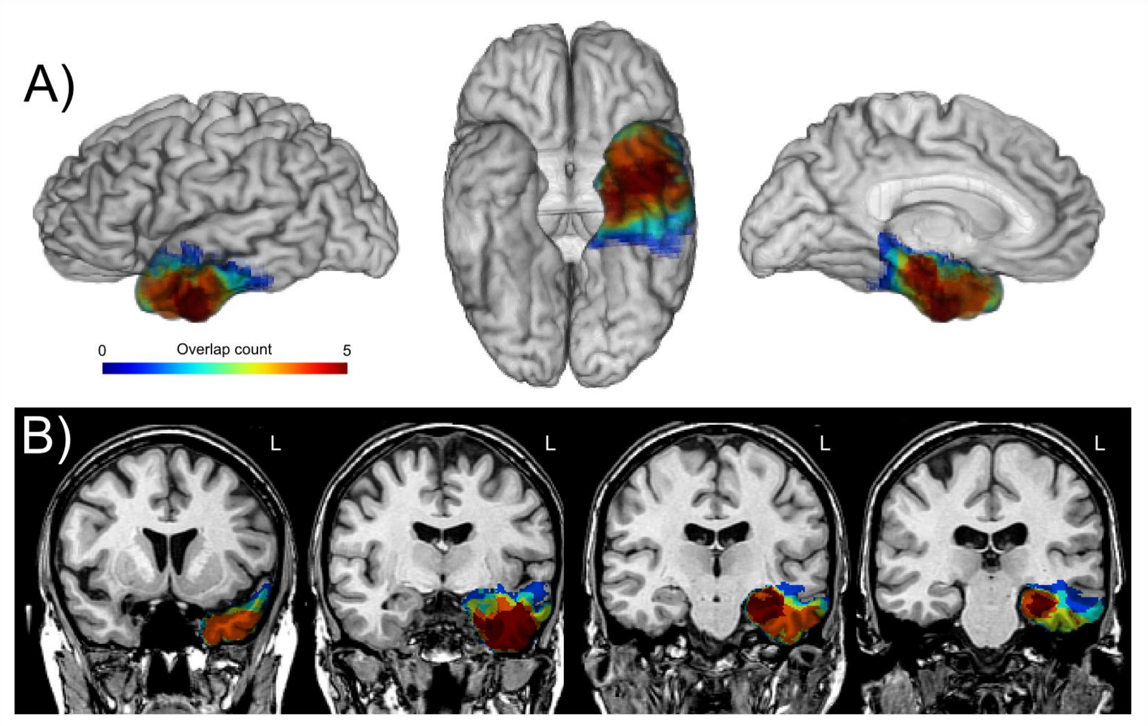
	Intelligence			Memory			Language				Executive Function	Visuo-Spatial Perception
Pt #	WAIS IV-FSIQ	VIQ	PIQ	WMS GMI	AVLT (5/DR)	CFT DR	WRAT IV	BNT	TT	COWA	WCST	CFT
2246	116	107	109	91	13; 8	*17*	117	*54*	44	61	6; 4	31
2403	93	89	92	88	11;*10*	12	102	57	44	59	*3; 37*	*31*
2555	96	85	94	91	13; 9	22	94	*52*	44	27	6; 9	30
3166	100	102	107	93	*11; 8*	25	99*	*50*	*38*	28	5; 28	36
3472	105	93	107	88	13; 7	14	90	51	41	39	3; 17	27
M	102. 0	95.2	101.8	90.2	12.2; 8.4	18.0	100.4	52.8	42.2	42.8	4.6; 19.0	31.0
SD	9.0	2.1	8.1	2.2	1.1; 1.1	5.4	10.4	2.8	2.7	16.4	1.5; 13.5	3.2

Note: WAIS = Wechsler Adult Intelligence Scale; VIQ = Verbal IQ; PIQ = Performance IQ; WMS GMI = Wechsler Memory Scale-III General Memory Index; AVLT (5/DR) = Auditory Verbal Learning Test (Trial 5; delayed response); CFT DR = Complex Figure Test – delayed response; WRAT-IV = Wide Range Achievement Test; NART = National Adult Reading Test; BNT = Boston Naming Test; TT = Token Test; COWA = Controlled Oral Word Association; WCS = Wisconsin Card Sorting Test (categories/ perseverative error); CFT = Complex Figure Test – copy score
M = Mean, SD = Standard Deviation
* denotes WRAT-R instead of WRAT IV score
Italicized scores indicate borderline deficient scores (i.e., 2 SDs below the means)

Table 3: Protocol

Phase	Duration (Approximate Minutes)	Description
Pre-Familiarity Rating	12	Rated familiarity of spoken words on 1-6 scale; 28 familiar items, 24 unfamiliar items
Study (Practice)	2	Practiced FM or EE study condition
Study (Main)	10	Studied new word/picture associations in FM or EE condition (see Figure 2)
Free Recall (Immediate)	3	Free recall of unfamiliar and familiar items from study set
Delay	30	Break followed by visual-perceptual task
Free Recall (Delayed)	3	Free recall of unfamiliar and familiar items from study set
Recognition (Practice)	2	Practiced 3AFC recognition task
Recognition (Main)	5	Performed 3AFC recognition task, all lures were uncommon items studied earlier in the session from same semantic category (see Figure 3)
Cued Recall (Visual Cue)	4	Cued recall of studied items with novel visual exemplar
Cued Recall (Visual Cue & Verbal Prompt)	4	Cued recall of studied items with visual exemplar same as previous phase and the first syllable of the item’s name (spoken by examiner)
Post-Familiarity Rating	12	Rated familiarity of spoken words on a 1-6 scale; same list of items and order of presentation as pre-familiarity rating phase

Figure 1: Neuroanatomy of the Lesion Extent in TL group

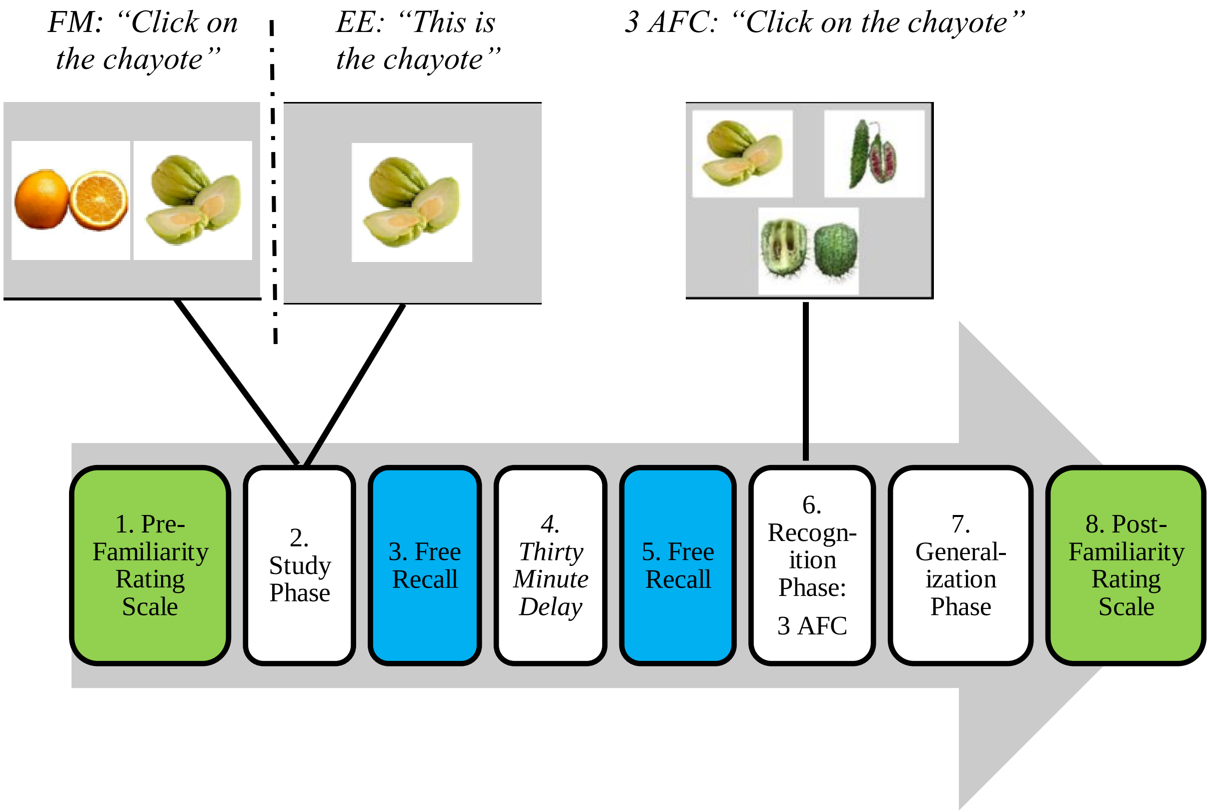


Note: All lesions (i.e., resections) were traced on a common template brain, and the extent and overlap of those lesions is presented here in the template brain's space. In both panels, hotter colors correspond to a larger number of overlapping lesions (see color scale at middle left).

A) Three-dimensional reconstruction of lesion overlap in the template space. Note the concentration of overlapping lesion extent in the left anterior temporal lobes.

B) Coronal slices through the template space illustrating the concentration of lesions in the anterior and medial temporal lobes. These images follow radiological convention (i.e., left is right). Left to right, these slices highlight: left temporal pole; the hippocampal head; the uncal apex; and hippocampal body. Note the concentration of lesion overlap in the temporopolar, ventral temporal, and medial temporal regions, especially in the left hippocampus throughout most of its extent

Figure 2: Procedure for FM and EE Conditions



CHAPTER III

RESULTS

All participants were able to complete all task requirements without any difficulty in the comprehension of task directions. All participants were successful eye tracked. As previously mentioned, eye-tracking data are not reported in this document.

Referent Selection Accuracy

Accurate referent selection is a crucial piece of any word learning task. Both groups were highly accurate in referent selection during the study phase in the FM condition (NC: $m = 97.5\%$, SE = 0.020, TL: $m = 97.0\%$, SE = 0.013) and there were no significant differences across groups ($Z = 1.435$, $p > 0.25$). The EE condition was assumed to be 100% accurate as there was a single choice presented and all participants completed the study phase in the EE condition without timing out on any item. Therefore, all participants were able to select the correct referent without any difficulty during the study phase in both conditions. There were no significant group differences in response time between groups with a marginally faster response time in the EE condition across participants ($F(1,9) = 4.285$, $p = 0.068$) which was likely attributable to the simpler response demands of the EE task (i.e., selecting from one item versus two in the FM condition). Figure 3 shows performance for both groups on referent selection accuracy during the FM study phase.

Free Recall Performance

The free recall portion of the experiment provided the first opportunity to showcase any learning of novel words that occurred during the study phase. As no specific cues were provided regarding the items previously viewed, this was a highly difficult task. For familiar items, the immediate versus 30 minute delayed recall were not significantly different across groups (group-by-delay interaction: $F(1,24) = 0.168$, $p > 0.5$). There was, however, a main effect of study condition with the FM condition resulting in a greater number of *familiar* items recalled than the EE condition (F(1,8) = 14.554. $p < 0.001$). This result is likely due to the familiar competitor objects being presented alongside the unfamiliar targets in the FM condition. There were no other main effects or interactions for the familiar items pre or post-delay. For an overview of participants' performance in recalling familiar items, refer to Table 4.

For unfamiliar item pre- and post-delay, there was no main effect of group (F(1,8)=3.449, p>0.1) and a marginal main effect of study condition (F(1,24)=3.981, p = 0.058), but delay itself was not significant (F(1,24)=0.442, p>0.5). There was a significant interaction between group and study condition (F(1,24)=5.419, $p < 0.05$). For post-delay only, there was a marginal main effect of group (F(1,8)=4.397, p = 0.693) and a non-significant interaction between the two group and study condition factors. As clearly represented by Figure 5, comparisons were able to name >0 items in either condition with TL participants were not able to name a single unfamiliar item on average. These results indicate that there was no benefit of the FM condition for participants with TL on this initial (albeit difficult) test of learning while NC participants showed signs of learning novel names. For an overview of performance, refer to Table 5, while Figure 4 illustrates mean performance by group and condition.

Recognition Accuracy

The 3AFC recognition test, administered following the delayed recall phase, tested recognition memory for unfamiliar item-name associations. The naïve comparison group (NN) was included in this analysis in order to compare how the participants with TL performed in respect to participants who had not studied the items and were given the 3AFC recognition test. There was a significant main effect of group (F(2, 22) = 18.443, $p < 0.001$) with the NC performing significantly better across both conditions compared with the TL and NN groups. The NC group was the only group to differ from chance (both conditions, each Z > 5.0, each $p < 0.001$). Interestingly, the NC group performed only marginally better than the TL participants in the FM condition (Z = 2.638, p = 0.086) despite a large performance difference overall (difference in proportion correct = 0.22), an effect that may have been due to relatively high variability in NC recognition performance in the FM condition. There were no significant effects of study condition (F(1,22)=1.166, $p > 0.2$), nor was there an interaction between group and study condition (F(2,22)=2.090, $p > 0.1$). There were no main effects or interactions for response time across groups or across conditions (main effect of group: F(2, 22) = 0.3312; main effect of study condition: F(1,22)=0.181; interaction term: F(2,22) = 2.366); each $p > 0.1$). Figure 5 shows the proportion correct responses on the 3AFC task for the TL, NC, and NN participants on both the FM and EE conditions. Table 6 provides the mean proportion correct responses across groups and conditions. In conclusion, there was no benefit to either the EE or FM condition for the TL participants on recognition performance.

Generalization Performance

As the TL participants had impaired learning of the unfamiliar items during the previous phases, it is unsurprising that the TL participants performed poorly on the generalization phase using a novel visual exemplar. There were main effects of group (F(2,19)=4.412, $p < 0.05$) and cue type (visual only vs. auditory-visual cues; F(1,55), 15.274, $p < 0.001$); NC participants remembered more items overall (F(2, 19)=4.412, $p < 0.05$), and more items were remembered in the auditory and visual cue condition than the visual cue alone condition (F(1, 55) = 15.274, $p < 0.001$). There was no significant main effect or interaction with study condition (each F < 1.0, $p > 0.1$). Collapsing across study condition, there was a significant interaction of group by cue type in that NCs benefitted more from the verbal and visual cue condition than the TL participants (F(1, 28)=9.429, $p < 0.001$). This is unsurprising as the performance of the TL participants up to this point indicated they did not learn the token unfamiliar item (as reflected in the 3AFC recognition performance). Table 7 provides a comparison of mean number of items recalled for both cuing conditions across participant groups. Figure 6 provides a graph of this data.

Pre-Familiarity Ratings and Rating Changes

Groups did not differ in pre-existing familiarity of words as evidenced by non-significant main effects and interactions (each $F<1.0$, each $p > 0.4$). The only significant main effect was observed in the factor for word commonality ($F(1,69)=9336.934$, $p < 0.001$). NC participants rated familiar words at a mean of 5.940 (SE = 0.023) while unfamiliar words were rated at a mean of 1.301 (SE = 0.029) on a scale from 1-6 before the study phase. The TL group rated familiar words at a mean of 5.845 (SE = 0.48) while unfamiliar words were rated at a mean of 1.413 (SE = 0.237) during the pre-familiar rating phase. Similarly, the NN group rated familiar words with a mean rating of 5.946 (SE = 0.007) and unfamiliar words at a mean rating of 1.345 (SE = 0.041).

The familiarity ratings at the *end* of the study showed numerically greater change in ratings for previously unfamiliar items for the NC group versus the TL group irrespective of condition. However, there was only a marginal effect of group for change in familiarity rating post-testing with NCs showing a slightly larger change in familiarity than the TL participants ($F(1,8)=4.191$, $p = 0.075$). There was no effect of study condition on change in familiarity ratings after testing ($F(1,8)=0.377$, $p > 0.5$). Table 8 provides the mean change in familiarity rating for the groups. Figure 7 represents this information in a graph.

Summary

As evidenced by severely impaired performance on free recall, recognition testing, and generalization tasks, the TL participants did not learn novel object-name associations despite a FM paradigm. While NC participants were able to acquire a rich representation of novel items (demonstrated by improved familiarity ratings and generalization of item names to novel exemplars), the TL group was grossly impaired in learning any novel names.

Table 4: Mean Number of Familiar Items Recalled

	Pre-Delay		Post-Delay	
	FM Condition	EE Condition	FM Condition	EE Condition
TL	7.0 (SE = 1.673)	4.6 (SE = 0.510)	8.2 (SE = 1.463)	4.6 (SE = 0.927)
NC	8.0 (SE = 1.924)	5.4 (SE = 0.400)	10.2 (SE = 1.934)	5.6 (SE = 0.245)

Note: SE = Standard Error

Table 5: Mean Number of Unfamiliar Items Recalled

	Pre-Delay		Post-Delay	
	FM	EE	FM	EE
TL	0.2 (SE = 0.200)	0.2 (SE = 0.200)	0.2 (SE = 0.200)	0.0 (SE = 0.00)
NC	1.2 (SE = .735)	2.8 (SE = 1.594)	2.0 (SE = 0.837)	3.0 (SE = 1.517)

Note: SE = Standard Error

Table 6: Mean Proportion Correct Response during the Recognition Phase

	FM	EE
TL	44.9% (SE = 0.034)	41.3% (SE = 0.076)
NC	67.2% (SE = 0.062)	82.8% (SE = 0.058)
NN	41.1% (SE = 0.033)	42.3% (SE = 0.036)

Note: SE = Standard Error Performance

Table 7: Mean Number of Items Recalled During Generalization Phase

	FM		EE	
	Visual Cue	Auditory & Visual Cues	Visual Cue	Auditory & Visual Cues
TL	0.0 (SE = 0.000)	0.2 (SE = 0.200)	0.0 (SE = 0.000)	0.6 (SE = 0.245)
NC	4.0 (SE = 1.095)	6.0 (SE = 1.844)	4.4 (SE = 1.400)	8.2 (SE = 1.772)

Note: SE = Standard Error

Table 8: Average Change in Pre-Familiarity Rating versus Post-Familiarity Rating of Unfamiliar Items

	FM	EE
TL	0.432 (SE = 0.132)	0.529 (SE = 0.109)
NC	1.088 (SE = 0.147)	1.174 (SE = 0.126)

Note: SE = Standard Error

Figure 3: Proportion Correct Referent Selection in Study Phase

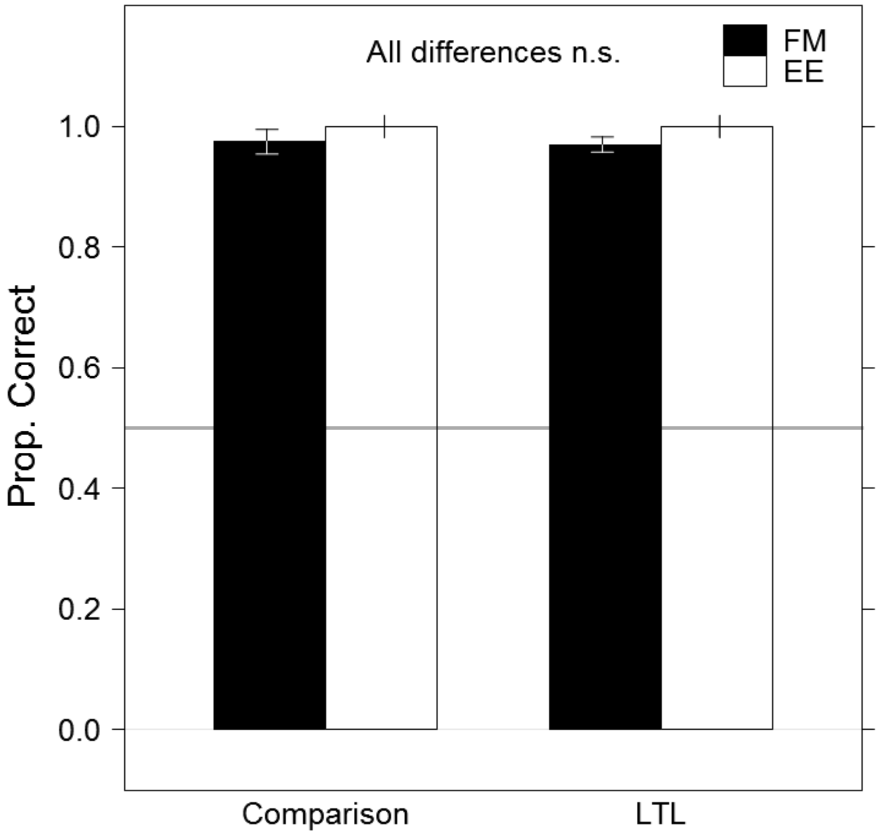


Figure 4: Number of Familiar and Unfamiliar Items Recalled during Free Recall Phase

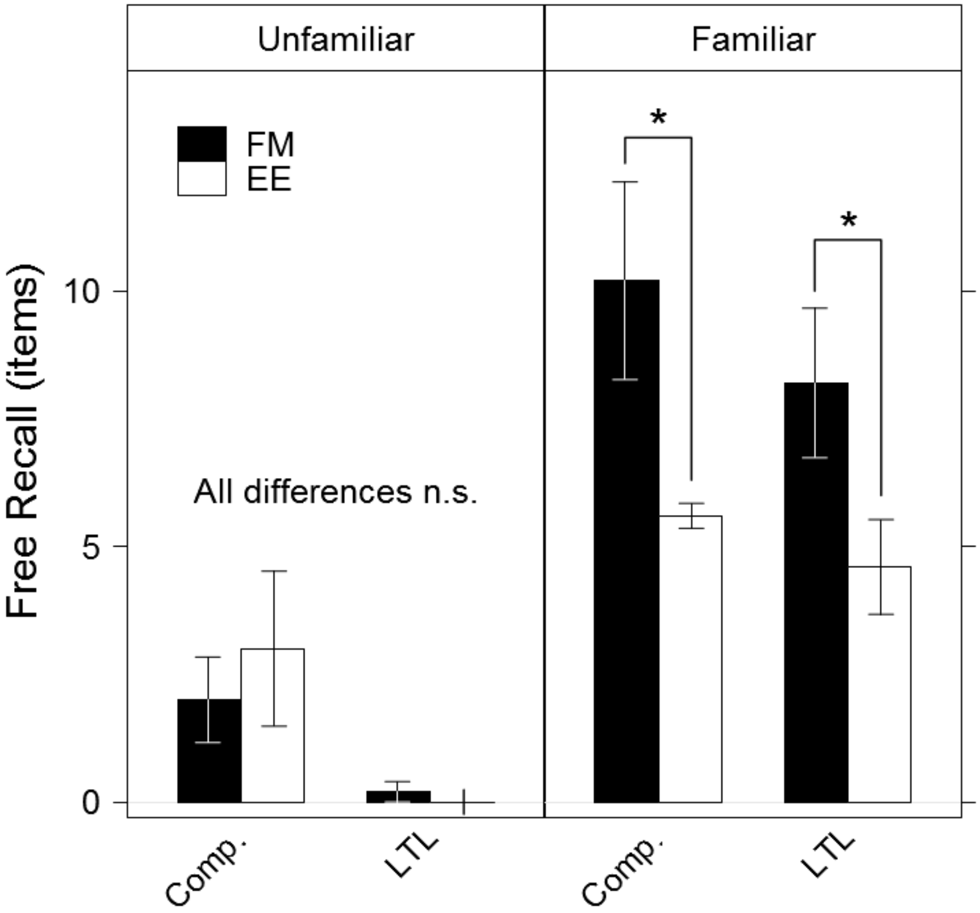


Figure 5: Proportion Correct Referent Selection in Test Phase

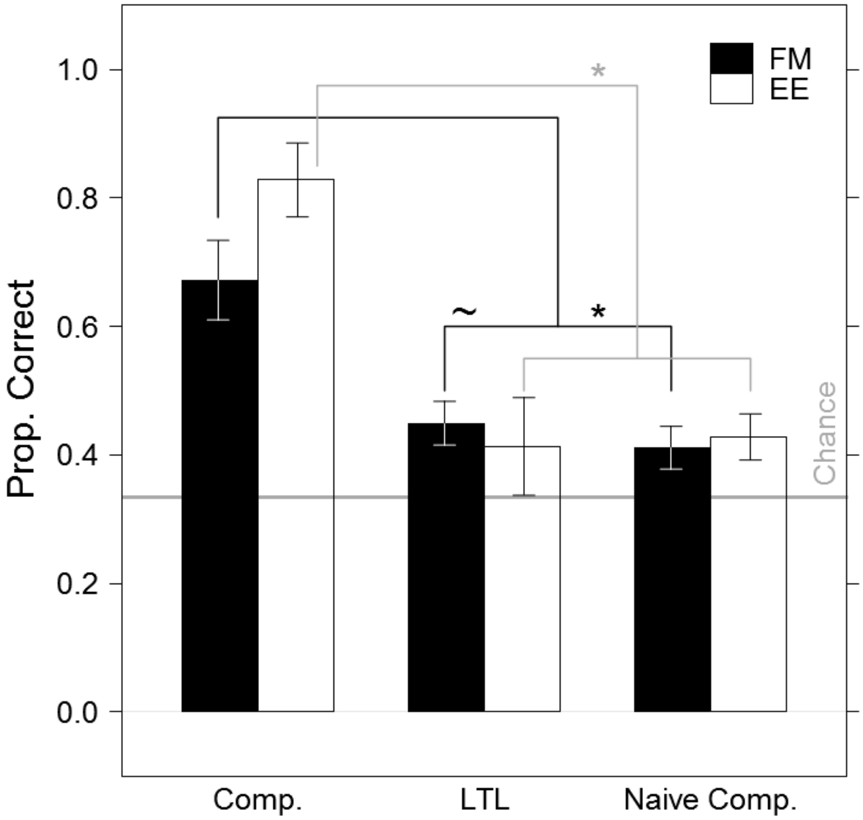


Figure 6: Number of Items Recalled during Generalization Phase

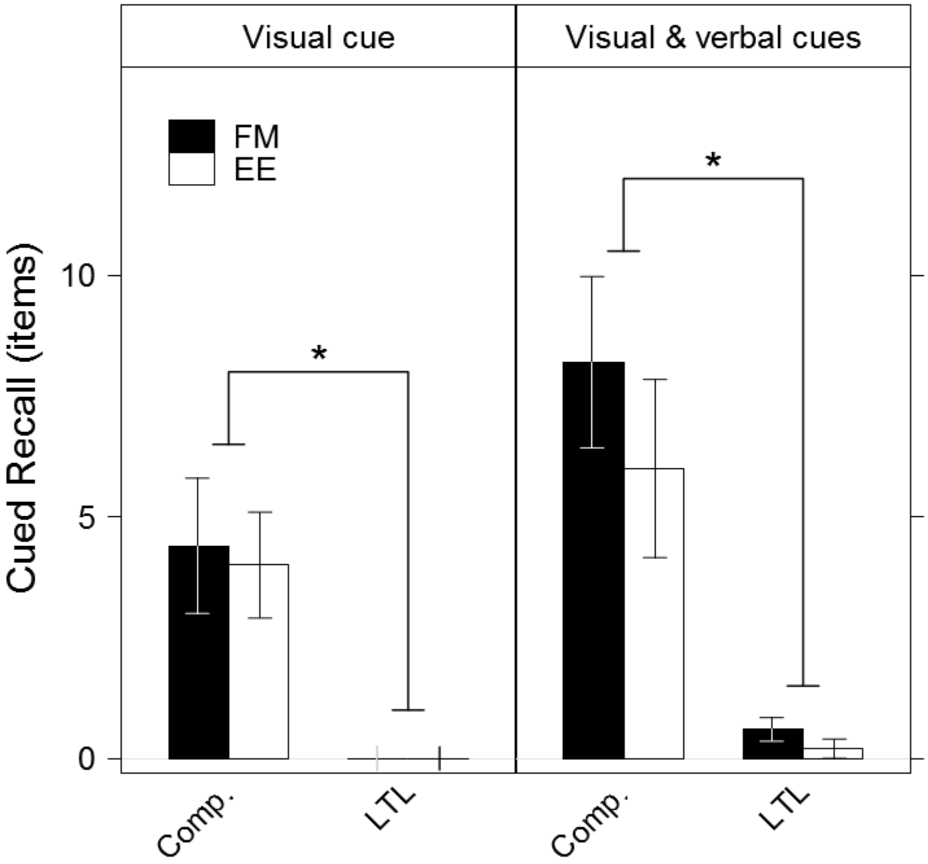
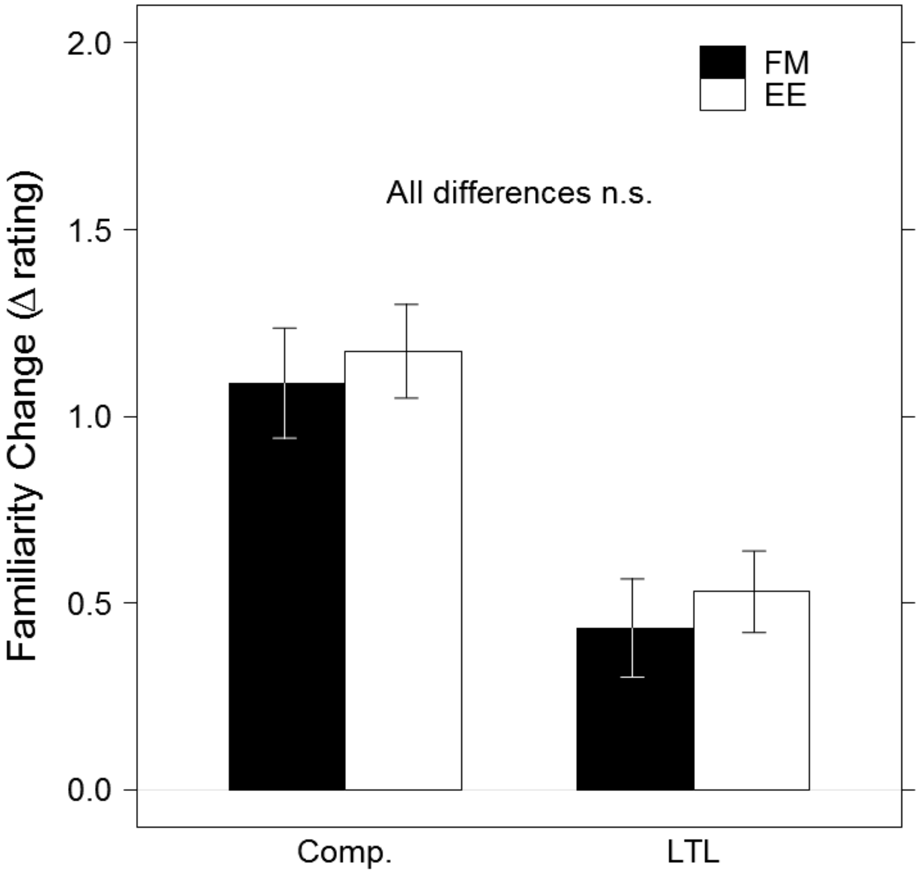


Figure 7: Change in Familiarity Rating of Unfamiliar Items from Pre- and Post-Familiarity Ratings



CHAPTER IV

DISCUSSION

Summary

The aim of this study was to extend the findings of Sharon and colleagues (2011) and Warren and Duff (2012) in order to determine if a fast mapping (FM) condition, in contrast with explicit encoding (EE), could promote word learning in participants with left temporal lobectomies due to epilepsy. The results of this study, in conjunction with the findings by Warren and Duff (2012), provided an opportunity to examine whether an alternative pathway for word learning may exist that bypasses the well-characterized hippocampal memory system. Across both word learning conditions, participants with TL were markedly impaired at learning the names of new words compared to healthy normal comparisons. Moreover, the performance of the TL group was as poor as that of individuals who did not have the benefit of any study exposure trials. While this study attempted to replicate this previous finding, there were methodological changes including additional behavioral measures to assess the graded nature of word learning. These measures will be discussed in greater detail in the implications section of the discussion. The results were consistent with the findings of Sharon and colleagues in that their two participants with left temporal lobe damage performed significantly worse than controls. These results alone could be construed as consistent with Sharon and colleagues' belief that FM learning may be mediated outside of the hippocampal structures. Similar to the participants with unilateral damage to the left polar temporal cortex from their study, the participants in this study with unilateral MTL damage were impaired at learning novel associations in both conditions. In Sharon and colleagues, one participant with impaired performance had significant damage to the left temporal pole as well as left MTL cortex and the other had no tissue in the left temporal pole and significant reduction of the left hippocampus and MTL cortex. The participants with bilateral hippocampal system damage, on the other hand, were found to have intact word learning performance. However, the current results may be most consistent with work by Warren and Duff (2012) who reported a severe disruption in word learning in the FM and EE in patients with bilateral damage to the hippocampus in absence of damage to the anterior temporal lobe. Thus, with all the available research literature integrated, the results align with the traditional interpretation for the neural substrates implicated in word learning. Because both the amnesic and TL participants from this line of studies were impaired regardless of study condition, the rapid, flexible associations normally produced by the hippocampal system are unavailable for word learning when this system is damaged.

Ways to Learn Words

The history of the childhood word learning literature implicates the fast mapping process as a first step in binding a name to a referent. Familiar items support the modification of existing semantic knowledge in order to aid word acquisition and create durable associations. As summarized earlier, the similarity in word learning between adults and children through the fast mapping process points to similar cognitive and neural substrates involved in fast mapping. The hippocampal system is required in order to create rapid acquisition of arbitrary stimuli. Based on the results reported here, individuals with bilateral *or* unilateral damage to the hippocampus are unable to use fast mapping as way to “bypass” the hippocampal system and learn new words.

There is a possibility, however, that these individuals could have mapped the novel items with partial categorical information (as shown in Sharon and colleagues). In their study, Sharon and colleagues contend that “the new learning acquired by the amnesic patients in this study constitutes a first report of rapid acquisition of arbitrary novel associations” (p. 1148). Even more remarkable, participants in that study retained the learned associations a week later following the FM condition but were markedly impaired on the EE recognition task even after a delay of just 15 minutes. These conclusions require a closer look into what behavioral performance was required in their study to show learning. Sharon and colleagues tested recognition memory using a 3AFC with 3 separate categories of items to select from (i.e., recognizing the correct semantic *category* of the item would have resulted in a correct selection). In general, those with TL have marked deficits in consolidation and retrieval of novel words. Being able to recognize the name for an animal, in a closed set with two different semantic categories, has very modest implications for the challenges encountered in daily life. Words are not merely recognized, but retrieved and expressed in order to communicate knowledge with others. While the patients studied by Sharon et al. may have mapped the novel items on a superordinate, categorical level, the real-world usefulness and application of this learning would be severely restricted. The learning shown in Sharon and colleagues study may also be consistent with the findings that when new semantic learning occurs for individuals with hippocampal damage, it is typically seen in the context of adding a new item to an already established category or semantic network (e.g., O'Kane et al., 2004).

The design of the current study provided a more robust, specific test of learning. The 3AFC sets in the recognition task were three novel items from the same semantic category (i.e., an animal target was presented with two other novel animals from the study). Testing the ability to recognize an item based on its features rather than its category alone is a more ecologically valid means of studying word learning. If an adult starts a new job and is introduced to a new coworker, it does little good if you can only remember that the name "Scott" is associated with a person rather than this specific example of Scott. The 3AFC setup in this study required a specific one-to-one binding of information in order to select the correct referent and the TL group performed at chance on this task while the NC group was able to recognize many recently-learned associations with little difficulty.

The Role of the Hippocampus in Word Learning

The poor performance of the TL group is striking given that their brain damage was unilateral, that is, these participants had an intact right hippocampus. Why did these participants perform as poorly as the severely amnesic patients with bilateral hippocampal damage from Warren and Duff (2012)? The left hippocampus is traditionally associated with verbal memory function, but reorganization to the right MTL is implied for individuals with left MTL pathology (e.g., Richardson, Strange, Duncan, & Dolan, 2003; Seidenberg, Hermann, Schoenfeld, Davies, Wyler, & Dohan, 1997). While there is no indication that the right hippocampus is damaged in our sample of participants, there is also little evidence that regions outside the left MTL can functionally take over residual verbal memory functions resulting in normal performance. It appears that individuals with unilateral hippocampal damage do not have the same profound memory impairments as those observed in individuals with bilateral hippocampal damage, but significant memory consequences related to word learning were observed in this study.

There was a great deal of attention and excitement following the release of the findings by Sharon and colleagues particularly because of the rehabilitation implications. Unfortunately, FM does not appear to “bypass” the MTL route of word learning to improve performance for individuals with localized damage to the hippocampal system. If in fact the FM condition, but not the EE, enabled associative learning in this study, FM could be considered a useful rehabilitation tool. However, the results of this study indicated that word learning through a FM process is not the easy remedy for these individuals. While rehabilitation can focus on word learning, it would depend upon the non-declarative system where such learning is slow, incomplete, and inflexible (e.g., McClelland, McNaughton, & O’Reilly, 1995; Bayley and Squire, 2002).

Developmental Hippocampal Dysfunction

With an early onset of seizure disorder and failure to learn any new words in the FM or EE conditions in this study, an important question to consider is how these individuals with hippocampal dysfunction have learned any words at all in their lifetime. While the hippocampus is critical for word learning, the participants in this study had verbal IQs in the normal range and have managed to learn all kinds of words while growing up. How have they accomplished this without two functional hippocampi?

One possibility arises from the complementary learning systems (CLS) framework (McClelland, McNaughton, & O'Reilly, 1995). In this model, the brain exploits two different systems to accomplish learning. One system relies upon changes in synaptic connections among the neurons themselves that are directly responsible for behavior and information processing (i.e., the neocortical processing system). The other system relies upon the hippocampus and related structures to adapt synaptic connections within the declarative memory system (i.e., the hippocampal memory system) (e.g., McClelland, et al., 1995). According to McClelland and colleagues, changes to the synaptic connections among many neurons in the neocortical system can accumulate over the course of many repetitions and can eventually lead to correct learning – such as an association between a word and its meaning. These small adaptive changes, however, do not allow for rapid learning of arbitrary associations. Acquiring new information in this way, while absolutely possible, is very slow and "insufficient for meeting the demands of everyday life, in which information must often be acquired and retained on the basis of a single exposure" (McClelland et al., 1995, p. 3440). Damage to the left hippocampus in this study would account for the failures in learning in the FM and EE conditions as both required rapid learning. Participants with intact hippocampal memory systems are able to explicitly recall new information due to substantial changes to the strengths of connections among neurons in the hippocampus. The arbitrary relationships are bound by the hippocampus and available for recall. As for how any words were acquired in the TL group’s vocabulary, the intact neocortical system would provide an alternative means for learning. There is only limited knowledge of what words these individuals know now as measured by standard neuropsychological tests. Furthermore, there is no information regarding how long it took them to learn these words or how many exposures were required.

Developmental amnesia is a prime example of a population who acquired language and significant vocabularies despite bilateral hippocampal damage (Vargha-Khadem, Gadian, Watkins, Connely, Van Paesschen, & Mishkin, 1997). These children had bilateral hippocampal damage acquired at birth in one case, by the age of 4 years old by another, and by the age of 9 years old for the third child. Despite profound episodic memory deficits, all three individuals attended mainstream schools and had low average to average range performance on speech, language, literacy, and factual knowledge assessments (e.g., Weschler Objective Reading Dimensions Test). The fact that these children could learn new semantic information (albeit in the low-average range) has led to the claim that only a subcomponent of declarative memory (episodic memory) depends upon the hippocampus while semantic memory can be acquired as a rapid process outside of the hippocampus. There should be some caution about this claim, however. The word learning ability of these developmental amnesic individuals has never been subjected to the kind of testing presented in this research. At what rate did these children learn words? Do their lexicons have similar depth and breadth as individuals without hippocampal damage? We strong suspect that their answer would be no, and this outcome would suggest that this learning was accomplished via the neocortical learning system described above.

The declarative/procedural model provided by Ullman (2004) conceptualizes the various domains of language as related to either the declarative or procedural memory systems. The mental lexicon is largely dependent on the MTL (declarative memory system) while the mental grammar depends upon a network of specific frontal, basal ganglia, parietal, and cerebellar structures (procedural memory system). It is interesting to consider the word learning deficits in SLI in this context. SLI has recently been linked to abnormalities in structures of the brain underlying procedural memory including the basal ganglia (particularly the caudate nucleus, SMA and the cerebellum (Ullman; Tomblin, Mainela-Arnold, & Zhang, 2007; Lee & Tomblin, 2012). The evidence suggests that individuals with SLI utilize the (relatively spared) declarative memory system in order to use language forms that are typically learned via the procedural memory system (e.g., regular past tense verb retrieval). At the same time, however, children with SLI have been reported to have vocabulary deficits. It has been suggested that children with SLI may need to hear a new word *twice as many times* as their peers before comprehending it and need *twice as many opportunities* to practice producing the word before independently using it (Gray, 2003). If that is the case, what is contributing to the deficit in word learning if the declarative memory system is intact?

One possibility is that word learning is best viewed as the convergence of the declarative and non-declarative memory systems (e.g., Gupta & Tisdale, 2009). Learning a word in fact requires both systems, although perhaps at different time scales. If one of these memory systems is not intact, then word learning is not normal. Secondly, even if the brain pathology is SLI is most evident in the basal ganglia, that fact does not necessarily mean that the hippocampus is functioning normally. That is, the hippocampus may not be able to fulfill its role if other structures are not working properly in the brain. While it is unclear if there is a functional connection between the two systems, there have been studies pointing toward an interaction between the declarative and non-declarative memory systems dependent upon learning demands. For example, event related fMRI of healthy participants reveals activation of the hippocampus early in learning and a deactivation for the rest of the learning up to 144 trials (Poldrack et al., 2001). One memory system does not act in isolation from the other and that both systems may contribute to learning (but with a different nature and perhaps and different times).

Limitations of the Study and Future Research

The small sample size of only female participants with TL (5 participants) makes it difficult to generalize the results of the current study. Constraints on recruitment were implemented to yield a better-characterized sample consisting solely of participants who suffered early onset epilepsy. Thus, it is not entirely clear how individuals with late onset epilepsy who have undergone a temporal lobectomy would perform. While neuropsychological performance of individuals with childhood-onset temporal lobe epilepsy has been found to be poorer than individuals with late-onset epilepsy (e.g., Hermann et al., 2002), it could be presumed that performance would be likewise impaired as the resected tissue would be comparable in these populations.

Future research should include replication of the results with a larger group of TL participants. Furthermore, comparing the performance of individuals with early and late onset epilepsy would help generalize the outcomes. As described by Hermann and colleagues (2002), individuals with early-onset temporal lobe epilepsy tend to have greater impairments on a variety of neuropsychological measures compared with individuals with late-onset epilepsy. However, considering that patients with superior neuropsychological measures prior to TL resection tend to have poorer memory outcomes after TL, a late-onset TL group hypothetically could have a better performance. On the other hand, later onset would imply a reduced chance of functional reorganization and thus resection of the MTL might grossly impair outcomes regardless. Another interesting avenue of exploration would be a FM paradigm where a dissociation could be setup between accurate learning of categorical information for an item versus impaired one-to-one name mapping. Considering the amnesic participants in Sharon and colleagues (2011) showed normal categorical learning while amnesic participants in Warren and Duff (2012) were grossly impaired, the methodological differences may point to a breakdown in what could be rapidly learned in a fast mapping paradigm beyond categorical information.

Conclusions

Based on the current study, it is clear that individuals with TL due to early onset temporal lobe epilepsy are severely impaired in learning new words. A fast mapping condition did not promote word learning for these individuals while normal control participants were able to acquire a rich representation of novel items regardless of learning condition. This finding reinforces the case that the hippocampus and related MTL structures are essential for rapid declarative learning. In order to successfully learn a new word, an arbitrary association between an object and its label must be formulated and encoded. Sharon and colleagues (2011) contend that the amnesic patients in their study demonstrated hippocampal-independent acquisition of arbitrary associations, however, their results have not been replicated and the depth of learning required in their FM paradigm is uncertain. These findings, in conjunction with broadly similar results obtained from hippocampal amnesic patients by Warren and Duff (2012), support the necessity of the hippocampus for rapid and flexible associations to be obtained via the declarative memory system.

APPENDIX A

PRE/POST FAMILIARITY RATING SCALE: CONDITION B FM

Word	Rating	Ex/Description	Word	Rating	Ex/Description
Rose	1 2 3 4 5 6		Sparrow	1 2 3 4 5 6	
Lion	1 2 3 4 5 6		Desman	1 2 3 4 5 6	
Marmoset	1 2 3 4 5 6		Acanthus	1 2 3 4 5 6	
Toucan	1 2 3 4 5 6		Blueberry	1 2 3 4 5 6	
Solenodon	1 2 3 4 5 6		Cantelope	1 2 3 4 5 6	
Raspberry	1 2 3 4 5 6		Motmot	1 2 3 4 5 6	
Lizard	1 2 3 4 5 6		Turtle	1 2 3 4 5 6	
Calathea	1 2 3 4 5 6		Saki	1 2 3 4 5 6	
Tomatillo	1 2 3 4 5 6		Wolf	1 2 3 4 5 6	
Broccoli	1 2 3 4 5 6		Chicken	1 2 3 4 5 6	
Wallaroo	1 2 3 4 5 6				
Ladybug	1 2 3 4 5 6				
Kobus	1 2 3 4 5 6				
Santol	1 2 3 4 5 6				
Giraffe	1 2 3 4 5 6				
Okapi	1 2 3 4 5 6				
Taro	1 2 3 4 5 6				
Basilisk	1 2 3 4 5 6				
Kiwi	1 2 3 4 5 6				
Mangosteen	1 2 3 4 5 6				
Romanesco	1 2 3 4 5 6				
Sapodilla	1 2 3 4 5 6				
Fritillary	1 2 3 4 5 6				
Dandelion	1 2 3 4 5 6				
Lily	1 2 3 4 5 6				
Squirrel	1 2 3 4 5 6				
Shipova	1 2 3 4 5 6				
Daisy	1 2 3 4 5 6				
Zucchini	1 2 3 4 5 6				
Pinecone	1 2 3 4 5 6				
Duck	1 2 3 4 5 6				
Rollinia	1 2 3 4 5 6				
Apple	1 2 3 4 5 6				
Turaco	1 2 3 4 5 6				
Longan	1 2 3 4 5 6				
Lettuce	1 2 3 4 5 6				
Gaur	1 2 3 4 5 6				
Peach	1 2 3 4 5 6				
Pear	1 2 3 4 5 6				
Mara	1 2 3 4 5 6				
Rhinoceros	1 2 3 4 5 6				
Cauliflower	1 2 3 4 5 6				

APPENDIX B

FREE RECALL FORM: CONDITION B FM

Post FM Study Free Recall				*Pre FM Test Free Recall*			
Word	*Recall*	*Word*	*Recall*	*Word*	*Recall*	*Word*	*Recall*
Acanthus		Sparrow		Acanthus		Sparrow	
Apple		Squirrel		Apple		Squirrel	
Basilisk		Taro		Basilisk		Taro	
Blueberry		Tomatillo		Blueberry		Tomatillo	
Broccoli		Toucan		Broccoli		Toucan	
Calathea		Turaco		Calathea		Turaco	
Cantelope		Turtle		Cantelope		Turtle	
Cauliflower		Wallaroo		Cauliflower		Wallaroo	
Chicken		Wolf		Chicken		Wolf	
Daisy		Zucchini		Daisy		Zucchini	
Dandelion				Dandelion			
Desman				Desman			
Duck				Duck			
Fritillary				Fritillary			
Gaur				Gaur			
Giraffe				Giraffe			
Kiwi				Kiwi			
Kobus				Kobus			
Ladybug				Ladybug			
Lettuce				Lettuce			
Lily				Lily			
Lion				Lion			
Lizard				Lizard			
Longan				Longan			
Mangosteen				Mangosteen			
Mara				Mara			
Marmoset				Marmoset			
Motmot				Motmot			
Okapi				Okapi			
Peach				Peach			
Pear				Pear			
Pinecone				Pinecone			
Raspberry				Raspberry			
Rhinoceros				Rhinoceros			
Rollinia				Rollinia			
Romanesco				Romanesco			
Rose				Rose			
Saki				Saki			
Santol				Santol			
Sapodilla				Sapodilla			
Shiopova				Shiopova			
Solenodon				Solenodon			

APPENDIX C

GENERALIZATION PHASE FORM: CONDITION B FM

Post FM Test Free Generalization w/ Visual			*Post FM Test Generalization w/ Visual & Verbal Cue*		
Word	*Order*	*Recall*	*Word*	*Order*	*Recall*
Acanthus			Acanthus		
Basilisk			Basilisk		
Calathea			Calathea		
Desman			Desman		
Fritillary			Fritillary		
Gaur			Gaur		
Kobus			Kobus		
Longan			Longan		
Mangosteen			Mangosteen		
Mara			Mara		
Marmoset			Marmoset		
Motmot			Motmot		
Okapi			Okapi		
Rollinia			Rollinia		
Romanesco			Romanesco		
Saki			Saki		
Santol			Santol		
Sapodilla			Sapodilla		
Shipova			Shipova		
Solenodon			Solenodon		
Taro			Taro		
Tomatillo			Tomatillo		
Turaco			Turaco		
Wallaroo			Wallaroo		

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