Age-Related Changes in Visual Spatial Working Memory Cognits: Frontal-Parietal EEG Coherence During Delay

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Abstract

This study explored changes in scalp electrophysiology across two Working Memory (WM) tasks and two age groups. Continuous electroencephalography (EEG) was recorded from 18 healthy adults (18-34 years) and 12 healthy adolescents (14-17) during the performance of two Oculomotor Delayed Response (ODR) WM tasks; (i.e. eye movements were the metric of motor response). Delay-period, EEG data in the alpha frequency was sampled from anterior and parietal scalp sites to achieve a general measure of frontal and parietal activity, respectively. Frontal-parietal, alpha coherence was calculated for each participant for each ODR-WM task. Coherence significantly decreased in adults moving across the two ODR tasks, whereas, coherence significantly increased in adolescents moving across the two ODR tasks. The effects of task in the adolescent and adult groups were large and medium, respectively. Within the limits of this study, the results provide empirical support that WM development during adolescence include complex, qualitative, change.

Keywords: Working memory, Adolescence, Electroencephalography, Frontal-parietal coherence

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CHAPTER ONE: INTRODUCTION

Working memory (WM) is critical for many cognitive functions (Funahashi, 2006; Kawasaki, 2012; Wager & Smith, 2003), including reasoning, language and goal-motivated behavior (Fuster & Bressler, 2012). Perhaps for this reason, WM has been described as "one of the most studied topics in cognitive psychology and cognitive neuroscience" (Wager & Smith, 2003, p. 255). Despite the depth and breadth of research on this topic (Funahashi, 2006; Fuster & Bressler, 2012), the neural substrate of WM remains unknown. Several models of WM, including modular cognitive models (Baddeley & Hitch, 1974; Baddeley, 1996; Cowan, 2001) and physiological network models (Fuster, 2008; Kotchoubey, 2006; Postle, 2006) have been developed.

Cognitive and physiological models put forward different definitions of WM. From a modular cognitive perspective, WM is generally described as a limited capacity system (Luck & Vogel, 1997) that actively maintains and manipulates information (Baddeley, 2010). Recent work has argued for separate WM for different cognitive domains (Cowan, 2001). Regardless of domain, WM is described as tri-phasic, entailing stages of encoding, maintenance and retrieval (Kawasaki, 2012). Some researchers argue that the cognitive model does not fully account for the immense physiological data that has been accumulating since the early 1900s (Fuster, 2009). For example, Postle (2007) reviewed several lines of research that would require the substantial disassociation of the cognitive models' domain specific modules. Thus, in response, physiological network models have been proposed (Fuster & Bressler, 2012; Kotchoubey, 2006; Postle, 2007). Physiological network understandings of WM are

grounded in evolution and the dynamic interplay between biology and experience (Fuster & Bressler, 2012; Kotchoubey, 2006). According to this view, WM evolved because it enables an organism to utilize information that is no longer present in the environment but is essential for the performance of adaptive behavior (Curtis, 2006; Kotchoubey, 2006; Fuster & Bressler, 2012).WM is defined from this perspective as widely distributed, long-term memory networks that are *temporarily* and *temporally* activated, and continuously updated to facilitate the planning of near-term, goal-directed actions (Fuster, 2008). That is, WM is posited as emerging on a temporal plane rather than as spatially localized modular functioning (Fuster, 2008). Thus, WM is understood as an evolved capacity, globally distributed, and dynamically activated on a temporal dimension (Fuster, 2008) and, importantly, dependent upon maturational factors (Asato, Terwilliger, Woo, & Luna, 2010; Klingberg, 2006). This latter feature is illustrated, for example, in behavioral and physiological studies demonstrating that structural and functional changes in the developing adolescent brain (Asato et al., 2010; Spear, 2002; Olesen, Nagy, Westerberg & Klingberg, 2003; Segalowitz, Santesso & Jetha, 2010) may underlie differences in WM performance between adolescents and adults (Geier, Garver, Terwilliger & Luna, 2009; Klingberg, 2014; Tamnes et al., 2013). Adolescence may represent a particularly intensive developmental period (Asato et al., 2010).

Adolescence is identified as a time of important development in humans, a transition period between child and adult (Dahl, 2008). Adolescence is biologically characterized as a time of significant developmental plasticity in several neural systems, including those underlying behavior, emotions, decision making, self-

regulation and executive functions (Dahl, 2008; Van Leijenhorst, et al., 2010). Specific changes occurring in the adolescent brain have been identified as underlying age-related improvements and qualitative shifts in cognitive functioning, including WM (Asato et al., 2010; Darki & Klingberg, 2014).

The present research is grounded in a physiological understanding of WM and is informed, in particular, by Fuster's (2008) physiological cognit model, where cognits describe widespread, hierarchical, overlapping, and emergent neural networks. The WM cognit is understood as a time-bridging function that mediates cross temporal contingencies when there is a delay between perception and action (Fuster & Bressler, 2012). Specifically, the biological principle called the Perception Action Cylce (PAC) describes that an organisms' actions follow from perception, and in turn modify perceptions, and so on, in an unbreakable cycle (Kotchoubey, 2006). However, if past environmental information is no longer present in the environment but is relevant to informing imminent action, then WM forms a temporal gestalt between the memory of the stimulus and the future goal-directed action (Fuster & Bressler, 2012). Thus paradigms investigating WM are operationally defined by the delay period (Fuster, 2008; Hunter, 1913).

As the delay period is what operationally defines all WM tasks, studies utilizing brain imaging techniques in the investigation of WM have focused on neurological activity occurring during the delay (D'Esposito, 2007; Fuster & Bressler, 2012). Much of this research has shown that WM correlates with persistent brain activity in the prefrontal cortex (PFC) as well as the modality dependent posterior region; that is, a frontal-parietal network seems to underlie WM (Fuster & Alexander, 1971; Funahashi,

Bruce, Goldman-Rakic, 1989; Olsen et al., 2003; Riggal & Postle, 2014; Ullman, Almeida, & Kingberg, 2014) and this network appears to develop well into adulthood (Geier et al., 2009; Klingberg 2014; Sander, Werkle-Bergner & Lindenberger, 2011; Ullman et al., 2014; Zollig, Martin & Kliegel, 2010). Additionally, electrophysiological research suggests that neuronal connectivity strength and rates of firing during the delay period are essential for determining cognitive capacity (Klingberg, 2014). Thus, due to its high temporal resolution, electroencephalography (EEG) has been used to investigate task-dependent and age-dependent brain changes on a millisecond timescale.

In the present study, EEG was recorded during the delay period of an oculomotor delay response task (ODR). An ODR task is a WM task that uses eye movements, called saccades, as the metric of motor response. Participants are presented with some form of visual stimuli. A delay ensues in which the stimulus is no longer present but must be remembered in order to successfully make a saccade when prompted. ODR tasks have been described as the gold standard for investigating WM because the visual system is well described in research and because eye movements generate less noise in the EEG signal than other motor responses (such as pressing a button with a finger) (Curtis, 2006).

EEG was recorded from 12 adolescents and 18 adults while they participated in an ODR task. The ODR task had two conditions called ‘Match’ and ‘Non-Match’ that place different demands on WM during the delay period (Curtis, 2006). In Match, participants performed memory guided saccades. That is, the visual stimulus could be used to plan the impending eye movement during the delay period. In Non-Match, the visual stimulus was of a ‘forbidden’ location where the participants were instructed not

to look when prompted to respond; thus eye movements could not be planned during the delay period. Two delay-period, frontal-parietal, alpha frequency coherence values (one value for the Match condition and one for the Non-Match) were calculated for each participant. It was expected that there would be differences in coherence across Conditions (Match, Non-Match) and across age Groups (Adolescent, Adult). These results were expected since, first, previous work shows that the Match condition biases participants towards a prospective coding strategy, and that the Non-Match biases participants towards a retrospective coding strategy (Curtis, 2006; Curtis, Rao & D'Esposito, 2004; Geier et al., 2009; Nichol, 2014), and, second, previous research shows that adults and youth utilize different brain regions during WM tasks owing in particular to maturational factors (Geier, et al.,2009; Klingeberg, 2006; Sanderson, 2013). Finally, an interaction effect was predicted as previous research found changes in the pattern of EEG activity in the Match condition between adolescents and adults (Sanderson, 2013).

EEG was used as the methodology because of its superior temporal resolution (Luck, 2005). Alpha was selected as the brain oscillation of focus for several reasons. Alpha was the first frequency discovered (Berger, 1929), is the most prevalent in the human brain (Basar, 2012; Klimesch, 1999), has been reported in many WM studies (Nichol, 2014; Palva, Monto, Kuashekhar, Palva & Kopell, 2010; Roux & Uhlhaas, 2014; Sanderson, 2013; Sauseng, Klimesch, Schabus & Doppelmayr, 2005) and has been described as fundamental (Basar, 2012), underlying cortical communication and cognition (Jensen & Mazaheri, 2010; Klimesch, Sauseng & Hanslmayr, 2007; Roux & Uhlhaas, 2014), and as integral for inhibition of task- irrelevant stimuli (Sauseng et al.,

2005; Roux & Uhlhaas, 2010; Palva & Palva, 2011). Three frontal electrode sites (F3, FZ, F4) and three parietal electrode sites (P3, PZ, P4) were combined to create a measure of frontal activity and a measure of parietal activity, respectively. The three electrodes from each the anterior and the parietal sites were sampled in order to achieve a general measure of frontal and posterior activity, respectively. The choice of these electrode signal-pair sites as indicative of brain activity in the regions beneath them, namely, the PFC and the parietal cortex, follows from research describing that the generators of EEG activity directly under the recording electrode produce at least half of the amplitude recorded, and generators of the EEG activity within a six cm diameter of the recording electrode produce at least 95% of it (Nunez & Srinivasan, 2006). Coherence measures of EEG have been used as a general index of the brain's functional connectivity (Lee, Wu, Yu, Wu & Chen, 2012). Coherence between frontal and parietal sites was of interest because several specific areas in these regions have been shown in the operation of WM (Curtis, 2006; Draki & Klingberg, 2014; Ullman, et al., 2014). Due to the protracted maturation of the prefrontal areas (Asato et al., 2010; Draki & Klingberg, 2014; Fuster, 2014; Segalowitz, Santesso & Jetha, 2010), coherence between frontal and parietal scalp sites was expected to reflect processing differences between age groups. Overall, this technique fits well in this study's investigation of the brain's task- and age-dependent activation patterns during the delay period of an ODR task.

The present study found a statistically significant Group x Condition interaction: delay-period, frontal-parietal, alpha coherence decreased in Adults moving across the levels (Match to Non-Match) of the ODR task whereas coherence increased in Adolescents. The effect of condition was medium in the Adults and large in

Adolescents. These results suggest, within the limits of this study, that WM during adolescence includes qualitative and complex changes in development.

CHAPTER TWO: LITERATURE REVIEW

In the following literature review I will outline the shift in approaching WM from a cognitive perspective to a physiological perspective. I will then provide a detailed outline of the cognit model, a physiological perspective model, put forward by Joaquin Fuster. This model will serve as the theoretical framework for the present research investigating delay period activity during WM. The significance of the delay period, and optimal delay task paradigms will be detailed. A brief review of brain maturation with a focus on WM development will be provided followed by the brain imaging techniques used to investigate WM. Finally, the rationale, research questions and hypothesis of the present study will be given.

From Cognitive Modular Models to Physiological Network Models

WM has been operationally defined from both cognitive and physiological perspectives (Fuster, 2008; Kotchoubey, 2006; Postle, 2006). Perhaps the most widely accepted cognitive model is that developed by Baddeley & Hitch (1974), according to which WM is understood not as a unitary storage system, but rather as a system entailing three components: the *Central Executive*, which is responsible from attentional control, and two limited capacity storage systems, namely, the *Visuo-spatial sketch pad* and *Phonological loop* (Baddeley & Hitch, 1974). Modifications to this model, including the addition of an *Episodic buffer* have since been made (Baddeley, 2012). From the cognitive perspective, WM is generally described as a limited capacity system (Luck & Vogel, 1997) and separate WM for different domains, specifically visual and verbal, have been empirically supported by research (Cowan, 2001). WM, regardless of domain, is described as tri-phasic, again, involving encoding, maintenance and retrieval

(Kawasaki, 2012). Finally, researchers adopting this perspective assert that they have identified the neural substrate of Baddley's Central Executive and storage systems, but the issue of how these modules temporally communicate has not been thoroughly elucidated (Kawasaki, 2012).

In consideration of cognitive functions such as attention, language, and intelligence, such modular models have been described as "empirically inconsistent with the recent literature" (Fuster, 2009, p. 2947) and have been criticized for requiring a potentially endless proliferation of new *modules* to explain new cognitive phenomena (Kotchoubey, 2006). Some researchers argue against the notion of specialized systems working in *isolation*, describing WM instead as an emergent property of dynamic neural networks; that is, there is co-ordination of evolved brain systems giving rise to higher cognitive functions (D'Esposito, 2007; D'Esposito, Postle & Rypma, 2007; Fuster, 2008; Kotchoubey, 2006; Postle, 2006). In response to criticism of modularity, Baddeley (2012) has argued that from the cognitive perspective certain processes are "tightly interlinked within the module and more loosely *linked* across modules" (p.7, emphasis added). However, according to Fuster and Bressler (2012) the physiological model is a network model and thus there are no *links*. WM from a physiological perspective is thus defined as networks that are widely distributed, temporarily activated and continuously updated toward the planning of near-term, goal-directed actions. From a physiological network approach, then, an understanding that the unit of representation and function *is* the network and not a discrete, autonomous anatomical region is paramount. Recently, brain imaging studies provide evidence of widely distributed, dynamic cortical networks (Curtis et al., 2004; Curtis, Sun, Miller &

D'Esposito, 2005). Thus the investigation of networks, including WM networks, and their development in humans is imperative in order to understand cognition. A model of cognits put forth by Joaquin Fuster is of particular interest and is outlined below (Fuster, 2008).

Fuster's Cognit Model

Fuster (2008) presents a Cognit Model which is not completely antithetical to modular cognitive models. A cognit is defined as a unit of memory. A cognit is comprised of a network of synaptically associated cortical neurons. These dispersed neuronal assemblies are synaptically associated by life experience. Cognits may encompass several cortical areas; however, network operations are irreducible to the operations of those areas. The cognit thus represents the epistemological floor for understanding WM. It follows that attempts to explain a cognitive function, such as WM, below this level will inevitably fail. The cognit model diverges from other networks such as that proposed by Hebb in several ways: First, cortical cognits overlap and share connectionist-like nodes of association, (thus, cognit boundaries are not clearly demarcated); Second, cognits are constantly changing; Third, cognits are characterized by reciprocal connectivity, both feedforward and feedback via a process termed reentry (Fuster & Bressler, 2012). Reentry is the coordination of distributed neural activity and is interpreted from synchronized oscillatory activity (Tallon-Baudry, Bertrand, & Fischer, 2001). Last, cognits are hierarchical, and nested (Fuster, 2008). Thus there are cognits at the lowest perceptual levels that are modular-like; however, these cognits are subsumed within higher cognits (Fuster, 2008). Thus, modular-like cognits are not *controlled by* an executive function, but are *part of* executive functions.

In the cognit model there is no need for endless modules, or a Central Executive (Fuster, 2008), and WM cognits may be understood in terms of perception and action.

The perception action cycle (PAC) and working memory (WM) cognits. WM is described by Fuster (2008) as the emergence of several overlapping WM cognits. Fuster's WM cognits may be loosely understood as belonging to one of two broad types of dynamically interacting cognits, namely, perceptual and action (Fuster & Bressler, 2012). Although widely distributed, the perceptual cognit is predominant in the posterior areas of the brain, and the action cognit, which also serves to integrate perceptions, is predominant in the PFC (Fuster & Bressler, 2012). Thus, these two networks, comprised of many other nested networks, communicate with each another through bidirectional feedback and feedforward connections via reentry. Reentry makes possible the coordination of action with information regarding the internal and external environment (Fuster & Bressler, 2012). When there is a delay between perception and action, WM performs the temporal integration of perception and action thus preserving the PAC (Fuster & Bressler, 2012). In short, WM serves the PAC.

The PAC describes a basic biological principle: all adaptive behavior is predicated upon the circular flow of information between organism and environment (Fuster 2008; Postle, 2014). The PAC is similar to other formulations of such evolved continuous interactions. Thus the organism makes predictions about the environment as well as the effects of future behavior on the environment and then tests these predictions through further perception and action (Kotchoubey, 2006). Specifically, perception initially moves upward through the perceptual cognit hierarchy and then dynamically interacts with potentially all levels of perception and action cognits,

whereas action initially moves downward through the cognit hierarchy and then likewise dynamically interacts with other cognits (Fuster & Bressler, 2012). This reentrant portion of the cycle is critical in WM (Fuster & Bressler, 2012). Thus, just as the PAC can be thought of as biphasic in the sense of being one part perception and one part action, it may also be thought of as biphasic in a temporal sense, being one part past (perception) and one part future (action). Crucially, when there is a delay between perception and action, a bridge must be formed (cross-temporal contingencies must be mediated) in order to connect both the environmental information of the past (perception) and the goals toward which future actions will be enacted (action). This bridge is WM (Fuster & Bressler, 2012).

Research supporting this model has been accumulating. For example, persistent firing of neurons in the PFC and parietal regions during the delay period has been observed using EEG (Dhawan, Deubel & Jonikatis, 2013; Fuster & Alexander, 1971) and fMRI (Curtis & D'Esposito, 2003; D'Esposito et al., 2000; D'Esposito, Ballard, Zarahn, & Aguirre, 2000). Importantly, if either the neuronal activity in the PFC or the posterior region is disrupted via permanent or temporary lesioning, then WM performance degrades in proportion to the disruption (Alexander & Fuster, 1973; Chafee & Goldman-Rakic, 2000; Fuster & Alexander, 1973; Goldman & Alexander, 1977; Nishino, Ono, Saskai, Fukuda & Muramoto, 1984; Sobotka, Diltz, & Ringo, 2005). Thus WM is not localized to one brain area but is widespread and emerges to bridge perception and action during the delay.

Oculomotor Delayed Response Tasks and Delay Period Activity

The delay period is what operationally defines all WM tasks (Fuster, 2008). WM

involves bridging the the gap between perception and action (Fuster & Bressler, 2012). Delay tasks were first devised by Hunter (1913) and characteristically have four phases: 1) *Stimulus*: the subject is presented a piece of information (stimulus/ to-be-remembered information); 2) *Delay*: the removal of the piece of information from the subject for an enforced duration of time; 3) *Cue*: presentation of objects/behaviors for choice; and 4) *Response*: the subject's choice of information or action. In order to complete the task successfully, subjects must: a) remember the rules and goals of the task; b) remember the cue during the delay; (retrospective coding); and, c) engage in prospective memory of the impending choice/action. Thus, phase 2, the delay period, is the crucial factor in the delay task as this is what operationally defines all such tasks (Fuster, 2008). WM is operational during the delay. The response (phase 4) is contingent on past information (phase 1), and so during the delay WM must mediate this cross-temporal contingency (Fuster, 2008). Previous work has shown that the "delay activity is the carrier of memory through the delay period" (Sobotka et al., 2005, p. 128). For example, WM performance and neuronal activity during the delay correlate in monkeys (Funahashi, Bruce & Goldman-Rakic, 1989) and in humans (Pessoa, Gutierrez & Bandettini, 2002). In addition, controlled disruption of delay period activity reduces both neuronal activity and behavioral performance; importantly, the magnitude of performance impairment is proportional to the magnitude of delay period disruption, suggesting a causal relationship (Sabotka et al., 2005).

WM is distributed across the brain (Fuster & Bressler, 2012). Initially, non-human primate electrophysiological recoding studies found persistent neuronal activity during the delay in the PFC (Fuster & Alexander, 1971). Subsequent studies have

demonstrated that there is persistent activity in widespread brain regions in animals and humans during the delay period of a WM task. For example, single-unit electrophysiological studies in primates have shown cells that persistently fire during the delay period of WM tasks in the thalamus, basal ganglia and infertotemporal cortex (Fuster & Jervey, 1982; Miller, Erickson & Desimone, 1996; Miyashita & Chang, 1988), the posterior parietal cortex (Mazzoni, Bracewell, Barash & Anderson, 1996), the visual processing cortices (Bisley & Pasternak, 2000; Miyashita & Chang, 1988) and, as stated, the PFC (Fuster & Alexander, 1971; Fuster, 2014). There is evidence that these dispersed neurons comprise a cognit, whereby WM arises from functional interactions between distant brain areas. Some of this evidence comes from lesioning studies. Lesioning is the inactivation of a neuron or groups of neurons either permanently, as in the case of ablation (that is the complete removal of some amount of brain tissue), or temporarily (Fuster, 2008). Temporary (reversible) lesioning is the temporary disruption of neuronal activity; for example, neuronal firing can be disrupted by either electrical interference, or by the cooling of a specific brain region, whereby at a certain reduced temperature (induced via invasive measures) neurons are not able to function (Fuster, 2008). Primate experiments that used microelectrode recording in combination with reversible lesioning generally have found that the cooling of one area (for example the PFC) depresses the activity of cells in a distant area (for example, the inferotemporal area) during the delay period and degrade the subjects' performance of the delay task (Alexander & Fuster, 1973; Chafee & Goldman-Rakic, 2000; Fuster & Alexander, 1973; Nishinoet al., 1984; Sabotka et al., 2005).

More recently, oculomotor delay response (ODR) tasks have been used to

investigate WM. ODR tasks are described as the gold standard of WM paradigms (Curtis & D'Esposito, 2003). ODR tasks are delay tasks that involve goal-directed generation of eye movements called saccades (Dhawan et al., 2013). To date, ODR research has suggested that delay period activity could represent the retention of sensory or motor information, retrospective or prospective coding (Curtis, 2006) or the suppression of attention (Dhawan, et al., 2013; Jonikaitis, Dhawan & Deubel, 2014), or other processes not yet elucidated (Riggal & Postle, 2012). Well-designed oculomotor paradigms allow for the manipulation of sensory and motor demands so as to answer these questions (Curtis, 2006). For example, several researchers have used a Match- versus Non-Match-to sample ODR task paradigm (see, Curtis et. al., 2004; Dhawan, et al., 2013; Geier, et al.,2009; Jonikatis et al., 2014). In this paradigm, visuospatial WM is investigated. During the delay period of the Match condition a saccade can be planned immediately and the execution of the saccade merely delayed until prompted (Curtis et al., 2004; Dhawan et al., 2013; Jonikaitis et al., 2014). Curtis (2006) described the Match task as biasing subjects towards a prospective motor code strategy. In the Non-Match condition saccades cannot be planned during the delay period (Dhawan et al., 2013). Curtis (2006) described this task as biasing subjects towards a retrospective sensory code strategy, and likened this to "sustained covert spatial attention" (p.174). Research on humans using fMRI has demonstrated that Match and Non-Match tasks elicit distinct patterns of delay period activity (Curtis, 2006; Curtis et al., 2004; Geier et al., 2009; Jonikatis et al., 2014). Specifically, event related fMRI studies have found that delay period activity in the frontal eye fields is greater in Match than in Non-Match, whereas delay period activity in the intraparietal sulcus is greater in Non-Match than Match

(Curtis et al., 2004). Additionally, children, adolescents and adults have been shown to differ in terms of brain regions recruited (Geier et al., 2009), suggesting that although WM is present at birth (Diamond & Goldman-Rakic, 1989), it matures across development via continued refinement of the recruitment of specific regions, including the frontal-insular-temporal regions (Darki & Klingberg, 2014; Geier et al., 2009; Fuster, 2008). Recently Sanderson (2013) found age-related differences in scalp-recorded slow wave amplitudes at frontal and parietal locations using the same ODR tasks that were used in the present study.

In adults, however, the meaning of the neural difference in delay activity between Match and Non-Match conditions remains unclear (Riggal & Postle, 2014). For example, research on humans using measurements of spatial allocation of attention during the delay has found that Match and Non-Match tasks lead to distinct attentional benefits and attentional costs, respectively (Dhawan et al., 2013). Thus, as stated, the difference in delay period activity may reflect a difference in strategy, namely, retrospective and prospective coding (Curtis, 2006), or the suppression of attention unique to the Non-Match task (Dhawan, et al., 2013).

Brain Maturation and Working Memory

Historically, the importance of the PFC in WM has been well established by ablation studies in primates (Jacobsen, 1935, 1936; Lashley, 1948; Spaet & Harlow, 1943) and rodents (Johnston, Hart & Howell, 1974). The severity and nature of the effect of ablation depends on age in primates, with some studies finding no effect for PFC ablations before age two (Harlow, Akert & Schilts, 1964). Reversible lesioning of the PFC via cooling have also been shown to lead to age-dependent deficits on

delay tasks (Goldman & Alexander, 1977). These findings suggest that at the level of ontogeny, the PFC develops gradually and only becomes committed to certain functions after birth. In humans, the development of the PFC may be particularly protracted (Asato et al., 2010; Spear, 2002), which may explain differences in WM between children, adolescents and adults (Klingeberg, 2006; Klingeberg, 2014). As stated, WM cognits are biological entities formed as a function of phylogenetic and ontogenetic experience (Fuster & Bressler, 2012); thus biological or developmental timetables along with species-typical experience may guide the ontogenetic development of WM (Klingeberg, 2014). Adolescence in particular has been described as a significant time of cerebral maturation (Asato et al., 2010; Jetha & Segalowitz, 2012).

Behavioral differences in WM across development. An inverse 'U' shaped pattern may characterize the efficiency of WM across development (Sanderet al., 2012; Zollig et al., 2010), with WM improving throughout childhood (Darki & Klingberg, 2014; Klingberg et al., 2002; Myatchin & Lagae, 2013), reaching maximum efficiency in young adulthood (Geier, et al., 2009; Sander, et al., 2011) and then declining in old age (Missonnier et al., 2011; Zollig, et al., 2010). This pattern may be explained by the breakdown of inhibitory controls in children (Sander et al., 2012) and older adults (Missonnier, et al., 2011; Sander et al., 2012) when WM load is high. Research has informed interpretations of WM as beginning to develop linearly after approximately the age of six (Klingberg, 2006). Thus, improvements in WM from this point onward until adulthood may be described as quantitative (Klingberg, 2006); however, very recent research suggests that WM may develop in a more complex manner (Draki &

Klingberg, 2014) with qualitative jumps in development occurring during adolescence (Asato et al., 2010).

Neurophysiological differences of WM across development. EEG and ERP studies have found clear, age-related differences in the speed and accuracy of WM (Alloway & Alloway, 2013; Draki & Klingberg, 2014; Geier et al., 2009; Myatchin & Lagae, 2013). A gradual increase in WM performance during a visual spatial WM task was found to occur with increasing age in a sample of nine to 18 year old children (Klingberg et al., 2002). Moreover, increased age was also correlated with greater activation of the superior frontal sulcus and intraparietal cortex (Zollig et al., 2010). Additionally, contralateral delay activity (CDA) was identified as a potential neural marker of WM capacity, where the CDA showed age-related differences reflecting limited top-down control in children (Sander et al., 2011).

With regards to frequency, alpha is the dominant frequency recorded in EEG in adults (Basar, 2012), but not in very young children (Saby & Marshall, 2012) or older children with learning disabilities or poor education (Klimesch, 1999); however, alpha power increases in children with age, beginning at posterior and ending at anterior recording sites (Klimesch, 1999). By about age 16 an increase in absolute upper alpha band power characterizes the brain (Klimesch, 1999). In sum, quantitative and qualitative changes in the structure and functioning of brain networks, may underlie age-related improvements in WM (Asato et al., 2010; Klimesch, 1999; Klingberg, 2006; Klingberg et at., 2002). Adolescence may represent a particularly intensive developmental period (Asato et al., 2010).

Adolescence is identified as a time of important development in humans, a

transition period between child and adult (Dahl, 2008). Adolescence is biologically characterized as a time of significant developmental plasticity in several neural systems, including those underlying behavior, emotions, decision making, self-regulation and executive functions (Dahl, 2008; Van Leijenhorst, et al., 2010). For example, fMRI research has recently shown support for behavioral research identifying adolescents as hypersensitive to reward (Van Leijenhorst, et al., 2010). Research shows that the areas associated with cognitive control, such as the PFC, are still developing well into adulthood, possibly as late as thirty (Crone & van der Molen, 2007; Steinberg, 2008). During development, specific changes occurring in the brain have been identified as underlying age-related improvements in cognitive functioning, (such as WM) and predictive of cognitive capacity (Darki & Klingberg, 2014). During adolescence there is an increase in white matter, as a result of *myelination*, (Asato et al., 2010; Barnea-Goraly et al., 2005; Darki & Klingberg, 2014; Klingberg, et al.,2002; Olesen et al., 2003; Segalowitz et al., 2010; Steinberg, 2008). Myelination is thought to increase the speed of transmission both within the local brain region as well as between the parietal and frontal areas (Klingberg, 2006; Klingberg, 2014). In turn, this is thought to create greater stability, less interference, and to foster the functioning and integration of a network (Klingberg, 2014). Further research using fractional anisotropy as a measure of myelination and axon thickness supports the correlation between increased white matter and increased brain activity (Asato et al., 2010; Barnea-Goraly et al., 2005; Darki & Klingberg, 2014; Klingberg, 2006). Another important change during adolescence is a decline in gray matter volume as a result of synaptic pruning (Paus, Keshavan & Giedd, 2008). Pruning is described in the language of natural selection, whereby unused or

lesser used synapses and axons do not survive (they are pruned), leaving only active and efficient brain material (Bjorklund, 2005; Paus et al., 2008; Klingberg, 2006). Again, this maturational process is thought to result in a more stable and more efficient network. Changes in cortical folding are also occurring, with recent research showing that during adolescence there is a reduction in gyrification, particularly in the frontal areas, which is presumed to also relate to cognitive development (Klein et al., 2014). Additional changes during adolescence include changes in neurotransmitter function (Segalowitz et al., 2010; Steinberg, 2008) and changes in the expression of genes (Klingeberg, 2014). Importantly, significant changes occur in the PFC, including some structural and functional changes as well as increasing connectedness between the PFC and other brain regions (Segalowitz et al., 2010). In general, these changes may be thought of as leading to a more *connected* brain. For example, Lee et al., (2012) found a correlation between global efficiency of brain networks and intelligence; a correlation between intelligence and white matter architecture, (where white matter may underlie efficiency in connecting brain regions); and a correlation between shorter characteristic path length and intelligence (perhaps resulting from efficient pruning). It is therefore plausible to assume that a more connected brain may result in better WM. Investigating changes in frequency coherence between spatially distant brain regions may elucidate WM development.

Electroencephalography (EEG), Event-Related Potentials and Neural Oscillations

Accumulating electrophysiological research shows that the neural processes implicated in higher cognitive functions, including perception, attention and motor actions, exist in segmented, discrete *time* periods (or time-windows), rather than spatial

locations (Palva & Palva, 2012). Evidence suggests that neural oscillations impose these time-windows (Palva & Palva, 2012). Neural oscillations are the rhythmic and repetitive activity of neural tissue, arising from individual neuron's particular mechanisms or from neuronal interactions (Thatcher, 2012). Neuronal interactions in turn may produce oscillations at frequencies different than the firing frequency of individual neurons; for example, alpha frequency activity is a well-known oscillation (Thatcher, 2012). Thus neural oscillations represent the temporal aspect of a spatial- temporal brain functioning dimension (Fries, 2005).

EEG is the brain imaging technique most sensitive to measuring information processing on a temporal plane (Luck, 2005). EEG is the recording of brain's electrical activity. EEG can record neuronal responses on a millisecond time scale (Luck, 2005). EEG can be recorded from the brain by microelectrodes and from the scalp using scalp electrodes (Collura, 1993; Luck, 2005). Whereas single unit recordings (the insertion of microelectrodes directly into the brain) record the action potentials of single neurons, EEG records the summation of the activity of similarly oriented post-synaptic pyramidal neurons (Luck, 2005; Kotchoubey, 2006; Sauseng & Klimesch, 2008). EEG cannot detect the activity from deep brain structures or dipoles that are parallel (rather than perpendicular) to the surface of the cortex (Luck, 2005). However, many higher cognitive functions, including WM, arise from the cortex (Luck, 2005).

Event-related potentials (ERP) are the brain activities elicited by specific sensory, cognitive or motor events (Luck, 2005). ERP are embedded within the continuous EEG and without particular averaging techniques, the ERPs are masked by an ongoing EEG biological and non-biological artifacts (Luck, 2005). Several ERP

components have been described. Most of these ERP components are identified by the scalp location of their peak amplitudes and latencies (such as P300) (Luck, 2005). Because the ERPs are time-locked, the latency of an ERP is described as indicating the timing of information processing (Luck, 2005).

In the last thirty or so years, some attention has been paid to the fluctuations in EEG oscillations and the possibility that these may provide an understanding of the coupling and uncoupling of functional networks that ERPs cannot provide (Bastiaansen, Mazaheri & Jensen, 2012). Neural oscillations are divided into frequency bands: Delta (0–4 Hz), Theta (5-8), Alpha (9-12 Hz), Beta (13-30 Hz) and Gamma (30-80 Hz) (Sauseng & Klimesch, 2008). Cognitive functions, ranging from basic to higher, have been related to different frequencies of neural oscillations (Roux & Uhlhaas, 2014). Recent evidence has shown that information is efficiently transmitted and coded for in distributed neuronal populations via neural oscillations (Havenith, et al., 2011; Bosman et al., 2012). For example, a review of research by Sauseng and Klimesch (2008) describes the different functions attributed to each band, including: delta's importance in large-scale cortical integration; theta's role in various memory processing; alpha's role in inhibition, as well as very specific perceptual, attentional and memory processing; beta's role in motor activity, attention and higher cognitive functions; and gamma's role in binding information, binding large-scale brain networks and retaining and retrieving information. Of relevance, the maintenance of information in WM has been postulated as one role of oscillatory activity (Roux & Uhlhaas, 2014).

Neural oscillations and coherence. As described previously, Fuster's (2008)

cognit model states that any given neuron can be recruited to one of several cognits at any given point in time. Cognits are hierarchically nested and so higher cognitive functions, such as WM, will emerge out of the activation of a cognit with many cognits nested within (Fuster, 2008). The instantaneous emergence of this spatially widespread cognit is described as owing to reentry (Fuster & Bressler, 2012). Specifically, reentry is the coordination of distributed neural activity and is interpreted from synchronized oscillatory activity (Tallon-Baudry, Bertrand, & Fischer, 2001). An investigation of non-phase-locked responses may reveal how smaller cognits (networks) can be recruited into multiple functional cognits in a dynamic fashion, thus shedding light on how information is integrated and represented in the brain (Bastiaansen et al., 2012). Specifically, synchronous firing of neurons is described as facilitating network integration as it raises the probability that widespread neurons will entrain one another (Knig & Schillen, 1991). Such a phenomenon has been termed binding and is further discussed below.

Initial observations of the synchronous firing of neurons in the visual cortex led to a theory of *binding*. Binding theory posits that through synchronous firing the various features of vision could cohere into a whole picture (Fuster & Bressler, 2012). Thus synchronous oscillations in many frequencies not only link areas to form a unified functional network, but also bind information (Varela, Lachaux, Rodrigues & Martinerie, 2001). Such a *relational code*, via oscillations, may operate at higher cognitive levels, including WM (Fuster & Bressler, 2012). Specifically, visual binding has been described as the synchronization (integration) of neurons on a local scale, whereas large scale synchronization, spanning multiple scales both spatially and

temporally in the brain, is evidenced to underlie higher cognitive functions (Varela et al., 2001). Large scale synchronization is possible because the neocortex is organized to accommodate dense local connections as well as long-range connections to distant cortical areas (Bastiaansen et al., 2012). Fries (2005) offers a theory of how neural oscillations produce cognitive processes; in effect, temporal windows for communication emerge when neuronal groups oscillate coherently. Following this, if neuronal coherence is absent the cognitive process is prevented (Fries, 2005). Importantly, neuronal coherence explains the flexibility and effectiveness of cognitive functions, where the mere anatomical connections between neurons do not (Fries, 2005; Fuster, 2008). In sum, synchronous electrical activity across brain regions suggests a functional relationship (Varela et al., 2001) and provides for an explanation for how the brain can perform tasks requiring immense cognitive flexibility (Fries, 2005).

Two important measures of functional interactions between pairs of signals have been identified, namely, measures of EEG currents or power, and measures of EEG network properties (Nunez & Srinivasan, 2007). Coherence (a correlation coefficient squared) is an example of the latter. EEG coherence, calculated as a function of frequency from signals being simultaneously recorded from pairs of distant electrodes, may be used to quantitatively measure synchrony (Halliday et al., 1995), including task-dependent and content-specific synchronization (Salazar, Dotson, Bressler & Gray, 2012). Distant synchronous activity is picked up by different electrodes (Tallon-Baudry et al., 2001) and increased synchrony results in increased stability of the phase difference of the two oscillatory field potentials, or *coherence*

(Bastiaansen et al., 2012). In sum, synchronization of several distant networks can be inferred from the coherence in a given frequency band between electrode sites (Bastiaansen et al, 2012) and this can be done for each frequency band (Nunez & Srinivasan, 2007). As coherence allows the monitoring of dynamic, large-scale synchronization of activity measured by distant electrodes (Weiss & Mueller, 2003), it is an important measure of the functional interactions between oscillating brain sub-systems (Nunez & Srinivasan, 2007).

Research suggests that different frequencies and relationships between frequencies, simultaneously recorded, underlie distinct functions (Roux & Uhlhaas, 2014; Weiss & Mueller, 2003); thus, it follows that research may focus on one or several frequency bands to disentangle function. For example, in an effort to understand WM, research has found that there is sustained oscillatory activity in the gamma band (30-60 Hz) for visual WM (Palva et al., 2010; Tallon- Baudry, Bertrand, Peronnet, & Pernier, 1998), for WM of face orientation (Jokisch & Jensen, 2007), in contralateral hemisphere to saccade direction in a Match-like delayed oculomotor paradigm (Medendorp, et al., 2006), and for auditory (Mendendorp, et al., 2006) and somatosensory WM maintenance (Haegens, Osipova, Oostenveld & Jensen, 2010). Last, the amplitude of gamma oscillations has been shown to be related parametrically to WM load (Roux, Wilbral, Mohr, Singer & Uhlhaas, 2012; Palva et al., 2010). Other frequency band oscillations have been observed. For example, during WM, in the sensory or association cortex, oscillatory synchrony may be observed with beta and theta ranges predominating in different areas according to the modality as well as the memory load of the to-be-remembered information (Fuster & Bressler 2012). Theta

activity has been found to increase parametrically with WM load and has been suggested as reflecting inhibitory processes (Jensen, & Tesche, 2002; Klimesch, Freunberger, Sauseng & Gruber, 2008). However, theta has also been described as underlying the organization of WM items that are ordered sequentially (Roux & Uhlhaas, 2014).

Alpha oscillations have become a particular focus of WM research and of EEG research more generally. Alpha oscillations have been described as the most frequent oscillations in the human brain (Klimesch, 1999), and thus fundamental (Basar, 2012). In a purely visual spatial WM task, frontal-parietal connectivity has been observed at the alpha frequency (9-12 Hz) (Palva et al., 2010; Sauseng et al., 2008). Alpha activity may play a role in the inhibition of irrelevant items during WM (Roux & Uhlhaas, 2014). Research has identified local alpha power modulations during WM tasks that require greater inhibitory processes in adults (and to a lesser degree in children and older adults) (Sauseng et al., 2005). Such inhibition may be of perceptual and action items. For example, posterior alpha activity has been interpreted as reflecting functional inhibition of distracting perceptual input during the delay (Sauseng et al., 2005). Research has localized alpha activity to the premotor cortex, suggesting that motor plans are inhibited during the delay (Roux et al., 2012). Formerly thought to index idling of the cortex, increasing evidence points toward alpha activity as implicated in cortical communication and cognition (Jensen & Mazaheri, 2010; Klimesch et al., 2007; Roux & Uhlhaas, 2014). Thus, research has suggested that alpha activity reflects that task-irrelevant information is being actively inhibited (Roux & Uhlhaas, 2014; Palva & Palva, 2011) and therefore that it reflects active processing

(Palva & Palva, 2011). Research has also investigated how coherence in alpha across brain regions may describe a functional network. EEG research may advance earlier fMRI findings.

To reiterate, during a WM task, the coherent activity in the prefrontal and posterior regions can be observed using fMRI (Curtis et al, 2004; Riggal & Postle, 2014) and EEG (Palva et al,, 2010; Roux et al., 2010; Roux & Uhlhaas). This prefrontal-posterior activation during a WM task is likely due to the short and long term cooperation between these networks, and their reciprocal control over one another. (Fuster & Bressler, 2012; Uhlhaas et al., 2010). It is proposed that this is manifested via neural reverberation (Fuster, 2006; Tallon-Baudry, 2001; Varela, et al., 2001). Coherence between frontal and parietal areas has also been interpreted as control over the level of cortical activation in higher visual areas, thus establishing biased attention to anticipated targets (Sauseng & Klimesch, 2008). Coherence patterns and levels may change across development.

Coherence may speak to the nature of *intelligence* more broadly (Lee et al., 2012; Thatcher, 2012). For example, Lee et al. (2012) found that coherence patterns correlated with several tests of intelligence, and these findings have been interpreted as supporting the notion that connectivity strength is a good indicator of general intelligence (Lee et al., 2012; Thatcher, 2012). Specifically, Lee et al. (2012) stated that "a smarter brain is associated with stronger interaction in the central nervous system" (p. 38). Extrapolating this, it is hypothesized that a *more connected brain,* as a function of maturation, may underlie the superior WM performance of adults compared to adolescents, and of adolescents compared to children. Relatively few studies have

investigated changes in frontal-parietal coherence across development (Tamnes et al., 2013). In a recent study, Cuevas et al. (2014) studied ten month olds and found that widespread cortical synchronization emerged during cognitive tasks demanding inhibition. Thus, using EEG coherence, this study suggests that even in infancy higher cognitive functions are performed by recruiting frontal and posterior brain regions into a WM network (Cuevas et al., 2014). A study comparing WM in eight year old children and adults found coherence in infero-temporal and parietal cortical regions in children as opposed to the frontal- parietal coherence found in adults (Machinskaya & Kurgansku, 2012). Comparing coherence between distant simultaneous electrode recordings between adults and adolescents is warranted.

Thus, although much research has attested to the distributed nature of cognitive processes including the functional integration of these dynamic areas via synchronous oscillations, specifically between the frontal and posterior areas (Fuster, 2009), more research is needed, especially in establishing whether dynamic network integration, as indicated by coherence between frontal and posterior electrodes, will similarly manifest in adolescence. As stated, the crucial function performed by WM is bridging the gap between perception and action during a delay by turning attention inward according to prospective goals for action and by temporarily activating pre-existing networks of long term memory (Fuster & Bressler, 2012). Additionally, as stated, cognits, including WM cognits, are biological entities formed as a function of phylogenetic and ontogenetic experience (Fuster, 2008). Thus biological or developmental timetables may guide the ontogenetic development of WM.

The Present Study

Purpose and rationale. The investigation of the communication between widely distant regions of the brain has been described as critical (Lee et al., 2012; Rodriguez et al., 1999; ten Caat, Lorist, Bezden, Roerdink & Maurtis, 2008; Thatcher, 2012; Uhlhaas et al., 2014). Specifically, research has identified the synchronization between frontal and posterior signal pairs in same or different frequencies as indicative of higher-level cognitive functioning (Constantinidis & Wang, 2004; Srimal & Curtis, 2008; ten Caat et al., 2008), pointing to frontal-posterior networks in such functioning (Constantinidis & Wang, 2004; Curtis et al., 2005; Fuster & Alexander, 1971; Funahashi et al., 1989; Geier et al., 2009; Riggal & Postle, 2014; Sander et al., 2010; Srimal & Curtis, 2008; Ullman et al., 2014). Thus the physiological network model of WM as distributed, hierarchical, dynamic (Constantinidis & Wang, 2004; D'Esposito, 2007; Fuster & Bressler, 2012; Postle, 2006) and developing into adulthood (Farber, & Beteleva, 2011; Geier et al., 2009; Klingberg, et al., 2002; Zollig et al., 2010) grounds the present study.

In sum, research has described that behaviorally and on an electrophysiological level, children, adolescents and adults differ in WM performance (Cuevas, 2012; Geier et al., 2009; Sander et al., 2012; Klingberg et al., 2002; Myatchin & Lagae, 2012; Zollig et al., 2010). Fractional anisotropy and fMRI research suggests that the structure and function of the brain is also changing across development (Asato et al., 2010; Barnea-Goraly et al., 2005). EEG provides the temporal resolution necessary to investigate how these differences may be explained by differences in functional interactions across brain regions. Specifically, EEG provides information regarding the human brain's electrical

activity at the time unit of a millisecond (Bosch, Mecklinger & Friederici, 2001). EEG phase synchronization, as measured by coherence, indexes the precise timing of communication between millions of neurons that may be spatially distant but functionally related (Sauseng & Klimesch, 2008). There is, however, a gap in the research: few studies look at the difference between adults and adolescents in terms of this functional connectivity on a temporal dimension.

The present study is a continuation of a broader research endeavor in the Developmental Neuroscience Laboratory (DNLab) in the department of Child and Youth Studies at Brock University. This endeavor seeks to describe WM across development using EEG recorded during the performance of an ODR task. Specifically, in the DNLab: first, Sanderson, (2013) found differences in EEG activity between adolescents and adults in the recruitment of frontal and parietal areas (a localized, anterior difference between adolescents and young adults was observed during the late delay period of the Match task); second, Nichol (2014) found differences in the alpha frequency between Match and Non-Match conditions in adults (alpha power during the delay period was higher in Match compared to Non-Match). Overall, the results of the DNLab show that there are different attentional demands required by the two conditions (Nichol, 2014). The findings of the DNLab are consistent with Fuster's (2008) theory: when the PAC is disrupted by a delay, as occurs with delay tasks, WM must mediate the gap between perception and action using retrospective and prospective coding, respectively. Depending on the demands of the WM task, coding strategy may differ (Curtis et al., 2005; Nichol, 2014) and there may also be age related differences (Klingberg et al., 2002; Sanderson, 2013).

Following the findings of Sanderson (2013) and Nichol (2014), in the present study, I investigated frontal-parietal synchronization as an index of anterior-posterior connectivity (WM cognits) during the delay period of two conditions (Match and Non-Match) of an ODR task in adults and adolescents. I focused specifically on alpha band synchronization between frontal (F3, Fz, F4) and parietal (P3, Pz, P4) electrode sites. I chose these three electrodes at each site because the goal was to sample from anterior and parietal sites in order to achieve a general measure of EEG activity in the frontal and parietal areas. This technique is consistent with the literature where typically only a few electrodes are chosen so as to decrease the chance of responses from other brain sites (Lee et al., 2012). These *anterio*r and *posterior* sites are the most traditionally selected (Lee et al., 2012). Finally, EEG activity directly under the recording electrode produce at least half of the amplitude recorded, and generators of the EEG activity within a six cm diameter of the recording electrode produce at least 95% of it (Nunez & Srinivasan, 2006).

Research questions and hypotheses. Given that the two ODR conditions place different cognitive demands on the participant during the delay period, task differences in frontal-posterior coherence were expected to reflect variation in cognitive processing. Moreover, given that adolescent brains are undergoing substantial maturation, including, presumably, the forming of more integrated and efficient networks (Klingberg, 2006; Fuster, 2008), differences in frontal-parietal coherence were expected between the two groups. Thus for this study I asked three research questions and proposed three hypotheses.

Research Question 1. Will delay-period, frontal-parietal, alpha coherence differ

across Conditions (Match and Non-Match)?

Hypothesis 1. Coherence will differ between the Match and the Non-Match conditions.

Research Question 2. Will delay-period, frontal-parietal, alpha coherence differ between Groups (Adolescents and Adults)?

Hypothesis 2. It is predicted that coherence will differ between groups.

Research Question 3. Will the combined effect of Condition and Group affect delay-period, frontal-parietal, alpha coherence?

Hypothesis 3. It is predicted that there will be a combined effect of Condition and Group on coherence.

CHAPTER THREE: METHODOLOGY

Participants

Data from 18 healthy adults aged 18-33 years (8 males, M = 24.25 years; 10 females, M = 21.55 years) and 12 healthy adolescents aged 14-17 years (7 males, M = 16.25; 5 females, M = 15.25) were collected as part of an ERP study approved by the Brock University Research Ethics Board (REB # 10-211) (Appendix A). Adult participants were recruited from graduate students and student volunteers from our lab and from Brock undergraduate students via poster announcements. Adolescents were recruited via snowball sampling from the community. Questionnaires were used to screen for possible neurological conditions, psychiatric challenges, or other chronic health problems that could affect either task performance or EEG recording (Appendix C). All participants spoke English as their first language and reported normal or corrected to normal vision. All participants signed informed consent (parental consent and assent for the adolescents) before their participation in the study (Appendix D). Participants received a $20 honorarium for their participation.

Data Recording

Continuous EEG data were recorded in a sound attenuated and electrically shielded chamber. 129-channel HydroCel Geodesic Sensor Net (Electrical Geodesic Inc. Eugene, OR) was used to record EEG. Vertex electrode was used as a reference. Sampling rate was 500 Hz. 0.1-100 Hz bandpass filters were used to filter the data during acquisition. Throughout the experiment electrode impedances were kept below 100 kHz. Eye movements were monitored by two infrared camera eye tracking system (Smart Eye Pro,Version 5.8) simultaneously with EEG recording.

Data Collection Procedures

Equipment was checked to ensure good working order and all materials necessary for data collection were gathered and prepared prior to each participant's arrival. The eye tracking system was calibrated by the researcher and re-calibrated when the participant arrived. The participants signed an informed consent prior to testing. To ensure participants were comfortable with the procedures and equipment, participants were guided by the researcher through the types of equipment that were used in data collection, and the requirements of the experimental conditions were outlined. The participants' heads were measured to determine the appropriate net size. The net then was soaked in a potassium chloride and baby shampoo solution. This solution was used to ensure the conductance of the electrical activity from the scalp to sensors. The net was then placed on the participant's head and adjusted to ensure that all electrodes were in the correct position and were touching the scalp.

Participants were taken to a dimly lit, sound attenuated testing room. This testing room was designed to eliminate external electrical interference that may affect the measurement of the electrical activity in the brain. Here the participants sat in an upright position on a chair approximately 45-55 cm from the Dell computer screen on which the task would be displayed. The net was then connected to the Net Amps 300 amplifier. The eye tracking was re-calibrated to the participant's specifications. Participants were instructed to maintain their position and minimize their movement throughout the recordings. Channel impedances were checked before beginning each condition and kept below 100 kΩ. Prior to each condition participants were read the task instructions and guided through an on-screen example of the task by the researcher. The participants had the opportunity to ask for clarification and complete five practice trials which were not recorded as data. Once the participant fully understood the instructions the researcher left the testing room and the task

was initiated through an external computer used for data collection. During the data recording, the researcher continuously monitored the data acquisition and eye tracking from the external data collection computers. At the half way point in each condition participants were prompted to take a break. During this break participants remained in the room but were allowed to rest their eyes or move if needed. Any adjustments to the equipment as well as impendence check were done during this time. When ready to resume, participants informed the researcher who started the second half of the condition. Upon completion of all three conditions participants were debriefed about the study and given the opportunity to ask questions (refer to Appendix B).

Oculomotor Delayed Response Tasks

The experimental tasks were created using E-Prime (Version 2) software (Psychological Software Tools, 2004). Three ODR conditions were developed namely, Match, Non-Match and Control. The control condition EEG data showed task effects (see Nichol, 2014) and, the research questions posed by this study were of Match and Non-Match conditions; thus the control condition was not investigated (see Appendix E for a description of the control condition). The conditions were displayed on a 19” Dell computer monitor with stimuli presented on a black background. Each condition had a total of 64 trials with a break in the middle of the condition (after 32 trials). Total running time per condition was approximately eight minutes. The order in which these conditions were completed was counterbalanced.

The paradigm. The ODR conditions were designed to be game-like. Each of these conditions required the participants to maintain their gaze on a central fixation mark until a single cue would appear in one of eight possible locations around the periphery of the fixation mark. The cue would disappear, a delay period would ensue,

and when prompted, the participant would make a saccade to a location depending upon task instructions. Participants were told try not to blink during the delay period (from the moment of the cue presentation to the saccade response). All three conditions had five phases in-line with Hunter's (1913) classic delay task paradigm: Fixation (-1500-0ms), Stimulus (0-200ms), Delay Period (200-2700ms), Cue to respond & Response (2700-4200ms), and Feedback (4200-4500ms) (see Figure 3 for a visual timeline of the ODR-tasks' events). After each trial there was a 1000 ms inter-trial interval. The trials went as follows: First, an image of planet Earth was presented at the center of the monitor (fixation). Second, a star would appear (stimulus) in one of 8 positions (360 degrees) about the earth and then disappear (delay). Third a star would appear over the earth cueing (cue) the participant to act (response): The goal of the game was to protect the planet Earth from the garbage-dumping aliens by "*blocking*" the aliens. Successful *blocking* differed by condition. The specific instructions for each task are explained below.

Match Condition. The Match condition (Figure 1) was designed as a memory-guided saccade paradigm: In Match a star would appear in one of eight possible locations cuing the future location of where the participant should make a saccade when prompted. During the delay the cue is not present and no response is required. When prompted, the participant *should* make a saccade to the location where the star had appeared (cuing the location of the invading aliens) so as to *block* the aliens. A breakdown of Match is as follows:

Fixation Phase - The participant fixates on *planet Earth*, (i.e. a fixation point located in the centre of an otherwise black screen).

Cue Phase - A star flashes in one of the eight possible locations around the Earth. The location of the Cue is where the participant *should* look following the delay when prompted. Successfully remembering the Cue and generating a saccade to this location when prompted to respond will result in successfully 'blocking the aliens'.

Delay Period – The cue is no longer present and no action is required. The participant remains fixated on the image of Earth.

Response - The image of the Earth disappears cuing the participant to generate a saccade. The participant *should* look in the blank space in which the star previously appeared in order to successfully block the aliens.

Feedback - The alien appears in the initially cued location. This indicates to the participant the correct location.

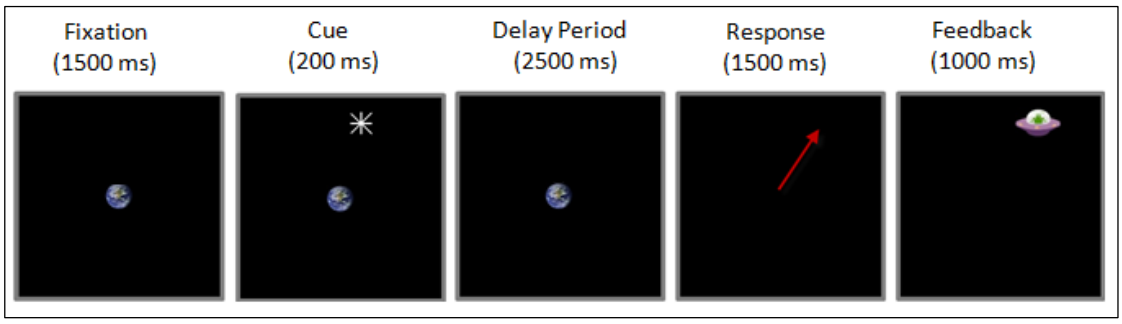

Figure 1: Match Condition Timeline. After fixation a cue appears to which particpants must look when prompted. During the delay participants fixate on the Earth until it disappears, prompting a response, i.e. participants make a saccade to the previously cued star's location. The red arrow (not actually present on the screen during experiment) shows where participants should make their saccade.

Non-Match Condition. The Non-Match (Figure 2) condition was designed as a variation of an anti-saccade task: In Non-Match the initial cue is actually of a 'forbidden' location to where the participant must *not* look when prompted. During the

delay period, the forbidden cued location is no longer present and no action is required. After the delay period, two stars appear, one of which is in the ‘forbidden’ location. This is when the participant must respond by generating a saccade to the non-forbidden (i.e. novel) location. If the participant were to make a saccade to the star that was in the new location then the aliens would be successfully blocked. Finally, feedback was provided: an ‘alien’ would appear at the correct location. A break-down of Non-Match is as follows:

Fixation Phase - The participant fixates on *planet Earth*, i.e. a fixation point located in the centre of an otherwise black screen..

Cue Phase - A star flashes in one of the eight possible locations around the Earth. This star is in the ‘forbidden’ location to which participants must *not* look when prompted. At the end of the Cue Phase the star disappears.

Delay Period - The participant remains fixated on the image of Earth. No cue is present and no action is required.

Response - The Earth disappears from the screen. Two stars appear in two of the eight possible locations, one of which is in the previously cued ‘forbidden’ location. Participants must look to the location of the new star to successfully block the aliens.

Feedback - The alien appears in the non-cued (i.e. novel) location. This indicates to the participant the correct location.

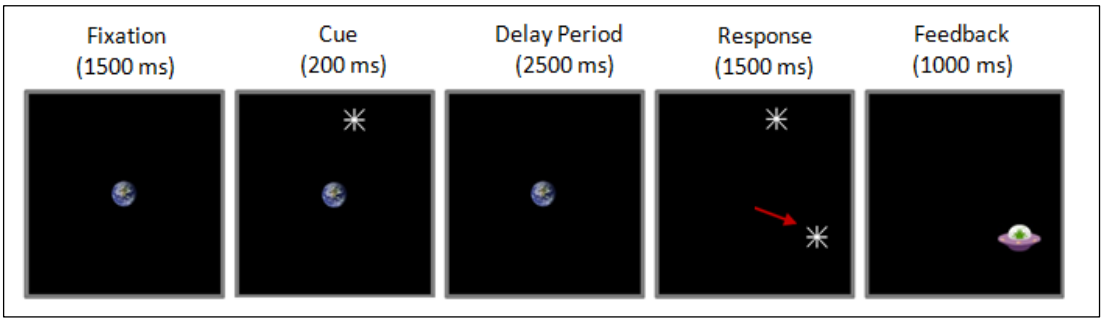

Figure 2: Non-Match Condition Timeline. After fixation on the earth a cue appears in a 'forbidden' location to which particpants must not look when prompted. During the delay, participants fixate on the Earth until it disappears. Two stars then appear one of which is in the previously cued forbidden location. Participants must make a saccade to the non-cued star. The red arrow (not actually present on the screen during experiment) shows where participants would make their saccade.

Thus, the different conditions necessitated unique cognitive processes whilst utilizing the same visual stimuli and methods of response.

Data Processing

Pre-processing and artifact rejection. Continuous EEG is a combination of physiological signals that originate from the cortex and that are related to processing, as well as signals that may not be elicited by the cortex (e.g., heartbeat, sweat, eye-movements, other movement artifacts, etc.). In cognitive EEG-ERP studies these artifacts should be cleaned from the continuous EEG before the signal processing. In this study automated pre-processing scripts were applied to both the Match and Non-Match ODR conditions. After pre-processing, the data were submitted to Infomax Independent Component Analysis (ICA) to further differentiate the biological artifacts from the cortical activity (Delorme & Makeig, 2004).

Automated pre-processing prepares the EEG data for further processing and most importantly eliminates the subjectivity of visual inspections and allows

standardizing of the data cleaning procedures. These automated pre-processing scripts were developed by Desjardins (J. Desjardins, personal communication, January 29, 2014) and were used in previous research (Desjardins & Segalowitz, 2013; Nichol, 2014). The automated scripts were run in the Shared Hierarchical Academic Research Computing Network (SHARCNet).

The pre-processing involved the following steps: 1) merging each condition (Match and Non-Match) across participants; 2) application of 2-30 Hz filters on EEG; 3) referencing the data on an average interpolated electrode; 4) identifying and rejecting noisy channels (the channels that were identified 10% of the recording were not included in the analyses); 5) identifying and rejecting bridged electrodes; (6) re-referencing the data to the averaged interpolated channel; and 7) identifying and rejecting the time windows that were contaminated by artifacts (if a designated time window was identified 10% of all the channels, that time window was not included in the analyses). The data were then submitted to Independent Component Analyses (ICA) with an N-1 channel Principal Component Analysis (PCA) reduction (Desjardin & Segalowitz, 2013). Given the fact that the EEG is composed of various sources of mixed signals, it is essential to extract the signals of interest. ICA categorizes the EEG signals as independent components, with different properties (see Hyvärinen, 2013, for the applications and recent developments of ICA). In this study ICA was used to separate cortical activity from biological artifacts (eye blinks, electromyogram, electrocardiogram, etc.).

Segmentation. Artifact free continuous EEG data from Match and Non-Match conditions were segmented using the “Cue” onset as 0 point in time. The period of -

2000 ms to 0 ms relative to the cue onset was used as the baseline and the period of 4500 ms was used as post-cue window (Figure 3). EEG for each participant was segmented according to the location of stimulus presentation (i.e., left visual field, right visual field) for Match and Non-Match conditions (i.e., 32 left match, 32 right match). Event Related Slow Potentials were plotted using Matlab, creating time frequency decompositions.

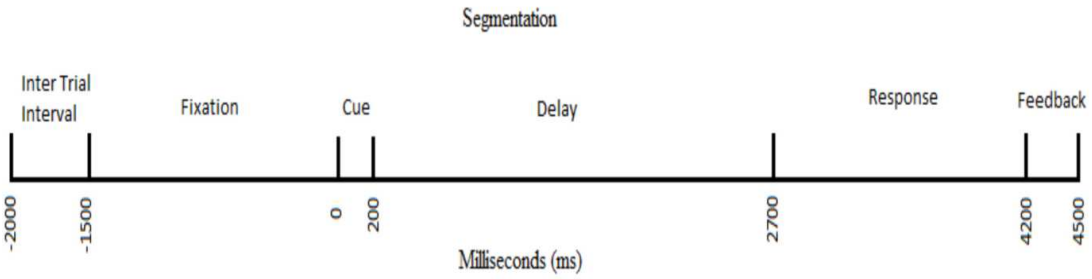

Figure 3. Segmentation of Data. Timeline of the data segmentation and the corresponding events. Copyright 2014 by Melissa Nichol. Reprinted with permission.

EEG Coherence

Time-frequency analyses and coherence statistics were computed in EEGLab (Version 13.1.1). The following steps were followed for both Match and Non-Match conditions: 1) segmented files were co-registered to the MNI head model and then standardized to 10-20 channel locations and were interpolated specifically for F3, Fz, F4, P3, Pz and P4 electrode sites; 2) a time frequency decomposition was applied to each trial of each channel using the newtimef function; 3) inputs to the function were specified to generate 600 time points for frequencies 2 Hz to 30 Hz (with a 1 Hz interval); 4) wavelet cycles started at 1 cycle at the lowest frequency and then increased by .5 cycles for each frequency up to the maximum frequency; 5) left, middle and right coherence

values were generated by calculating the correlation coefficient at each time point and frequency between F3 and P3, Fz and Pz, and F4 and P4 on the absolute values of the time-frequency complex coefficients (abs function in Matlab) using the default parameters to the corrcoef function in Matlab; this generated an r value at each time and each frequency for left, middle and right frontal-parietal power coherence; 6) the window of 500 ms to 2700ms (representing the delay period) in the alpha frequency (10Hz) was isolated and selected for each segmented file's r array; 7) the grand averages of the arrays for the electrode sites F3, Fz, F4 and the electrode sites P3, Pz, P4 were collapsed to create measures of frontal and posterior activity, respectively; and 8) a pre-written coherence function was run on the collapsed frontal and posterior sites generating two r values per participant. The two values represented delay-period, frontal-parietal, alpha coherence in the Match and Non-Match conditions. The coherence values were then entered manually into SPSS.

CHAPTER FOUR: RESULTS

Overview

Delay-period, frontal-parietal, alpha coherence values for each Match and Non-Match conditions for each participant were used in the analysis (Table 1 shows the means and standard deviations of coherence values). The data analyses were conducted in IBM SPSS (*Version* 21).

Table.1 Means and Standard Errors of Coherence Values (*r* values between frontal and parietal sites)

Table 1	Adult		Adolescent		Total	
	M	SE	M	SE	M	SE
Match	.268	.022	.207	.021	.244	.016
Non-Match	.231	.022	.298	.035	.257	.020
Total	.249	.016	.252	.022		

All data exploration and statistical analyses were performed using IBM SPSS (*Version* 21). Before the analyses the data were screened for outliers using the Boxplot function. Exploration of the data revealed two upper value outliers in the Match condition: one from the Adult group and one from the Adolescent group, and one upper value outlier in the Adult, Non-Match condition. The outliers were transformed by changing the score to the mean plus two standard deviations (Field, 2011). This method is advantageous because it reduces the severity of the score while preserving it as extreme. Following the transformation, the data was explored, and a 2 (Group) x 2 (Condition) factorial ANOVA with repeated measures on the second factor was performed. Alpha was set a .05 for all statistical analyses. Normality was assessed using Kolmogorov-Smirnov's statistic. Homogeniety of variance was assessed using

Leven's statistic. Effect sizes were reported as Pearson's Correlation Coefficient *r*.

Research Question 1. Will delay-period, frontal-parietal, alpha coherence differ across Conditions?

Hypothesis 1. Frontal-parietal, alpha coherence will differ between the Match and the Non-Match conditions.

Cell sizes were equal; there were 30 observations in Match and 30 observations in Non- Match. The data was normally distributed in Match, $D(30) = .13$, $p > .05$ and in Non-Match, $D(30) = .10$, $p > .05$.

There was a significant effect of Condition on frontal-parietal coherence, $F(1, 28) = 6.20$, $p = .019$, $r = .43$. The confidence interval for the difference between the two means did not cross zero, 95% CI [0.005, 0.049]. Frontal-parietal coherence was significantly greater in the Non-Match condition compared to the Match condition.

Research Question 2. Will delay-period, frontal-parietal, alpha coherence differ between Adolescents and Adults?

Hypothesis 2. Frontal-parietal, alpha coherence will differ between Adults and Adolescents.

Cell sizes were unequal; there were 36 observations in the Adult group and 24 observations in the Adolescent group. The data was normally distributed in Adults, $D(36) = .11$, $p > .05$ and in Adolescents $D(24) = .10$, $p > .05$. The assumption of homogeneity of variance was met $F(1, 58) = 97$, $p > .05$.

The main effect of group was non-significant, $F(1, 28) = .01$, $p = .923$, $r = .02$. The confidence interval for the difference between the two means crossed zero, 95% CIs [-0.074, 0.067]. The frontal-parietal coherence in Adults was not significantly lower

than in Adolescents.

Research Question 3. Will the pattern of change in delay-period, frontal-parietal, alpha coherence moving from Match to Non-Match differ between Adolescents and Adults?

Hypothesis 3. It is predicted that there will be a combined effect of Condition and Group on coherence.

Cell sizes were unequal; there were 18 observations in both Adult-Match and Adult-Non-Match, and there were 12 observations in both Adolescent-Match and Adolescent-Non-Match. The data was normally distributed for Adult-Match, $D(18) = .13$, $p > .05$, Adult-Non-Match, $D(18) = .13$, $p > .05$, Adolescent-Match, $D(12) = .21$, $p > .05$ and Adolescent-Non-Match, $D(12) = .17$, $p > .05$. The assumption of homogeneity of variance was met for Match, $F(1, 28) = 0.24$, $p > .05$ and Non-Match, $F(1, 28) = 0.24$, $p > .05$.

There was a significant Group X Condition interaction, $F(1, 28) = 35.31$, $p = .000$, $r = .75$. The observed effect was large (Field, 2011). A disordinal interaction was visibly apparent (see Figure 4).

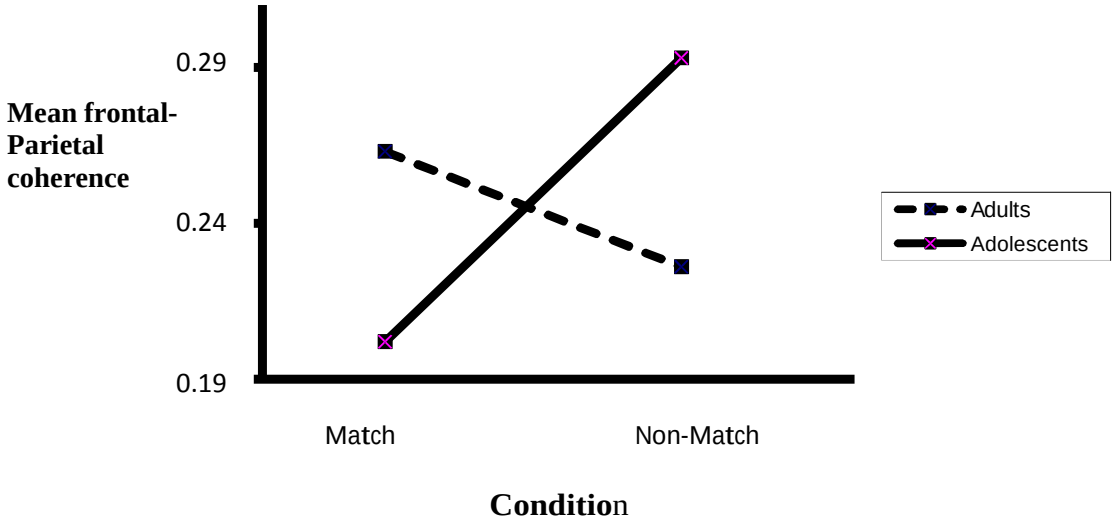

Figure 4. Group x Condition Interaction

The Group x Condition interaction was further analyzed to investigate the simple effects. First, the simple effect of Group (Adult, Adolescent) within each level of the ODR condition was analyzed. Cell sizes were unequal for the simple effect of Group.

Within the level of Match, the effect of Group was non-significant, $F(1, 28) = 3.50$, $p = .072$, $r = .33$. The confidence interval for the difference between the two means crossed zero, 95% CI [-0.006, 0.126].

Within the level of Non-Match, the effect of Group was also non-significant, $F(1, 28) = 2.87$, $p = .102$, $r = .30$. The confidence interval for the difference between the two means crossed zero, 95% CI [-0.148, 0.014].

Second, the simple effect of Condition (Match, Non-Match) within each level of group was analyzed. Cell sizes were equal for the simple effect of Condition.

Within the Adult group, the effect of condition was significant, $F(1, 28) = 7.45$, $p = .011$, $r = .45$. The confidence interval for the difference between the two means did not cross zero, 95% CI [0.019, 0.056].

Within the Adolescent group, the effect of condition was also significant $F(1, 28) = 29.63$, $p = .000$, $r = .71$. The confidence interval for the difference between the two means did not cross zero, 95% CI [-0.141, -0.04].

Therefore, in Adults, delay-period, frontal-parietal, alpha coherence was significantly higher in Match compared to Non-Match. The size of this effect was medium (Field, 2011). In Adolescents, coherence was significantly lower in Match compared to Non-Match. The size of this effect was quite large (Field, 2011).

CHAPTER FIVE: DISCUSSION

Research has elucidated developmental brain changes during adolescence; however, research into neural oscillation and development is rather limited (Basar, 2012). ODR tasks in particular activate frontal-parietal regions and are thus deemed valuable tools in the investigation of WM in relation to brain development (Curtis, 2006; Geier et al., 2009; Klingberg, 2006; Klingberg et al., 2002; Machinskaya & Kurgansky, 2012). The overall goal of this study was to explore delay-period, frontal-parietal EEG coherence in the alpha band frequency as an index of possible developmental change across two age groups, as well as a possible index of change in cognitive strategy across tasks. This study is unique as it is one of the few studies to combine EEG with ODR tasks to explore WM across tasks and across development. For example some studies have used ODR tasks to investigate changes in brain activity across WM tasks using EEG (see for example, Dhawan et al., 2013) and fMRI (see for example a review by Curtis, 2006), and some studies have investigated WM across development (see for example, Klingberg et al., 2002; Machinskaya & Kurgansky, 2012); however, no study has yet looked at how EEG coherence patterns may show unique task-dependent changes depending upon age. Using EEG was of particular importance as other techniques, such as fMRI, rely on the change in resource allocation to neuronal populations in order to infer brain region activity; in contrast, changes in EEG, such as signal amplification and coherence, can be detected regardless of resources used (Thatcher, 2012). Thus, for example, the firing of neurons in synchrony can amplify an electrical signal geometrically without a geometric increase in resources, resulting in EEG's provision of purer and greater information about the activity of the

brain compared to other brain imaging methods (Thatcher, 2012). Hence, EEG may be useful in ascertaining the subtle changes that occur during development and may subsequently inform early detection measures and interventions of WM difficulty (Klingberg, 2014). In fact, if the normal electrophysiological developmental trajectory of WM is well understood, then EEG may be used to detect difficulties before they can be accurately detected by behavioral measures (Klingberg, 2014). Early identification is one of the most important factors in successful intervention (Bjorklund, 2005).

The present study used a two-leveled, ODR-WM task to investigate delay-period, frontal-parietal, alpha band, EEG coherence changes across ODR tasks (Match, Non-Match) and across age groups (Adult, Adolescent). A significant Group x Condition interaction was found and this effect was large. Adolescents showed greater coherence during Non-Match than Match, whereas Adults showed the opposite pattern. The effect of Condition within the Adolescent group was large, whereas the effect of Condition within the Adult group was medium. The interaction, interpreted within the limits of this study, suggest that complex qualitative changes may be occurring during adolescence. Luna, Garver, Urban, Lazar and Sweeney (2004) found that cognitive processes including, reaction time, cognitive control and WM, develop non-linearly from childhood to adulthood. Moreover, fMRI research has offered empirical support that there are qualitative differences in structural brain development (Draki & Klingberg, 2014), brain region recruitment (Geier et al., 2009; Luna et al., 2001), and functional connectivity (Fair et al., 2009) between children, adolescents and adults. In particular, the development and refinement of white matter is thought to underlie many cognitive skills, including WM (Asato et al., 2010; Barnea-Goraly et at., 2005), where white

matter has also been described as developing non-linearly (Lebel, Waker, Leemans, Phillips & Beaulieu, 2008). Importantly, adolescence was described as involving a "qualitatively unique state of white matter maturation" (Asato et al., 2010, p. 2128). The uniqueness of adolescent brain development may be related more so to puberty (which correlates with age) than with age itself (Dahl, 2008; Spear, 2000; Steinberg, 2008), where this would also offer some explanation regarding sex differences in trajectories of both cognitive and white matter development (Asato et al., 2010). Qualitative changes in white matter development during adolescence could underlie the observed significant interaction between age group and type of WM task and the large effect of condition on adolescent coherence values.

The present research showed that WM resources may be recruited differently by adolescents and adults depending upon the specific demands of the ODR-WM task (Match, Non-Match). Specifically, adult coherence values were significantly higher in Match than in Non-Match, whereas Adolescent coherence values were significantly lower in Match than in Non-Match. Both Dhawan et al., (2013) and Curtis et al., (2005) used a very similar ODR-WM paradigm with comparable Match and Non-Match levels to investigate WM in adult participants. Their findings contradict one another yet may offer some context for the specifics of the present study's findings. First, Dhawan et al., (2013) described that there were attentional costs to the cued location in Non-Match and enhanced attention to the cued location in Match. The attentional costs (also referred to as selective inhibition) observed during Non-Match were posited as owing to the conflicting cognitive demands unique to the Non-Match task (i.e. the demand on WM to remember the location of the 'forbidden' cue, as well as the conflicting demand to generate a saccade to the non-forbidden location in the near

future) (Dhawan, et al., 2013). Dhawan et al., (2013) concluded that these conflicting demands in Non-Match were resolved by reducing attention to the cue in order to permit flexible responses when prompted (where participants presumably relied on only a faint memory trace of the forbidden cued location to inform saccade genration). Second, contrary to Dhawan et al., (2013), Curtis et al., (2005) described enhanced attention to the cued location during Non-Match. Curtis et al., (2005) posited that the Non-Match task biased participants toward a retrospective coding strategy; participants were presumably rehearsing the location of the forbidden cued location. In the present study the results do not necessarily indicate enhanced attention, attentional costs, or retrospective coding strategy. This is because coherence in the alpha band was measured, and, as described, there is no consensus as to the exact function of alpha (Basar, 2012). Specifically, the significantly higher coherence in Non-Match within the Adolescent group could represent either enhanced attention (such as retrospective rehearsal), or increased inhibition (reducing attention to the forbidden cue), where, again, the opposite pattern was observed for adults.

In sum, within the limits of the present study, the interaction finding holds particular developmental significance and indicates that adults and adolescents may recruit frontal-parietal resources differently depending upon the specific demands placed on WM by the task at hand; however, whether changes in alpha coherence reflect enhanced attention, inhibition or other cognitive processes, cannot be concluded.

Overall, this study contributes to a growing understanding of the electrophysiological, developmental trajectory of WM.

Limitations and Future Directions

Overall, it seems that different task demands result in different strategic uses of WM

resources in adolescents and in adults. In adolescents this effect is large. These strategy changes may follow from the differences in the structure and function of the underlying networks (i.e. more myelinated fiber tracts between frontal and posterior brain regions resulting in faster communication between these areas) (Asato et al., 2010). Unfortunately this study did not collect data regarding the accuracy of the eye movements generated; it is possible that differences in accuracy between adults and adolescents occurred in one or both of the conditions. Knowing the differences in accuracy between groups could offer some indication as to whether the potentially different strategies used by the adolescents were advantageous or detrimental to task performance. More research is needed to elucidate the cognitive strategies that may underlie the different patterns of coherence in each of the age groups.

Second, sample size, unequal cell sizes and non-random sampling limits this study. For example, the simple effects analysis did not reveal any significant difference between age groups within either level of ODR condition; that is, within Match, coherence was not significantly higher in Adults than in Adolescents and within Non-Match, coherence was not significantly lower in Adults than in Adolescents. However, cell sizes were small and unequal in this particular portion of the analysis (18 and 12, for Adults and Adolescents respectively). A larger sample size (and equal cell sizes) would have provided greater precision of the averaged EEG data and increased statistical power, possibly revealing that adult and adolescent coherence values differ significantly within each level of the condition. Additionally, snowball and convenience sampling was used. Random sampling of a larger population would have offered greater confidence in the independence of observations and supported generalizability. Finally, this study followed the Null Hypothesis Significance Testing model with alpha set at the typical level of .05.

This model is intrinsically flawed (see Cohen, 1994; Field, 2011). However, the present study attempted to address some of the limitations of this model by including effect sizes and 95% confidence intervals of the mean differences (see Cohen, 1994; Field, 2011). Third, research using scalp EEG electrode site coherence to investigate higher cognitive functions is relatively new (see for example, Lee et al., 2012; ten Caat et al., 2008) depriving this study of substantial context. Moreover, this study offers only a very limited glimpse into what is happening in the brain during the delay period of WM. For example, while not addressing the question as to the overall functionality of alpha activity, this study used coherence in the alpha frequency as an index to elucidate possible differences in delay period activity across Age and Condition. Alpha represents only a small band of a range of frequencies produced by the brain (Luck, 2005). As an analogy, many neurotransmitters and hormones are implicated in any given higher cognitive function (Sapolsky, 2012). Moreover, neurotransmitters and hormones have different actions at different sites and in different contexts (Sapolsky, 2012). Likewise, other frequencies may synchronize during WM (Palva & Palva, 2011) and may do so between different brain regions (Roux & Uhlhaas, 2014). Specifically, coherence can be investigated in same frequency bands (e.g., alpha-alpha) (Palva & Palva, 2012) and different frequency bands (i.e. alpha-gamma) (Roux & Uhlhaas, 2014). For example, research by Roux and Uhlhaas (2014) suggests that the coding of distinct WM information is accomplished via the coupling of alpha-gamma and theta-gamma, and research by Kawasaki and Yamaguchi (2013) suggests that theta and beta synchronize when a monetary reward is expected for successful WM performance. Finally, research has also begun to investigate phase-amplitude coupling (see, for example, van der Meij, Kahana, & Maris, 2012). Thus this study is

limited in scope.

Fourth, the use of averaging in this study is another limitation. Recent research using fMRI with adolescent and adult subjects has shown age-dependent lateralization during spatial WM tasks (Nagel, Herting, Maxwell, Bruno, & Fair, 2013). However, in the present study, the EEG data from three electrode sites were combined to create a frontal index and a posterior index of alpha activity. It is possible that investigating coherence between any two distant electrodes rather than the two groups of three electrodes, could have produced different results (Lee et al., 2012). For example, the electrodes on one hemisphere may show greater or lesser coherence than the electrodes on the other hemisphere (von Stein, Rappelsberger, Sarnthein, & Petsche, 1999). Moreover, cues came either to the left of right visual fields and it is possible that coherence may also change as a result of hemi-field presentation; for example a hemi-field presentation effect has been observed for semantic stimuli (Coulson, & Van Petten, 2007). This study also averaged the EEG activity from the entire delay period (500ms-2700ms). Nichol (2014) and Sanderson (2013) found that there are differences in slow wave activity in early versus late delay. It is possible that alpha coherence may also differ across the delay period time window.

Fifth, the lack of a good control condition limits this study. Future researchers should include a well-designed control condition so as to investigate how each age group differs from its own baseline.

Sixth, the present study analyzed EEG data only. In the future, other behavioral measures such as accuracy and reaction time should be recorded (for example through the utilization of eye tracking technology and software). Other aspects of context could

also be explored. For example, in a unique, recent EEG-WM study, with adult participants, Kawasaki & Yamaguchi (2013) found an effect of reward on coherence; specifically, there was synchronization of beta and theta only under high reward conditions. These results suggest a functional dynamic link between WM and reward networks (Kawasaki & Yamaguchi, 2013). Research has shown that adolescents respond differently than adults depending on context (e.g., the possibility of reward and the presence of peers) (Albert, Chein & Steinberg, 2013), and brain imaging techniques have described this difference physiologically (Van Leijenhorst et al., 2010). Given these past studies, it would be interesting to replicate the present study and add the possibility of different levels of reward or add the presence of peers, and compare adolescents and adults under these conditions.

Seventh, the present study investigated the difference in coherence between two age groups: Adolescents (14-17) and Adults (18-33). It is important to replicate this study with younger (<14) and older (>33) participants in order to capture the entire developmental trajectory of coherence during WM. It may also be useful to use a regression analysis to track age changes rather than divide participants into age groups. This study did not investigate possible sex differences, where differences in myelination patterns and WM ability may differ by sex in adolescence (Asato et al., 2010). Interestingly, there is evidence that separating adolescents according to pubertal status (and sex), rather than age, may be a better strategy; pubertal status correlates more strongly with white matter development in the adolescent brain than age, and white matter development may underlie cognitive development (Asato, et al., 2010). Additionally, a recent study found a significant relationship between WM

performance and cortical volume reduction in frontal and posterior brain regions that was not explained by gender, intelligence, or age differences (Tamnes et al., 2013). In this study, age did not interact with this relationship; thus its findings strongly support the view that structural maturation of the frontal-parietal cortical network underlies WM development (Tamnes et al., 2013).Unfortunately, overall, research in this area is lacking (Tamnes et al., 2013).

Finally, the data from this study were collected from healthy participants. This data may be used as a baseline for future research into clinical populations (e.g., anxiety disorders, learning disabilities, and ADHD).

Conclusion

WM is critical for many cognitive functions (Funahashi, 2006; Kawasaki, 2012; Klingberg, 2014; Wager & Smith, 2003), and persons with clinical conditions such as learning disabilities, ADHD and borderline personalities all show low WM abilities (Alloway & Alloway, 2013). Importantly, WM is responsive to intervention in adults (Brehmer et al., 2012) children (Alloway & Alloway, 2013; Klinberg, 2014), and children with identified WM difficulty (Green et al., 2012; Holmes et al., 2009; Klingberg et al., 2005). Thus, elucidating how WM networks operate across development and according to differing task demands is critical in informing future interventions (Klinberg, 2014). The findings of the present study hold developmental significance and indicate that adults and adolescents may recruit frontal-parietal resources differently depending upon the specific demands placed on WM according the context of the task. Research has already elucidated developmental brain changes during adolescence; however, research into neural oscillation and development is rather limited (Basar, 2012; Tamnes et al., 2013). ODR tasks in particular activate frontal-parietal

regions and are thus deemed valuable tools in the investigation of WM in relation to brain development (Curtis, 2005; Draki & Klingberg, 2014; Geier et al., 2009; Olsen et al., 2003). The overall goal of this study was to explore how delay-period, frontal-parietal EEG coherence in the alpha frequency may indicate possible developmental changes across age, as well as different cognitive strategies across tasks. This study is unique as it is one of the few studies to combine EEG with ODR tasks to explore WM in this manner (see also, Dhwan et al., 2013; Geier et al., 2009).

The present EEG ODR study was grounded in literature suggesting that neural oscillations are instrumental in generating transient, widespread networks (D'Esposito, 2007; Fries, 2005; Fuster, 2008; Fuster & Bressler, 2012; Thatcher, 2012). Further, consistent with the findings of the present study, other fMRI and EEG research using similar paradigms have demonstrated that different networks are implicated in Match versus Non-Match WM tasks (Curtis & D'Esposito, 2003, Curtis et. al., 2004; Dhawan, et al., 2013; Geier, et al., 2009). These findings can be interpreted within the context of the PAC. For example, Fuster (2008) describes that WM bridges perception and action when the perceived stimulus is no longer present in the environment but is necessary for informing imminent action. Curtis (2006) notes that WM operates differently depending on the task demands; specifically, Match and Non-Match bias coding to be prospective and retrospective, respectively. Dhwan et al. (2013) further claim that Non-Match also requires the specific suppression of attention, while Hanslmayr et al., (2011) contend that attention may be more internally focused in Match-like conditions and externally focused in Non-Match conditions. Thus WM, understood from the cognit model, may in fact represent several WM cognits, each operating under specific conditions and

demands. This study investigated this possibility, as well as the possibility of age-related changes in these networks.

This study averaged EEG data recorded during the delay period of a WM ODR task from three frontal and three parietal scalp electrode sites. An average coherence value between these two locations for the entire delay period was calculated for each participant in each condition. The results of the present study suggest that WM cognits develop qualitatively. Adolescents' frontal-parietal coherence was greater in Non-Match condition than Match, whereas Adults' frontal-parietal coherence was greater during Match condition than Non-Match. The effect of condition within the adolescent group was large. This result is consistent with recent longitudinal research showing that white matter development and WM functioning (Asato et al., 2010) and changes in cortical and subcortical volume (Tamnes et al., 2013) may be developing in a more dynamic and less quantitative manner during adolescence than previously thought (Draki & Klingberg, 2014). Such complex development, as is suggested by this study, is also congruent with theories that describe higher cognitive functioning as an emergent property of the brain (D'Esposito, 2007; Fuster, 2008; Fuster & Bressler, 2012; Postle, 2006; 2014); that is, understood as an emergent property, WM could demonstrate the inverse U-shaped pattern consistently observed across the human lifespan (Sander et al., 2012; Zollig et al., 2010) while not necessarily corresponding on a one-to-one scale with changes to any given brain structure (for example, white matter) or function (for example, alpha coherence). In conclusion, this study offers a small but important contribution to an area of investigation requiring more research.

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Appendix A

Brock University
Research Ethics Office
Tel: 905-688-5550 ext. 3036
Email: reb@brocku.ca

Ethics Board

Certificate of Ethics Clearance for Human Participant Research

13

PRINCIPAL INVESTIGATOR: TEKOK-KILIC, Ayda - Psychology

E: 10-211 - TEKOK-KILIC

Faculty Research STUDENT: SUPERVISO Ayda Tekok-Kilic

TITLE: Visual spatial working memory: What does saccade-related brain activity tell us?

ETHICS CLEARANCE GRANTED

Type of Clearance: RENEWAL Expiry Date: 3/31/2014

The Brock University Bioscience Research Ethics Board has reviewed the above named research proposal and considers the procedures, as described by the applicant, to conform to the University's ethical standards and the Tri-Council Policy Statement. Clearance granted from **3/19/2013 to 3/31/2014.**

The Tri-Council Policy Statement requires that ongoing research be monitored by, at a minimum, an annual report. Should your project extend beyond the expiry date, you are required to submit a Renewal form before **3/31/2014.** Continued clearance is contingent on timely submission of reports.

To comply with the Tri-Council Policy Statement, you must also submit a final report upon completion of you project. All report forms can be found on the Research Ethics web page at http://www.brocku.ca/research/policies-and-forms/research-forms.

n addition, throughout your research, you must report promptly to the REB:

a) Changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) All adverse and/or unanticipated experiences or events that may have real or potential unfavourable implications for participants;
c) New information that may adversely affect the safety of the participants or the conduct of the study;
d) Any changes in your source of funding or new funding to a previously unfunded project.

We wish you success with your research.

Approved:

Brian Roy, Chair
Bioscience Research Ethics B

Brock University is accountable for the research carried out in its own jurisdiction or under its auspices and may refuse certain research even though the REB has found it ethically acceptable.

Appendix B

Developmental Neuroscience Lab, Brock University
Feedback Form
Project Title: Visual spatial working memory: What does saccade-related brain activity tell us?

Dear Participant,

Thank you for taking part in this study. Without the help of volunteers like you, this research would not be possible.

As you know we measured EEG and monitored your eye-movements while you completed very simple computer games that required you to maintain specific spatial locations in mind. Holding or manipulating information in your mind over a short period of time is referred to as "working memory" and is fundamental to both basic and complex thinking in human beings. In this study, we are specifically interested in how children and young adults are able to hold spatial information in working memory and use that knowledge to properly guide the eyes to the locations required in our computer game.

The working memory functions you needed to use in this study are supported by various regions of the brain including the dorsolateral prefrontal cortex and frontal eye fields (both in the front of the brain) as well as the inferior parietal lobule (located about several centimetres behind and above your ears). Understanding how these different areas support the storage of spatial information and are used to guide the movement of your eyes is of great interest to cognitive neuroscientists. By recording brain responses in children of various ages, we can chart the development of the different neural structures involved in spatial working memory and the control eye movements. This information can also be used to identify and understand abnormal developmental trajectories in spatial working memory as well how damage to the brain (from head injuries or disease) can be expected to impact mental skills and behaviour.

As you are aware from the consent form, all of your data will be kept strictly confidential and when the data is presented, you will not be identified in any way.

If you would like to learn more about the results of this study, feel free to contact the principle investigator (see below). However, please be advised that it takes several months to complete data collection and then to process the data and perform necessary analyses. Thus, preliminary results are not likely to be ready before the summer of 2011.

If you have any issues that you would like to discuss regarding your involvement in this study, you may contact the Brock Research Ethics Board through the Research Office at 905-688-5550, Ext: 3035, File # 10-211.

Thank you again for taking part in this study. Your help was very much appreciated. Principle Investigator:

Dr. Ayda Tekok-Kilic
atekokkilic@brocku.ca
Lab Phone: 905-688-5550, Ext: 3347 Office Phone: 905-688-5550, Ext:3937

Appendix C

TELEPHONE SCRIPT – For Undergraduate Volunteers

Name _____ Phone _____

Thank you for calling. My name is _____. Let me first tell you about the study. We are interested in how thebrain supports performance on tasks requiring attention and memory. We are studying brain and cognitive development as humans grow and change from young children into adults. We would like you to come to the Developmental Neuroscience Lab at Brock University for a single 2 hour session. During this session, you will complete 3 versions of a computerized memory task in the form of a game while we use EEG to monitor your naturally occurring brain response and visual sensors to monitor the direction of your eye movements.

Of course, we will explain all procedures to you fully when you arrive at the lab before you begin. But I

can answer any general question you might have right now (give any practical or technical information required). If you think you might be interested, can I ask you a few health-related questions to see if the study would be appropriate for you. Is this alright? This and all other information is kept strictly confidential.

1. What is your birth date? _____
2. Approx years of education? _____ Right or left-handed? _

3. Do you have any visual problems? _____ Yes No

4. Do you have any major health conditions? _____ Yes No

6. Do you have any conditions that could affect nervous system function? Yes No

(e.g., multiple sclerosis, epilepsy, fibromyalgia?)

7. Do you have diabetes, 83ypoglycaemia, lupus, chronic fatigue syndrome? Yes No

8. Have you ever had any serious psychiatric difficulties? Yes No

(e.g. diagnosed ADD, clinical depression___, other?_____)

9. Have you ever had a head injury or concussion? If yes:_____ Yes No

If serious visual problems, or serious physical, neural or mental condition say.....

Having _____ could affect the physiological responses that we will be measuring so I'm afraid that this study won't be appropriate for you . However, if you are still interested, we could send you some information about the outcome of the study when it's ready. Also, there may be other studies coming up where _____ would not be an issue. If you like, I can put your name on a list and we could contact you about participating at another time.

If health screening is passed say: That all seems fine. However, since we will be collecting EEG, there are a couple of other things I have to ask:

Do you use non-permanent hair dye? _____

Is your hair extremely thick? _____

In corn rolls? _____

Dreadlocks? _____

Anything else that might make fitting a tightly fitting cap difficult?

Would it be alright for you to not wear makeup (or remove any makeup) the day you come for the study?

If they meet criteria and are willing to participate …

OTake contact info, arrange an appointment, and describe how to get

to the lab.

O If they wear contacts, suggest wearing glasses that day instead.

O Remind them that this is entirely voluntary and that they are free to withdraw at any time if they wish.

O Tell them that we can email or call to give a reminder prior to their visit. O THANK THEM!

Contact Information: Appointment Date:

Appendix D

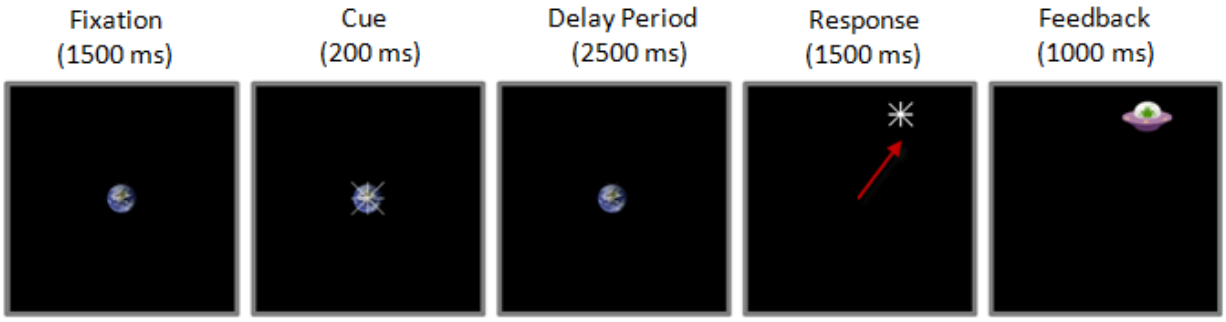
Dear Participant:
This form provides you with the information you will need to make an informed decision about whether or not you would like to participate in our study on working memory development. Please read it over carefully and if you have any questions, you are welcome to phone the research coordinator, William Tays (905) 688-5550 ext. 3347 or, or myself (Dr A. Tekok-Kilic) at ext. 3937 for clarification.
The goal of this study is to investigate brain function while participants take part in game-like computer tasks. We believe that this study will lead to a richer understanding of the brain mechanisms underlying the functionality of working memory processes and its development.
WHAT IS INVOLVED
The study will take place at the Developmental Neuroscience Lab. You will be asked to come to the lab for a 2 hour session. All of the tasks and procedures will be explained to you and we will review this letter with you so you have a full understanding of what is involved before we begin.
A soft, elasticized sensor cap is placed on the head to record naturally-occurring brain activity while you engage in a series of game-like computer tasks. The tasks do not involve motor responding (such as pressing a key) but they involve directing eye gaze to specific locations cued by visual stimuli on a computer screen. Eye gaze is measured by analyzing real-time images taken from two digital cameras attached to the computer monitor. These cameras do not store the images they measure. They only record digitized landmarks that represent your eyes and face. It will take about 30 minutes for all of the set-up we require, during which time you can relax or ask us questions. There will be three 15 minute computer tasks presented sequentially during the study. Including extra time for breaks, the entire session is expected to take 2hours and there will be a $20.00 honorarium for volunteering your time. POTENTIAL RISKS AND BENEFITS
There are no risks involved in this study. Benefits include introducing participants to research. The techniques and procedures will be fully explained to you and you will be free to ask questions throughout. Most participants find it interesting to see their brain waves and eye tracking on the computer screen. As well, young people often feel good about taking part in a project that could increase our scientific understanding of the factors that influence brain development.
CONFIDENTIALITY
All information gathered is kept completely confidential. Names are replaced with code numbers and it is these code numbers that are entered into our data base along with the physiological information. They will be stored in a restricted-access laboratory, only researchers working on this project will have access to these data and all records of the information will be destroyed when no longer required. You would
never be identified in any way when the data are published in academic journals or presented at scientific conferences.
PARTICIPATION IS VOLUNTARY
Participation in this study is entirely voluntary. You may refrain from participating in any component of this study. As well, you may decide to withdraw from this study at any time without penalty even after signing this form.
SECONDARY USE OF THE DATA
The present investigation is designed as a pilot project and therefore the results will be preliminary. The researchers may decide to re-analyze the data in the future. This is considered as “secondary data analyses” and will only be conducted if you give your consent.
CONTACT INFORMATION
If you have any questions about this study or if you would like further information, please contact the project coordinator, Carleigh Sanderson (contact information above). This study has received ethics clearance from the Research Ethics Board of Brock University (#10-211). If you have any comments or concerns about the rights of a research participant, please contact the

Research Ethics Office at 905-688-
5550, Ext. 3035.
Thank you for considering this project. If you would like to participate, please return a signed copy to the lab in the envelope provided but keep the extra copy for your records.
CONSENT
I agree to participate in the study described above. I have made this decision based on the information provided above and have had the opportunity to receive any further details and understand that I am
welcome to ask any further questions in the future. I also understand that I can withdraw this consent at any time without penalty even after signing this form.
Participant's Name: _____
Signature: _____Date: _____
I also agree on the secondary use of the data collected for this research by the researchers in future research.
Participant's Signature: _____
This participant received research participation hours ( ) or an honorarium ( ).

Appendix E

Control Condition

The control condition was designed to provide a baseline measure of EEG data, saccadic movement, and cortical activation. The cue stimulus was overlaid on the fixation stimulus and participants were instructed to prepare for the generation of a saccade. During the response period, a star stimulus (identical to the cue stimulus) was presented in one of the eight spatial locations around fixation. Participants were required to make a saccade to the cued location and maintain gaze until feedback stimulus appeared.



Control Condition Timeline. Participants fixate on the Earth until it disappears and participants make a guided saccade to the star. The red arrow (not actually present on the screen during experiment) shows where participants would make their saccade.

Fixation Phase – The participant is instructed to fixate on an image of the planet Earth which is located in the centre of the screen on a black background.

Cue Phase – A star flashes on top of the Earth to warn the participant that the alien is about to appear in one of the eight locations surrounding the Earth.

Delay Period – The participant must remain fixated on the image of planet Earth waiting for the alien to appear.

Response – The planet Earth disappears from the screen and a star appears in one of the 8 possible locations. The participant must look to that location, as the star is an indicator that an alien will be appearing in that location to dump its garbage on Earth.

Feedback – The star disappears and the alien appears in that location indicating that the alien was coming from that location to dump its garbage. The participant looks at the alien.