Examining the effects of aerobic exercise and bilateral movement on frontal alpha asymmetry

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Robert Allan Hicks

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Robert Allan Hicks

Abstract

Determining the effects of different interventions on brain activity related to depression is imperative to prevention and treatment of the disorder. One measure of brain activity related to depression, called "frontal alpha asymmetry" (FAA), measures differences in resting brain activity between the left and right prefrontal cortices. Using electroencephalography, measuring differences in resting alpha activity between these two regions is theorized to help quantify an individual's predisposition to depression. This thesis, comprised of two studies, aimed to investigate the influence of aerobic exercise and bilateral rhythmic movement on FAA in young healthy adults. Study 1 investigated the test-retest reliability of FAA within a two-day period in order to first understand the short-term stability of FAA. Results showed that FAA has low to moderate test-retest reliability in this time period, while its contributing alpha powers had moderate to high test-retest reliability. It was concluded that FAA is stable to use in a repeated measures design, however, should be accompanied by its contributing alpha powers to inform any observed changes. Study 2 aimed to investigate the effects moderate aerobic exercise and bilateral rhythmic movement on FAA. Results showed that aerobic exercise caused a significant increase in FAA scores 22-38 minutes post intervention. Furthermore, bilateral rhythmic movement did not lead to a significant change in FAA at any time point post intervention. Results from this study suggest that there must be some physical demand to positively influence FAA. Further research should investigate these effects in a clinically depressed population to help understand how aerobic exercise may help in treatment of depression.

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1.0 Introduction

There is developing evidence of unique relationships between asymmetrical brain activity and observable behaviours. It is well established that the left and right hemispheres of the brain are not symmetrical, neither in structure nor function. Obvious examples of this include language comprehension and production, both of which are mainly processed in the left hemisphere (Cohen, 2012). It is likely that more subtle differences between the left and right hemispheres exist as well that will provide insight to how different processes lead to certain behaviours. This is of particular importance when considering these asymmetries and how they contribute to the understanding of dysfunction and mental illness. Another important component to this field of research is determining factors or stimuli that influences these asymmetries. Harnessing the utility of these factors can lead to better interventions to influence a person's behaviour in a positive way. Of interest are factors that influence prefrontal cortex (PFC) activity due to its role in cognition and behavioural control (Miller & Cohen, 2001). The PFC is responsible for top-down control of human behaviour that is formed by internal goals or intentions (Miller & Cohen, 2001). This control is commonly referred to as "executive function", which is a multidimensional construct of "effortful" processes that inhibit stereotyped behaviour in order to execute those that will result in goal achievement (Banich, 2009). There is growing evidence that the PFC has asymmetrical processing in the left and right hemispheres (Coan & Allen, 2004; Sterpenich et al., 2014; Xue et al., 2013). For example, compared to healthy people individuals suffering from depression commonly exhibit a relative decrease in left frontal activity compared to the right (Henriques & Davidson, 1991). This difference is thought to contribute to a lack of motivation which is a common symptom in depression. Interestingly, increasing the activity of

the left PFC in individuals with depression via transcranial magnetic stimulation (TMS) has been shown to decrease symptoms (George et al., 2000; Vanneste et al., 2014). It has yet to be determined, however, whether this results in increased motivation related behaviours in this population.

This relationship between left and right PFC activity is commonly referred to as "frontal asymmetry" and has been demonstrated to relate to both trait and state modulations in an individual's affect and motivational tendencies (Coan & Allen, 2004). Frontal asymmetry is most commonly measured using electroencephalography (EEG) by the difference in the alpha frequency band (8-13 Hz) power density between left and right frontal electrodes. Alpha frequencies are used as an inverse measure of cortical activity as it is hypothesized to correspond with cortical inactivity or idling (Laufs et al., 2003; Oakes et al., 2004). Therefore, greater alpha power levels in left versus right electrodes would exhibit relatively greater right than left cortical activity. This specific measure is referred to as frontal alpha asymmetry (FAA).

FAA has been used in several types of studies that investigate it both as a trait measure and as a state-related measure. Although it has been shown to relate to trait constructs of emotional processing (Davidson, 2002) it is well established that it is subject to state fluctuations (Hagemann et al., 2002). Studies investigating the test-retest reliability of FAA have shown low to moderate stability over periods of 2-weeks to 3 years with retest correlations between 0.50 and 0.79 depending on electrode and reference scheme used (Allen et al., 2004; Tomarken & Davidson, 1992). The high level of variability of this measure means conclusions regarding its changes along with motivational processing must be considered with skepticism until the sources of state fluctuations are determined. A potential state influencer that has been investigated in this field is aerobic exercise and its relationship to FAA both in trait and state paradigms. It has been

shown that 30 minutes of moderate intensity aerobic exercise promotes an asymmetry having relatively greater left than right cortical activity (Woo et al., 2009, 2010). These findings would suggest a beneficial effect of aerobic exercise on state-related FAA and may provide a partial explanation to the preventative effects of aerobic exercise on mood disorders.

In the present thesis, young healthy adults were recruited to investigate the potential influence of aerobic exercise and bilateral movement on FAA. The first objective of this thesis was to measure the short-term stability of FAA over two daytime periods and between two days. This knowledge is necessary to better understand the reliability of using state changes in FAA to form adequate conclusions for subsequent studies focused on within-subject differences associated with exercise. The second objective was to further establish a possible influence of aerobic exercise on FAA. This was conducted using a resting control and a 'no load' cycling task to determine if these effects are due to the movement component of exercise or due to the exercise itself. This research will lead to a greater understanding of the important relationship between aerobic exercise and brain activity related to motivation. It may guide future research on the use of aerobic exercise in the prevention and treatment of mood disorders.

2.0 Literature Review

2.1 Cortical Asymmetry: Structures and Functions

It is well established that significant asymmetries exist in the human brain. This includes both structural and functional differences between the left and right hemispheres. Gross structural examples include protrusion of the right hemisphere past the left anteriorly and vice versa for the left posteriorly. Also the right frontal region is commonly wider than the left and vice versa for the occipital region (Cohen, 2012). One major functional example is the differences between the left and right hemispheres in language and auditory processing. Both language comprehension and speech production occur mainly in the left hemisphere while pitch and musical processing mainly occurs in the right hemisphere (Cohen, 2012). This processing of sound occurs in Brodmann's area 22, which also has structural differences between the two hemispheres. Neuronal clusters in the left area 22 are spaced approximately 20% further apart and are interconnected via longer axons when compared to area 22 in the right hemisphere (Galuske et al., 2000). Language processing asymmetry is evident in development as well. When infants begin to babble, most commonly babble with right mouth asymmetry, which may be an indication of prelanguage development as opposed to random motor activity (Holowka & Petitto, 2002). This functional asymmetry corresponds with a large structural asymmetry that occurs in the planum temporale, an area just posterior to the auditory cortex. In 65% of people the left planum temporale is larger in the left than the right (Galaburda et al., 1978). Interestingly, musicians who have perfect pitch have a larger leftward asymmetry in the planum temporale compared to non-musicians or musicians without perfect pitch (Schlaug et al., 1995).

Complementary to language production occurring in the left hemisphere, specialized visuospatial processing is commonly attributed to occur mainly in the right hemisphere (Mesulam, 1981). This complementary relationship of lateralization between language and visuospatial processing appears to be an innate bias (Cai et al., 2013). In a study by Cai et al (2013), individuals with abnormal right hemisphere language processing in all cases exhibited left hemisphere visuospatial processing, which is opposite to the average population. Another example of a functional asymmetry occurs with facial expression recognition. When left side damage occurs in the insula and putamen, individuals lose the ability to recognize disgust facial expressions but retain the ability to perceive other facial expressions (Calder et al., 2000). Handedness is an interesting lateralization due to its translation in to an asymmetrical outward behaviour. Although the large majority of the human population exhibits right hand preference, neural differences are evident between left and right-handed individuals. Morphometric studies have shown that right handed individuals have larger left than right parietal and occipital widths compared to left handed individuals (Kertesz et al., 1990).

Although asymmetries in the brain reveal information about specialized functions such as language, they can also provide mechanisms of dysfunction and illness. For example, aphasia (inability to produce speech) is often caused by damage to cortex along the left sylvian fissure (Kandel et al., 2000). Interestingly, individuals who suffer from aphasia retain the ability to swear (Cohen, 2012). This is attributed to formulaic linguistic capabilities of the right hemisphere, which is also responsible for processing negative emotions (Van Lancker & Cummings, 1999). Lateralization of motivational processing of emotion has also been demonstrated between the left and right hemispheres (Harmon-Jones, 2004). This is important to consider for different psychopathologies in which their mechanisms may be further understood

from these asymmetries. A relevant paradigm of motivational processing is Davidson's model of affective processing, which attributes production of withdrawal-avoidance behaviours mainly in the right frontal hemisphere while production of approach-motivation behaviours occurs mainly in the left frontal hemisphere (Coan & Allen, 2004; Davidson, 2002). This model has been applied to several disorders such as depression, obsessive-compulsive disorder and attention-deficit/ hyperactivity disorder (ADHD) and consistently corresponds to dysfunctional behaviours related to motivation and emotion (Ischebeck et al., 2014; Keune et al., 2014). For example, it is well established that a common feature of major depression disorder (MDD) is hypoactive left prefrontal cortex (PFC) activity (Henriques & Davidson, 1991; Minnix et al., 2004; Stewart et al., 2014). According to Davidson's model, the left PFC is responsible for initiating approach motivational behaviours. A common symptom in MDD is a decrease in approach motivational behaviours, which may be explained at least in part by the decrease in left PFC activity (Shankman et al, 2007). ADHD on the other hand is classified by a dysfunction in approach motivational behaviours in that there is an abnormal increase in these behaviours. It has been shown that severity of ADHD symptoms is associated with a greater left than right activity asymmetry (Keune et al., 2014). Lateralization of emotional and motivational processes in the PFC appear to be important in understanding how it influences behaviour, as it is essential for decision-making and cognition.

2.2 Approach and Avoidance Motivation

Motivation is the drive that causes an individual to do an action in order to achieve a goal (Pessoa, 2009). Models of motivation include two types of motivation related responses to

stimuli (Elliot et al., 2013; Elliot & Covington, 2001). The first is an approach-appetitive

response in which the organism responds to a stimulus by approaching or engaging with the

stimulus. The second is a withdrawal-avoidance response in which the organism responds by

avoiding or retreating from the stimulus. Both approach and avoidance responses to stimuli are

necessary for survival in an organism. Approach behaviours facilitate things like getting food

and mating, while avoidance behaviours facilitate things like defensive behaviours and flight.

There is evidence of organisms across a wide spectrum of complexity that exhibits approach-

withdrawal mechanisms (Schneirla, 1959). For example, single cell organisms such as the

Amoeba approach to light for energy production processes. The Amoeba will withdraw from

light, however, if the intensity is too high (Elliot, 2008). As organisms get more complex (along

with their behaviour) they begin to exhibit more variability within species to how they respond to

stimuli. Therefore, examining approach-withdrawal behaviours in humans will very much

depend on the individual, as well as the state of the individual. An example of this is the

primitive eye blink reflex in humans during a startle response. The reflex is thought of as an

involuntary avoidance response to a high intensity stimulus that acts to protect the eyes (Lang,

1995; Ohman, 1986). Interestingly, when an individual is primed to a negative emotional state

their eye blink response has a shorter latency and greater magnitude compared to a positive or

neutral emotional state (Lang et al., 1990). This innate response, however, is not indicative of the

complex mechanisms behind most human approach-withdrawal behavioural responding.

Although most if not all stimuli carry an emotional association when evaluated (Zajonc, 1998)

human behavioural responses are highly influenced by top-down executive approach-withdrawal

mechanisms based on greatly prioritized goals (Elliot, 2008). A common example of this

executive control is with diet and food responses (Elliot, 2008; Lowe et al., 2014). Although

certain appetitive foods will cause an initial tendency to approach, the top-down influence of a weight loss goal may cause the person to avoid the food. Lowe et al. (2014) demonstrated the influence of continuous Theta Burst Stimulation causing down regulation of the left dorsolateral prefrontal cortex (dlPFC) on these responses in individuals who were presented with appetitive food stimuli. Results showed that with decreased left dlPFC activity, participants on average consumed a greater amount of food compared to the sham condition (Lowe et al., 2014). This result is an example of the potential role of the dorsolateral prefrontal cortex in motivational processes and its effects on outward behaviour and decision-making.

2.3 Frontal Asymmetry in Motivational Processing

There is a large body of evidence that shows lateralized processing of emotional and motivational information in the left and right prefrontal cortex. Models of motivational processing involve responses to either withdraw from, or approach to emotionally evoking stimuli (Elliot & Covington, 2001). More specifically, it has been shown that left PFC activity is increased with approach-related behaviours while right PFC activity is increased in withdrawal-related behaviours (Coan & Allen, 2004; Harmon-Jones et al., 2003; Poole & Gable, 2014)

Original models of frontal asymmetry were tested using a valence model of emotion (Wheeler et al, 1993). Valence models of emotion categorize emotional states by the positive or negative experience or subjective feeling associated with these emotions (Watson & Tellegen, 1985). Although related in some cases to motivational responses, positive and negative valence emotions are not all associated with approach and withdrawal behaviours, respectively. One such emotion is anger, a negative valence emotion that tends to cause approach related behaviours.

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This gap in the valence model of frontal asymmetry has been tested repeatedly and has provided consistent results. For example, Harmon-Jones and Allen (1998) and Harmon-Jones (2000) reported greater relative left frontal activity was associated with higher levels of trait anger. This finding has been replicated in other studies (Coan & Allen, 2003) and strengthens the argument that frontal asymmetry is more associated with motivational processing related to emotion, as opposed to reflecting valence of emotional traits or state within an individual.

The above examples refer to resting frontal asymmetry, which is hypothesized to tap into trait components of motivational responding. However, similar to emotional models of frontal asymmetry, motivational models exhibit trait and state components as well. Resting state frontal asymmetry is referred to as "activity", where as a state change in frontal asymmetry from pre to post stimuli is referred to as "activation". This is particularly important as it may provide greater insight into how a person responds to specific stimuli as opposed to predicting motivational tendencies based on "types" of stimuli. The latter inherits a subjective value based on the researcher, while the participant in the study may interpret specific stimuli in a different manner. An example of this may occur with fear inducing stimuli. A person who is afraid of dogs when presented with a dog will likely exhibit a relative right-sided activation and respond by withdrawing from the dog. However, a person who enjoys the company of dogs will likely exhibit left sided frontal activation and respond by approaching the dog. If this is true, learned associations to stimuli may be revealed by frontal asymmetry activation, and in turn predict how a person's behaviour will correspond to the frontal asymmetry activation.

Some of the earliest studies demonstrating state FAA changes associated with anger have shown that increases in anger after presentation of a stimulus reveals FAA activation resulting in greater left than right relative activity compared to prestimulus (Harmon-Jones et al., 2003).

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Interestingly, a study by Harmon-Jones et al. (2003) revealed that the left frontal activation only occurred when retaliatory behaviour was possible to counter-act the anger eliciting stimuli. In the study, undergrad student listened to fake announcements regarding tuition increases at their school. Individuals who listened to clips explaining the decision had been finalized did not exhibit left frontal activation, whereas the individuals whose clip said the decision was still being considered did exhibit left frontal activation. Numerous additional studies have been conducted that support the motivational model of FAA (Poole & Gable, 2014; Wacker et al., 2013). This is particularly important as it provides insight to the mechanistic nature of frontal asymmetry on motivational processes, as opposed to emotion alone.

2.4 Frontal Asymmetry in Emotional Processing – Relation to Depression

Frontal asymmetry has been implicated to exist in two possible relationships to an individual's emotional processing. Frontal asymmetry has been shown to relate to trait-related constructs of emotional responding, while also showing state-related changes in response to emotionally provoking stimuli. Initial work by Schaffer et al. (1983) showed that higher Beck Depression Inventory (BDI) scores (more likely to be clinically depressed) were associated with greater relative right side activity while resting in a group of undergraduate participants. This relationship has been replicated in several studies (Henriques & Davidson, 1991; Minnix et al., 2004) and provides interesting insight into a possible mechanism for the decreased motivational behaviours associated with depression. Henrique and Davidson (1991) further revealed that the greater relative right side activity in this population was due to decreased left frontal activity (higher alpha power in left sites) as opposed to increased right-sided activity. This leads to

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further speculation that the left PFC is significant in controlling approach motivation behaviours. This decrease in left PFC activity in depressed individuals has been shown using other techniques such as fMRI (Liston et al., 2014). Interestingly, increasing the activity of this area via methods such as transcranial magnetic stimulation (TMS) has been shown to decrease symptoms of depression (Dannon & Grunhaus, 2003; Manes et al., 2001; Nahas et al., 2004). Importantly, frontal asymmetry differences in healthy individuals have been shown to be associated with emotional tendencies. Two studies (Tomarken et al., 1990; Wheeler et al., 1993) found that resting frontal asymmetry was able to predict emotional reactivity to emotional film clips. More specifically, individuals with relatively greater right frontal activity at rest experienced greater levels of negative emotions while watching negative valence films. Also, individuals who exhibited relatively greater left frontal activity experienced greater levels of positive emotions to positive valence films.

Although resting frontal asymmetry may reveal a trait measure, it is likely that these asymmetry measures are affected by the state within the network. State changes of frontal asymmetry in response to emotionally provoking stimuli have also been well established and may provide greater insight into how individuals respond to certain stimuli. Davidson et al. (1990) showed systematic changes in frontal asymmetry while participants viewed emotional film clips. Interestingly, these differences did not emerge over that span of viewing the clips, but did so when participants exhibited emotionally expressive facial expressions while viewing. More specifically, films that evoked disgust revealed relatively greater right activity while happy films revealed relative greater left activity. Due to these findings, Davidson (1993) proposed "that frontal EEG asymmetries reflect the activity of brain systems that moderate trait tendencies

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to approach, and withdraw from, novel stimuli, and mediate approach and withdrawal-

motivational tendencies that underlie state emotional responding" (from Coan & Allen, 2004).

2.5 The Role of Prefrontal Cortex Subdivisions and their Asymmetries in Emotional Processing

The prefrontal cortex (PFC) of the human brain is crucial for coordinating behaviour in order to achieve a desired goal. This ability to coordinate behaviour is most commonly referred to as executive function, which is an overarching term for several subcomponents of mental processing that assist with goal achievement. The PFC is responsible for continually updating and representing internal goals and how to achieve them (Miller & Cohen, 2001). When in an unfamiliar situation, one will try a variety of different behaviours to reach a goal. Once success occurs, reinforcement signals from brainstem systems associated with reward strengthen networks involved in executing that behaviour (Miller & Cohen, 2001). Emotional processing is a critical component to this process as it is responsible for signalling value (degree of reward or punishment) of stimuli and behaviour. Ultimately it is the guiding force that produces motivated behaviours both in the approach and withdrawal contexts.

Animal models have provided evidence that substructures within the PFC are more strongly connected with certain systems within the central nervous system. This in turn gives reasonable support that these different areas are responsible for performing different processes of executive function. Some examples include the dorsal PFC, which has stronger connections with motor system structures as compared to other PFC regions. Another includes the lateral and mid-

dorsal PFC as they receive strong connections from association sensory cortex. The orbital and medial PFC are linked with medial temporal limbic structures, which are crucial for long-term memory, emotional processing and motivation. Of particular importance is the abundant interconnections within the PFC. This allows for PFC regional afferents to communicate with other substructures within the PFC allowing for large amounts of information processing from many different networks in the brain in a relatively local area (Miller & Cohen, 2001). Three main functional subdivisions of the PFC include the dorsolateral (dlPFC), ventromedial (vmPFC) and orbitofrontal (oPFC) divisions. There is evidence that these subdivisions are each responsible for separate, yet highly related processes in guiding behaviour. There is also evidence for lateralization of processes between the two hemispheres within these regions.

Ventromedial Prefrontal Cortex (vmPFC): The vmPFC is highly connected with limbic structures responsible for emotional processing as well as subcortical structures such as the amygdala and hypothalamus (Miller & Cohen, 2001). Therefore, it is thought to be responsible for evaluating the emotional states (Rolls, 2003). In particular, due to its strong connections with the amygdala, it is implicated in decision making relating to threat (Bechara, 2004) as well as anticipation of future emotional consequences (Davidson, 2002). For example, patients with bilateral vmPFC lesions exhibit decreases in electrodermal activity prior to a risky choice when compared to control subjects (Bechara et al., 1999). Furthermore, rats with lesions to this area prolong the time period of maintaining an aversive conditioned response (Gewirtz et al., 1997; Morgan et al., 1993). Importantly, it may also modulate activation of the amygdala, implying it may play a role in cognitive control over emotional responding (Davidson, 2002; Quirk et al.,

2003). Its functions are highly related to those of the oPFC, which may be due to inconsistencies between studies of defining anatomical borders of these areas.

Orbital Prefrontal Cortex (oPFC): The oPFC also has a critical role in goal-oriented behaviour. It is strongly linked to cortical substructures such as the amygdala and hypothalamus, which are responsible for somatic signalling such as thirst and hunger and mediate arousal levels in response to threat (Kandel et al., 2000). It also receives input from all sensory systems including the gustatory and olfactory systems. The oPFC plays an important role in emotional processing related to rewarding or aversive stimuli (Kandel et al., 2000). Specifically, this subsection is thought to provide affective association to stimuli and influence behaviour accordingly (Rolls et al., 2003). Further support for this hypothesis is apparent considering the strong connections between the oPFC and the dlPFC (Rolls, 2000). The relationship between these two subsections is evident in a study by Wallis and Miller (2003) in which they measured neuronal responses within two rhesus monkeys. During a reward preference task, both the dlPFC and the oPFC activity coded for reward amount, however, only the dlPFC activity predicted whether or not the monkey would respond. Also, the reward related neuronal response occurred more rapidly in the oPFC than the dlPFC. The authors proposed that the oPFC is responsible for representing reward information that is then passed to the dlPFC in order to control behaviour (Wallis & Miller, 2003).

Dorsolateral Prefrontal Cortex (dlPFC): The dorsolateral prefrontal cortex (dlPFC) contributes to cognitive control of behaviour. Lesions to this area result in preservative errors and abandoning of successful rules for a behaviour unnecessarily (Kandel et al., 2000). Rules

that can be learned in order to perform behaviours to reach a goal successfully are weakened. Random behaviours that may be normally suppressed occur more and more frequently. The Wisconsin card-sorting test is a prominent example of the role of the dlPFC in behavioural control. When a rule for card sorting is changed, healthy subjects are able to quickly change strategies and maintain sorting using the new rule. In contrast, individuals with dlPFC lesions typically continue to use previous sorting strategy long after it is deemed incorrect. This subdivision of the PFC is thought to be responsible for cognitive processes as well as modulating emotional influences on behaviour. The dlPFC has strong connections to the premotor cortex and may be a major input to planning and execution of motor behaviour. The dlPFC is also important in initiation of goal-directed behaviour, due to its role in the mesolimbic and mesocortical dopamine systems (Salamone et al., 2007). In a study by Ballard et al., (2011) the authors investigated the functional connectivity of the dlPFC to the ventral tegmental area (VTA) and nucleus accumbens (NAcc), which are highly depended subcortical areas for initiation of motivated behaviour and movement. Using fMRI causal modelling, the results showed that the dlPFC has direct efferent connections to the VTA and the NAcc. The authors argue that this shows the dlPFC is the exclusive entry of reward value in this network, and thus being mainly responsible for initiation of reward-motivated behaviour.

PFC Asymmetries: There is significant evidence that there are functional differences in these PFC subdivisions between the left and right hemispheres. Initial evidence was from impairments exhibited post stroke to areas in the left or right PFC. However, these findings are not entirely sufficient to explain the observed dysfunctions as some may require both hemispheres to be operational and healthy. The most famous example is Phineas Gage, who

suffered a traumatic industrial accident that severely damaged his left frontal cortex. Although most of his functions were unaffected, reports from his doctor as well as friends stated that he began to exhibit a complete personality change. Prior to his accident he was described as a well-tempered person. However, after his accident he was described as irrational, short-tempered and was no longer able to control his emotions. This famous case led to the notion that the left frontal cortex played an important role in emotions and regulating behaviour accordingly (Damasio et al., 1994).

Stroke patients with unilateral left PFC damage exhibit greater depression symptoms than their unilateral right PFC damaged counterparts (Gainotti, 1972), especially if the stroke causes focal lesions (Morris et al., 1996). Conversely, stroke patients with right PFC damage have difficulty processing cues that are sensitive to punishment (Tranel et al., 2002). Furthermore, patients with damage to the right vmPFC (but not the left) exhibit abnormal decision making related to emotion (Clark et al., 2003).

Neuroimaging studies have significantly improved our ability to observe lateralized processing between the left and right PFC. Accumulating evidence suggest, in general, that the left PFC is responsible for processing emotions related to approach and reward motivation, while the right PFC is responsible for processing emotions related to avoidance and punishment motivation. A recent study by Xue et al., (2013) demonstrated using fMRI that during a reversal learning by reward or punishment, the right lateral oPFC and dlPFC activated during reversal learning trials for both reward and punishment. However, the right lateral oPFC and dlPFC activated more readily to punishment trials compared to their corresponding left regions. This demonstrated that the right oPFC and dlPFC in error signalling for behavioural adjustment, particularly for punishment (Xue et al., 2013). Another recent study by Sterpenich et al., (2014)

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investigated differences between viewing positive, neutral or negative pictures in individuals

who score high or low in a test of internally driven motivation (that is without immediate

reward), which they referred to as high or low persistence. Results showed that individuals with

low persistence scores demonstrated higher levels of activity in the amygdala and right oPFC,

and decreased activity in the left oPFC while viewing negative pictures. Low persistence

individuals also exhibited decreases in activity in regions (striatum) when viewing positive or

neutral pictures compared to high persistence individuals. Furthermore, low persistence

individuals showed a greater asymmetry toward the right oPFC while viewing negative pictures.

This study strengthens the support for the role of the right PFC in withdrawal related processing

of emotions and motivation. A study by Beraha et al., (2012) simply compared fMRI

asymmetries during presentation of negative and positive pictures between the left and right

hemispheres. The left mPFC showed a significant difference compared to the right during

presentation of positive stimuli whereas the right dlPFC showed a significant difference

compared to the left during presentations of negative stimuli.

2.6 Measurement of Frontal Asymmetry: The Frontal Alpha Asymmetry (FAA)

In light of the potential importance of PFC asymmetry the next important matter to

discuss is the methods of assessment. More recently, measures of PFC asymmetries have been

conducted using fMRI and PET to measure perfusion and glucose metabolism in certain regions

of interest and have shown supporting results for Davidson's model of motivational processing

(e.g. Sterpenich et al., 2014). However, the activity of the left and right PFC in this context is

most commonly measured by electroencephalography (EEG) alpha power differences between

the left and right sides (Coan & Allen, 2004). Although spatial resolution of EEG is inferior to neuroimaging techniques such as fMRI, it provides superior temporal resolution, which is crucial for understanding state related brain activity. Alpha waves are associated with cortical inactivity or idling, thus alpha power displays an inverse relationship to underlying cortical activity (Larson et al., 1998). This difference in alpha power between the left and right sides is referred to as "frontal alpha asymmetry" (FAA) and is calculated by subtracting the natural log of the left alpha power from the natural log of the right alpha power (Ln[R] – Ln[L]) (Davidson, 1988). Therefore, a positive value of this measure means a relatively greater left activity asymmetry whereas a negative value indicates a relatively greater right activity asymmetry (based on inverse relationship of alpha power and cortical activity). The natural log is employed in order to normalize the alpha power values, which tend to be a positively skewed distribution (Davidson, 1988).

Since the discovery of the alpha wave in electroencephalography (EEG) by Hans Berger in 1929, there has been discussion of its functional meaning with regards to brain activity. Due to its predominance over occipital areas during eyes closed, it was originally associated with cortical inactivity (Laufs et al., 2003). This notion has been supported by several neuroimaging studies in which alpha power negatively correlated with cortical perfusion or glucose metabolism (Cook et al., 1998; Goldman et al., 2002; Larson et al., 1998; Laufs et al., 2003; Oakes et al., 2004). This has been shown both for regional (Laufs et al., 2003) and overall global alpha power (Larson et al., 1998). Furthermore, the synchronization of EEG rhythms (resulting in greater power) is thought to result from thalamocortical relay neurons (Olejniczak, 2006). With that in mind, there appears to be an inverse relationship between thalamic metabolism and alpha power

(Larson et al., 1998). This result suggests that an increase in thalamus activity will result in a desynchronization of alpha activity at a given electrode.

2.7 Reliability of Frontal Alpha Asymmetry

Although a significant amount of research has found relationships between FAA and motivational processing (see Coan and Allen, 2004), there have been concerns regarding the test-retest reliability of this measure. Initial reports showed moderate test-retest intraclass correlations (between 0.50 to 0.79) across a two-week period depending on the reference scheme used (Tomarken et al., 1992). Similar reports have confirmed this moderate reliability more recently as well (Vuga et al., 2006). One major issue in the development of using FAA as biomarker of certain processes was the inconsistency in methodologies used by different groups (see Hagemann et al., 2002). It is important to the reliability of FAA measurements to consider the length of recordings. For example, recordings of 30 seconds compared to 8 minutes do not adequately show differences between healthy and clinically depressed individuals (Hagemann et al., 1998). This length of collection may partially explain null findings in studies that employ this procedure. Collecting for 8 minutes has good internal consistency with Cronbach's alpha values reported at approximately 0.8 to 0.9 (Hagemann et al., 1998; Reid et al., 1998; Tomarken et al., 1992), whereas collections of 30 seconds have weak to moderate internal consistency with Cronbach alpha values at approximately 0.5 (Hagemann et al., 1998). Reference montage is another methodological inconsistency in the measurement of FAA. A few studies have investigated the differences between using a common vertex (Cz reference) and a linked mastoid reference scheme (Hagemann et al., 1998, Reid et al., 1998). Although reliability for both

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reference schemes in these studies were good (r ~0.8), the average correlation between these two montages was r=-0.004 (Hagemann, 2004). However, the correlation between linked mastoids and an average reference montage was r=0.81 (Hagemann et al., 2001; Reid et al., 1998) suggesting that a Cz reference montage may measure a psychometrically different property of brain activity (Hagemann, 2004). The Cz reference, although commonly used, has an unfavourable signal to noise ratio and when used may not reflect differential activity at midfrontal electrode sites. Whereas the linked mastoid reference has a larger signal to noise ratio and is more likely to reflect asymmetrical processing (Hagemann, 2004). Experimental conditions are also important to control as these may influence a person's measured FAA.

2.8 Trait versus State Components of Frontal Alpha Asymmetry

Using FAA as a measurement of motivational responses to stimuli has been used in two main constructs. Originally proposed as a trait measure, resting FAA was believed to reflect a diathesis in the diathesis-stress model of psychopathology that reflected an individual's predisposition to how they emotionally respond to stimuli. It has also been used in a state-dependent construct in which fluctuations of FAA are measured in response to emotional stimuli (Coan and Allen, 2004). The first construct, trait, usually relies on what is commonly referred to as "activity", whereas the second, state, usually measures what is commonly referred to as "activation": a change in FAA pre to post stimulus (Coan & Allen, 2004). Unfortunately, although there is likely a trait component to FAA and motivational responding, it is unlikely to measure trait FAA due to state fluctuations between measuring sessions. In turn, this has raised concerns of its validity as a trait measure, or whether it has a trait component at all. Using

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Steyer's latent state-trait model (Steyer et al., 1992), Hagemann et al. (2002) estimated the variance in resting FAA due to state and trait, across four sessions. Their conclusions stated that a latent-trait model was not acceptable for any areas of the scalp recordings; however, a latent state-trait model was accepted for all areas. Their final estimations attributed approximately 40% of the variance across the four recordings were due to person-situational (state) effects, where as 60% of the variance was stable across the four recordings and constitutes individual differences in FAA. Although this provides insight into the sources of variance in this measure, by no means are these values more than an estimate that shows close to half of the variance is situational. This may partially explain null findings in this field, especially when investigating individual differences and risk for certain psychopathologies.

Interestingly, a study by Stewart et al. (2014) found that FAA activation during an emotionally challenging task better predicts lifetime occurrence of major depressive disorder (MDD) compared to resting FAA activity. That is, compared to controls, FAA during an emotional facial expression task MDD positive individuals exhibited the greatest difference in a decrease in left frontal activity. Resting FAA did not as strongly predict those who are MDD positive compared to controls.

The effect of certain stimuli on state FAA is a less explored area in this field, even though it may be a more promising practice for determining individuals' motivational tendencies. With that in mind, the short-term stability of FAA is not well established. Therefore, the first objective of this thesis project is to determine the test-retest reliability of FAA within and between days. Once this is established, state changes in FAA from pre to post-intervention can be confirmed with greater certainty, as this measure tends to fluctuate between measurements. Ultimately this

study will inform the second objective of this thesis project, which is to determine the effects of moderate intensity aerobic exercise on state FAA.

2.9 Relationships between Aerobic Exercise and Frontal Alpha Asymmetry

Traditionally, research investigating the effects of physical activity on humans has focused on cardiovascular health benefits. More recently, however, there has been an increased understanding and consensus that aerobic exercise can have positive effects on an individual's mental health (Ekkekakis et al., 2008; Park et al., 2011). Aerobic exercise and physical activity have been shown to decrease risk for mood disorders such as major depressive disorder and anxiety disorder (Park et al., 2011) and decrease symptoms in these populations (Malchow et al., 2013). The mechanism by which this occurs is not well understood (Crone et al., 2005; Petruzzello & Landers, 1994) and is likely due to complex interactions between physiological, biochemical and psycho-social factors (Biddle & Mutrie, 2001). It has been shown that moderate aerobic exercise decreases emotional reactivity to negative stimuli in both healthy and MDD positive patients (Crabbe et al., 2007; Mata et al, 2012). It remains unclear, however, whether this effect is due to changes in frontal alpha levels, particularly between the two hemispheres (Crabbe & Dishman, 2004). Crabbe and Dishman (2004) performed a quantitative synthesis of changes in brain activity during and after aerobic exercise and determined that although absolute alpha levels increase during and immediately post aerobic exercise, it does not change as a relative power of other frequency bands such as beta, gamma and theta. This effect was not specific to the frontal regions; although the authors qualify this by stating there was not a "statistically powerful test for regional differences" in their analysis.

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Several studies have investigated the effects of aerobic exercise on FAA and emotional responding. Overall, there is a significant amount of evidence that suggests aerobic exercise causes an increase in positive affect and these responses correspond with FAA (Ekkekakis et al., 2008; Hall & Petruzzello, 1999; Petruzzello & Tate, 1997; Woo et al., 2009, 2010). Initial work in this field by Petruzzello and Landers (1994) revealed that pre-exercise FAA significantly predicted the amount of variance in post-exercise anxiety reduction after 30 minutes of treadmill running at 75% VO_2max. Also, state anxiety measures were significantly decreased post-exercise compared to pre-exercise, which corresponded with a relative increase in left frontal activation compared to right activation. However, although within subject correlations between changes in FAA and anxiety were not significant, they followed theoretical predictions. FAA has been shown to predict affective responses to aerobic exercise both in terms of pre-exercise activity and post-exercise activation. The details of these relationships, however, appear to be inconsistent. This is likely due to heterogeneity between samples in terms of fitness level, exercise intensity and duration as well as measurement tools used for affective responding. For example, Petruzzello and Tate (1997) found no significant relationships between FAA and changes in state anxiety and affect at a moderate exercise intensity (55% VO_2max), whereas Woo et al., (2010) found significant increases in FAA scores and positive affect at all exercise intensities performed (45%, 60%, 75% VO_2max) but no significant differences between intensities. This difference in results between these two studies may be due to the high fit individuals in the first study compared to moderately fit individuals in the second study. There is evidence that fitness level of an individual may mediate relationships exhibited between FAA and affective responses to aerobic exercise (Petruzzello et al., 2001). Duration of exercise also appears to affect the level to which FAA is changed post-exercise (Woo et al., 2009). Specifically, it appears that 30 minutes

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of aerobic exercise may have the most beneficial effects on increasing FAA scores compared to 15 or 45 when exercising at 60% VO_2max (Woo et al., 2009).

A major concern regarding the literature on aerobic exercise effects of FAA is the use of valence models for self-reported affect. As mentioned in previous sections, it is strongly supported that although there may be a relationship to affective valence, FAA most likely reflects motivational processes in terms of approach and avoidance. The studies mentioned above may show mixed results due to the self-report valence model based questionnaires used, which do not necessarily measure state or trait approach-avoidance motivation.

3.0 Rationale

Aerobic exercise has many beneficial effects on both physical and mental well-being in humans. The positive effects of aerobic exercise on mental wellness include a decreased susceptibility to mood disorders as well as acute improvements on mood. Although this is understood on a large scale, the mechanisms of how aerobic exercise influences mood at the individual level are not fully known. One measure that has been consistently linked to risk for developing mood disorders is the relative brain activity between the left and right hemispheres in the prefrontal region, which is referred to as "Frontal Alpha Asymmetry" (FAA). This measure is thought to relate to individuals emotional and motivational responses to stimuli, both in trait and state-dependent constructs. Interestingly, it has been shown that this measure can be influenced by aerobic exercise (Petruzzello & Landers, 1994; Woo et al., 2010). Previous research investigating relationships between aerobic exercise and FAA have shown mixed results. This is likely due to the differences in samples used between studies (High vs average fitness individuals), using pre or post-exercise FAA to predict emotional responses, and exercise parameters (duration, intensity, and mode).

One factor that may impact the usefulness of studying FAA in test-retest paradigms (e.g. such as before and after exercise) is the reliability of the measure. Across long time periods (weeks), FAA has been shown to have moderate test-retest reliability (Hagemann, 2004). Some researchers have suggested that large fluctuations in FAA within an individual across measurements show that it is highly subjected to state influences. Since investigating the influence of aerobic exercise on FAA inherently indicates a state influence on FAA, the short-term stability of this measure needs to be established. Without this information, conclusions

regarding the influence of a bout of aerobic exercise on FAA may be questionable. Therefore, establishing the short-term reliability of FAA is a necessary first step before investigating the effects of aerobic exercise on FAA. Examining the test-retest reliability of FAA within a day (morning and afternoon) and between consecutive days is the first proposed objective of this thesis.

The primary goal of the thesis is to explore the influence of aerobic exercise and bilateral movement on the changes in FAA. Previous studies examining FAA post-exercise have either used no controls, or a resting control in which the participants sit quietly for the same duration as the exercise bout. Although this method may be appropriate, the movement component of the exercise bout may influence FAA by an independent mechanism compared to the aerobic exercise alone. Therefore, a secondary objective of this thesis to compare the effects of aerobic exercise versus non-aerobic bilateral rhythmic movement on FAA. This research may potentially further our knowledge of the influence of aerobic exercise on mood related brain activity and may lead to further research investigating the mechanisms behind this changing brain activity to understand aerobic exercise as a preventative intervention of mood disorders.

4.0 Research Objectives

Study 1: **Examining the reliability of frontal alpha asymmetry both within a day and between consecutive days**

The objective of study 1 was to evaluate the test-retest reliability of frontal alpha asymmetry between the morning and afternoon of two consecutive days. This information is important for studies investigating within-subject changes in frontal alpha asymmetry such as the proposed Study 2 in the current thesis.

Study 2: **The effect of a single session of moderate aerobic exercise on frontal alpha asymmetry: are changes due to bilateral movement or aerobic exercise?**

The objective of study 2 was to test and compare the influence of a non-aerobic movement task versus aerobic exercise on frontal alpha asymmetry. The effects of these conditions were also tested for individual hemispheric influences. The similarities and differences between the changes in these conditions may provide insight into the mechanisms of how these factors influence frontal alpha asymmetry.

5.0 Study 1: Examining the reliability of frontal alpha asymmetry both within a day and between consecutive days

5.1 Introduction

Depression is increasingly recognized as a significant health care concern in young adults (Hasin et al., 2005). A better understanding of the factors associated with mood and depression is key to assess potential future interventions for the disorder. There are potentially important links between the characteristics of brain activity and fundamental human behaviours such as motivation, which is strongly implicated in depression. Several studies have shown relationships between resting asymmetrical frontal brain activity (FAA) and motivational/approach or withdrawal/avoidance behaviours. Typical measurement of FAA is conducted using electroencephalography (EEG) alpha activity (8-13 Hz), which is commonly associated with cortical inactivity or idling (Goldman et al., 2002; Laufs et al., 2003). Alpha power differences in left and right electrode pairs on the anterior region of the scalp are used to quantify FAA. More specifically, relatively greater activity in the left frontal cortex is associated with approach-motivation related behaviour while relatively greater activity in the right frontal cortex is associated with withdrawal-inhibitory related behaviour (Davidson et al., 1990). Individual differences in FAA, particularly greater right activity, may increase risk for mood disorders such as depression. It is common in these disorders for individuals to exhibit abnormal decreases in motivational behaviours and increases in withdrawal behaviours. An important line of future inquiry is determining the cause/effect relationship between FAA and motivational state and in turn possible factors that may alter FAA. One potential factor to alter FAA and motivational state

is the use of aerobic exercise. Aerobic exercise has been shown to increase approach

motivational state measures and alter FAA corresponding to these behaviours (Woo et al., 2010).

Although proposed as a trait measure, this asymmetrical frontal brain activity is subject to

state-dependent fluctuations, which also may relate to state emotional processing (Hagemann et

al., 2002). These state-dependent fluctuations introduce a considerable amount of variability that

may cause methodological issues when investigating FAA in different contexts, including studies

with repeated-measures designs. In a study by Hagemann et al., (2002) trait variance and state

variance were estimated using a latent trait-state model. FAA was measured on 4 occasions with

4 weeks between measurements and it was estimated that 60% of the variance was due to

individual differences while 40% was due to task or state dependent fluctuations.

To determine the stability of the FFA measure over time, several studies have evaluated

test-retest reliability. Such studies have shown modest correlations over test-retest time periods

of 2-weeks to 3 years. For example, Tomarken and Davidson (1992) measured mid-frontal alpha

power asymmetry over a 3-week period and revealed stability correlations of 0.53 to 0.79

depending on the reference scheme and statistical test used. Allen et al., (2004) showed similar

results with intraclass correlations of 0.41 to 0.76 depending on the reference scheme and frontal

sites used across 3 assessments within an 8-week period. The focus of all of these studies has

tended to be directed to long test-retest intervals (weeks/months). Although these results may

suggest FAA as an acceptable measure to compare results between individuals across longer

time intervals, the stability of FAA across shorter time periods (within and between days) is not

well established. The latter is specifically important for a focus on potential state/task dependent

modulators of FFA.

The FAA is most widely being used as a trait measure that is subject to state fluctuations depending on a person's exposures or current processing. In this context it has been most commonly used as a potential biomarker of risk for a mood disorder such as depression. However, more and more evidence is emerging that shows state/task influences, such as processing of emotional stimuli, may be best for predicting a person's likelihood for a mood disorder (Stewart et al., 2014). With this in consideration, it is imperative to understand the state dependent fluctuations in this composite measure within a short time period and understand how it varies within and between subjects. This will lead to a greater understanding of short-term interventions that may cause an effect on resting FAA to show what may be beneficial or detrimental to a person's resting FAA. Therefore, testing FAA reliability within a shorter interval (days) will provide further understanding of the fluctuations of this measure for two critical time periods: within day and between days. A focus on such shorter time intervals is specifically relevant for studies that explore factors that affect state-dependent FAA. This would be especially true in repeated measures designs when comparing between resting FAA and the effects of exercise.

The purpose of this study was to evaluate the stability of FAA in healthy young adults across multiple sessions within a two-day period. Subjects' FAA was measured in the morning and afternoon of two consecutive days in order to measure within and between day stability. It was hypothesized that FFA will be reliable between and within days as supported by significant intraclass correlation coefficients (>0.5), similar to the values previously reported for longer time intervals (Tomarken & Davidson, 1992).

5.2 Methods

Participants: Sixteen participants were recruited and all were young healthy adults without a prior psychological diagnosis (age 24.7 ± 3.7, 9 females, 7 males). Sample size was determined prior to collection based on recommendations by Donner & Eliasziw (1987) for the hypothesized ICC values. No participants were excluded during the collection of this experiment. All subjects completed all four required sessions within a two-day period. Subjects were instructed to refrain from exercise on the days of testing. Subjects were also instructed to refrain from caffeine intake during the days of testing. However, they were allowed to have a morning cup at least 2 hours prior to morning sessions if necessary to avoid withdrawal effects.

Procedure: Participants attended a total of four sessions within a two-day period. On each day, sessions occurred in the morning at approximately 9:30am and in the afternoon at approximately 2:30pm. Within each session, participants underwent preparation for EEG, including electrooculography (EOG) and mastoid electrodes. Following EEG preparation, they entered a soundproof booth located inside the lab where they then underwent a 10-minute resting period while seated comfortably in a chair. After the 10-minute resting period, participants were instructed to sit comfortably and fixate on a fixation cross on the wall of the booth. Participants were instructed to rest either with eyes open or eyes closed for 1-minute while EEG was collected. Participants underwent a total of eight 1-minute collections within each session in a counterbalanced order of eyes open or eyes closed (COOCOCCO or OCCOCOOC) predetermined by the examiner. This order was randomized between subjects.

EEG Parameters: EOG was collected in order to identify ocular artefacts to be removed during analysis. EEG was collected from a total of 10 channels (FP1, FP2, F3, F4, F7, F8, FC3,

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FC4, Fz, and FCz) with linked mastoids used as the reference. EOG and mastoid sites were abraded and cleaned using Nuprep skin gel and alcohol. EOG sites included sites lateral to both eyes and above and below the left eye. Electrodes for these sites were filled with conductive gel and attached to the sites with adhesive tape. The participant's head was measured for cap placement by the halfway point between their nasion and inion as well as the halfway point between the pre-auricular points on either side of the head. Once this site was determined, it was used for placement of the Cz electrode when applying the cap. A 10-20 system electrode stretch Lycra cap was placed on the participant's head and electrode sites were prepared by a disposable, blunt needle that was inserted into the reservoir between the electrode and scalp through a hole in the electrode. The needle was moved in a circular motion to move the hair out of the way and lightly abrade the scalp. Conductive gel was released from the syringe into the reservoir. Continuous EEG was collected at 1000Hz using Neuroscan for all 1-minute trials. At the time of collection all electrode impedances were below 5kOhms.

EEG Analysis: All EEG data was processed using EEGLAB software (Delorme & Makeig, 2004). EEG data was down sampled to 250Hz, and filtered using a 1Hz high-pass and a 50Hz low-pass finite impulse response filter. Data was referenced to linked mastoid (A1+A2) reference. The eight 1-minute trials for each collection were appended and then analysed using independent component analysis (ICA). Components for artefacts such as eye blinks and eye movements were removed from the signal, followed by a visual inspection for confirmation. Spectral power density was determined using a Fast Fourier Transform (Hamming window of 2.048 seconds overlapping by 0.5 seconds) at both the F3 and F4 electrode sites within the alpha band (8-13 Hz). FAA score was calculated by subtracting the natural log of alpha power at F3 from the natural log of alpha power at F4 (FAA = ln[F4] – ln[F3]).

Statistical Analysis: A two-way repeated-measures analysis of variance (ANOVA) was conducted with factors of within day (two levels - morning and afternoon) and between days (two levels - day 1 and 2). Test-retest reliability was examined by conducting intraclass correlations (ICC (3,1) equation) for both within day measurements as well as between day measurements (Shrout & Fleiss, 1979). Between day measurements were compared between day 1 and day 2. Within day measures were compared between data collected on mornings versus afternoons.

5.3 Results

FAA within and between day differences

Table 5.3.1 shows the average FAA scores across all sessions. Overall the average FAA scores ranged from 0.072 to 0.086 across all four sessions. The between subject variability, as reflected by the standard deviations within sessions, was similar. A two-way repeated measures ANOVA revealed no significant effects of daytime (morning vs. afternoon, $F_{(1, 15)} = 0.55$, $p = 0.47$) or day (day 1 vs. day 2, $F_{(1, 15)} = 0.04$, $p = 0.84$). Figure 5.3.1 and Figure 5.3.2 show the grand average changes across these time points.

Table 5.3.1: Summary of average frontal alpha asymmetry (FAA) scores and standard deviations (SD) for each day and session.

FAA Scores	Session				Daytime		Day		
	1	2	3	4	Morning	Afternoon	1	2	All
Average	0.072	0.083	0.076	0.086	0.074	0.085	0.078	0.081	0.079
SD	±0.098	±0.089	±0.083	±0.076	±0.089	±0.081	±0.092	±0.078	±0.085
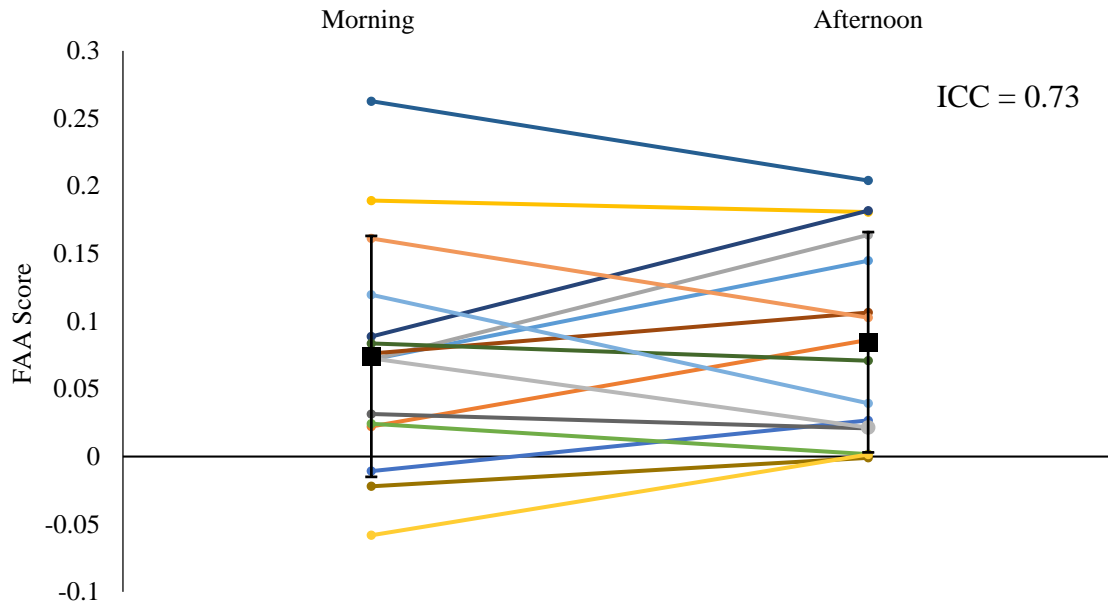
Figure 5.3.1: Frontal alpha asymmetry (FFA) scores between morning sessions and afternoon sessions shown for each subject. Averages for morning and afternoon collapsed across all subjects are shown as black squares (error bars represent standard deviation).
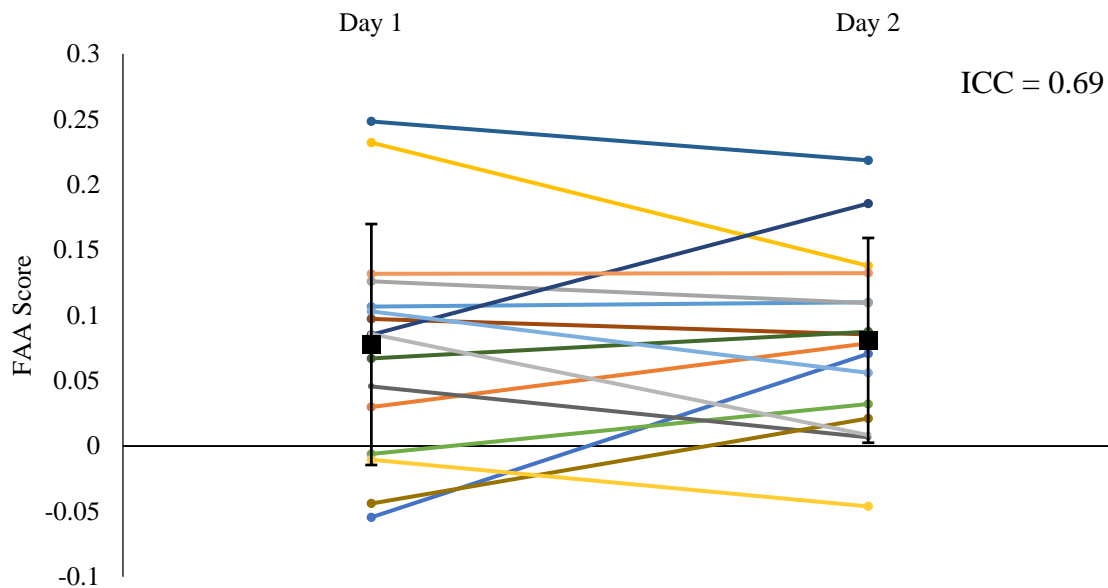
Figure 5.3.2: Frontal alpha asymmetry (FAA) scores between day 1 sessions and day 2 sessions from each subject. Averages for day 1 and day 2 collapsed across all subjects are shown in black squares (error bars represent standard deviation).

FAA reliability

Intraclass correlation analysis revealed a test-retest reliability of 0.73 for within day comparisons when FAA scores were collapsed for morning and afternoon sessions as shown in Figure 5.3.1. Test-retest reliability for between day comparisons was determined to be 0.69 when FAA scores were collapsed for day 1 and day 2 sessions as shown in Figure 5.3.2.

Individual ICCs between sessions are summarized in Figure 5.3.3. Within day comparisons (top row) showed ICCs of 0.69 (Morning 1 to Afternoon 1) and 0.48 (Morning 2 to Afternoon 2). Between day comparisons across matched daytimes (middle row) showed ICCs of 0.62 (Morning 1 to Morning 2) and 0.52 (Afternoon 1 to Afternoon 2). Remaining between day comparisons across unmatched daytimes (bottom row) showed ICCs of 0.74 (Afternoon 1 to Morning 2) and 0.35 (Morning 1 to Afternoon 2).

The lowest ICCs occurred between the farthest two time points; morning 1 and afternoon 2. The highest ICCs occurred between afternoon 1 and morning 2. Interestingly, the results show the lowest ICCs all occurred in comparisons that include the afternoon 2 time point (Figure 5.3.3). Furthermore, this decrease in test-retest reliability occurred in both F3 and F4 electrodes, suggesting the low FAA ICCs for afternoon 2 are not driven by one electrode in particular.
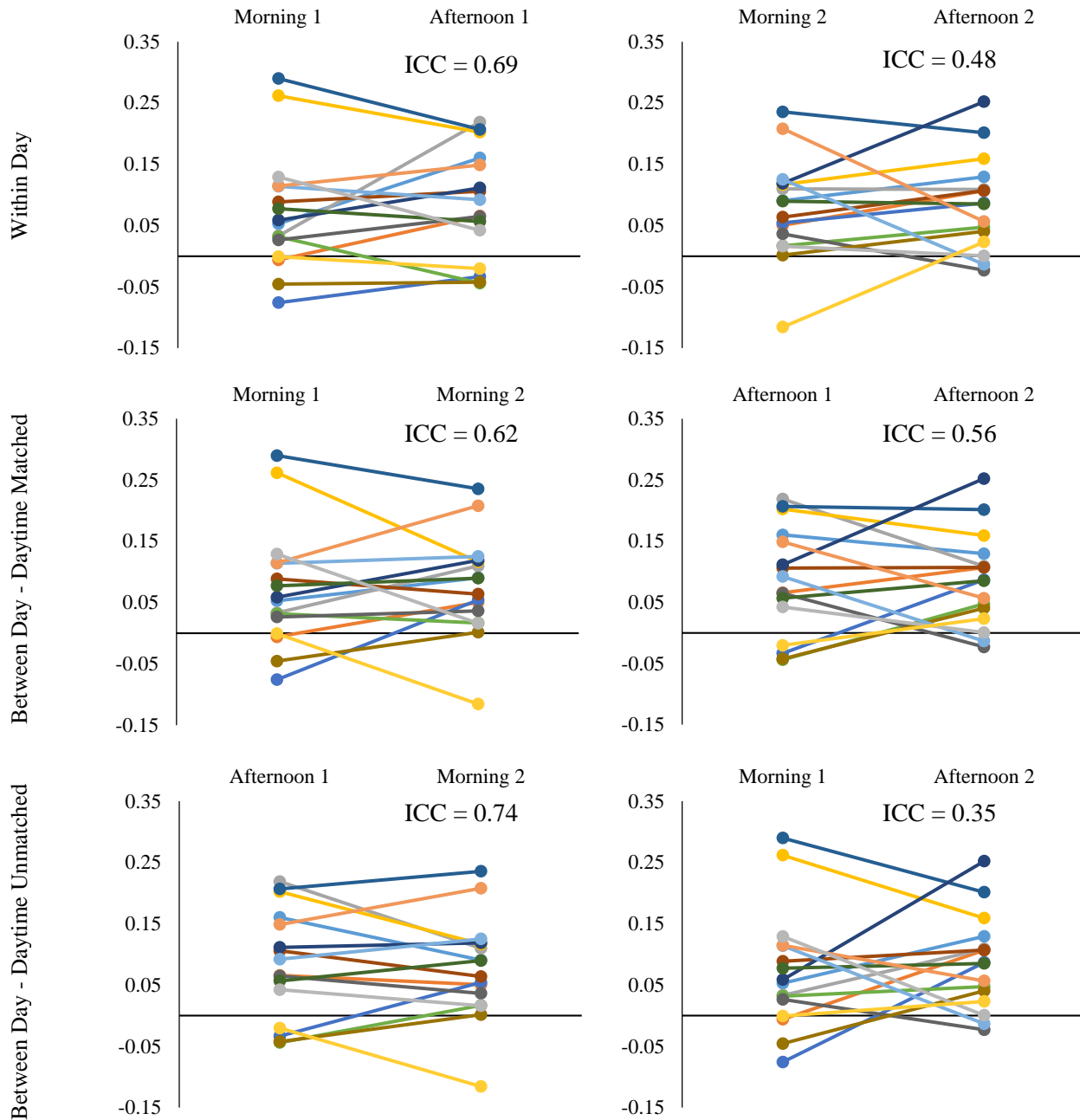
Figure 5.3.3: Frontal alpha asymmetry score (FAA) for individual subjects plotted for each comparison between individual sessions. Intraclass correlations are shown for each comparison. Within subject scores are connected between the two points.

While the average data was comparable and the within session variability was similar it was clear that there were consistent differences between individuals. Figure 5.3.4 provides FAA scores for each subject for each session and their average FAA. The data reveals that while there are between session differences the between subject differences are quite large. That said there is some evidence of larger within subject variability in some subjects while subjects 8 and 12 display individual session scores that do not vary very much from their mean FAA scores. Subjects such as 4 and 5 have a higher but even spread of FAA scores around their mean. Alternatively, subjects 11 and 16 show one session FAA scores that appear quite different form the other sessions.
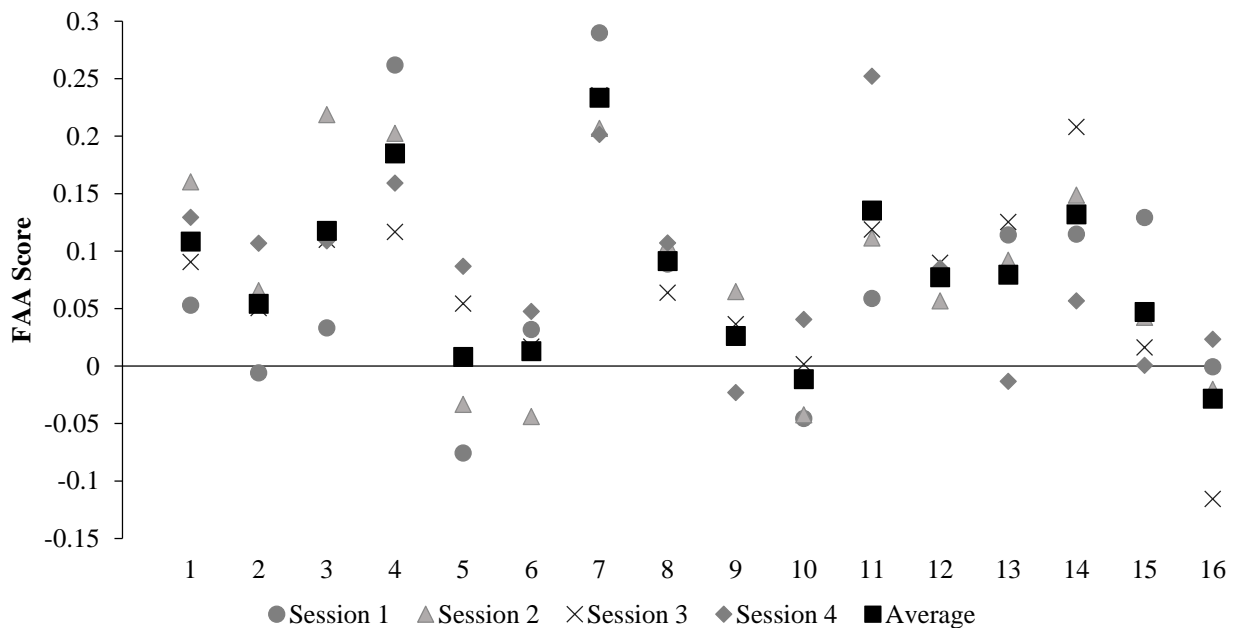
Figure 5.3.4: Subjects' individual session and average frontal alpha asymmetry (FAA) scores. Session frontal alpha asymmetry scores are shown in grey shapes. Subject averages collapsed across all session is shown in black squares.

Hemispheric Alpha Power Reliability (F3 F4)

To address whether differences in the FAA may have been associated with differences in F3 and/or F4 alpha activity analysis was conducted on F3 and F4 separately from FAA. A two-way repeated measures ANOVA revealed no significant effect of daytime ($F_{(1, 15)} = 0.22$, $p = 0.64$) or day ($F_{(1, 15)} = 0.40$, $p = 0.53$) on F3 alpha power. Similarly, a separate two-way repeated measures ANOVA revealed no significant effects of daytime ($F_{(1, 15)} = 0.44$, $p = 0.52$) or day ($F_{(1, 15)} = 0.30$, $p = 0.59$) on F4 alpha power.

Test retest reliability of F3 and F4 alpha powers between sessions is summarized in Table 5.3.2 with the corresponding FAA ICCs. All comparisons for both F3 and F4 showed ICCs of 0.8 or greater, with the exception of Morning 2 to Afternoon 2 and Morning 1 to Afternoon 2. Also, all electrode alpha power ICCs were higher than their corresponding FAA ICCs for each comparison.

Table 5.3.2: F3 and F4 alpha power intraclass correlations between sessions [F3, F4 (FAA)].

Session ICCs	Morning 1	Afternoon 1	Morning 2
Morning 1			
Afternoon 1	0.80, 0.82 (0.69)		
Morning 2	0.88, 0.88 (0.62)	0.88, 0.90 (0.74)	
Afternoon 2	0.68, 0.69 (0.35)	0.87, 0.86 (0.56)	0.72, 0.75 (0.48)

5.4 Discussion

The current study set out to determine the test-retest reliability over short intervals (within and between days) in order to provide a reference for future studies exploring task/state dependent changes within this time period. The current results confirmed the hypothesis revealing no significant effects of daytime or day on FAA. This suggests that it is unlikely that systematic changes occur in FAA from morning to afternoon and that any changes observed within day may be due to random effects in this composite measure. Although this study showed no significance of daytime it was not specifically designed to explore the specific possible influence of circadian effects. Results indicated no significant differences between days on FAA scores across subjects as well, suggesting FAA scores may be suitability stable across days to use multiday study protocols to test explore factors that may influence the FAA (e.g. exercise).

Furthermore, test-retest reliability of FAA was low to moderate as hypothesized. Similar to previous literature (Allen et al., 2004) when FAA scores are collapsed between two time points, test-retest reliability was increased, with ICC values of 0.73 (within day) and 0.69 (between day), compared to individual time point ICCs. Comparisons between individual time points revealed a range of ICCs from low to moderate depending on the time point comparison. More specifically, test-retest reliability of FAA scores within a two-day period showed similar results to previous studies with ICCs ranging in this study from 0.35 to 0.74.

Comparisons between collapsed time points show a better test-retest reliability, which has been shown in previous studies (Allen et al., 2004; Tomarken & Davidson, 1992). This suggests that multiple baseline measures may be beneficial when trying to distinguish FAA scores

between participants. When scores were collapsed, ~70% of the variance in FAA scores were due to between subject differences. This is better compared to some direct time point comparisons in which between subject variance accounted for between 35-74% of the variance in FAA scores. The data in this study showed that there is a greater risk of poor reliability when only comparing a single FAA measurement between subjects. This certainly leads to the important point that study designs should depend on within subject rather than between subject approaches to explore factors that influence FAA levels.

While the FAA composite measure has been the primary index there are obvious questions about whether the contributions from is components (F3 and F4) are differentially contributing to the FAA score. F3 and F4 alpha power showed moderate to high test-retest reliability with ICCs ranging from 0.68 to 0.90. This result of relatively higher ICCs in the electrode alpha power compared to the composite measure (FAA) has also been shown in previous studies (Tomarken et al., 1992). Interestingly, this study showed in general that higher ICCs in the individual electrode alpha powers resulted in higher FAA ICCs in the corresponding comparison.

Such difference in test-retest reliability in FAA compared to the individual electrode alpha powers has been repeatedly shown to occur in similar studies (Tomarken & Davidson, 1992). It is rather concerning that the composite measure itself has low-moderate ICCs whereas the electrode alpha powers have moderate-high ICCs. It is likely that relatively smaller levels of variability in both individual electrodes alpha levels results in a greater relative variability in the FAA measure as calculated. With that in mind it is unlikely to be due to using the natural log of each alpha power as multiple studies have shown that the natural log both normalizes the alpha scores with no effect in test-retest reliability of the FAA measure (compared to a normalized

ratio score for example) (Davidson, 1988). Therefore, since FAA is a ratio of two separate variables it would inherit the measurement error that is associated with both components leading to greater levels of random error within the composite measure. The lower test-retest reliability of the composite measure compared to its contributing components highlights that there is independent variation in the component scores. If the hemispheric alpha power co-varied evenly between the two sides the composite measure would maintain a more consistent value as with the contributing components. Due to the fact that this measure is a composite score of two separate dependent variables, as previously suggested, it is recommended to report individual hemispheric effects in this two-day time period. In part this recommendation is linked to the observation of differences in the repeatability between the components (F3 and F4) and the composite (FAA) measure. However, the second reason is it is possible that the changes in F3 and F4 may have important psychological differences. Specifically, it may represent differences in their resting motivational state between measurements. As a results the knowledge of which hemisphere may be causing a change in FAA is imperative to make conclusions for intervention effects. The results from this study further emphasize the strength of reporting individual electrode alpha powers versus only the FAA score, even within this short time period of two days. Individual electrode alpha power provides more information and has greater test-retest reliability.

Overall, this study showed that FAA has moderate test-retest reliability over a two-day period, with similar ICC values as those previously reported over larger time periods. Furthermore, it was determined that FAA does not significantly change in a systematic fashion within a day or between consecutive days. With the understanding of the variability within a person and lack of changes across the subjects as a group within a short time period, the following study of this thesis will investigate the potential influence of aerobic exercise and

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bilateral rhythmic movement on FAA. When effects are determined, this current study will help by informing the relative size of these effects and how they relate to the individual subjects' variability reported in this study. The test-retest reliability of FAA in this study was not higher than other studies that have tested its reliability in longer time periods suggesting that FAA varies within a person a similar amount in a two-day period as a longer time period such as a week or years (Allen et al., 2004; Gold et al., 2013; Tomarken & Davidson, 1992). This result gives a better understanding of the dynamics of changes in FAA within a person over time in that its degree of change within and between consecutive days is the same as the change within a person over other periods observed. This has important implications for future studies that investigate changes in FAA over these different time periods. If changes in FAA are determined due to a certain intervention, it is vital to understand if the given effects occur within this individual subject variability over time or if its effects cause an FAA outside of this variability band. If the within subject effects in these future studies are within this variability band, it would suggest that any main effects observed would be due to promoting a person's upper or lower "limit" of their FAA. However, if an intervention changed a person's FAA scores beyond this variability band, this would suggest the intervention changes FAA within a person greater than this "limited" FAA. This is key to understand for investigating interventions for people who have negative FAA scores, which may put them at a greater risk for mood disorders. If it is possible to improve their FAA scores to a positive score outside of this regular variability band, this suggests that it is a correctable issue. If, however, an intervention merely promotes there "best possible" FAA, it may not be able to improve their predisposition to mood disorders necessarily.

6.0 Study 2: The effect of a single session of moderate aerobic exercise on frontal alpha asymmetry: are changes due to bilateral movement or aerobic exercise?

6.1 Introduction

There is substantial evidence that relative differences between alpha band (8-13Hz) brain activity in the left and right prefrontal cortex can predict risk for mood disorders and how people may motivationally respond to stimuli (Coan & Allen, 2004). Specifically, greater left than right alpha activity is associated with an increased risk for developing depression and a decrease in approach-motivation related behaviours, whereas greater right than left alpha activity is associated with a decreased risk for depression and an increase in approach-motivation behaviours (Davidson, 2004). In this context, alpha is used as an indicator of regional cortical activity due to its inverse relationship with underlying cortical activity (Larson et al., 1998; Laufs et al., 2003; Oakes et al., 2004). This differential brain activity is commonly referred to as "frontal alpha asymmetry" (FAA) (Coan & Allen, 2004).

Of specific interest in the present study is the link between aerobic exercise and its effects on FFA. Aerobic exercise has been shown to have positive effects on mental well-being both in a chronic and acute setting (Mata et al., 2012; Park et al., 2011). Previous literature has shown that FAA does change post-exercise and in a few studies does predict post-exercise affect (Woo et al., 2009, 2010). In addition, there has been some work to suggest that resting FAA prior to aerobic exercise has been shown to predict an individual's post-exercise affect (Ekkekakis et al., 2008; Hall et al., 2007, 2010). These mixed results reveal there exists no definitive evidence of the relationship between FAA, aerobic exercise and changes in mood. However, it has been

established that aerobic exercise has an overall positive influence on FAA post aerobic exercise (Petruzzello & Tate, 1997; Woo et al., 2010). Therefore, while there are many possible factors that might account for the positive influence of aerobic exercise on mood the current work is specifically focused on the link between aerobic exercise and the FAA. Speculation about the link between FFA and aerobic exercise is influenced, in part, whether one assumes the FFA is reflective of personal trait or whether is dependent on state changes. There are concerns about whether FAA is a reliable trait measure of emotional responding (Hagemann et al., 2002). Rather, aerobic exercise may be a moderator of emotional responding by influencing neurotransmitter availability in the areas responsible for producing an emotional response. This implies that it may be best to investigate aerobic exercise in a state dependent paradigm for its effects on FAA. The current work is focused details of the effects of aerobic exercise on FAA in order to better understand the potential short-term state changes in FFA linked to single bout of aerobic exercise.

As noted there is evidence of the influence of exercise on FAA (Petruzzello & Landers, 1994; Woo et al., 2010) however the potential mechanisms of this change remains unclear. Specific factors related to exercise that have been associated with changes in FAA include the intensity and duration of the exercise bout, as well as the timing of the FAA measurement post-exercise (Ekkekakis et al., 2008; Hall et al., 2010; Woo et al., 2009). As discussed in the subsequent paragraph there are mixed views on the association with exercise intensity and FFA (Hall et al., 2010; Woo et al., 2010). Exercise duration influences post-exercise FAA and specifically, 30 minutes of aerobic exercise has been shown to promote the greatest amount of relative left frontal activation compared to 15 or 45 minutes (Woo et al., 2009).

With respect to effect of intensity initial findings suggest that only exercise of a sufficient intensity (~70% VO$_2$max) will cause an increase in left frontal hemisphere activation post-exercise. These studies, however, used highly fit young individuals (95th percentile VO$_2$max) (Petruzzello & Landers, 1994; Petruzzello & Tate, 1997). In a more recent study with average fit participants (Woo et al., 2010), it was shown that regardless of exercise intensity there was an increase in relative left frontal activation post exercise. The apparent absence of a relationship between intensity of exercise and effects on FAA post-exercise in non-elite fitness participants raises the possibility that the link between aerobic exercise and the influence on FAA may be simply due to the movement in this population. The potential importance of physical movement (bilateral; lower limb movements), rather than the associated cardiorespiratory challenge, could be linked by the association between dopaminergic and serotonergic activation linked with the coordination of bilateral rhythmic movement (Kiehn & Kjaerulff, 1996; Sharples et al., 2014). Striatal initiation and coordination of movement relies on dopaminergic activation from the ventral tegmental area (Kandel et al., 2000). This activation may be crucial as there is significant evidence that dopamine plays a crucial role in FAA, particularly in left hemispheric activation (Nestler & Carlezon, 2006; Wacker et al., 2013). Serotonin activation via the Raphe nuclei has also been shown to contribute to the control of rhythmic bilateral movement (Gackiere & Vinay, 2014). This activation has been shown to correlate with changes FAA post exercise as well (Ohmatsu et al., 2014). Therefore, the rationale for including such a task is that a) modes of aerobic exercise commonly use bilateral rhythmic movements (i.e. cycling or running) and b) bilateral rhythmic movements involve high recruitment of dopaminergic and serotonergic pathways (Kiehn & Kjaerulff, 1996; Sharples et al., 2014). Understanding of the potential mechanisms of exercise-mediated influences on FAA

would be informed by better understanding the relationship between movement, cardiovascular load and their influences on state FAA. In light of the potential importance of separating movement from cardiorespiratory effects, the primary objective of this study is to compare the effects of bilateral rhythmic movements with and without significant cardiovascular workloads on FAA state.

With respect to timing of FAA, assessment previous research has shown that FAA is significantly increased at approximately 20 minutes post exercise (Petruzzello & Landers, 1994; Woo et al., 2010). However, the time course of the effects of exercise on FAA remain unclear. Furthermore, the inclusion of a bilateral movement task and the time course of its effects on FAA may provide greater insight to the potential mechanisms that lead to changes in FAA post exercise. Therefore, one goal of this work is to assess the time course of the effects of exercise on FAA during the recovery period post-exercise as it may provide greater detail of the effects of exercise on FAA at the individual level. In light of the findings of the first study the design will focus on within-subject design, which will require running testing conditions on different days. Fortunately, as noted in the previous study, the FAA along with the F3 and F4 responses are stable across days within subjects.

Overall, the purpose of this study was two-fold: 1) to examine the effects of a single bout of moderate intensity aerobic exercise and of 'no' intensity bilateral movement on FAA compared to a resting control and 2) to assess the time-course of these effects during the post-recovery period. With respect to the difference between exercise and movement, it was hypothesized that both will cause a greater right than left alpha power FAA; however, the timing of this effect in the movement task will occur earlier than exercise. More specifically, it was hypothesized that aerobic exercise would cause a greater right than left alpha power FAA

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compared to the pre measurement at 20-minutes post condition, whereas movement would cause this effect immediately post condition. Based on previous literature, it was hypothesized that frontal alpha levels immediately post exercise will be elevated compared to pre-exercise in both the left and right hemisphere (Crabbe & Dishman, 2004). At the 20-minute post exercise mark, frontal alpha levels will return near baseline levels with increased cortical activity (lower alpha power) in the left hemisphere.

6.2 Methods

Participants: Twelve participants were recruited for this study and all were healthy young adults with no prior psychological diagnoses (ages 22.3 ±3, 5 male, 7 female). As well, none were taking any psychotropic medication at the time of the study. Sample size was rationalized based on the effect size of exercise after collection of 6 subjects using a pairwise main effects comparison model. Self-reported activity levels were collected prior to the start of the study (see Table 6.2.1). Types of activities listed by the participants included resistance training, cycling, running and various sports.

Table 6.2.1: Individual subject characteristics along with heart rate (bpm) target and performed ranges for exercise and movement tasks

Subject	Sex	Age	Activity	Exercise			Movement		
				Target Range (60-70% max HR)	Performed Range	RPE	Target Range (Rest - +10bpm)	Performed Range	RPE
1	M	22	High	119 - 138	127 - 133	5	58 - 68	58 - 61	0
2	M	25	Average	117 - 136	117 - 126	4 - 5	65 - 75	68 - 75	0
3	F	24	Average	118 - 137	120 - 133	4 - 5	57 - 67	62 - 66	0
4	F	19	High	121 - 140	120 - 127	4 - 5	70 - 80	75 - 86*	1
5	F	19	High	121 - 140	122 - 138	4	62 - 72	71 - 75*	0
6	M	19	Average	121 - 140	127 -137	4 - 5	60 - 70	61 - 68	1
7	F	18	Average	121 - 141	124 - 137	3	73 - 83	80 - 84*	0
8	M	22	Low	119 - 138	128 - 137	3	76 - 86	80 - 82	0
9	F	23	Average	118 - 138	122 - 124	3	77 - 87	87 - 91*	1
10	F	28	Average	115 - 134	122 - 131	4 - 5	62 - 72	70 - 72	0
11	M	23	High	118 - 138	126 - 132	4	60 - 70	60 - 66	0
12	F	26	Average	116 - 136	116 - 120	4 - 5	77 - 87	77 - 83	0

*indicates a performed range that is outside of the preferred target range

Task conditions: Participants underwent separate sessions on three different days in the lab, which were completed within a 2-week period. Each session involved a pre-intervention baseline measurement, followed by the intervention (exercise, movement, or control), and followed by a post-intervention measure. The order of the session interventions was randomized prior to subjects coming for their first session. Within each session, participants underwent preparation for EEG, including EOG and mastoid electrodes. Following prep, they entered a soundproof booth located inside the lab where they underwent a 10-minute resting period while seated comfortably in a chair. After the 10-minute resting period, participants were instructed to sit comfortably and be still as to prevent movement artifacts and other potential disturbances. Participants were instructed to rest with eyes open or eyes closed for 1-minute while EEG is collected. Participants underwent a total of eight 1-minute collections within each session in a counterbalanced order of eyes open(O) or eyes closed(C) (COOCOCCO or OCCOCOOC) predetermined by the examiner. Following collection, participants underwent one of the three conditions: 1) aerobic exercise (moderate workload), 2) movement (no workload), and 3) control (no movement).

Aerobic exercise: The aerobic exercise bout included a 30-minute bout of moderate intensity exercise on a recumbent cycle machine. Moderate intensity was determined using 60-70% subjects' age predicted heart rate maximum (calculated by: [220 – Age]*0.6). During exercise, participants were instructed to pedal at 50 rpm (displayed on cycle monitor) and workload was increased gradually every 2 minutes until target heart rate was reached. Once at target, they continued to exercise for 30 minutes. Rate of Perceived Exertion (RPE) was collected at 10, 20 and 30-minute time points of exercise bout.

Movement (no load): The movement condition involved the participant sitting on a recumbent bicycle in the lab and pedalling at 50 rpm for 30 minutes against nominal load and to avoid increasing their heart rate above rest by more than 10bpm.

Control (no movement): The control condition had participants sitting in a comfortable office chair in the lab quietly for 30 minutes.

After each task condition, participants immediately re-entered the soundproof booth and sat in the same arrangement as the pre measure. EEG electrode impedances were checked and fixed if necessary. This delay between intervention performance and EEG collection was 6 minutes. Once ready, participants underwent 32 minutes of EEG collection, alternating EO or EC in the same order as the pre measure. EEG was collected for a total of 32 minutes post intervention. Figure 6.2.1 shows a timeline of a session.

Figure 6.2.1: Timeline of the procedures within a session. The time in minutes is shown for each FAA collection and the performance of the intervention. 8-minute EEG collections for FAA are represented by the boxes

Data Collection: During the aerobic exercise and movement conditions subjects' heart rate was monitored using a polar heart rate tracker device and watch to ensure the parameters of each condition mentioned above. Heart rate was monitored by the experimenter and kept within the target heart rate range for the aerobic exercise and movement conditions.

EEG was collected from a 32 channel cap with linked mastoids used as the reference. EOG was collected in order to identify ocular artefacts to be removed during analysis. EOG and mastoid sites were abraded and cleaned using Nuprep skin gel and alcohol. EOG sites prepared include lateral sites to both eyes and above and below the left eye. Electrodes for these sites were filled with conductive gel and attached to the sites with adhesive tape. The participant's head was measured for cap placement by the halfway point between their nasion and inion as well as the halfway point between the pre-auricular points on either side of the head. Once this site was determined, it was used for placement of the Cz electrode when applying the cap. A 10-20 system electrode stretch Lycra cap was placed on the participant's head and electrode sites were prepared by a disposable, blunt needle that was inserted into the reservoir between the electrode and scalp through a hole in the electrode. The needle was moved in a circular motion to move the hair out of the way. Conductive gel was released from the syringe into the reservoir. Continuous EEG was collected at 1000Hz using Neuroscan software. All electrode impedances were below 5kOhms.

EEG Analysis: All EEG data was processed using EEGLAB software (Delorme & Makeig, 2004). EEG data was down sampled to 250Hz, and filtered using a 1Hz high-pass and a 50Hz low-pass finite impulse response filter. Data was referenced to linked mastoid (A1+A2) reference. Spectral power density will be determined using a Fast Fourier Transform (Hamming window of 2 seconds overlapping by 0.5 seconds) at both the F3 and F4 electrode sites within the alpha band (8-13 Hz). FAA score was calculated by subtracting the natural log of alpha power at F3 from the natural log of alpha power at F4 (FAA = ln[F4] − ln[F3]). The post condition EEG collections were analyzed in four segments that were 8-minutes long each (6-14 minutes, 14-22

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minutes, 22-30 minutes, and 30-38 minutes). These four time periods are referred to as post 1, post 2, post 3 and post 4 in the analysis and results.

Statistical Analysis: A two-way repeated measures ANOVA was conducted for FAA with factors of intervention (exercise, movement, control) and time (pre, post 1, post 2, post 3, post 4) to reveal any between intervention effects or interactions. To test the hypotheses of each intervention's effects, separate one-way repeated measures ANOVAs were conducted comparing FAA at the different time points (pre, post 1, post 2, post 3, post 4) for the exercise, movement and control conditions. Also, separate one-way repeated measures ANOVAs comparing F3 or F4 alpha at the different time points (pre, post 1, post 2, post 3, post 4) for the exercise, movement and control conditions. Tests of the hypotheses conducted using apriori contrasts between pre intervention and each post intervention time period. Additional comparisons were conducted using post-hoc pairwise comparisons (Tukey's) upon determining any main effects.

6.3 Results

Frontal Alpha Asymmetry

A two-way repeated measures ANOVA (Intervention [3 levels] X Time [5 levels]) revealed a significant main effect of time on FAA ($F_{(4, 44)} = 0.259$, $p = 0.049$). However, a Tukey's post-hoc test showed no significant difference between time periods for FAA. There was no significant effect of intervention ($F_{(2, 22)} = 0.01$, $p = 0.99$) or any significant interaction effects ($F_{(8, 88)} = 0.85$, $p = 0.56$) on FAA. Table 6.3.1 summarizes the FAAs measured at each time period and intervention as well as the averages collapsed across interventions.

Table 6.3.1: Frontal alpha asymmetry means and standard deviations for each time period and condition (95% confidence interval)

Condition		Pre	Post 1	Post 2	Post 3	Post 4
Exercise	Mean	0.042 (-0.010, 0.093)	0.055 (0.007,0.103)	0.049 (0.004, 0.095)	0.077 (0.028, 0.127)	0.073 (0.028, 0.119)
	SD	0.081 (0.057, 0.139)	0.076 (0.054, 0.129)	0.071 (0.051, 0.121)	0.078 (0.055, 0.132)	0.072 (0.051, 0.121)
Movement	Mean	0.060 (0, 0.120)	0.051 (-0.025, 0.127)	0.072 (0.003, 0.140)	0.065 (-0.008, 0.139)	0.068 (-0.007, 0.143)
	SD	0.090 (0.067, 0.160)	0.120 (0.085, 0.204)	0.107 (0.076, 0.183)	0.116 (0.082, 0.196)	0.118 (0.084, 0.201)
Rest	Mean	0.046 (-0.025, 0.117)	0.070 (0.003, 0.137)	0.066 (-0.0003, 0.133)	0.057 (-0.002, 0.116)	0.061 (0.017,0.106)
	SD	0.112 (0.079, 0.190)	0.105 (0.074, 0.178)	0.105 (0.074, 0.178)	0.093 (0.066, 0.158)	0.070 (0.050, 0.119)
All	Mean	0.049 (0.017, 0.081)	0.059 (0.025, 0.092)	0.063 (0.031, 0.094)	0.067 (0.035, 0.099)	0.068 (0.038, 0.097)
	SD	0.094 (0.077, 0.123)	0.099 (0.081, 0.130)	0.094 (0.076, 0.122)	0.094 (0.076, 0.123)	0.087 (0.071, 0.114)

Exercise effects: A one-way repeated measures ANOVA revealed a significant effect of time on FAA in the exercise condition ($F_{(4, 44)} = 2.67$, $p = 0.045$). However, a Tukey post-hoc analysis showed no significant difference between any time period for FAA. Furthermore, apriori contrasts between pre-exercise FAA and each post-exercise FAA showed a significant difference at the third post-exercise time period (22-30 minutes post, p=0.011) and fourth post-exercise time period (30-38 minutes post, p=0.022) as shown in Figure 6.3.1A. Figure 6.3.1B displays mean and standard deviations of the FAA change scores from pre to each post-exercise time period. The increase in FAA is clearly displayed for the post 3 and post 4 time periods in comparison to the post 1 and post 2 time periods.

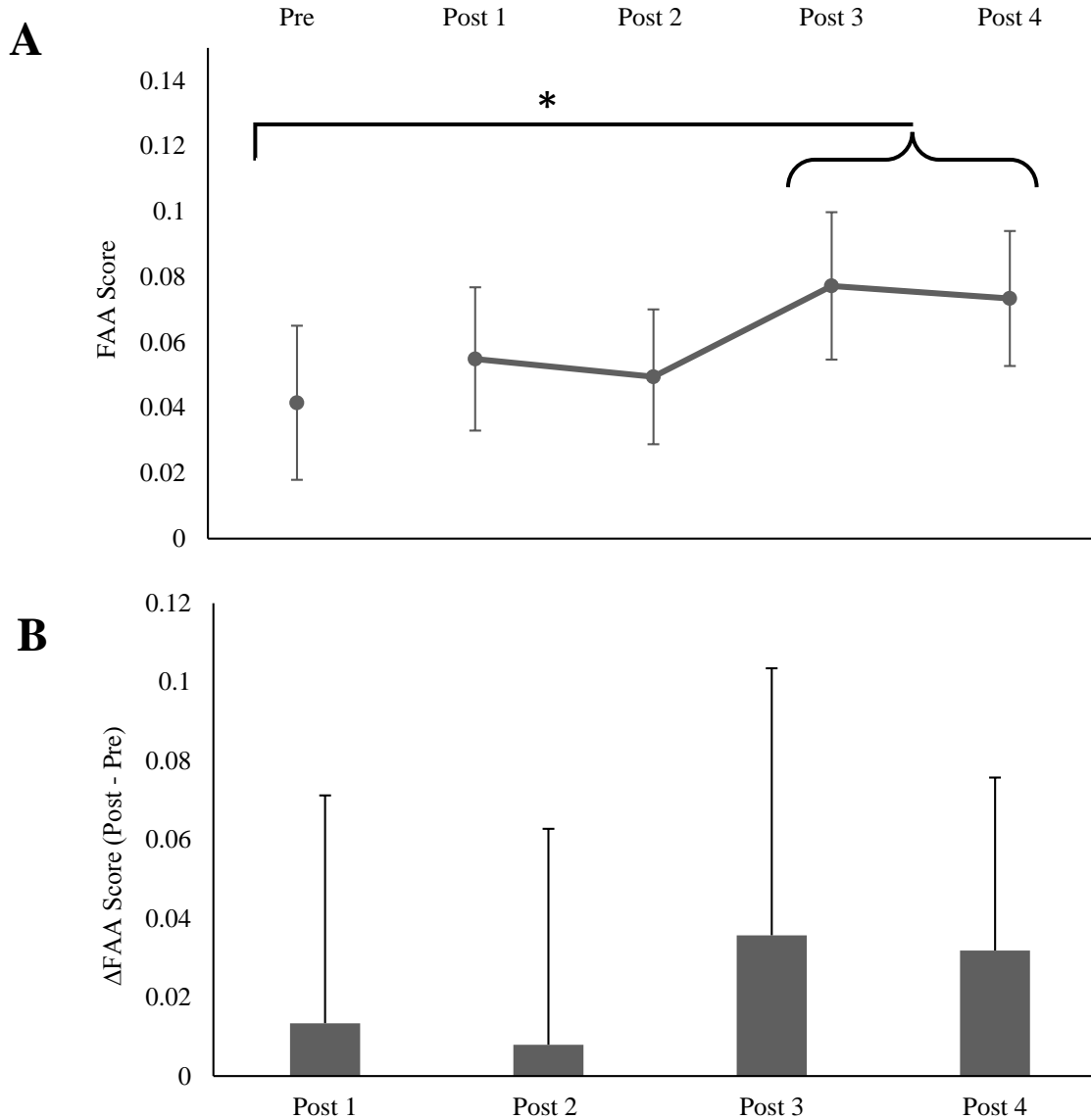Figure 6.3.1 **A**: Average frontal alpha asymmetry scores for pre-exercise and each post-exercise time point collapsed across participants. Error bars display standard error. *denotes a significant increase in FAA between pre and both post 3 and post 4 ($p<0.05$). **B**: Average change in frontal alpha asymmetry from pre-exercise to each post-exercise time point. Error bars display standard deviation.

Movement effects: A one-way repeated measures ANOVA revealed no significant effect of time on FAA in the movement condition ($F_{(4, 44)} = 0.70$, $p = 0.60$). Apriori contrasts showed no significant differences between pre-movement and any post-movement time periods as shown in Figure 6.3.2A. Figure 6.3.2B displays the mean and standard deviations of the FAA change scores from pre to each post-exercise time period. In contrast to the differences in post 3 and post4 time periods observed following exercise there is no evidence of change in the FAA after 'no load' pedalling.

Figure 6.3.2 **A**: Average frontal alpha asymmetry scores for pre-movement and each post-movement time point collapsed across participants. Error bars display standard error. **B**: Average change in frontal alpha asymmetry from pre-movement to each post-movement time point. Error bars display standard deviation.

Control Effects: A one-way repeated measures ANOVA revealed no significant effect of time on FAA in the rest condition ($F_{(4, 44)} = 0.59$, $p = 0.67$). Apriori contrasts showed no significant differences between pre-rest and any post-rest time periods as shown in Figure 6.3.3A. Figure

6.3.3B shows that mean and standard deviations of the FAA change scores from pre to each post-exercise time period. There is no significant change in the FAA value over time. It is noteworthy that the variability in the FAA at time periods was comparable across the task conditions regardless of the task effects.
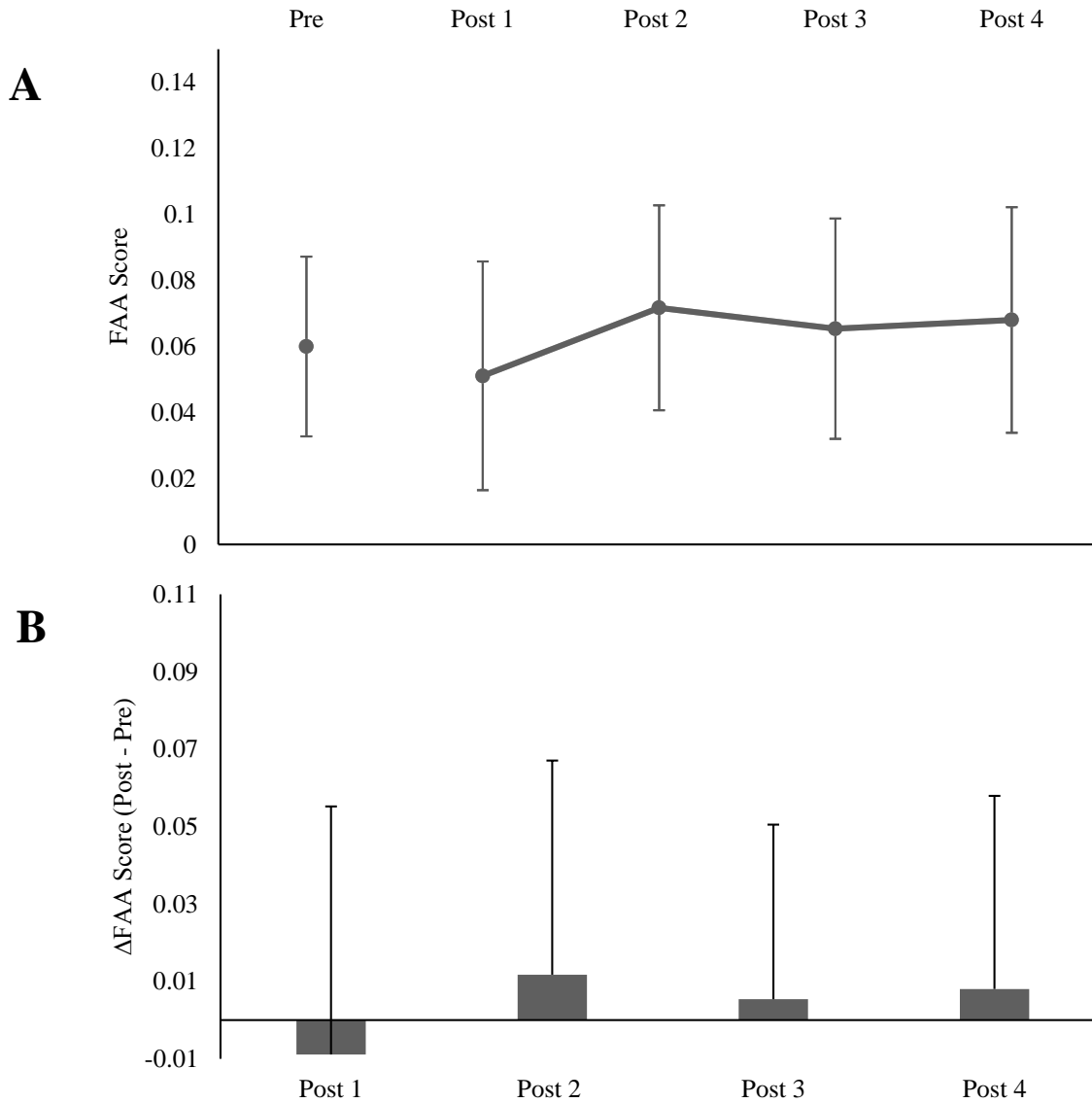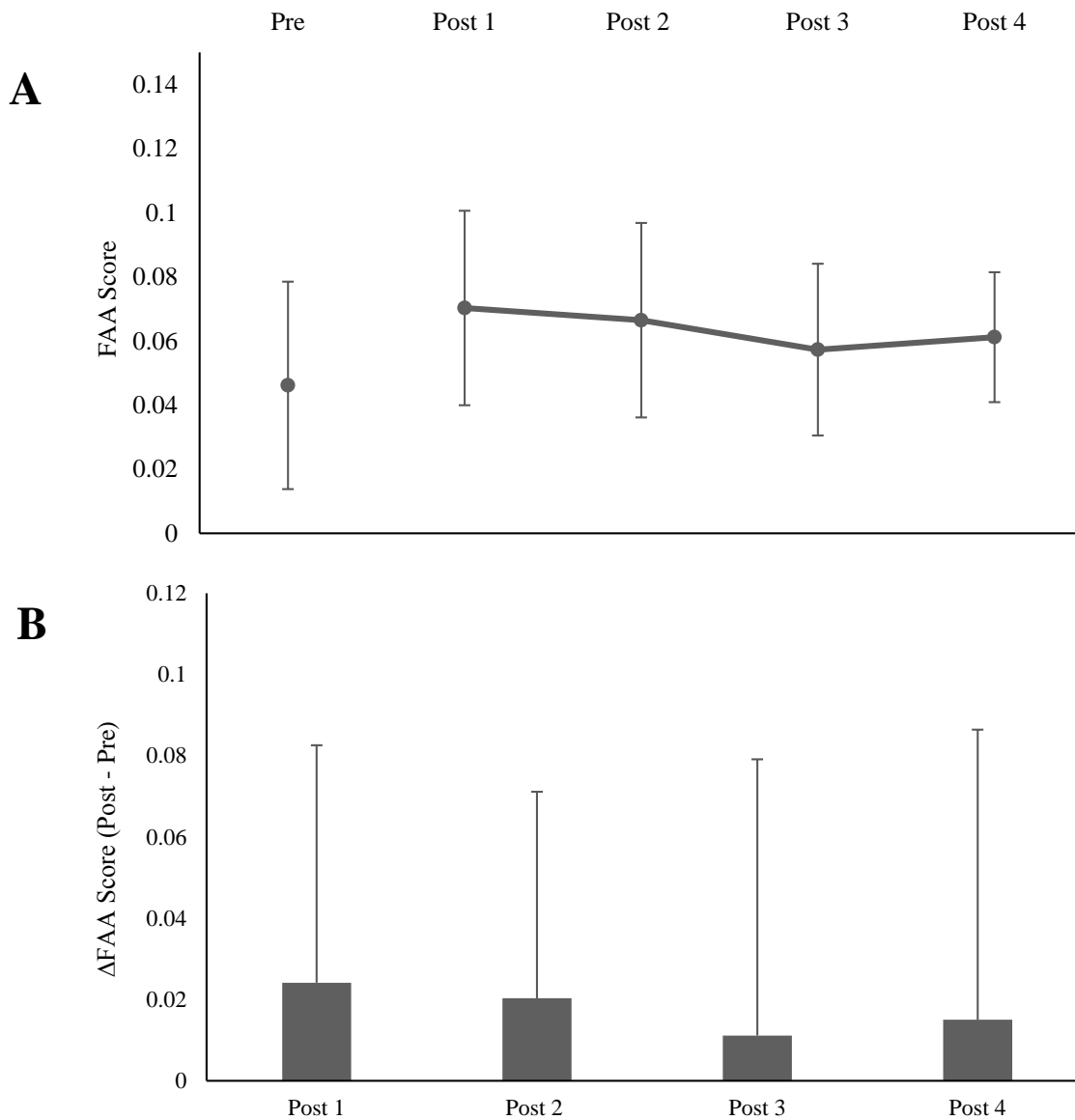

Figure 6.3.3 **A**: Average frontal alpha asymmetry scores for pre-control and each post-control time point collapsed across participants. Error bars display standard error. **B**: Average change in frontal alpha asymmetry from pre-control to each post-control time point. Error bars display standard deviation.

F3 and F4 Alpha Power

Exercise effects: Separate one-way repeated measures ANOVAs revealed a significant effect of time on F3 alpha power ($p<0.01$) and F4 alpha power ($p<0.0001$). A Tukey post hoc test revealed a significant difference between pre-exercise alpha powers compared to all post-exercise alpha powers for both F3 and F4. No other significant differences were found (see Figure 6.3.4.
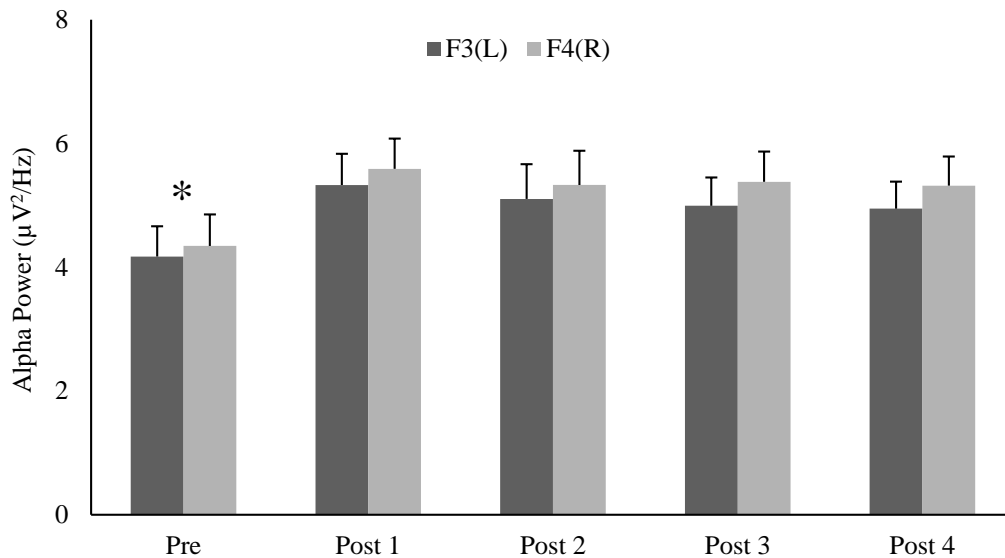
Figure 6.3.4: Exercise alpha powers for the F3 and F4 electrodes for each time period. * denotes a significant difference between pre exercise to each post exercise time period ($p<0.05$).

Movement effects: Separate one-way repeated measures ANOVAs revealed a significant effect of time on F3 alpha power ($p=0.0014$) and F4 alpha power ($p=0.002$). Tukey post hoc tests for both F3 and F4 revealed significant differences between post 1 and pre as well as post 1 and post 3 (see Figure 6.3.5).
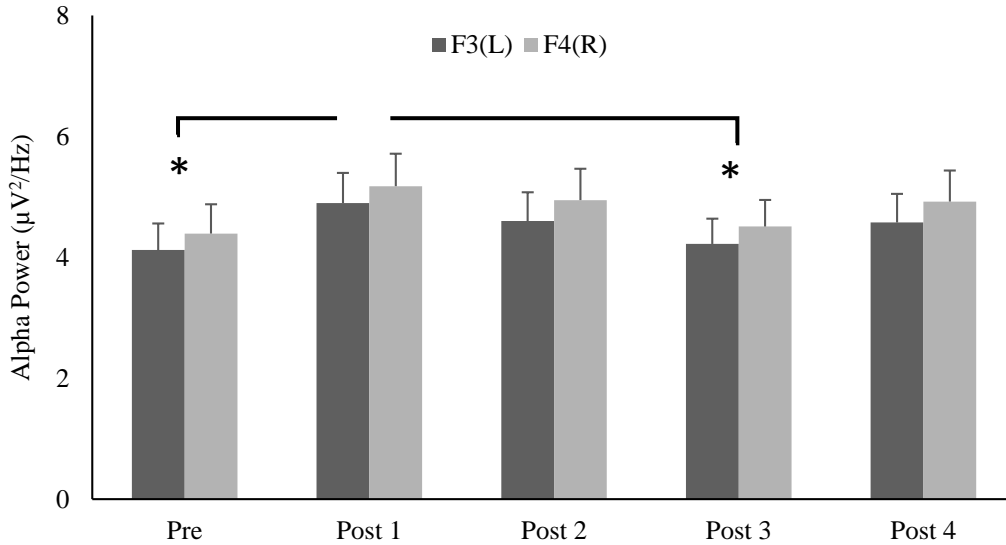
Figure 6.3.5: Movement alpha power for the F3 and F4 electrodes for each time period. * denotes significant differences for both F3 and F4 electrodes between the pre-movement and post 1 time periods as well as the post 1 and post 3 time periods ($p < 0.05$).

Control effects: Separate one-way repeated measures ANOVAs revealed no statistically significant effects of time on F3 ($p = 0.33$) or F4 alpha power ($p = 0.26$) (see Figure 6.3.6).
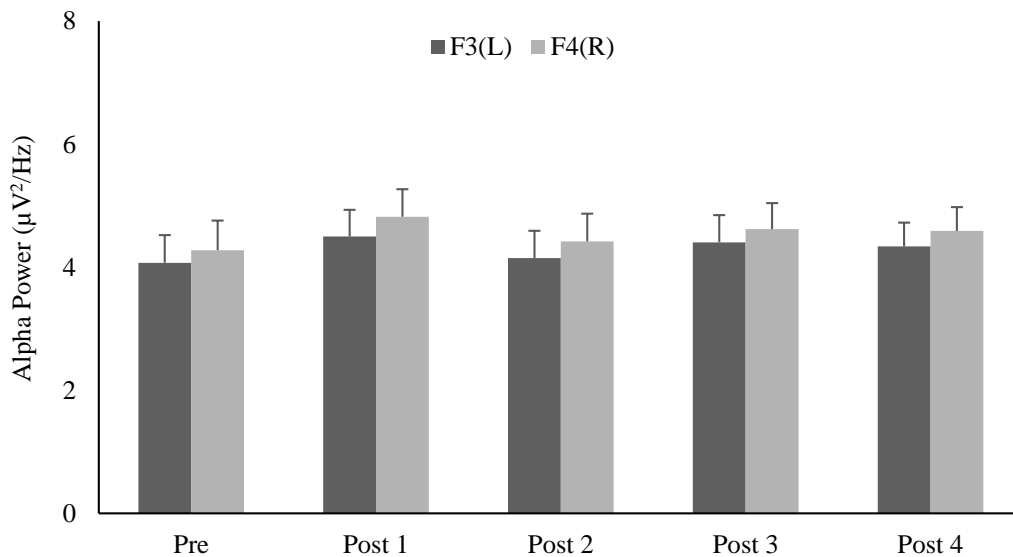

Figure 6.3.6: Control alpha powers for the F3 and F4 electrodes for each time period. No significant differences were found for either electrode at any time period ($p > 0.05$).

The current results revealed that both exercise and movement significantly increased F3 and F4 alpha power. However, this effect in the exercise condition occurs at all four post-exercise time periods. In the movement condition, F3 and F4 alpha powers were significantly elevated in the post 1 time period compared to the pre and post 3 time periods. Within the context of the differences in the alpha levels between F3 and F4, significant changes in FAA leads to question of which of these electrodes is causing the change, in regards to the exercise effects. From Table 6.3.2 it is clear that the increase in FAA in the exercise condition at the post 3 and post 4 time periods is mostly due a greater decrease in F3 alpha power rather than an increase in F4 alpha. Specifically, F3 alpha levels from post 2 to post 4 decrease by $0.16 \, \mu V^2/Hz$ where as F4 only decreases by $0.01 \, \mu V^2/Hz$.

Table 6.3.2: Average F3 and F4 alpha powers ($\mu V^2/Hz$) for each condition and time period.

Time Period	Exercise		Movement		Control	
	F3	F4	F3	F4	F3	F4
Pre	4.17	4.34	4.12	4.39	4.07	4.28
Post 1	**5.33**	**5.59**	**4.90**	**5.18**	4.50	4.82
Post 2	**5.10**	**5.33**	4.60	4.95	4.15	4.42
Post 3	**4.99***	**5.38***	4.22	4.51	4.40	4.62
Post 4	**4.95***	**5.32***	4.58	4.92	4.34	4.59

*denotes time periods in which FAA was significantly increased compared to pre within its condition. Bolded numbers are alpha powers that are significantly greater compared to pre alpha powers within their condition ($p<0.05$).

Secondary Analysis

Correlations between the subjects' pre intervention FAA scores and their average post intervention change scores were analyzed. This was done to determine if there is a relationship between the subjects' pre score and the amount the FAA changes post intervention. This analysis revealed r-squared values of 0.27 ($p = 0.086$), 0.04 ($p = 0.21$), and 0.45 ($p = 0.017$) for the exercise, movement and control conditions respectively. The correlation between these two variables was only statistically significant in the rest condition, however, the exercise condition appears to be approaching significance (see Figure 6.3.7).
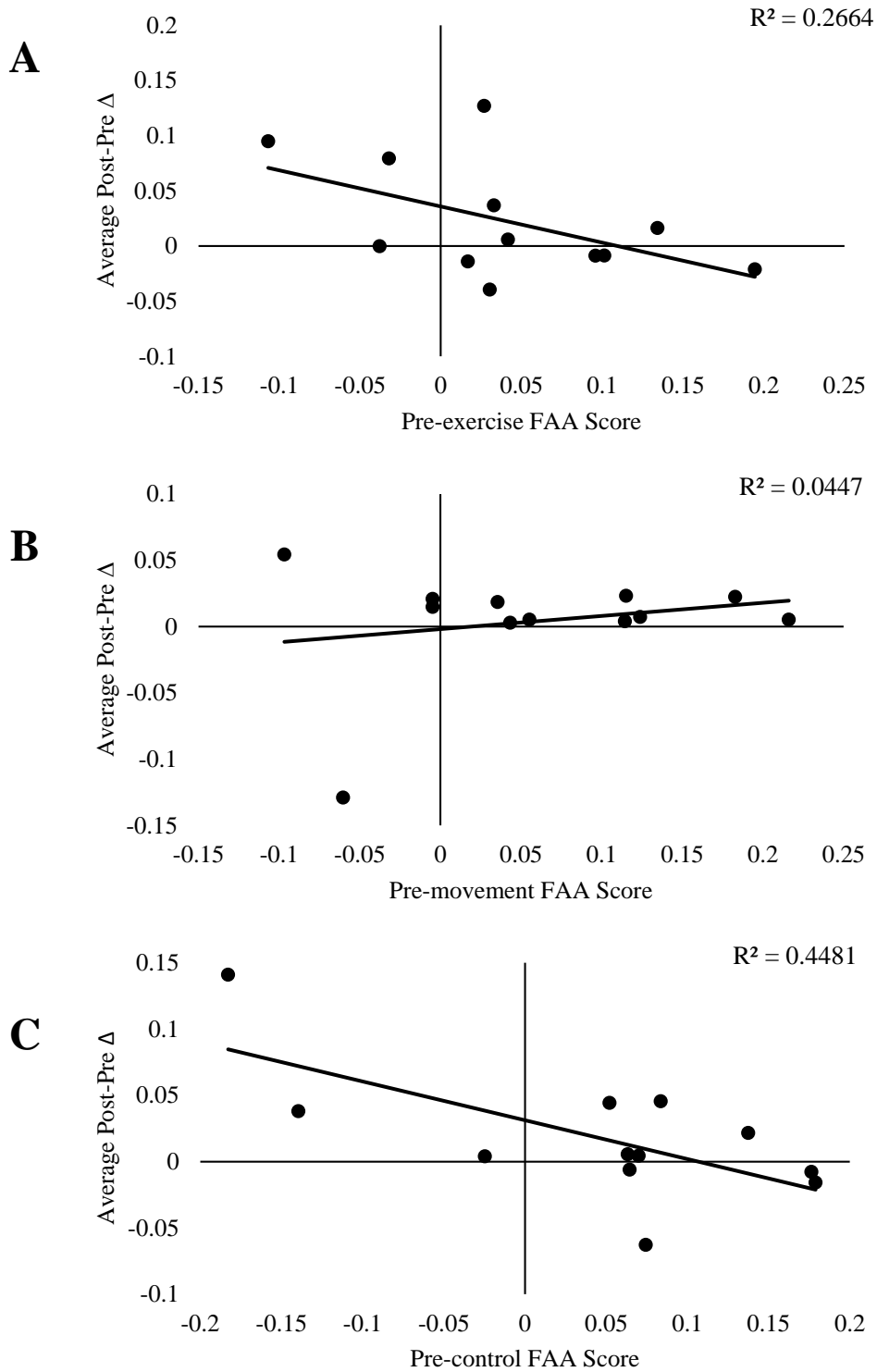
Figure 6.3.7: Correlations between subjects' pre intervention FAA scores (x-axis) and subjects' average post intervention change score (y-axis) for exercise (**A**), movement (**B**) and control (**C**) conditions.

6.4 Discussion

The purpose of this study was to investigate the effects of aerobic exercise and a matched bilateral movement task on the FAA. Contrary to the hypothesis the movement condition did not result in a significant increase in FAA post-movement leading to the view that the cardiorespiratory demand of the task is a critical determinant of the influence of cortical excitability. However, the results confirmed the hypothesis of an increased FAA in the exercise condition from pre to the post 3 and post 4 time periods (22 - 38 minutes after the end of exercise). This result both confirmed the hypothesis of the timing of the exercise effects on FAA while replicating previous literature that has also shown the effect in this time window (Petruzzello & Landers, 1994; Woo et al., 2010). As hypothesized, alpha levels post-exercise were significantly elevated for both F3 and F4 compared to pre-exercise. With that in mind, the increase in FAA that was observed post-exercise appears to be due to a relative decrease in F3 alpha power compared to F4 alpha power levels which remained relatively stable post-exercise. Interestingly, in the movement condition F3 and F4 alpha powers were increased in the first post-movement time period when compared to pre-movement. This suggests that bilateral rhythmic movement does influence overall alpha levels, but does not sustain the increase compared to exercise. Finally, the results confirmed the hypotheses that the control intervention would lead to no significant changes in FAA or alpha power levels.

Exercise and bilateral movement effects on FAA

Results from the exercise intervention coincides with previous literature that showed a similar increase in FAA after 20 minutes post exercise (Petruzzello & Landers, 1994; Petruzzello & Tate, 1997; Woo et al., 2010). Interestingly, Woo et al., (2010) demonstrated that this increase in FAA at this time point post-exercise did not depend on the intensity of the exercise bout. Thus, the inclusion of a bilateral movement task (loadless cycling) was to test if these effects are indeed due to the cardiovascular response to exercise or possibly the movement component of the exercise. Results revealed no significant effects of the bilateral movement task on FAA at any time period post-movement. These results suggest that the effects of exercise on FAA are potentially linked to the cardiovascular response to the exercise bout. The potential explanations for the absence of the anticipated effects in the movement condition may be associated with 1) the characteristics of the movement and/or 2) statistical power. As noted it was anticipated that movement would have a modulatory influence FFA mediated through serotonergic and dopaminergic activation. It is possible that the characteristics of this movement specifically the intensity of the associate neural drive (muscle contraction) may be an important determinant of potential influence on cortical excitability. The current approach was to use a very low load level of activity which would feature sensory inputs but low CNS drive to muscles. The rationale for this was to ensure little to no cardiorespiratory demand. If in fact neural drive is important then a paradigm focus on small muscle groups that would not concurrently increase cardiorespiratory demands would be a more appropriate task conditions to evaluate. There is some concern that the study may have been underpowered to see an overall effect on FAA due to the movement task. Only 12 subjects were needed to detect a significant effect in the exercise task, however, the size of the effect in the movement task may be smaller and thus be hidden due

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to the between subject variability. Finally, it is also possible that there is no measurable influence of bilateral movement limb movement on FAA. Certainly, whatever effect size may or not be related to movement the possible influence of the associated cardiorespiratory demand is much larger. The partial eta-squared values for exercise ($\eta^2_{partial} = 0.20$), movement ($\eta^2_{partial} = 0.06$) and control ($\eta^2_{partial} = 0.05$) reveal a relatively large effect due to exercise compared to the movement and control conditions. This suggests that the movement task in this study did not have a meaningful effect on FAA rather than reflecting an inability to detect differences due to a small sample size.

Timing of the effects

The timing of the changes in FAA post-exercise provide may provide some insight into the potential mechanisms of the exercise induced changes in FFA and its potential clinical utility. Cardiovascular exercise is known to increase activity of several neuromodulator systems corresponding with the increase in physiological arousal required to perform exercise. Of these neuromodulators, the two that are most frequently implicated in FAA research are serotonin and dopamine (Papousek et al., 2013; Wacker et al., 2013) In regards to exercise, Ohmatsu et al. (2014) showed that FAA after undergoing a pedalling exercise were positively correlated with increases of urinary serotonin levels. This suggests that the overall increase in FAA at the 22-38 minute time periods in this study may have been when serotonin increases were the largest post-exercise. This delayed increase in serotonin levels may related to the recovery from exercise (Ohmatsu et al., 2014). With respect to potential dopaminergic effects, there is substantial evidence of a link between left dorsolateral prefrontal cortex activity and dopamine. Interestingly, dopamine's effects on prefrontal cortical activity depends on the types of available

receptors, while also having a biphasic effect on cortical activity if release is sustained (Seamens & Yang, 2004). Specifically, it has been shown to have initial decreases in certain physiological measures followed by an increase. It may be possible that this delay in increasing activity due to dopamine may coincide with the delay in increasing relative left PFC activity (increased FAA) post-exercise. However, it is highly likely that the effects of exercise on FAA are due to a complex interaction between neuromodulators, individual differences in receptor distributions and genetic polymorphisms related to these systems. It is important to consider that FAA was significantly increased from pre-exercise in both the 22-38 minutes post-exercise time periods. This suggests that further research needs to be conducted to extend this post-exercise window to time periods greater than 38-minutes. It is possible that this increase in FAA will be sustained for longer periods as serotonin levels may continue to rise or be sustained past this time period. If this is true it is important to understand for exercise as an intervention for depression risk.

Individual electrode effects (F3 and F4)

Frontal alpha asymmetry represents differences in resting brain activity between two competing behavioural systems (Davidson, 2002). These theorized competing systems are an approach behavioural system and a withdrawal behavioural systems (Elliot & Covington., 2001). Thus, a ratio is used in order to quantify the resting differences between these two systems within an individual. Differences in resting activity in these systems are shown to relate to an individual's predisposition for developing a mood disorder such as depression. However, in order to properly understand changes in frontal alpha asymmetry across measurements it is important to consider the individual contributions of each electrode to the ratio. More specifically, are the exercise mediated changes observed in both F3 and F4 sites or is the

influence asymmetrical. Similar to Woo et al., (2010), this study showed that the increase in

FAA due to exercise after ~20 minutes post-exercise is due to a relative decrease in F3 alpha

power, suggesting a relative increase in relative left PFC cortical activity compared to the right

PFC. The mechanism of the differential changes in cortical activity between left and right PFC is

likely due to an increase in serotonin levels post exercise. Although Ohmatsu et al, (2014) related

increased serotonin levels to changes in FAA as previously mentioned, they did not report the

individual electrode contributions to these relative increases. However, studies such as Mann et

al., (1996) have shown that increasing serotonin levels via fenfluramine in healthy individuals

increased left PFC activity specifically. Therefore, it is possible that the exercise mediated

effects on FAA are due to a relative increase in serotonin levels that specifically increase the

resting cortical activity of the left PFC. This is particularly important for informing the clinical

utility of exercise in depression. It has been repeatedly shown that individuals suffering from

depression have decreased resting activity in this region compared to healthy individuals.

Therefore, this relative increase in left cortical activity indicates a potential mechanism for the

role of exercise in preventing and possibly treating depression. With this in mind, it is important

to indicate the contributions of each electrode to FAA as opposed to only reporting the ratio by

itself in future studies.

These results and their implications for exercise as an intervention to change brain

activity relating to depression risk needs to be taken with caution. Although there is an overall

effect in the exercise condition on FAA, this increase did not occur in every subject. There was

considerable variability in the difference scores when explored across subjects which occurs for

all three interventions. Some subjects exhibited relatively large increases in the control and

movement sessions, which suggests the exercise effects on FAA may not be clinically meaningful. Secondary analysis of the relationship between subjects' pre FAA scores and their average change post intervention showed moderate negative correlations for both the exercise and control conditions. Specifically, the relationship revealed that the lower a subject's pre FAA score, the greater the positive change post intervention. There are two potential explanations for this finding. 1) An individual's state pre-intervention determines the size of the effect. If a subject's pre-intervention FAA measure was towards a more negative state, this would potentially lead to a greater change or return back to a more neutral or positive state post-intervention. Or 2) individuals who are predisposed to having a more negative FAA are most greatly affected by the interventions themselves. If the correlation between pre FAA and post FAA change scores only occurred in the exercise condition, this would imply the second explanation. However, since this relationship occurred in the control condition as well it is more likely that it is the first explanation. This relationship may be crucial to understand intervention effects in a depressed population.

Comparing between interventions, there was a significant main effect of time on FAA with no significant interaction between intervention and time. This suggests that regardless of the intervention performed, FAA changed over time. The difference scores for all interventions at all post time periods (except movement post 1) showed a relative increase in FAA. Although not significant, the tendency for FAA to increase from pre to post intervention suggests there may be factors effecting FAA negatively due to the initial stages of the collection (i.e. EEG prep) or some factors effecting FAA positively in the post intervention stages. Alternatively, the state of the subjects when entering the lab for testing may have influenced their pre measures. This

potential issue may be improved by having more control over subjects before they enter the lab

for things such as eating and fatigue as examples that may have affected their pre measures.

7.0 General Discussion

7.1 Conclusions

Asymmetry in frontal brain activity has been repeatedly associated with motivational responses to emotional stimuli. This relationship has many implications for different mood disorders in which emotional responding may affect daily functioning. This asymmetry is most commonly characterized by measuring alpha power differences between homologous frontal electrode pairs via electroencephalography. The purpose of this thesis work was to investigate the influences of aerobic exercise and bilateral rhythmic movement on frontal alpha asymmetry in young healthy adults to provide insight into a potential mechanism by which physical activity helps prevent mood disorders such as depression.

Measuring resting state brain activity differences at F3 and F4 frontal electrodes is most commonly associated with Davidson's model of affective processing (Davidson, 2001) in which the left and right prefrontal cortices correspond to competing motivational/emotional systems. Specifically, the left prefrontal cortex is part of an approach motivation behavioural network, most commonly associated with approach responses to positively valued stimuli, while the right prefrontal cortex is part of a withdrawal motivation behavioural network, most commonly associated with withdrawal/avoidance behaviours to negative stimuli. Measuring the difference of resting brain activity (via alpha power) between these two proposed networks is thought to predict an individual's predisposition of motivational behaviour. As such, a person's predisposition may put them at greater risk for certain emotional disorders such as depression, which is associated with a decrease in approach motivation behaviours and an increase in

withdrawal motivation behaviours compared to a healthy population. Although this model of asymmetrical brain activity is commonly thought of as a trait predisposition, several studies has shown that this frontal alpha asymmetry is subject to state related fluctuations (Coan & Allen, 2003).

The state and trait dependent determinants of the F3, F4 and FAA raise concern about the stability or reproducibility of the measure. The initial study determined that the measure of frontal alpha asymmetry is overall a moderately reliable measure in a two-day period with intraclass correlations ranging from 0.35-0.74. This is similar to previous research that has investigated FAA test-retest reliability over longer time periods such as a week or greater (Allen et al., 2004; Gold et al., 2013; Tomarken & Davidson, 1992). Both F3 and F4 alpha power had high test-retest reliability with no discernible difference in the reliability between these two electrodes. This suggests that the lower test-retest reliability in the frontal alpha asymmetry is not due to any one electrode in particular, but may inherit the error in both electrodes. Furthermore, the use of this measure in this time period should be accompanied by individual electrode power that is contributing to the overall ratio.

The focus of the second part of the thesis was exploring the link between exercise and changes in cortical activity. There is are many studies that have revealed the link between short term exercise and cortical activity (see Crabbe & Dishman, 2004). Specific to the current work there have been several that have revealed such effects linked to alpha power of F3 and F4 (and FAA) (Petruzzello & Landers, 1994; Petruzzello & Tate, 1997; Woo et al., 2010). Importantly these differences observed did not appear linked to movement alone but rather when there was some degree of effort. That is the movement likely requires cardiovascular demand and/or higher levels of muscle recruitment than the movement task in study 2. A potential explanation for this

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may the brains control of the sympathetic and parasympathetic nervous systems (Craig, 2009). There is mounting evidence that like approach and withdrawal motivation, sympathetic and parasympathetic control is divided between right and left frontal cortical areas respectively (Craig, 2005). During an exercise or higher neural recruitment movement task there is an increase in sympathetic nervous system activity (Roatta & Farina, 2010). After cessation of this effortful task, parasympathetic activity would likely increase to maintain homeostasis and counteract the previous activity of the sympathetic nervous system. This upregulation in parasympathetic activity would be controlled by increasing activity in the left frontal regions of the brain (mainly anterior insular cortex) and decreasing activity in the regions controlling sympathetic activity (the right anterior insular cortex). This change in autonomic control after the effortful task may be at least partially responsible for the relative desynchronization of alpha activity (decreased alpha power) in the left frontal regions compared to the right. The potential relationship between left and right frontal cortex networks and their roles in autonomic nervous system control, emotion and motivation have important implications in the use of exercise and/or movement in the treatment of clinical depression. Specifically, movement must be effortful enough to cause an increase in sympathetic nervous activity in order to then cause a later increase in parasympathetic activity. Increasing the activity in the parasympathetic control network may result in increases in brain regions known to be hypoactive in depression, like the left PFC.

Comparing the results from both studies suggests that the influence of exercise on FAA is greater than the variability of FAA seen in study one. For example, the largest mean difference for FAA in study 1 occurred between morning 1 and afternoon 2 in which the mean FAAs were 0.072 and 0.086 respectively (a difference of 0.014). In study 2, however, the mean difference of

the significant effects on FAA due to exercise was 0.035 suggesting an effect size greater than different time points in study 1. Also, the effect size of exercise ($\eta^2_{partial} = 0.20$) compared to the reliability study ($\eta^2_{partial} = 0.01$) further emphasizes this point. The largest mean difference of FAA in the movement condition from pre to post was 0.012, a similar no significant effect to that in study 1. The between subject variability in this task however, appears greater in the movement task than those in the exercise task and in study 1. It remains a possibility that study 2 may be underpowered to see any movement effects, however, the lack of a larger effect size suggests otherwise. Importantly, this effect size on FAA due to exercise approximately similar findings by Petruzzello & Landers (1994) who found a mean increase in FAA of 0.033 from pre to post exercise at 20-minutes post.

In study 2, this thesis also showed that aerobic exercise causes a significant increase in frontal alpha asymmetry. Also, this increase in FAA occurred at 22-38 minutes post-exercise, confirming previous literature that shows a delay in this effect (Petruzzello & Landers, 1994, Woo et al., 2010). Conversely, bilateral rhythmic movement did not cause a change in FAA. With the competing behavioural systems implicated in the FAA measure, this research shows that the change in FAA due to exercise occurs by increasing the relative cortical activity in the F3 electrode, which corresponds to an approach motivational system. These combined results of cardiovascular exercise and bilateral movement have implications for the role of physical activity in the prevention of mood disorders such as depression, which is often associated with a decrease in approach motivational behaviours. It is concluded that in order to positively influence frontal alpha asymmetry, there must be cardiovascular demand in the task being conducted. Future research will need to investigate the length of these effects of exercise on FAA in order to fully understand the potential for exercise as a preventative intervention in mood disorders.

7.2 Limitations and Future Directions

Several limitations in this thesis may influence the interpretation of the results for these two studies. Limitations of this research include the recruitment of young healthy individuals exclusively. The effects of exercise on FAA in study 2 may be exclusive to this population and thus may not occur similarly in older or clinically depressed individuals. Further research will need to be conducted in order to test these effects in different populations. Sample size in study 2 is also a potential limitation. Only 12 subjects were recruited which may have been too small to detect an effect in the bilateral movement condition. Therefore, more subjects may need to be collected and analyzed in order to see any effects.

Priorities for future research include conducting similar exercise experiments in a clinically depressed population. The effects of exercise shown in this thesis and other studies have shown a positive effect in healthy individuals only. This may benefit the understanding of exercise in preventing depression, but does not imply the effects are the same in a clinical population. Therefore, this research is imperative to understand the potential mechanisms of exercise as a treatment for depression. Another important question for future studies is linking the short-term effects of exercise on these measures to how it effects them long-term. Having short-term benefits of exercise on mood disorder symptoms and related brain activity is useful, however, it ultimately does not solve the underlying issues. Understanding if exercise is able to progressively change a person's resting FAA, for example, in order to decrease their risk for symptoms in the future may partly answer the question of how long-term exercise habits decrease the risk of mood disorders as observed by Park et al., 2011. It may be possible that repeatedly promoting a healthier FAA state via exercise may result in more long-term plastic

changes in the prefrontal cortex. This may be further supported by other long-term plastic effects shown due to exercise due to its increasing of brain-derived neurotrophic factor and mediators of long-term plasticity (Cotman & Berchtold, 2002).

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