# Dynamic fluctuations in emotion and spatial representation: A functional cerebral systems approach to right hemisphere dysfunction

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## Abstract

This study proposed an experimental test of theoretical models related to emotion and space representation in the brain. Previous research has established that emotion is represented, processed, expressed, and regulated largely by the right hemisphere. Furthermore, there is evidence from experimental paradigms and clinical case reports to suggest that the same hemisphere plays a dominant role in the processing of external space. A conceptual difficulty of clinical and neural network overlap arises when right hemisphere disorders of emotion are compared with those of spatial representation. The current experiment tested some of these hypotheses about emotion regulation and spatial representation in the right hemisphere using nonclinical subjects under a cortical stress paradigm designed to mimic the conditions of cortical duress. An additional goal was an extension of a previous study that examined emotional influence on spatial orientation. Results did not support our initial hypotheses. Subsequent analyses did provide some evidentiary support for some theories related to emotion and brain function. Additionally, patterns of subject performance were observed that support traditionally held theories of differential hemispheric function with regard to emotion and spatial behavior. These findings are discussed within the context of theories of emotion, spatial function, and disorders secondary to right hemisphere damage.

## General Audience Abstract

This is a study examining the role of emotion and stress on the allocation of attention in the individual's external environment. Further examined was the role that brain systems involved in attention, emotion, and spatial representation and the correlation with brain damage and syndromes that result in disruption to these systems. Conceptual difficulties regarding overlapping brain areas that contribute to different functions serve as the foundation for understanding both how these systems work and the behavioral manifestations of their dysfunction. Finally, further elucidating the role of these neural systems in contributing to self-awareness, emotion regulation, and the representation of external space was the ultimate objective of this study.

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# Chapter 1
# Introduction

The basis for exploring the relationship between emotion processing and spatial representation in the human brain is derived from some historical principles of higher cortical function and the clinical case literature, replete with reference to interference in these systems and subsequent neuropsychological dysfunction. This paper seeks to expound upon a theoretical model of right hemisphere dysfunction from the perspective of relationships between emotion regulation and spatial processing systems. In doing so it may be that there is evidence of a functional overlap between these disparate mechanisms that contribute to awareness states while supporting the notion of a cardinal syndrome of right hemisphere dysfunction that results from the interaction of these systems.

## *Fundamental Considerations*

The English neurologist John Hughlings Jackson (1879) proposed that the brain is structured hierarchically with higher cortical structures, primarily telencephalic, developing after lower-order, and evolutionarily older, rhombencephalic and mesencephalic brainstem structures that give rise to primitive survival reflexes (Tucker, Derryberry, & Luu, 2000). Thus, Jackson proposed an inhibitory hierarchical functional system in which brainstem mechanisms are vertically integrated with higher cortical functional systems that serve to modulate lower order systems. Following from this, the principle of encephalization makes reference to the evolutionary processes by which the opposing cerebral hemispheres assume increasingly complex functional control of lower cortical brain systems due to their phylogenetically superior complexity (Tucker et al., 2000).

Asymmetries in hemispheric function have their basis in the now defunct phrenological theories of Franz Joseph Gall and Johann Kaspar Spurzheim (Kolb & Whishaw, 2015). This movement produced a notable historical rivalry led by Pierre Flourens who, by way of lesion-ablation paradigms, insisted that localization of higher functions was not probable. Paul Broca (1865) under influence of Gall's defender Jean Baptiste Bouillaud, was able to convincingly demonstrate such localization via his now infamous expressive aphasic patient Leborgne. This

was followed by Carl Wernicke's discovery of the anatomic basis of receptive aphasia in the left posterior temporal lobe in 1874.

Despite these developments, debates about the nature of functional localization continued until the colossal disconnection work of Roger Wolcott Sperry, Joseph Bogen, and Phillip Vogel in which so-called "split-brain" patients were examined in terms of competing hemispheric functions (Sperry, 1961; Sperry, Gazzaniga, & Bogen, 1969; Sperry, 1977). Sperry and his colleagues were able to state convincingly that the hemispheres were significantly different in their respective functions while possessing a similar, but opposing, conscious state.

An integrative perspective that considers the aforementioned principles may be found in the work of Alexander Romanovich Luria who proposed a theory of functional cerebral systems (see Luria, 1976; 1980). His proposition consisted of three primary functional units: the first functional unit consisting of the mesencephalic reticular formation within medullar and pontine brainstem regions that is responsible for maintaining cortical tone and altering arousal. The second functional unit consists of the posterior regions of the cerebral hemispheres, primarily the occipital, parietal, and temporal lobes that are responsible for the reception, analysis, perception, and integration of multimodal sensory information relayed from the primary sensory modalities. The third functional unit consists primarily of the frontal lobes and primary anterior portions of the two hemispheres. This region is responsible for regulatory control over the other two functional units as well as providing for behavioral output. Luria's approach has provided a basis for understanding the brain as a highly interconnected modular system in which behavior is dependent upon a reciprocal interaction between multiple functionally separate brain areas.

### *Functional Considerations*

Laterality research has revealed significant differences between the two cerebral hemispheres in terms of both function and dysfunction. Prior to the work of Sperry and his colleagues, the left hemisphere (LH) was considered the dominant hemisphere due to its capacities for the production and reception of language and subsequent propositional (logical) speech, the serial processing of information, arithmetical and motor programming (praxis) operations, and general ability to directly communicate with the external world in a manner easily understood by opposing brains (see Harrison, 2015; Kolb & Whishaw, 2015 for a review of hemispheric differences). By contrast, the right hemisphere (RH) was considered "dumb" or

"retarded" as satirically referenced by Sperry (1981) in his acceptance speech for the Nobel Prize in Physiology and Medicine. This prevailing view came largely from practice in clinical neurology in which it was observed that focal left hemisphere lesions gave rise to significant and apparent deficits (predominantly apraxic and aphasic deficits) in an individual patient whereas similar lesions to the right hemisphere did not yield these same problems (Sperry, 1981). Thus it came to be viewed that the right hemisphere was subservient and "lacking also in the higher cognitive faculties associated with language and symbolic processing" (Sperry, 1981) and was also incapable of the same consciousness that the left so displayed.

The research to date has dispensed with this view almost entirely while also adding a significant basis for considering the hemispheres to be functionally distinct and oppositional in their directives. The previous findings of language dominance for the LH remain, as well as its role in arithmetical and serial processing operations. However, the RH appears to be dominant for the processing and regulation of spatial operations, nonverbal (prosodic) language, and the regulation, comprehension, and expression of emotion. Furthermore, in contrast to the left hemisphere's serial and binary processing abilities, the right hemisphere appears capable of a global and parallel processing that allows it to analyze sensory information holistically and rapidly for what some have surmised is partially its evolutionary role in threat detection/avoidance, preservation and dominance of its organism, and its control over the sympathetic branch of the autonomic nervous system, a point addressed shortly (Elias & Saucier, 2006; Harrison, 2015; Kolb & Whishaw, 2015; Palmerini & Bogousslavsky, 2012; Ziadel, Iacoboni, Berman, Zaidel, & Bogen, 2012).

*Emotional Asymmetry*

In reference to previously discussed phylogenetic principles of brain organization, much research has supported the notion of right hemisphere dominance for the comprehension, processing, expression, and regulation of emotion. Furthermore, the right hemisphere contribution to speech in the form of prosodic intonation has been repeatedly noted in the literature.

Gainotti (1972) confirmed earlier suppositions and reports that left-hemisphere damage results in a depressive-catastrophic reaction, whereas right hemisphere lesions result in acute indifference, black humor, and inappropriate reactions. As regards RH contributions to language,

Heilman and colleagues (1975; see also Tucker, Watson, & Heilman, 1977) provided the first distinct evidence of what they termed an *auditory affective agnosia* in which patients with right hemispheric lesions, particularly within the temporo-parietal junction, specifically at the middle-inferior parietal and posterior-superior temporal area, exhibit a deficit in the comprehension of affect in speech. This would later be classified as a *receptive (sensory) aprosodia* (from the Greek "a" = without, "prosodia" = prosody) in which patients are unable to recognize emotion and prosodic intonation (prosody = coloring, melody, cadence of speech and gesture) despite preserved ability to express these same faculties (Ross & Mesulam, 1979; Ross, 1981). Patients unable to express emotion in speech, gesture, and behavior have been classified as possessing an *expressive (motor) aprosodia* in which they present as flat, bland, monotone, unconvincing, sometimes unable to express sadness or joy motorically (crying/laughing), with a reduction in gesturing, and an inability to vary intonation (Ross & Mesulam, 1979; Ross, 1981); this resulting from lesions to the right inferior frontal lobe overlapping the primary motor and premotor cortical areas. Further research elucidated eight categories of aprosodias resulting from lesions of the right hemisphere that map to specific lesions sites corresponding to the homologous regions of the left hemisphere specialized for propositional language functions and for which damage results in many of the classic aphasic syndromes (Caplan, 2012; Ross, 1981).

These and other findings gave rise to theoretical models of emotion laterality. Much of these models rest on assumptions about the inhibitory role of the frontal lobes, bilaterally, particularly over posterior cortical regions via the longitudinal tracts (Tucker & Derryberry, 1992) in addition to the postulate of Denny-Brown (1956) of a reciprocal inhibitory relationship between the frontal and parietal cortical areas. In Denny-Brown's conceptualization, the frontal and parietal lobes are mutually inhibitory with the frontal lobes tending toward withdrawal behaviors and the parietal lobes tending toward approach behaviors. Complimenting an anterior-posterior dichotomy, Tucker (1981) proposed that the hemispheres are also reciprocally balanced and mutually opposing such that each function via commissural connections to excite or inhibit the other hemisphere.

Initial research paradigms and clinical evidence of emotion laterality suggested different possible outcomes: that the right hemisphere is dominant for processing of emotion, that regulation of emotion and emotional behavior are a function of the right hemisphere, that the right hemisphere is specialized for negative emotion while the left is specialized for positive

emotion, or an integration of these (see Borod, 1992; Harrison, 2015; Demaree, Everhart, & Youngstrom, & Harrison, 2005; Silberman & Weingartner, 1986 for review).

The *Right Hemisphere Hypothesis* (Blonder, Bowers, & Heilman, 1991; Borod, 1992; Borod et al., 1998; Borod, Bloom, Brickman, Nakhutina, & Curko, 2002) states that the RH is specialized for emotional perception, comprehension, and expression, regardless of its valence. In this theoretical model, anterior regions of the right hemisphere (primarily right frontal) are responsible for the expression and production of emotion, whereas the posterior regions of the same hemisphere are responsible for reception, perception, and comprehension of emotion across sensory modalities. Evidence for this theory has come from multiple channels and across sensory modalities (see below).

In addition to a RH superiority for emotion, the *Valence/Balance Hypothesis* proposes differential roles for the hemispheres, and left/right frontal lobes respectively, in the processing and expression of emotion per valence (Davidson, 1984). The first variation on this model assumes the LH is specialized for positive emotional expression whereas the RH appears specialized for negative emotional expression (Davidson, 1992a; Davidson, 1992b; Sackheim et al., 1982). A second variation of this hypothesis proposes that the RH is specialized for the perception and expression of all emotional valences, whereas the LH is specialized for only positive emotional experience and expression (Davidson, 1984). In this second derivation, it is proposed that right hemisphere dominance stems from right posterior regions and that the right frontal lobe remains specialized for the expression/regulation of emotion, whereas only the left frontal lobe is involved in positive affect expression (Davidson, 1984).

Extension of the balance models led to a proposal the frontal lobes were differentially involved in activation states and approach and withdrawal. The *Behavior Inhibition/Behavior Activation System (BIS/BAS)* developed by Gray (1981; 1990) postulates three primary emotion systems, the primary two of which are that associated with activation and that associated with inhibition. Support for hemispheric involvement in this model has been found with higher scores on BAS measures (Carver & White, 1994) corresponding to left anterior activation and higher scores on BIS measures corresponding to right anterior activation (Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997). The BIS/BAS model corresponds appropriately with further emotion-derived asymmetries. The *Approach/Withdrawal Hypothesis* extends notions of asymmetries of emotional valence and regulation while adding that the left frontal lobe appears specialized for

approach behaviors while the right frontal lobe is specialized for withdrawal-avoidance behaviors (Davidson, 1992c; Davidson, 1993; Davidson, Ekman, Senulis, & Friesen, 1990). More specifically, it was argued that the fundamental dichotomy was not between positive and negative emotions but that approach behavior and withdrawal behavior are the phylogenetically basic behavioral outputs with which we associate affective valence. So that what we traditionally associate as a negative affect tends toward withdrawal behaviors (e.g. anxiety, depression, phobic reactions) whereas what we associate as positive affect has an approach component (happiness reflected in social approach and a Duchenne smile). Furthermore, situations in which the emotion is processed (e.g. felt) but behavioral output is absent (lack of physical approach/withdrawal) show decreased anterior (frontal) cortical activity with preserved posterior activity.

Other models have extended upon and advanced the asymmetric control of human emotion systems. Manuck and colleagues (2000) proposed that activation of left frontal regions results in positive anticipation of future events whereas activation of right frontal regions results in negative reflection of past events. Demaree and colleagues (2005) sought to explain some issues with current models via their *Dominance/Submission* model. Specifically, fear and anger are both considered negative emotions but the first involves approach behaviors (classically left frontal and positive) while the latter withdrawal behaviors (right frontal and negative). Additionally, both involve high arousal states (typically a right hemisphere function). Thus they accept the idea of approach and withdrawal but suggest that the findings of left frontal activation are associated with dominance states (anger and aroused approach) while right frontal activation is associated with submissive states (fear and aroused withdrawal). This model assists in also explaining why some states, notably anxiety, have been found to result in high right posterior activity with low right frontal activity.

To assist in explaining why differential intrahemispheric arousal exists within the same affectively valenced emotions, our laboratory has proposed the *Quadrant Model* (Shenal, Harrison, & Demaree, 2003). Referencing the findings of Denny-Brown (1956) and Tucker (1981) in describing intra- and interhemispheric mutual reciprocal activation-inhibition among different brain regions, four quadrants (left and right posterior, left and right anterior) are proposed in which dysfunction in one quadrant (e.g. right frontal dysfunction) results in a cascade effect in which opposing brain regions are thereby uninhibited (e.g. right posterior

uninhibited and left frontal uninhibited) and experience arousal (see Foster, Drago, Ferguson, & Harrison, 2008; Harrison, 2015 for review). Thus, affective states, the level of arousal associated with those states, and the behavioral output of the organism may be explained via this activation/deactivation paradigm of specific brain regions that are associated with different emotion functions (see above).

In their review, Silberman and Weingartner (1986) concluded that the right hemisphere is both specialized for the regulatory control, processing, and behavioral output of emotion as well as expressing superiority in negative emotion; the left hemisphere is more often associated with positive emotional processing. Furthermore, Tucker (1981) proposed that the right hemisphere's dominant role in emotion processing is a result of specific features of right hemisphere function: namely that the right hemisphere tends to represent information in an analogical format and that emotional behavior is a function of the RH ability to process and integrate information in a syncretic and holistic manner. This references the parallel processing nature of the RH contrasted with the sequential, linear nature of LH processing. It has further been suggested that the RH role in emotion is a purely spatial function, a suggestion first put forth by Gardner and colleagues (1983). These authors suggested that it is the exceptionally high sensitivity required to understand complex and subtle relationships between emotional valences that guides behavioral output (i.e. what does the organism do in space).

This proposition may be compared with the notable observation that the approach/withdrawal models are inherently spatially-circumscribed models requiring activation of regions of the brain necessary for movement in coordinate space. Demaree and colleagues (2005) added that the approach/withdrawal conceptualization appears to be a better fit to the existing data as compared to a particular valence of emotion. Adolphs and Demasio (2000) proposed that the differential lateralization of emotion to right hemisphere function may be due to the fact that human emotion involves a complex system of enteric, autonomic, and neuroendocrine connections that facilitate processing of peripheral somatic information. Additionally, they note that, given the reliable literature on awareness states and body representation in the RH, it is likely that human emotion systems developed in parallel with those specialized for representation of the body space and that in all likelihood, emotion and representation of the body are different aspects of the same overall integrated functional system.

In further support of these models, research has consistently found the aforementioned deficits associated with the aprosodias in addition to defects in the processing of specific external stimuli. Further support is found in the right hemisphere's dominance for processing emotion in the tactile, auditory, and visual sensory modalities. Borod and colleagues (1983) provide a strong review of the right hemisphere dominance for emotion and evidence of its processing of emotion via multiple sensory modalities. Thus, right hemisphere dominance for processing emotional faces (visual) and intonation in the voice (prosody-audition) has been a consistent finding. Specifically, via the visual modality, a right hemisphere dominance for the perception of negative emotional faces has been found (Adolphs, Damasio, Tranel, & Damasio, 1996; Herridge, Harrison, Mollett, & Shenal, 2004; Mandel, Tandon, & Asthana, 1991; Wittling & Roschmann, 1993). Via the auditory modality, the aforementioned dominance of the right hemisphere in emotion-laden speech (prosody) has been a consistent finding (Borod et al., 1998; Borod, 2000, Emerson, Harrison, & Everhart, 1999). Bryden and MacRae (1989) found a right hemisphere advantage for identification of emotion via the left ear and others have found the same advantage for processing the emotive quality of tones and sequences (Bryden, Ley, & Sugarman, 1982). Additionally, evidence for right hemisphere dominance via the tactile (somatosensory) modality has been found for negative emotion-facial gesturing (Herridge, Harrison, & Demaree, 1997). Examining affectively valenced faces and words, Demakis and Harrison (1994) found a left hemisphere advantage for processing happy faces but decreased left hemisphere performance in an affective word interference task. These findings were interpreted as lending support to the right hemisphere's advantage in cerebral activation.

Previous research has found functional asymmetry for the processing of faces with more rapid perception of facial affect found in the right hemisphere (Harrison, Gorelzcenko, & Cook, 1990). Additional research indicates that facial expression of emotion may be largely right hemisphere dependent Dimberg and Patterson (2000) and Borod and colleagues (1997), in a review of 49 facial asymmetry studies, found that the left hemiface was more involved in the motoric expression of emotion than the right hemiface. Electroencephalograpic (EEG) studies have found significant positive correlations between the rated subjective intensity of negative emotional memories and cortical activation across right frontal, temporal, and occipital lobes (Foster & Harrison, 2002). Overall, research has indicated that emotion has considerable influence over visual (Klaassen, Riedel, Deutz, & Van Praag, 2002; Coupland et al., 2004),

somatosensory (Herridge et al., 1997; Lee, Meador, Loring, & Bradley, 2002), motor (Demaree, Harrison, & Everhart, 2002), auditory (Gadea, Gomez, Gonzalez-Bono, Espert, & Salvador, 1995), and cardiovascular (Snyder, Harrison, & Shenal, 1998) functions.

*Anatomy and Physiology of Emotion in the Right Hemisphere*

The neuroanatomy of emotion systems is intricate and highly developed. A complete discussion of these systems can be found elsewhere (see Adolphs & Damasio, 2000; Tucker & Williamson, 1984; Tucker, Derryberry, & Luu, 2000 for reviews), but a brief few points and basic overview will serve to highlight some of the laterality issues within these systems and provide a basis for our spatial systems.

Integrative rhomboencephalic (brainstem) subsystems comprising of efferent and afferent projections from the medulla (particularly the reticular activating system), the pons, and the cerebellum comprise three disparate functions for emotion control: 1) descending efferent control of peripheral cell groups to control organ systems and motor limb function, 2) spinal transmission adjustments by way of descending monoaminergic (serotonin, dopamine, and norepinephrine) into the ventral horn of the spinal cord serve to both adjust the gain of efferent motor neuron projects as well as to inhibit sensory afferent transmission within the dorsal horn during high stress situations, 3) the ascending projections primarily from the reticular activating system comprise the catecholamine neurotransmitters from the locus coeruleus (norepinephrine), dorsal/medial raphe nucleus (serotonin), ventral tegmental nuclei (dopamine) and the cholinergic projections from the nucleus basilis (acetylcholine). These neurotransmitter systems are both lateralized and associated with separate excitatory, inhibitory, and arousal functions.

Dopaminergic and cholinergic projections appear to be greater to the left hemisphere, supporting previous research on some of the prominent motor features of Parkinsonism and the degenerative deterioration of left hemispheric functions seen in schizophrenia (Glick, Ross, & Hough, 1982; Tucker & Williamson, 1984). This asymmetry in cholinergic projection has led to research on control of the parasympathetic branch of the autonomic nervous system (ANS) by the left hemisphere (Harrison, 2015). The LH dominant role in motor programming and the fact that language production requires a motor program for speech output, necessitate the use of neurochemical motor projections. In contrast, the right hemisphere's role in spatial perception, topographic mapping, and parallel holistic processing necessitate that it draws heavily on arousal

systems from brainstem components. Thus, serotonergic and noradrenergic distribution projects heavily to the right hemisphere (Tucker & Williamson, 1984). Serotonin has a significant role in arousal systems and norepinephrine has been found to the be primary sympathetic ANS neurotransmitter supporting research indicating a right hemisphere dominance for modulation of arousal and control of sympathetic nervous function (Harrison, 2015). Consideration of the evolutionary role of emotion in human behavior lends further support to the need for neurotransmitter systems that subsume arousal and homeostatic functions.

Cortical and subcortical systems, comprising traditional limbic mechanisms, include hypothalamic reception of multicomponent interoreceptive and exteroreceptive sensory information and in turn innervates the aforementioned brainstem mechanisms for higher regulatory control of homeostatic functions. The hypothalamic nuclei are densely interconnected with the pontine periaqueductal gray (PAG) area that is responsible for the aforementioned control of peripheral autonomic and modulatory functions. Hypothalamic fear responses typically concern the classic fight/flight response that acts to facilitate the defensive and avoidance postures in threat situations. However, these systems are not isolated and are reciprocally interconnected with higher cortical systems via projections to the amygdala in the temporal lobes. The amygdala has been found to function as an extension of this sympathetic response by providing a more flexible set of response options by way of anticipatory or active avoidance (Gray & McNaughton, 1996). The lateralized sympathetic drive that results in fearful withdrawal, escape behavior, or the classic fight/flight response is dependent upon further hierarchical control via descending projections from the frontal lobes, that serve to modulate the temporal amygdala response to threat-based situations. Thus, as noted by Tucker and colleagues (2000), the evolutionary progression in a hierarchical fashion can be viewed as beginning with basic adaptive reflex states to systems capable of modulating the lower functions and maintaining an active emotional state to those that are capable of maintaining these behaviors over extended periods of time or producing highly complex emotional behaviors (e.g. personality functions and social intelligence).

Although not discussed above, memory systems are integral to these emotion systems. Through vertical integration via phylogenetic development, emotion systems have developed to encompass subcortical circuits subserving primitive need states, higher mechanisms for maintaining homeostatic drives, and higher cortical functions necessary for veridical cognitive

representation that comprise the complex human self-representation. Thus, the right hemisphere appears particularly adept at regulation and extension of this human emotion reflex-arc in space and time.

*Anatomy and Asymmetry of Spatial Systems*

Similar to emotion, the representation and coding of coordinate space within the human brain is exceedingly complex and a complete review of these systems and their anatomy is beyond the scope of this discussion (see Berti & Rizzolati, 2003; Galletti & Fattori, 2003; Ladavas, 2003 for reviews). A brief overview of what is known about these systems provides the basis for understanding their dysfunction. Much of what is known is derived lesion-ablation studies and neuroimaging findings.

Vernon Mountcastle and colleagues (1975; Mountcastle, 1976) first found that different parietal regions correspond to separate "selective attention" to immediate space (that close to the person) in work with rhesus monkeys. From this he and others assumed the first notions of "immediate peripersonal space" (Mountcastle, 1976). Giacommo Rizzolati and colleagues (1981a; 1981b) made similar advancements studying the premotor cortices of macaque monkeys and proposed dividing external space into two primary sectors: peripersonal (egocentric) and extrapersonal (allocentric). These radial sectors of space are further subdivided, a point which is better elucidated by the unilateral neglect literature. In their review of the research concerning neuronal coding of coordinate space, Berti and Rizzolati (2003) have concluded that near and far space are indeed coded separately in distinct parietal regions. However, they note that what has yet to be explained is both why this is from an evolutionary standpoint and then how space becomes a unitary phenomenological construct for the individual.

It is also apparent that visually perceived space is coded via two distinct neural mechanisms (see Galletti & Fattori, 2003 for review). The first is retinotopically distributed and dependent upon eye movement, position, and retinal coordinates. These retinotopically mapped circuits are highly interconnected with oculomotor neurons in the premotor regions of the frontal lobes bilaterally. The other mechanism involves neurons coding for direct, anchored, real-position sense that is independent of retinal mapping. This second mechanism is, like the other, capable of providing encoding for the location of an object in space that is independent of the

fixation of foveal or peripheral vision. However, in order to produce a so-called "spatial map" of what is perceived, both mechanisms are highly interconnected and dependent upon the other.

More importantly this provides further support for the notion of frames of reference for spatial dimensions: egocentric (with reference to the body), peri-personal (physical space around the body), and allocentric (extrapersonal-with reference to objects outside the body; Buxbaum et al., 2004). Given the close association with the body space and that space within limb reach, peripersonal space is considered to be a component of egocentric (personal) space (Guariglia & Antonucci, 1992). None of these frames of reference are dependent upon retinal coordinates or foveal perception (Galletti & Fattori, 2003) and research has indicated these cellular mechanisms are based primarily in posterior parietal regions that correspond to clinical data (particularly with regard to spatial neglect and optic ataxia) suggesting that this area of the parietal lobe represents visual space (Bisiach & Luzzati, 1978; Bisiach & Vallar, 2000; Vallar, 2001).

As mentioned, the mapping of space and the corresponding notion of "attention" to spatial frames is quite complex. Functional models of these neural systems tend to focus on dysfunction within the systems and the consistent, yet paradoxical, finding that disorders of space representation occur almost exclusively (with rare exception) after damage to right posterior brain damage. The understanding that space is primarily represented in the right hemisphere is not a new conception. Harrison (2015) provides a cogent review of the spatial frames and notes that it is the right hemisphere that appears to be particularly dominant for spatial analysis of regions outside the physical body and its parts.

However, the reasons for asymmetric space representation have been a matter of contention since the first clinical case reports on right hemisphere spatial dysfunction. The question of why the right hemisphere appears dominant for processing and representing external is derived largely from the neglect and associated disorders literature (discussed below). Two types of theoretical models have attempted to explain why right hemisphere lesions result in spatial dysfunction disproportionately more often than left hemisphere lesions: stimulus-bound models and representational models. It is likely that a combination of both of these propositions is correct. Stimulus-bound models generally take a stance that the right hemisphere has a dominant role in attending to the spatial half-fields.

Kinsbourne (1970; 1977) proposed that the hemispheres compete for control of brainstem mechanisms responsible for directing attention ipsilaterally, thus there is a balance in normal

hemispheric function. Furthermore, the LH possesses language functions that mediate arousal in cases of lesions to either hemisphere. Thus, with RH lesions (left spatial neglect) the LH becomes hyperactive (uninhibited), is further aroused by language systems in constant use, and biases attention to right hemispace. With LH lesions, the same language systems are still capable of producing sufficient arousal to counteract the undamaged RH attempt to orient solely toward left hemispace, thus there is no right hemispatial neglect (*Hypoactive Hypothesis*).

Heilman and colleagues (1977; 1978) agreed with Kinsbourne's idea of hemispheric balance/imbalance but proposed that the issue was that the RH becomes hypoaroused rather than the LH becoming hyperaroused (*Hyperarousal Hypothesis*). Neglect and spatial disorders are thus conceived of as an orienting deficit resulting from damage within a corticomedullary white matter tract that projects to unimodal association cortex via the nucleus reticularis of the thalamus. The mesencephalic reticular formation is responsible for mediating cortical arousal via this feedback loop and damage along this line produces a hypoarousal state for the hemisphere in which the tract is damaged. The imbalance that results allows the intact hemisphere's arousal systems to bias it contralateral to the damage (see Heilman, Watson, & Valenstein, 2012 for review; Mennemeier, 1994). These researchers further proposed that each hemisphere was responsible for mediating behavior in contralateral hemispace (LH-right space; RH-left space) and that the right hemisphere, for reasons unclear, was capable of controlling arousal-activation for both itself and the left hemisphere, whereas the LH was capable only of mild activation of RH systems (Heilman & Valenstein, 1978; Heilman & Van Den Abell, 1979). Thus, the right hemisphere is specialized for control of "spatial attention" in both left and right hemispace, whereas the left hemisphere is only capable of mediating attentional mechanisms in the right hemispace.

Other authors have provided similar explanations for the repeated finding of spatial deficits from right, but not from left, hemisphere lesions and the supposed right hemisphere dominance for a spatial attention or representation. Mesulam (1981) proposed that the RH contains more synaptic neuronal space devoted to attentional functions than the LH and that some form of attentional or spatial gradient exists that is in favor of right hemispace (Weintraub & Mesulam, 1987). The hypothesis of an attentional gradient was supported by Kinsbourne (1993) who proposed that an attention gradient existed in which the hemispheres orient in a lateral manner such that attention is not bisymmetrical in two separate hemispaces (left versus

right) but rather is extended across the spatial array but with an increasingly strong bias toward right hemispace as a function of the movement toward that space (*Orientation-Bias Model*). The distinction made by Kinsbourne is that spatial disorders are the result of this gradient of attention and the loss of an active hemisphere to oppose the gradient across space, rather than as a loss of one of two opponent processors with subsequent loss of attention to hemispace. Kinsbourne's model also does not seek to explain a RH dominance for attention but rather states simply that attention is biased toward right hemispace. Posner (1984) attempted to explain the RH dominance by explaining that the RH is specialized for attentional orienting and that spatial dysfunction (primarily neglect disorders) is due to an inability of an individual, following RH lesions, to disengage attention to right hemispace (Danckert & Ferber, 2006)

Representational models of space have attempted to explain some of the more unusual and labyrinthine manifestations of right hemisphere spatial dysfunction. Indeed, many of the stimulus-bound attentional models fail to account for some of these manifestations as well as the distinct overlap of spatial disorders with awareness disorders (discussed below). Ennio de Renzi and colleagues (1970) first proposed that space is *represented* in the right hemisphere. Bisiach and colleagues (Bisiach & Luzzatti, 1978; Bisiach, Luzzatti, & Perani, 1979) provided distinct evidence that patients with neglect disorders manifest the syndrome in memory, mental imagery, and provided evidence that these disorders are topographically mapped somewhere in the right hemisphere. Bisiach and Berti (1986) proposed that spatially-based disorders resulting from right hemisphere dysfunction are the result of damage to a complex network of cell assemblies residing in multimodal association cortex (parieto-occipito-temporal area) of the right hemisphere. In this sense, RH spatial processing is dependent upon a system that topographically represents external stimuli across internally circumscribed space. Thus, represented space is isomorphic with external space (Bisiach, Capitani, & Porta, 1985). The neural network underlying this system is highly differential but corresponds appropriately to the aforementioned findings on dual-cell processing (retinotopic and real-position/anchored cell types) that have been found in cytological studies of cortical cell columns in the parietal lobes and adjacent tissues (see Bisiach & Berti, 1987 for review of the neural network). Further research has supported the processing characteristics and fundamental assumptions of this model (Rizzolati & Berti, 1990; Rizzolati & Berti, 1993).

*Disorders of Emotion and Space*

Right hemisphere dysfunction entails disruption of the aforementioned spatial and emotional systems and tend to include significant arousal deficits. Four primary syndromes of right brain dysfunction are discussed, that are traditionally conceptualized into one of four types: one awareness, one emotional, one spatial, and one mixed. Some other disorders of right cerebral dysfunction are included to elucidate the emotional-spatial nature of these brain regions. These disorders comprise a clinical basis for the many theoretical arguments put forth previously. Furthermore, the provide the clinical picture of right posterior brain damage mirrored in a lesser form by our study.

Originating with Josef Babinski's (1914; 1918) descriptions in a patient with left hemiplegia following cerebrovascular lesions to the right cerebral hemisphere, *anosognosia* (from the Greek *a* = without, *noso* = disease, *gnosis* = knowledge; Heilman & Harciarek, 2010) is perhaps the hallmark awareness syndrome. The disorder refers specifically to a lack of awareness of deficit, denial of illness, a failure to recognize and assign implications to deficits, or a failure to consciously maintain awareness of neuropsychological dysfunction resulting from impairment or disruption of cortical networks necessary for the operation of a particular function (Adair & Barrett, 2012; Bauer, 2012; Bottini, Paulesu, Gandola, Pia, Invernizzi, & Berti, 2010; Kolb & Whishaw, 2015; Orfei, Robinson, Bria, Caltagirone, & Spalletta, 2008; Prigatano, 2010).

Anosognosia manifests as simply the patient's apparent lack of awareness of deficit. And the deficits that patients deny or fail to acknowledge are almost always very severe (Adair & Barrett, 2012). Typically, these deficits are a left sided paresis or plegia, anesthesia, or other loss of left sided function. There is no apparent confusion associated with this loss of awareness, as patients simply do not acknowledge it. The syndrome is by definition dissociable from sensory deficits such the hemianesthesia and hemiplegia with which it commonly co-occurs (Vuilleumier, 2004). Thus, it occurs and presents as a loss of awareness not attributable to damage to corticofugal or corticopetal tracts (Blumenfeld, 2011; Waxman, 2013). It has been described in so many clinical case reports and within the context of such a variety of brain dysfunction that Fisher (1989) proposed that it be considered a "principle of cerebral dysfunction in humans" (p. 127).

Vocat and Vuilleumier (2010) have noted some trait characteristics of anosognosia: the disorder tends to fluctuate in time characterized by patients giving different answers to the same

questions about their deficits over the course of just a few moments, there tend to be discrepancies in patient remarks, and the loss of awareness may concern different implications related to their paralysis (e.g. reasons why they are in the hospital or excuses for their inability to perform certain actions as a result of their paralysis). These fluctuations are the object of speculation regarding the component systems that are disrupted in the disorder, specifically the influence of emotion systems. The neuropathology of anosognosia involves lesions (damage) to the right infero-posterior parietal lobe, right posterior insular, right thalamic nuclei and basal ganglia (lenticular nucleus) regions, and right dorsolateral prefrontal and premotor cortices, with the most common lesion pattern involving the fronto-parietal convexity of the RH and/or their connections (Adair & Barrett, 2012; Appelros, Karlsson & Hennerdal, 2007; Baier & Karnath, 2008; Berti et al., 2005; Bisiach et al., 1986; Bottini et al., 2010; Craig, 2010; Karnath, Baier, & Nagel, 2005; Karnath & Baier, 2010; Meador, Loring, Feinberg, Lee, & Nichols, 2000; McGlynn & Schacter, 1989; Orfei et al., 2007; Orfei et al., 2008; Pia et al., 2004; Starkstein et al., 1992; Stone et al., 1993).

Now regarded in the neuropsychological literature as a distinct syndrome of emotion dysfunction in the right hemisphere, *alexithymia* (from the Greek "a" = lack, "lexis" = word, "thymos" = mood/emotion) was originally defined as the inability to identify one's emotions using semantic language (Sifneos, 1973). However, it has since been further described as a restriction of emotional functioning and a general failure of the ability for right hemisphere emotion systems to contribute to social behavior (Heilman & Harcierek, 2010). Alexithymia thus has been conceptualized as a primary disorder of emotion in the right hemisphere.

The disorder was extensively studied in the Los Angeles series of surgical commissurotomy patients initiated by Roger Sperry and Joseph Bogen (Sperry, Gazzaniga, & Bogen, 1969). These researchers found alexithymic characteristics to be most prominent in these so-called "split-brain" patients and attributed the deficits to a failure of interhemispheric transfer (Hoppe & Bogen, 1977). The contemporary description of the disorder includes the loss of emotional awareness, a paucity of dreaming by whatever mechanism, inability to represent fantasy scenarios, and what is referred to as a "concrete cognitive style" in which patients describe endless mundane details of events and environment without notable substance (Fricchione & Howanitz, 1985; Gardos, Schniebolk, Mirin, Wolk, & Rosenthal, 1984; Jorge, 2010). Patients with alexithymia present as bland, sparse, and with flat affect; they are described

as boring and void of substance in interaction. They exhibit profound difficulties with finding the appropriate ways of describing their emotional state, report a loss of imaginal dreaming, and extremely rigid and sclerotic interpersonal and social interactions (Apfel & Sifneos, 1979).

Heilman and Harcierek (2010) noted that alexithymia is a defect of emotion in the right hemisphere. The neuropathology of this disorder has been regarded as resulting from an interhemispheric transfer deficit in which emotional information from the right hemisphere is not transferred nor incorporated into left hemisphere behavioral outputs (typically language or social approach; Hoppe, 1977; Hoppe & Bogen, 1977; Shipko, 1982; Tabibnia & Zaidel, 2005). This results from one of two possible pathways: either damage to the commissural fibers connecting the two hemispheres or damage to the posterior regions of the right hemisphere specifically involved in processing and comprehending emotional information (Tabibnia & Zaidel, 2005). Furthermore, this right hemisphere dysfunction is conceptualized as damage to the same area which results in receptive aprosodia, and both alexithymia and aprosodia appear to share neural correlates (Lane, Ahern, Schwartz, & Kaszniak, 1997). Spalletta and colleagues (2001) found that alexithymia resulted from damage to territories served by the right middle cerebral artery, particularly the right temporal and parietal regions as well as the lenticulostriate branches.

Described very early in the neuropsychological literature, *hemispatial neglect* is a syndrome whereby a patient fails to report, respond or orient to, explore, or otherwise direct attention toward the visual or body space contralateral to a lesion (Bisiach, 1999; Buxbaum et al., 2004; Halligan & Marshall, 1993; Heilman, Bowers, Valenstein, & Watson, 1987; Heilman, Watson, & Valenstein, 2012; Kinsbourne, 1970; Mesulam, 1981; Rizzolati & Berti, 1993; Vallar, 1993; Vallar, 1998). The disorder is also considered to be the manifestation of a loss of represented left hemispace. With reference to the previously mentioned spatial frames of reference, a patient might exhibit neglect in personal, peripersonal, and extrapersonal space (Buxbaum et al., 2004). Thus, spatial neglect may be egocentric (body-centered) or allocentric (externally object/location centered). Within the aforementioned egocentric spatial frame (the mid-saggital plane of the body), patients may neglect objects (generally visual or auditory) in personal space (the patient's body) or in peripersonal space within specific sectors such as objects within hand reach or within the auditory radial plane. Dysfunction within the allocentric spatial frame concerns the contralesional side of objects in extrapersonal space independent of their position with regard to the patient's body. Thus, a patient may neglect the left half of an

object irrespective of its relation to the body center or neglect the left half of an object regardless of where it is in the patient's visual space (i.e. object-centered deficit). Further complicating this picture of neglect dissociations is that the notion of *allocentric* space directly refers to extrapersonal space that is outside of hand-reach and thus encompasses the larger spatial coordinate system within which the body behaves. Thus, patients may exhibit neglect within peripersonal space while able to orient to object appearing farther from them in extrapersonal space (Halligan & Marshall, 1991). There may be a rotation of the egocentric spatial frame toward the ipsilesional side of space, that the side ipsilateral to the lesion (the right side) is comparatively spared and a lateral spatial-attentional gradient may remain in which the patient experiences a general decrease in the ability to orient into the affected hemispace (from right hemispace decreasing toward left hemispace; Kinsbourne, 1993; Vallar, 1998). Furthermore, space extends horizontally, vertically, and radially. Thus, spatial neglect may occur in all 3 visible dimensions, the most common type of neglect being that of left horizontal, lower vertical, proximal radial hemispace (Gawryszewski, Riggio, Rizzolatti, & Umilta, 1987; Ladavas, 1993; Shelton, Bowers, & Heilman, 1990; Heilman et al., 2012). Hemispatial neglect is our primary disorder of spatial functions.

Research has indicated that damage to the right inferior parietal, posterior-superior temporal lobe, the anterior portion of the right angular gyrus involving the parietal-occipital-temporal heteromodal association cortex, right thalamic nuclei, and the right basal ganglia nuclei (caudate and putamen) are necessary for the production of neglect with the most critical lesion site involving the inferior parietal and posterior temporal lobes at the tempero-parietal junction (Bisiach, 1999; Corbetta, 2014; Corbetta et al., 2005; Gainotti et al., 1972; Halligan et al., 2003; Heilman et al., 2012; Karnath, Ferber, & Himmelbach, 2001; Karnath, Berger, Kuker, & Rorden, 2004; Mort et al., 2003; Vallar & Perani, 1986; Vallar & Perani, 1987; Vallar, 1993; Vallar, 1998, Vallar, 2001).

Considered to be one variation of the *productive* behaviors that patients exhibit following right sided brain damage, Gerstmann's (1942) *somatoparaphrenia* (from the Greek "soma" = body, "para" = next to/in addition, "phren" = nerve) is the clinical construct of denial of limb ownership, a deficient body part, and/or of ascribing the ownership to another (Bisiach, Rusconi, & Vallar, 1991; Bottini et al., 2010; Critchley, 1957; Cutting, 1978; Halligan, Marshall, & Wade, 1995; Karnath & Baier, 2010; Sandifer, 1946; Vallar & Ronchi, 2009). This disorder seems to be

a complex form of bodily integrity dysfunction that is related directly to anosognosia. The disorder manifests when a patient begins expressing delusional beliefs about the affected parts of the body, usually on the left side. They typically will deny ownership of the extremity, attribute its ownership to someone else, and/or make claims about their limbs that are absurd (Gandola et al., 2012; Halligan et al., 1995; Karnath & Baier, 2010; Vallar & Ronchi, 2009).

Patients tend to also "personify" or react with very strong emotions toward their paralyzed limbs. Typically, the emotional reaction manifests as a negative one in which patients express hatred for their limb and a desire to see it removed, a phenomenon known as *misoplegia* (Critchley, 1974; Karnath & Baier, 2010). This may also be the converse with *acute hemiconcern* in which the patient overvalues the paralyzed extremity and seeks to protect it, even from medical intervention (Bogousslavsky, Kumral, Regli, Assal, & Ghika, 1995). Both hatred and love can occur in the same patient with the same deficit over a period of only a few hours, thus providing evidence of some of the fluctuations also seen in anosognosia (Loetscher, Regard, & Brugger, 2006). Personification manifests in assigning the paralyzed limb a personality or anthropomorphizing their deficit (Critchley, 1957; Critchley, 1955), giving the limb a name and talking with it (Vallar & Ronchi, 2009). Anosognosia is usually present with these patients but must remit to some degree in order for the patient to acknowledge the limb. However, it remains apparent in the individual's inability to understand how their behavior and the alienation of their limb is abnormal. Additionally, the actual loss of the limb is really a loss of awareness of limb ownership. Somatoparaphrenia may thus be understood to possess overlapping characteristics of the previous three disorders: a spatial delusion with an emotional component and awareness difficulties. This disorder tends to fluctuate considerably while possessing these components.

The right hemisphere *aprosodias* have been discussed, with reference to other emotional disorders, and the overlap of aprosodia with alexithymia. Other disorders of spatial function generally present in tandem with the more prominent syndromes mentioned before. Topographical disorientation manifests in several forms but generally patients with these lesion patterns lose the ability to navigate in space, experience directional confusion, and landmark agnosia (Aguirre & D'Esposito, 1999; Farah, 2003; Farah & Epstein, 2012). Additionally, patients experience impaired ability to draw and dress themselves in the form of constructional and dressing apraxias, respectively (Farah & Epstein, 2012). Lastly, dysfunction in these same spatial systems may affect left lateralized language systems: neglect dysgraphia and neglect

dyslexia present as very precise displacement of words, parts of words, and letters in both writing and reading (Vallar, Burani, & Arduino, 2010).

*Sympathetic Arousal and the Right Hemisphere*

Right hemisphere control of the sympathetic branch of the autonomic nervous system has been investigated extensively. Wittling (1995) has described the extensive anatomy and physiology of cerebral control of these functions and their respective laterality. Moruzzi & Magoun (1949) first identified the role of the reticular system in arousal, particularly following stimulation of right mesencephalic regions. Arousal dysfunction is most prominent following damage to right prefrontal and mesial frontal regions due to a failure to regulate descending corticofugal pathways to these brainstem reticular systems. Evidence suggests that right frontal regions exert regulatory control via corticofugal pathways over sympathetic arousal. Unilateral stimulation of insular regions in both hemispheres has been found to affect the regulation of sympathetic nervous activity differentially (Oppenheimer, Gelb, Girvin, & Hachinski, 1992) and hemispheric inactivation via the Wada procedure (intracarotid sodium amobarbital injections) has resulted in differential effects of left versus right hemispheric inactivation (Zamrini et al., 1990). Posterior regions of the right hemisphere have been associated with irregular cardiovascular reactivity including tachycardia and cardiac arrhythmia (Marshall, Westmoreland, & Sharbrough, 1983). Additionally, the previously discussed neurotransmitter asymmetries provide further evidence that those neurochemicals associated with arousal and recruitment of brainstem systems are distributed primarily to the right hemisphere. Furthermore, we have presented evidence of differential effects of emotional stimuli across sensory modalities on the right hemisphere (see above). Harrison (2015) provides a cogent and thorough review of findings related to sympathetic regulation by the right hemisphere and provides significant evidence that the left hemisphere may be responsible for the regulation of the parasympathetic branch of the autonomic nervous system.

*Integrating Spatial and Emotional Behavior*

Similar to integrated theoretical positions on emotion systems, representational theories of right hemisphere spatial dysfunction are based upon suppositions about right hemisphere function. Bisiach and Berti (1987) proposed that the right hemisphere possesses characteristics

that differentiate it from the left hemisphere in terms of the way external sensory information is received, integrated, and processed for later behavioral output. Thus, spatial awareness and processing of external coordinate space is dependent upon a system that functions via a non-propositional analog manner as contrasted by the left hemisphere's propositional coding. The strength of these models of space representation are their accounting for the same holistic, parallel, multimodal sensory processing capabilities that are assumed to be the basis for the lateralization of emotion systems to the right hemisphere (see above).

With regard to our previously discussed right brain disorders, alexithymia, neglect, and anosognosia have been found to disrupt higher cognitive functions including memory, sleep, attention, language, mental imagery, dreaming, and hallucinations (Baxter & Warrington, 1983; Berti, 2004; Bisiach & Luzzati, 1978; Buchanan, Waterhouse, & West, 1980; De Renzi, Faglioni, & Scotti, 1970; Fricchione & Howanitz, 1985). The fluctuations seen in somatoparaphrenia and anosognosia are an indication of a system that is changing while dysfunctional and this is not a characteristic seen in left hemisphere syndromes (Bisiach et al., 1991; Prigatano, 2010; Ramachandran, 1995; Rubens, 1985; Turnbull, Jones, & Reed-Screen, 2002). This point lends credence to the differential processing modes of the two hemispheres, the right hemisphere's role in sympathetic arousal, and the dynamic fluctuation of emotion that is characteristic of normal brain function. These systems occupy the same functional cerebral space (see Kinsbourne, 1980). The emotional nature of alexithymia, anosognosia, and somatoparaphrenia has been well documented. But researchers have also indicated that information processing in spatial neglect has a subtle, but likely strong, emotional component, particularly with regard to exhibited attitudes toward the neglect side of space (Bisiach, 1994; Turnbull et al., 2002). Everhart and colleagues (2001) investigated the propensity for right hemisphere patients to experience spatial delusions. Referencing the unusual lateralization of misidentification syndromes and delusional behavior following right hemisphere damage, they found dysfunction in right temporoparietal regions during the neuropsychological evaluation as well as decreased cortical beta activity on qEEG. Furthermore, they found increased beta activity over homologous left hemisphere regions during an affective arousal task. These authors note that the results support the notion of the right posterior region's role in awareness with relation to coordinate space.

Theoretical models of anosognosia, body schema dysfunction, and emotional disorders have sought to explain the overlapping presentation these disorders and their overlapping anatomy. Multiple perspectives have been put forth and are beyond the scope of this discussion, however the problem has been well documented (Bisiach & Berti, 1987; Cutting, 1978; Karnath & Baier, 2010; Marcel, Tegner,& Nimmo-Smith, 2004). The previously reviewed findings on right hemisphere functions and the lateralization of emotional and spatial systems begs the question of how do the two interact. The model proposed by Bisiach and Berti (1987) provides for underlying neural networks for these disorders as well as a framework for considering them as part of a larger syndrome. Karnath and Baier (2010) proposed that the deficits of these systems in right brain damage are akin to a "disturbed sense of ownership" of left sided body space and body parts. They provide evidence that this dysfunction arises from insular cortical regions in the right hemisphere (see Craig, 2010 for insular contributions), but do not account for the spatial disruptions.

A more compelling proposal has recently been put forth by Turnbull, Fotopoulou, and Solms (2014) stating that deficits of awareness are a direct consequence of disruption of *veridical spatial cognition*, which they define as realistic and accurate spatial knowledge. Drawing heavily from emotion research and anosognosia, they propose that the damage seen in anosognosia and other disorders causes disruption of the normal mechanisms involved in right hemisphere regulation of emotion systems. That right brain damage results in left sided spatial deficits related to body parts and space that also tend to fluctuate in a manner that is inherently emotional, is taken to mean that these systems are interdependent. Thus, a patient is unable to perceive their deficit because they are unable to take a spatial perspective other than that of self-centeredness (e.g. there is nothing wrong with me; there is something wrong with how you perceive me). There is no "theory of mind" or "taking another's perspective" behavior. The individual sees only what was previously encoded and what is desired (egocentric spatial cognition). Citing evidence from the available research indicating that manipulation of the emotional significance of a deficit can alter awareness (Fotopoulou et al., 2010; Ramachandran & Blakeslee, 1998), it is proposed that the ability to regulate strong emotional valences is required to maintain integrity of spatial systems that subserve the ability to take an allocentric (outside) spatial perspective. In this case, damage to the overlapping emotional and spatial centers leave the emotion systems unregulated and thus patients are, for reasons not clearly

understood, unable to "move" within space because to do so would require "tolerance" (read regulation) of strongly valenced negative emotion (e.g. realization of an extreme deficit such as paralysis). To be clear these are not psychogenic or psychodynamic arguments but rather these researchers have proposed that space is emotionally constrained which requires understanding that either emotion and space are the same functional output of anatomically isometric systems or that an unknown mechanism governs the strong connection between these two constructs.

Previous experimental research has examined the role of emotion in attending to coordinate space. Foster and colleagues (2008) sought to explain how the lateralization of emotion systems might bias attention to hemispace with reference to some of the models of spatial attention previously discussed. On the basis that asymmetric hemispheric arousal results in allocation of attention to the contralateral hemispace and the proposition that the left hemisphere is capable of mediating attention in proximal (peripersonal) space (Heilman, Chatterjee, & Doty, 1995), these authors proposed that the mutual reciprocally balanced relationship between the frontal and posterior regions of each hemisphere would affect the influence of emotion systems on spatial attention. In a paradigm utilizing a pegboard in which subjects placed emotionally-labeled pegs while thinking of how the emotion felt to them, the researchers found that positively-labeled emotional pegs were placed in distal left radial hemispace. Furthermore, they found that the negative emotional pegs were placed in proximal right radial hemispace relative to the positive pegs. The authors note that, consistent with the *quadrant model*, the positive emotional pegs resulted in left frontal lobe activation, a corresponding inhibition of left posterior regions, inhibition of right frontal lobe, and activation of right posterior regions. Thus, the activation in the right posterior region biased attention to left hemispace and the corresponding left frontal activation biased the affective valence in favor of positive emotion. Furthermore, the findings were taken to support the notion that the right hemisphere has a particular affinity for distal hemispace. The placement of the negative emotional pegs was interpreted as right frontal activation resulting in right posterior inhibition, left posterior activation and a bias toward right hemispace and proximally, supporting the potential role of the left hemisphere in proximal right hemispatial relationships.

This experiment is novel in that it directly tests the role of emotion in a task that is arguably measuring a spatial relationship. Our laboratory has previously proposed a theoretical model to explain how functional neural systems, in the right brain in this case, operate to result

in highly intense emotional states. This model has been described extensively elsewhere but the basic tenets will be discussed. The *Dynamic Functional Capacity Model* (Carmona, Holland, & Harrison, 2009; Harrison, 2015; Mitchell and Harrison, 2010; Williamson and Harrison 2003) has hypothesized that right hemisphere regions responsible for regulation of emotion and cortical arousal have a limited functional capacity that may thus be exceeded and dysfunction via overwhelming external stimuli or damage. The basis for this model derives from the notion that prefrontal neural systems have limited cellular metabolic resources in which to exert regulatory control over posterior and subcortical brain regions. Thus, prefrontal cortical regions effect regulatory control over arousal systems and emotion systems in response to sensory stimulation. This model is based upon basic cortical anatomy and our previously discussed models of cortical function (e.g. inter- and intra-hemispheric balance). Because the cellular resources of any brain tissue are finite, the resources of regions involved in regulatory control may be depleted or exceeded with the input of sufficient external (sensory) or internal (damage) stress. When these regulatory neural systems fail, it is reasonable to expect disinhibition of posterior sensory and subcortical arousal systems. Beyond disinhibition, it may be expected that general dysregulation leaves these systems functioning in an aberrant manner.

With regard to our previously described systems, models, and disorders, it is possible that the disruptions to awareness, spatial, and emotion systems in the right hemisphere results from damage to brain tissue that leaves these systems unregulated. This damage occurs either by way of exceeding capacity limitations of our prefrontal systems or by disconnecting the prefrontal regions from the posterior systems. Thus, these shared neural systems may experience both unbridled activation and dynamic oscillations leading to behavioral outputs that correspond with such activity.

*Summary and Purpose of the Current Experiment*

We have established a basis for understanding that 1) emotion systems appear lateralized largely to the right hemisphere, 2) the right hemisphere plays a significant role in negative, withdrawal, protective, defensive emotion states, 3) the right hemisphere appears to be specialized for processing and regulation of external coordinate space, 5) the right hemisphere, via reciprocal cortical-subcortical connections with specific brainstem areas, possesses a dominant role in recruiting arousal and sympathetic autonomic systems, 6) the left and right

hemispheres process external sensory stimuli and internal system representations in different but mutually beneficial manners, and 7) the right hemisphere possesses significant neurophysiological mechanisms for the aforementioned systems that are clearly differentiated in both anatomy and function from those of the left hemisphere but which appear to share an overlapping neural architecture.

Given the aforementioned points, it has been proposed that spatial and emotional systems in the right cerebral hemisphere are possess overlapping cortical anatomy and, via their dysfunction, may possess an overlapping, if not similar, functional nature. Thus, space and emotion should vary as a function of the other and that spatial relationships should be dependent upon emotional regulation. We seek to test hypotheses regarding the systems and models discussed by way of a cold pressor paradigm in which subjects are interacting in a spatial task with emotional stimuli. The cold pressor task serves as both an arousal of these systems and a stressor on frontal capacity via pain (see Mitchell & Harrison, 2010). The spatial-emotional task seeks to extend the aforementioned study by Foster and colleagues (2008) by way of testing whether emotion and space are bidirectionally influenced as it relates to cerebral dysfunction in such a way as to mimic conditions of right brain damage in healthy subjects. Further proposed are different hypotheses regarding the outcome of exposure to emotional stimuli and external stressors.

In a normal functioning brain, there should be a left hemispatial bias for negative emotion and a right hemispatial bias for positive emotion. Under conditions of cortical duress such as a cold pressor, over-stressing the right posterior regions might produce the conditions necessary for dysregulation of right posterior regions by the right frontal lobe, thereby disrupting normal right hemisphere spatial and emotional control. Per our theoretical bases, in right side stroke patients, the RH ceases to be able to regulate salient negative emotion as well as experiencing disruption to spatial attention in the left hemispace. Therefore, the ability to project awareness of space leftward and distally is disrupted. The result may be an egocentric or peripersonal spatial bias and a preference toward right hemispace generally. A similar result may be expected in this paradigm in which a cortical stressor is introduced in addition to emotionally valenced stimuli, the type of which corresponds differentially to left or right cerebral activation. Generally there should be a disruption of allocentric spatial cognition in the presence of cortical stress that leaves the right brain unable to properly address negatively valenced external stimuli.

# Chapter 2

## Method

*Emotional-Spatial Hypotheses*

1) It is expected that facial stimuli will trend toward biasing subjects toward left hemispace.
2) It is expected that verbal stimuli will trend toward biasing subjects toward right hemispace.
3) At baseline, it is expected that negative emotional stimuli will bias subjects to distal left hemispace, generally.
4) At baseline, it is expected that positive emotional stimuli will bias subjects to proximal right hemispace, generally.
5) Under cold pressor stress, it is expected that exposure to negative emotional stimuli will result in a proximal left hemispatial bias whereas exposure to positive emotional stimuli will result in a proximal right hemispatial bias.
6) Under cold pressor stress, negatively valenced facial stimuli should produce the greatest spatial bias into proximal left hemispace.
7) Under cold pressor stress, positively valenced verbal stimuli should produce the greatest spatial bias into proximal right hemispace.

*Physiologic Hypotheses*

1) It is expected that cold pressor stress will alter sympathetic drive evident on cardiovascular measures of heart rate and systolic blood pressure.

*Sex Difference Hypotheses*

1) It is expected that male subjects will exhibit greater laterality in the placement of emotional stimuli
2) It is expected that cold pressor stress will have a greater effect on the placement of emotionally valenced stimuli by male subjects relative to female subjects.

3) It is expected that the greatest laterality biases will be exhibited by high-hostile male subjects under cold pressor stress when exposed to emotionally valenced stimuli, relative to female subjects in general.

*Subjects*

Subjects consisted of 52 individuals, both male (n = 17) and female (n= 35), with an age range of 18-22 years. Subjects included Caucasian, Indian, African, Latino-Hispanic, Arabic, and Asian ethnicities. They were recruited from an undergraduate population at a major university. Education level was consistently between 13 (first year of college) and 16 (last year of college) years. Subjects were screened for an exclusionary criteria consisting of a history of neurological insult or illness, a history of mental illness, major medical systemic illness, current use of neuro/psycho tropic medications, visual and hearing impairments (uncorrected), and left-handedness. Subjects provided written informed consent to participate and approval for this research design was granted by the Institutional Review Board of Virginia Polytechnic Institute and State University.

In order to obtain relevant information pertaining to subject selection, individuals will were screened for demographic information, medical history, mental health history, medication history, and laterality preference (see below).

*Screening Questionnaires*

*Medical History Questionnaire*: Our medical history questionnaire consists of questions designed to determine whether a subject may be excluded based upon a preexisting condition that met our exclusionary criteria (e.g., Mitchell & Harrison, 2010).

*Beck Anxiety Inventory (BAI)*: The BAI (Beck & Steer, 1990; Bardhoshi, Duncan, & Erford, 2016) is a 21-item self-report Likert scale designed to assess the presence of generalized anxiety and anxiety disorders. The items are designed for individuals to rate the degree to which they have been bothered by such symptoms in the past week. Each item is endorsed on a 4-point scale with a range of possible scores from 0 to 63. The BAI has been found to have strong internal consistency and reliability in addition to higher convergent and discriminant validity

than other measures of anxiety (Fydrich, Dowdall, & Chambless, 1992). This questionnaire was used to screen for a history of anxiety.

*Beck Depression Inventory-II (BDI-II)*: The BDI-II (Beck, Steer, & Brown, 1996) is a 21-item self-report Likert scale designed to assess the presence and degree of self-reported depression. The items are related to different symptoms commonly associated with clinical depression. Each item is endorsed by the patient on a scale of 0 to 3 with a range of possible scores from 0 to 63. The BDI-II has been shown to have a high internal consistency and strong concurrent validity for the measurement of depression, particularly in college-age samples (Storch, Roberti, & Roth, 2004). This questionnaire was used to screen for a history of depression.

*Cook-Medley Hostility Scale (CMHS)*: In order to screen for cynical hostility and to group the subjects according to trait hostility levels, the CMHS will be used. The CMHS is a 50-item true/false self-report questionnaire derived from the Minnesota Multiphasic Personality Inventory that is designed to assess the presence of hostility, anger, and resentment (see Smith & Frohm, 1985). The CMHS has been classified as a state measure of hostility and it has been shown to exhibit validity in the measurement of the same (Demaree & Harrison, 1997). The CMHS has also been shown to possess a high degree of reliability (Smith & Frohm, 1985) as well as convergent and discriminant validity (Raikkonen, Matthews, Flory, & Owens, 1999) with regard to physiologic measures. For the purposes of our design, subjects scoring below 19 would be identified as low-hostile whereas those scoring above 29 would be identified as high-hostile. This categorical classification has historically been used in our research laboratory with reliable results (see Rhodes et al., 2017; Williamson & Harrison, 2003).

*Coren, Porac, and Duncan Laterality Questionnaire (CPD)*: The CPD (Coren, Porac, & Duncan, 1979) is a self-report questionnaire consisting of 13 items designed to assess the patient's lateral preferences for the foot, hand, eye, and ear. Items are scored as +1, -1, or 0 for "right", "left", or "both" respectively, with a range of scores from -13 to +13. A score of greater than or equal to +7, indicating a right lateral preference, was required for further participation.

*Demographics Questionnaire*: Basic demographics were obtained including race, sex, age, date of birth, years of education, place of birth/origin, and current educational/employment status.

*Toronto Alexithymia Scale-20 (TAS-20)*: The TAS-20 (Taylor, Ryan, & Bagby, 1985; Bagby, Parker, & Taylor, 1994) is a twenty-item self-report measure designed to identify the construct of alexithymia in patients. The overall scale is derived from 3 factors: difficulty identifying emotions and distinguishing them from physiological sensations of emotion (Factor 1), difficulty describing feelings/emotions to others (Factor 2), and an externally directed pattern of thinking (Factor 3). Research has consistently supported its use in identifying the disorder of alexithymia, as defined, and the scale has shown good convergent and concurrent reliability as well as discriminant validity across samples and across languages (see Bagby, Taylor, & Parker, 1993; Taylor, Bagby, & Parker, 2003; Parker, Bagby, Taylor, Endler, & Schmitz, 1993). The scale is administered in a 5-point Likert format with individuals rating the degree to which each statement agrees with their subjective experience. The questionnaire basic range is from 20 to 80 with a cutoff score of 61+ indicating the presence of alexithymia as a clinical construct. This questionnaire was used to screen for a history of alexithymia as a disorder of emotional awareness, although subject selection was not affected by the results of this measure.

*Apparatus*

*Affective Auditory Verbal Learning Test (AAVLT)*: The AAVLT (Everhart, Demaree, & Harrison, 2005; Mollet & Harrison, 2007; Snyder & Harrison, 1997; Snyder, Harrison, & Shenal, 1998) is a 45-word affectively-based supraspan-word list designed to provide an objective measure of emotion-based auditory verbal learning. Three separate sub-lists of 15 words each: 1 emotionally negative, 1 emotionally positive, and 1 emotionally neutral, were derived for this purpose. An equal proportion of one- and two-syllable affective words comprise the lists. The positive and negative lists, which are comprised of those words rated highest and lowest in pleasantness, respectively, were adapted from the Toglia and Battig (1978) index of word norms. The neutral word list was adapted from the Rey Auditory Verbal Learning Test (RAVLT; Rey, 1964). For the purposes of this experiment, words were taken from the positive and negative lists to create our verbal spatial array.

*Pictures of Facial Affect*: The Pictures of Facial Affect (Ekman, 1976) are a series of 110 black/white photographic slides consisting of individuals, both male and female, mimicking 6 distinct emotions (happiness, sadness, fear, anger, disgust, and surprise). Within the original set are an equal number of "neutral" emotional expressions. From this set we selected 15 photographs each, with one set identified as "positive" and the other identified as "negative."

*Cold Pressor*: The cold pressor is a standard clinical cardiovascular and pain stressor designed to elicit or induce systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) reactivity. The cold pressor stress test consists of placing the hand in ice water (measured at 0-3 degrees Celsius) to just above the wrist radiocarpal joint (approximately 2.54 centimeters) and holding it in place for a duration of 45 seconds. Water temperature is maintained at 0-3 degrees Celsius and monitored by the use of a calibrated H-B Instrument B60303 Glass Thermometer. The water is kept in an insulated container, which is placed at approximately the same level as the heart ($4^{th}$ intercostal space). The procedures for this method are derived from those by Hines & Brown (1936).

*Physiologic*: Physiological data was acquired via the use of a Biopac Systems Inc. MP150 SW Data Acquisition Platform with a UIM100C interface module. The main platform is connected to an ECG100C electrocardiographic amplifier with shielded pinch leads (for recording of heart rate and cardiac electrophysiology) and a NBIP 100D Continuous Noninvasive Arterial Pressure monitor (for the measurement of arterial blood pressure) with associated cuffs. Data acquisition and analysis will be conducted with the use of Biopac Systems Acq-Knowledge 4.4 Software.

*Spatial Array*: Our spatial array consists of a square flat galvanized magnetic steel board measuring 24" x 24" that is divided into four equal quadrants (Left-Horizontal/Distal-Radial, Left-Horizontal/Proximal-Radial, Right Horizontal/Distal-Radial, and Right-Horizontal/Proximal-Radial). The division of quadrants is via the use of an overlay that subjects did not see.

- AAVLT Words: All positive (15) and negative (15) words from the AAVLT are grouped randomly.
- Ekman Faces: Negative faces (15) and positive (15) faces are grouped together on 2”x2” photographs.

*Procedure*

Subjects were recruited via the SONA system from within the Psychology Department research pool. Upon arrival at the laboratory subjects completed a written Informed Consent Form and were given an opportunity to ask all relevant questions related to participation in this project. Once consented, subjects completed the demographics questionnaire, Medical History Questionnaire, BAI, BDI-II, CPD, and CMHQ.

Subjects were then seated in a chair in front of a table on which the Spatial Array was placed. They were seated in a fixed position measured 6” from the table such that the board is centered in the subject’s midsagittal plane. The cold pressor cooler was placed next to the subject’s left arm but within adequate reach to ensure compliance with American Heart Association guidelines for the accurate measurement of blood pressure (see Harrison & Kelly, 1987; Harrison, Gorelczenko, & Kelly, 1988; Pickering et al., 2004). To ensure further accuracy in BP measurement, each subject was instructed to keep their legs uncrossed and feet flat on the floor in a relaxed position.

Each subject was then fitted with the physiological recording equipment. Lead placement for the electrocardiograph will follow the Einthoven Triangle Potential Measurement 3-Lead ECG. Specifically, electrodes will be placed with one on the right inner wrist medially, one on the left inner wrist medially, and one on the right inner leg above the ankle. Following the oscillometric method (see Harrison & Kelly, 1987; Harrison, Gorelczenko, & Kelly, 1988; Pickering et al., 2004), the left upper arm was fixed with a calibrated non-invasive BP monitoring cuff for the recording of SBP and DBP. A period of approximately 2 minutes was provided for subjects to adjust to the setting and to the recording equipment. Each subject was told that recordings would be taken.

***Condition 1 (Words)***

*Baseline (Physiologic)*

Subjects were instructed to remain seated with their feet flat on the floor shoulder-width apart. They were told "*Recordings will now be taken which include your heart rate and blood pressure, so please remain still with your feet flat on the floor and arms resting on the chair."* Heart rate, systolic, and diastolic blood pressure were collected twice in succession following the adjustment period. To determine the accuracy of the readings, a third reading was taken if the first two recordings differ by 6 beats per minute (HR) or by 20 mm Hg on the systolic BP measurement).

*Baseline (Spatial Placement)*

Following the collection of initial values, subjects were provided the following instructions: *"In front of you is a collection of individually laminated words. When instructed please take individual words from the collection, read each one to yourself, and place them however you wish on the board in front of you. Please place the words until you have them all on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."* Subjects will then be asked to begin placing the words on the tray and timing will commence.

*Stress (Cold Pressor)*

Subjects will then be given the following instructions: *"When instructed, please place your left hand in the water to a point about 1 inch above the wrist. You will be asked to hold your hand in the water for 45-seconds after which you will be told to remove it. This will be difficult due to some discomfort, but please try and to keep your hand in the water until instructed to remove it. (Ready the stopwatch to time) Please place your hand in the ice water."* Subjects will then be asked to place their hand in the water and after 45-seconds subjects will be asked to remove their hand from the water.

*Post-Stress (Spatial Placement)*

Subjects will then be given the following instructions: *"As before, when instructed you will begin taking words from the collection in front of you, reading each one to yourself, and placing them however you wish on the board. Please place the words until you have them all on the board. You will have approximately 3 minutes to do this. Let us know when you are done.*

*(When ready) Please go ahead."* Subjects will then be asked to begin placing the words on the tray and timing will commence.

*Post-Stress (Physiologic)*

Immediately following the conclusion of the post-stress word placement task, subjects will be asked to remain in their chair for a final recording of physiologic data. Heart rate and blood pressure values will then be recorded.

***Condition 2 (Faces)***

*Baseline (Physiologic)*

Following the conclusion of the final recordings of the first condition, subjects will remain seated. They will be told *"Recordings will now be taken which include your heart rate and blood pressure, so please remain still with your feet flat on the floor and arms resting on the chair."* Heart rate and blood pressure values will then be recorded.

*Baseline (Spatial Placement)*

Following collection of initial values, subjects will be given the following instructions: *"In front of you are several cards with faces on them. When instructed please take each face from the collection, look at each one, and place them on the board however you wish so that each face is visible. Please continue until you have placed all the faces on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."* Subjects will then be asked to begin placing and timing will commence.

*Stress (Cold Pressor)*

Subjects will then be given the following instructions: *"When instructed, please place your left hand in the water to a point about 1 inch above the wrist. You will be asked to hold your hand in the water for 45-seconds after which you will be told to remove it. This will be difficult due to some discomfort, but please try and to keep your hand in the water until instructed to remove it. (Ready the stopwatch to time) Please place your hand in the ice water."* Subjects will then be asked to place their hand in the water. After 45-seconds subjects will be told to remove their hand from the water.

*Post-Stress (Spatial Placement)*

Subjects will then be given the following instructions: *"As before, when instructed please take each face from the collection, look at each one, and place them on the board however you wish so that each face is visible. Please continue until you have placed all the faces on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."* Subjects will then be asked to begin placing the faces onto the tray and timing will commence.

*Post-Stress (Physiologic)*

Immediately following the conclusion of the post-stress spatial placement, subjects will be asked to remain in their chair for a final recording of physiologic data. Heart rate and blood pressure values will then be recorded. At the conclusion of data recording, subjects will be asked to complete a questionnaire about the cold pressor task (adapted from Dr. Gina Mollet's dissertation; see Mollet, 2006) and then be dismissed from the experiment.

# Chapter 3
## Analyses

Initial analyses were performed by separating the groups by sex (male/female). Our design consisted of a mixed factorial design with fixed effects of group and repeated measures on the spatial variables. The between-subjects variable consisted of two levels (male/female) with repeated measures of Condition (words/faces), Valence (positive/negative), Stressor (pre/post), and Quadrant (left distal, left proximal, right distal, right proximal) were used. The dependent variable consisted of the number of stimuli placed in each quadrant.

Initial analyses of our questionnaire measures (BDI-II, BAI, TAS-20, CMHQ) indicated three subjects who demonstrated alexithymia on the TAS-20 and three subjects with significantly elevated generalized anxiety on the Beck Anxiety Inventory. No significant elevations were demonstrated on the BDI-II or the Cook Medley Hostility Questionnaire. None of the subjects with alexithymia or anxiety demonstrated significant findings with regard to spatial placement.

A 5-way mixed repeated measures ANOVA was then conducted to determine whether our subject's spatial location placement differed on the basis of group (sex). In some cases the assumption of sphericity was violated and in these cases, either the Huynh-Feldt or Greenhouse-Geisser corrections were used as needed. In all other cases, the assumption of sphericity was met as well as other assumptions of the mixed factorial analysis of variance. Descriptive statistics are included in Table A1. No significant differences $F(1, 50) = .342$, $p = .561$ were found between males (n = 17) and females (n = 35) across condition, valence, stressor, or quadrant on the spatial placement of stimuli (see Table A2).

Further analyses examined whether our subject's placement of stimuli differed on the basis of the quadrant, condition, valence, or the application of the stressor (see Table A3). No main effects were found for Cold Pressor (Stressor; $F(1,50) = .157$, $p = .694$), Condition ($F(1,50) = 1.085$, $p = .303$), or Valence ($F(1,50) = 1.143$, $p = .290$). There was a main effect of Quadrant. Mauchly's test indicated that the assumption of sphericity had been violated so the Greenhouse-Geisser correction was used. Results were significant ($F(1.998, 99.898) = 7.028$, $p = .000$)

indicating that subject placement of stimuli different on the basis of quadrants on the spatial array (see Table A4 and Graph B1 for estimated marginal means).

Post-hoc pairwise comparisons, using a Bonferroni correction for the familywise error rate, were conducted to compare our main effects (see Table A5 for estimated marginal means and pairwise comparisons). Significant differences were found in the number of stimuli placed within *left distal* and *right proximal* hemispace ($p = .029$) with greater stimuli placed within the right proximal hemispace. When compared to the *right distal* hemispace, subjects placed more stimuli within the *left proximal* hemispace ($p = .021$). Lastly, comparison of the *right distal* to *right proximal* indicated subject preference for the right proximal location ($p = .016$).

There was a significant interaction effect ($F(2.411, 120.555) = 8.820$, $p = .000$) between the quadrant in which stimuli were placed and the particular type of stimuli (words versus faces) that were placed (see Table A3). Subjects placed more faces within the distal left and right hemispace while placing more words within the proximal left and right hemispace (see Table A6 for interaction effects between Quadrant and Condition). Overall, there tended to be a preference for placement of words within proximal peripersonal space bilaterally and for faces within distal peripersonal space bilaterally (see Graph B2 for interaction effects).

Groups were split by sex and intra-group analyses were conducted to determine again whether placement differed on the basis of our independent variables of quadrant, condition, valence, or the application of the stressor (cold pressor). A 5-way repeated measures ANOVA was conducted with variables consisting of 2-level repeated measures variables of Condition (words/faces), Valence (positive/negative), and Stressor (pre/post) and one 4-level repeated measures variable of Quadrant (left distal, left proximal, right distal, right proximal). Our dependent variable consisted of the number of stimuli placed in 1 of 4 locations (left proximal, right proximal, left distal, right distal).

Males (n= 17) were analyzed first (see Table A7 for Descriptive Statistics). No main effects were found for Valence ($F(1,16) = .190$, $p = .668$), Cold Pressor (Stressor; $F(1,16) = .895$, $p = .188$), Quadrant ($F(1.602, 25.627) = 3.551$, $p = .053$) or Condition ($F(1, 16) = 1.895$, $p = .188$; see Table A8 for Within Subjects Effects). Post-hoc analyses using the Bonferroni correction for the familywise error rate were not significant. However, there was a significant interaction effect between the quadrant of placement and the particular stimuli ($F(1.615, 25.832) = 4.794$, $p = .023$) indicating that male subjects tended toward placement of a greater number of

faces within distal left and right hemispace, while placing more words within proximal bilateral hemispace (see Table A9 and Graph B3 for the interaction effects between Quadrant and Condition).

No main effects for females (n = 35) were found for Cold Pressor ($F(1,34) = 2.482$, p = .124), Valence ($F(1,34) = 2.203$, p = .147), or for Condition ($F(1, 34) = 1.337$, p = .256). However, a main effect for Quadrant was found ($F(2.365, 80.406) = 4.680$, p = .008; see Table 11 for Within Subjects Effects). Mauchly's test of sphericity was significant so the Huynh-Feldt correction was used. Post-hoc analyses indicated a significant pairwise comparison (p = .016) between the right distal and right proximal quadrants; more stimuli were placed within the right proximal quadrant than the left (see Tables A12 and A13 for pairwise comparisons and estimated marginal means; see Graph B4 for female placement of stimuli). A significant interaction effect was found again for the quadrant of stimuli placement and the particular stimuli (words or faces) placed ($F(3, 102) = 5.040$, p = .003) indicating that female subjects also tended toward placement of a greater number of faces within distal hemispace bilaterally and placement of words more proximally (see Table A14 and Graph B5 for interaction effects between Quadrant and Condition).

Subsequent analyses were performed to determine whether differences in physiological variables could be found prior to or after introduction of the cold pressor. A mixed factorial repeated measures multivariate ANOVA was conducted (4x2). Repeated measures consisted of Trial (pre-CP 1, post-CP 1, pre-CP 2, post-CP 2) and a between subjects factor of Condition (counterbalanced words/faces). The Condition variable was examined to determine whether there was a significant effect of the type of stimuli on changes in any of the physiologic variables. Analyses were performed to determine the effects of cold pressor stress on systolic blood pressure (sBP), diastolic blood pressure (dBP), and heart rate (HR). See Table A15 for Descriptive Statistics of our Physiologic Variables.

Omnibus multivariate analyses indicated a main effect of Trial ($F(9,39) = 3.022$, p = .008) indicating significant change across the four trials (see Table A16 for multivariate omnibus analyses). There was no significant main effect for Condition ($F(3,45) = .614$, p = .609). Follow-up univariate ANOVAs indicated significant main effect for diastolic blood pressure (Trial; $F(1.966, 92.396) = 4.059$, p = .012). There was a linear trend of increasing diastolic blood pressure values from beginning to end (see Graph B6).

There was no significant effect of cold pressor stress on systolic blood pressure ($F(3, 141) = 1.831$, $p = .144$). Neither was there a significant main effect of heart rate across conditions ($F(2.612, 122.75) = 1.53$, $p = .222$). No significant post-hoc comparisons were noted. There were no significant interactions between the condition and specific changes in physiologic values.

# Chapter 4
# Discussion

*Findings*

The findings of our primary analyses did not support the hypotheses that male subjects would exhibit greater laterality in the placement of emotional stimuli. Neither was it found that cold pressor stress would have a greater effect on the placement of emotionally valenced stimuli by male subjects. Overall, no significant sex differences were found. Certainly, the limitations of our study design (described shortly) may have contributed to a lack of sex difference findings. Given the findings of increased hemispheric interaction in females and greater lateralized behavior in males, it may be expected that further stressing a particular brain region in males would exacerbate preexisting lateralized functions based upon sex. The effects of an external stressor such as a cold pressor were designed to mimic conditions of cortical function under duress (e.g. damage in the case of a stroke). Currently there is not a sufficient body of research examining sex differences amongst clinical populations presenting with neglect, anosognosia, or body schema disturbances. There is evidence for sex differences in alexithymia (see Levant, Hall, Williams, & Hasan, 2009). Given these findings, or lack thereof, conjecture about the reasons for a lack of sex differences from homologous paradigms in healthy individuals is difficult even controlling for the limitations of our study. Lastly, given our lack of high-hostile subjects, conclusions regarding our hypotheses with regard to sympathetic arousal and cold pressor stress cannot be made.

Primary analyses of our spatial data did not yield support for our hypotheses that either facial stimuli would bias subjects toward left hemispace or verbal stimuli would bias subjects toward right hemispace (Hypotheses #1 and #2). Furthermore, there was no direct support for the more specific hypotheses that negative emotional stimuli would bias placement toward distal left hemispace or that positive emotional stimuli would bias subjects to proximal right hemispace (Hypotheses #3 and #4). Neither did the addition of cold pressor as a stressor significantly affect the placement of negatively or positively valenced stimuli of either type (words or faces). Thus no support was found for our most direct hypotheses that cortical stress and emotional valence

would influence the ability of a subject to interact with allocentric left hemispace in particular (Hypotheses #5, #6, #7).

However, results were found suggestive of a spatial bias for both words and faces both radially and horizontally. More specifically placement of stimuli within quadrants was compared and overall, individuals demonstrated a preference for placement of stimuli within right proximal hemispace. Further analyses found that subjects demonstrated a preference for placement of stimuli by type (words versus faces). In this case the placement varied by radial space (distal and proximal). Placement of words was more common within the proximal left and right hemispace while the placement of faces within the distal left and right hemispace.

In the secondary intra-group analyses of male and female subjects, similar results were found across both groups. Both males and females exhibited a preference for placement of faces within distal bilateral hemispace and the placement of words within proximal bilateral hemispace. However, our post-hoc comparisons indicated that females showed a preference for right proximal hemispace in their placement of stimuli. This particular finding is interesting given that there was also preferential placement for words proximally. Conjecture about this particular finding in females is difficult although it may be considered in the context of general brain sex differences and the effects of brain damage. Research has consistently shown greater interhemispheric connection and consequentially communication in females than in males (see Ingalhalikar et al., 2014). In the case of damage to the right side of the brain (or in this case a pain stressor) it may be that the left hemisphere reacts differently in females than in males. So the placement of a left hemisphere stimulus (words) in the left hemisphere's dominant spatial orientation (right proximal hemispace) by our female subjects may be the result of stress to the right side resulting in left hemisphere priming by not only the stimulus itself but as a result of disinhibition due to right cerebral weakness. Thus, the left hemisphere is more activated because it is no longer balanced by the right. This may be more likely to occur due to aforementioned female interhemispheric connections that are not seen as predominantly in males. This finding does lend some support to Hypothesis #2 that verbal stimuli will bias subject placement toward right hemispace.

Regarding our physiologic variables of blood pressure and heart rate, there was not sufficient support for the hypotheses that cold pressor stress would significantly alter sympathetic drive via systolic blood pressure and heart rate (Hypothesis #1). Similarly, the

secondary hypotheses related to sympathetic arousal and hostility (Hypotheses #2 and #3) were not met. This was primarily due to limitations of our study and the lack of available high-hostile subjects. Across trials there was a trend of increasing diastolic blood pressure. This trend was likely the result of increasing exposure to the cold pressor over two trials as well as subject arousal increasing over the course of the experiment. However, although previous studies have done so, no conclusions can be drawn regarding the level of sympathetic arousal as a result of cold pressor stress.

Although unable to determine whether the predominant right proximal placement of stimuli occurred prior to or following the introduction of our stressor, given the normal right hemisphere dominance for processing spatial orientation, this may suggest that the effects of the cold pressor were enough to decrease the overall spatial bias of the right hemisphere. This would result in a left hemisphere control of the spatial orientation and preference for both right sided and proximal hemispace. However, without significant findings related to cold pressor stress, only conjectures can be made regarding this particular finding.

Given a left hemisphere bias for processing of propositional, language-derived stimuli (e.g. words, phonemes, etc.) and a right hemisphere bias for the processing of holistic, nonpropositional gestalt (e.g. faces, emotion, etc.) the finding that word and face placement varied by radial orientation lends support to the extant literature's reports on preferences for radial space by hemispheres. In this case, not only does the left hemisphere process words with greater ease, but also has a spatial preference for peripersonal or corporeal space (e.g. the body space itself). This is contrasted with the right hemisphere's bias for extrapersonal or extracorporeal space, hence the finding of greater face placement within distal quadrants. However it must be noted that although there does tend to be a hemispheric preference for both radial and horizontal space, there is still sufficient evidence that the right hemisphere is dominant for spatial processing overall and possesses greater capacity for right hemispatial processing than does the left hemisphere for ipsilateral space.

The study conducted by Foster and colleagues (2008) was modified to both include a stimulus-bound condition (words/faces) and a cortical stress paradigm (cold pressor) in order to mimic conditions of right brain damage in healthy subjects. The proposed findings differed from the previous study based upon the theoretical notions put forth in the *Capacity Theory* and those by Turnbull, Fotopoulou, and Solms' (2014) notion of *veridical spatial cognition*. Hypothesized

for this study was that with exposure to negatively valenced stimuli in a normal functioning brain, there should be a predominant left hemispatial bias with the converse being true for exposure to positively valenced stimuli. Further expectations included that with the addition of a cold pressor task as a cortical stressor, there would be a disruption of the subject's ability to appropriately interact with allocentric space and specifically within left hemispace.

Unfortunately no support was provided for these hypotheses. Our findings also did not directly support the hypotheses of the previous study (Foster et al., 2008). However, the finding of majority right proximal placement of stimuli may lend support for the *Quadrant Model* in that it indicates that with cold pressor stress and corresponding down regulation of the right posterior regions, there is a corresponding release of the left posterior region and consequent direction of attention toward right hemispace. Furthermore, independent of the valence of the stimuli or the presence of a cold pressor, the stimuli type influenced the area of radial space in which it was placed, lending further support to the previous research.

Three subjects elevated the alexithymia measure. From a theoretical standpoint, an expectation would be that subjects with alexithymia would have more difficulty with allocentric spatial interactions than those without. The reason for this is related to the models of the disorder positing that it is the result of dysfunction to the brain areas discussed. But more specifically it is a result of a particular individual's inability to adequately understand or recognize (i.e. process) their own emotion. However, due to the small sample size, no significant results were derived from these individuals.

Two observations were noted that may be regarded as unexpected findings. These may also be regarded as potential limitations to the study. The first is that subject placement behavior appeared to be random at times. This was also a direct result of our instructions and lack of direction when moving the subjects through the trials. It would be possible to better control for the confound of random placement via more specific guidance and instructions to subjects. However, this would also confound the ecological validity of the subject interaction during the task. Thus maximum freedom was allowed in subject placement without attempting to influence the way in which they did it. Secondly, an interesting phenomenon was noted in that a number of the participants appeared to group words and faces together based upon their valence. For example an individual subject would place all of the negative words in the upper right quadrant and place all of the positive words in the lower left. This same pattern was observed for the facial

stimuli. The most parsimonious explanation for this is related to simple semantic grouping in which individuals tend to cluster objects or stimuli according to semantic categories. In this case subjects likely identified stimuli as *positive* or *negative* and grouped them accordingly.

Both of these particular behaviors might be viewed as confounds but also necessary consequences of allowing subjects the freedom to interact with their environment under the controlled conditions (stimuli exposure and cold pressor). In other words, a stroke patient exposed to the same stimulus (valenced words/faces) would also be influenced by these same factors. Furthermore, this particular phenomenon shows how influential speech and language are over an individual's environmental behaviors. Even with the dominance of the nonverbal right hemisphere and stimuli that are primarily processed by that hemisphere (e.g. faces), individuals still use semantic language grouping in order to determine their placement of stimuli. This exposes the much larger limitation of attempting to design experiments examining laterality in nonclinical populations. Namely the difficulty in separating the use of language from any paradigm and relying solely on the abstract, nonverbal, and spatial functions of the right hemisphere. One last observation related to these points was noted: a very small number of individuals, when clustering the positive words in one quadrant and the negative words in another, would place the word "slay" in the wrong semantic category. This particular word is found within the negative word list on the AAVLT (Everhart, Demaree, & Harrison, 2005; Mollet & Harrison, 2007; Snyder & Harrison, 1997; Snyder, Harrison, & Shenal, 1998) but it was found that some subjects, when performing this grouping, would place "slay" with the positive words. Our undergraduate researchers were able to provide insights into how this particular word had come to be considered positive by younger populations, particularly in terms of a verb (e.g. "I slayed that test").

This small observation suggests an interesting hypothetical consideration: language appears malleable to change over time as influenced by culture whereas the social functions of the right hemisphere (e.g. facial analysis) do not appear to do the same. Thus negative facial expressions are always viewed as having some sort of negative quality (e.g. angry face). While cultural factors influence how gestural and facial behavior is viewed, there is significant evidence of universal basic emotions and their attachment to particular behaviors (e.g. angry face). This may be evidence of the ability of the left hemisphere to independently "decide" or assign values to the information it processes (i.e. a particular word is assigned or linked to an

emotional valence). With regard to our study, an interesting question would be whether individuals with right posterior cortical damage are still able to also process language accurately. Thus, without the right hemisphere's dominant emotional systems, can the left accurately assess the valence of language even though words have premorbidly been assigned to general categories such as "negative" or "positive". Clinical evidence suggests this is the case. Alexithymia as a brain disorder prevents patients from assigning meaning to emotions using language and furthermore impairs their ability to process emotion accurately. In our study there was no evidence that the three alexithymic participants lacked the ability to assign meaning to words. However, further studies might examine the degree to which this may be a fundamental principle of asymmetric cortical function in healthy individuals.

*Limitations*

There were several limitations to our study. First the methodological limitations included procedural difficulties, particularly related to the instructions to subjects. Foster's (Foster et al., 2008) study instructed subjects to feel the emotion they were identifying (e.g. the peg was labeled "happy" and thus they were to try and feel happy) prior to placement. Subjects were not asked to "feel" the emotion they were identifying (e.g. the word *cruel* should induce negative emotion) but rather instructed subjects to place the words as they "wished" (see instructions above). A modification to ask subjects to place words or faces however they "feel" might induce a greater emotional response. Subjects were instructed that they would have 3 minutes to place stimuli, whereas the previous study allowed subjects to take their time and did not indicate a time limit. In practice subjects were not stopped if they exceeded the 3 minute time limit but in instructing them that it existed, it may have induced a hasty response that was more methodical and possibly random than induced by emotional response.

We recreated the stimulus board (spatial array) used in the previous experiment with some modifications (e.g. ours was a metallic board as opposed to felt). One particular limitation related to this was that our subjects did not see the overlay used to divide the quadrants. Instead they only saw a 24"x24" white board on which they were permitted to place stimuli anywhere they desired. The lack of definitive divisions (boundaries) between the 4 quadrants certainly meant that subjects did not pay attention to the external space in terms of divisions (e.g. left proximal). Furthermore, our board restricted subjects to the aforementioned size of space in

order to approximate the interaction of an individual with space in arms-length (personal – peripersonal – extrapersonal). However, most individuals interact with space using visual direction visa vi line of sight. This also means that individuals tend to see and analyze their environment farther out in space than arms-length. Both of these factors limit the degree to which inferences can be made about how an individual might normally react in a similar situation in the "real world".

Subject recruitment was difficult and contributed to our unequal sample size. This was primarily a factor of the difficulty of recruiting within an academic university department from a population consisting of predominately undergraduate students with ages typical of that populace. Furthermore, our exclusionary criteria were found to be particularly stringent when correlated with the actual presentation of most subjects (e.g. a large percentage of recruited subjects were being treated for psychiatric illness or taking neurotropic medications) and thus prevented us from running a larger sample size. Furthemore, our restricted age range does not capture the typical ages at which patients tend to experience stroke or other neurologic insult (typically later in life).

A difference between the current and previous study, and a possible limitation, was that the previous study conducted a separate analyses to determine whether subject stimuli placement significantly differed from zero (i.e. the vertical (or radial) and horizontal bisection of the board). This allowed them to compare significant differences in radial placement within the horizontal and radial planes. This was not done because a greater number of stimuli (15 negative and 15 positive) was used than in the previous study (3 positive and 3 negative) making distance measurements difficult for the size of the board used. However, it may be that measuring for significant differences in spatial placement distance might lend insights into the way subjects interact in radial space independent of the horizontal or vertical planes. This particular methodological difference is something to consider in future studies and one that would likely be incorporated in any replication study.

*Future Directions*

As previously discussed, future studies should consider using the analysis technique of Foster and colleagues (2008) in which they measure the distance from true center for the placement of stimuli. This would require some adjustments to the amount of stimuli used to be

sure. Other considerations include having subjects experience the emotion subjectively, adjusting instructions, using different emotional stimuli, and other minor procedural changes. Furthermore, a larger sample size with a greater age range would be warranted. This would allow the capture of more individuals with alexithymia and possibly allow an analysis of how individuals with anxiety and depression are affected by the task. The use of functional magnetic resonance imaging (fMRI) has been considered in similar paradigms and may be a possible future direction using healthy subjects. However, the primary goal for a future replication study would be to conduct this study or a version thereof with a clinical population. Specifically, it would be interesting to have right hemisphere stroke patients engage in a spatial placement paradigm using emotional stimuli. Removal of the cold pressor task and increasing the size of the placement area (spatial board) would increase the ecological validity of the study. It would be interesting to note which disorders our subjects displayed most prominently and how these affected their spatial interactions. This would allow us to see how neglect, anosognosia, and other disorders directly affect the processing of emotional stimuli and the external environment.

# Appendix A

## Tables

*Table 1*
*Descriptive Statistics for Spatial Analyses*

| *Variable* | *Sex* | *Mean* | *Standard Deviation* | *N* |
|---|---|---|---|---|
| Left-Dist-Pre-Pos-Word | 1 | 2.41 | 3.104 | 17 |
| | 2 | 3.94 | 5.302 | 35 |
| | | | | |
| Left-Dist-Pre-Pos-Face | 1 | 3.24 | 2.728 | 17 |
| | 2 | 4.17 | 4.169 | 35 |
| Left-Dist-Pre-Neg-Word | 1 | 2.47 | 3.243 | 17 |
| | 2 | 3.20 | 4.079 | 35 |
| Left-Dist-Pre-Neg-Face | 1 | 3.94 | 2.839 | 17 |
| | 2 | 3.23 | 3.059 | 35 |
| Left-Dist-Post-Pos-Word | 1 | 2.06 | 3.132 | 17 |
| | 2 | 3.34 | 4.940 | 35 |
| Left-Dist-Post-Pos-Face | 1 | 3.00 | 2.693 | 17 |
| | 2 | 3.77 | 3.473 | 35 |
| Left-Dist-Post-Neg-Word | 1 | 2.41 | 3.355 | 17 |
| | 2 | 3.60 | 4.279 | 35 |
| Left-Dist-Post-Neg-Face | 1 | 3.82 | 3.226 | 17 |
| | 2 | 3.46 | 3.184 | 35 |
| Left-Prox-Pre-Pos-Word | 1 | 4.24 | 4.280 | 17 |
| | 2 | 4.37 | 5.168 | 35 |
| Left-Prox-Pre-Pos-Face | 1 | 2.24 | 2.195 | 17 |
| | 2 | 2.63 | 3.273 | 35 |
| Left-Prox-Pre-Neg-Word | 1 | 6.47 | 5.051 | 17 |
| | 2 | 3.54 | 3.988 | 35 |
| Left-Prox-Pre-Neg-Face | 1 | 5.41 | 2.717 | 17 |
| | 2 | 4.51 | 3.100 | 35 |
| Left-Prox-Post-Pos-Word | 1 | 3.41 | 4.317 | 17 |
| | 2 | 4.00 | 5.058 | 35 |
| Left-Prox-Post-Pos-Face | 1 | 2.76 | 2.705 | 17 |
| | 2 | 3.43 | 4.354 | 35 |
| Left-Prox-Post-Neg-Word | 1 | 6.88 | 5.207 | 17 |
| | 2 | 3.46 | 3.988 | 35 |
| Left-Prox-Post-Neg-Face | 1 | 5.24 | 3.093 | 17 |
| | 2 | 4.26 | 3.165 | 35 |
| Right-Dist-Pre-Pos-Word | 1 | 3.18 | 4.812 | 17 |
| | 2 | 2.69 | 3.724 | 35 |
| Right-Dist-Pre-Pos-Face | 1 | 4.76 | 3.649 | 17 |
| | 2 | 4.09 | 4.196 | 35 |

| | | | | |
|---|---|---|---|---|
| Right-Dist-Pre-Neg-Word | 1 | 2.12 | 3.120 | 17 |
| | 2 | 2.11 | 3.008 | 35 |
| Right-Dist-Pre-Neg-Face | 1 | 2.53 | 2.625 | 17 |
| | 2 | 3.26 | 2.694 | 35 |
| Right-Dist-Post-Pos-Word | 1 | 2.88 | 4.910 | 17 |
| | 2 | 2.43 | 3.500 | 35 |
| Right-Dist-Post-Pos-Face | 1 | 4.88 | 3.407 | 17 |
| | 2 | 4.06 | 4.151 | 35 |
| Right-Dist-Post-Neg-Word | 1 | 1.94 | 2.585 | 17 |
| | 2 | 2.91 | 3.617 | 35 |
| Right-Dist-Post-Neg-Face | 1 | 2.82 | 2.744 | 17 |
| | 2 | 3.31 | 3.075 | 35 |
| Right-Prox-Pre-Pos-Word | 1 | 5.12 | 5.110 | 17 |
| | 2 | 4.31 | 5.460 | 35 |
| Right-Prox-Pre-Pos-Face | 1 | 4.76 | 2.990 | 17 |
| | 2 | 4.54 | 4.730 | 35 |
| Right-Prox-Pre-Neg-Word | 1 | 3.82 | 3.557 | 17 |
| | 2 | 5.60 | 5.123 | 35 |
| Right-Prox-Pre-Neg-Face | 1 | 3.12 | 2.736 | 17 |
| | 2 | 3.77 | 3.309 | 35 |
| Right-Prox-Post-Pos-Word | 1 | 6.65 | 5.873 | 17 |
| | 2 | 5.09 | 5.474 | 35 |
| Right-Prox-Post-Pos-Face | 1 | 4.35 | 3.239 | 17 |
| | 2 | 3.69 | 4.398 | 35 |
| Right-Prox-Post-Neg-Word | 1 | 3.76 | 4.070 | 17 |
| | 2 | 4.94 | 5.567 | 35 |
| Right-Prox-Post-Neg-Face | 1 | 3.12 | 2.891 | 17 |
| | 2 | 3.94 | 3.404 | 35 |

*Table 2*
*Between-Subjects Effects for Spatial Variables*

| *Source* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta*$^2$ |
|---|---|---|---|---|---|
| Intercept | 1 | 20507.116 | 707808.503 | .000 | 1.00 |
| Sex | 1 | .010 | .342 | .561 | .007 |
| Error | 50 | .029 | | | |

*Table 3*
*Within-Subjects Effects for Spatial Variables*

| *Independent Variable* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta Squared* |
|---|---|---|---|---|---|
| Quadrant | 3,99.898 | 230.820 | 7.028 | .001 | .123 |
| Quadrant * Sex | 3,150 | 34.213 | 1.564 | .200 | .030 |
| Cold Pressor | 1,50 | .004 | .157 | .694 | .003 |
| Cold Pressor * Sex | 1,50 | .076 | 2.802 | .100 | .053 |
| Valence | 1,50 | .791 | 1.143 | .290 | .022 |
| Valence * Sex | 1,50 | .671 | .969 | .330 | .019 |
| Condition | 1,50 | .200 | 1.085 | .303 | .021 |
| Condition * Sex | 1,50 | .056 | .302 | .585 | .006 |
| Quadrant * Cold Pressor | 3,150 | .853 | .380 | .767 | .008 |
| Quadrant * Cold Pressor * Sex | 3,150 | 1.515 | .675 | .568 | .013 |
| Quadrant * Valence | 2.725,150 | 139.234 | 1.726 | .169 | .033 |
| Quadrant * Valence * Sex | 3,150 | 92.445 | 1.262 | .290 | .025 |
| Cold Pressor * Valence | 1,50 | .984 | 1.450 | .234 | .028 |
| Cold Pressor * Valence * Sex | 1,50 | .849 | 1.252 | .269 | .024 |
| Quadrant * Cold Pressor * Valence | 2.2,112.89 | 5.121 | .390 | .703 | .008 |
| Quadrant * Cold Pressor * Valence * Sex | 3,150 | 1.860 | .188 | .904 | .004 |
| Quadrant * Condition | 2.5,129.62 | 118.574 | 8.820 | .000 | .150 |
| Quadrant * Condition * Sex | 3,150 | 19.089 | 1.643 | .182 | .032 |
| Cold Pressor * Condition | 1,50 | .076 | .408 | .526 | .008 |
| Cold Pressor * Condition * Sex | 1,50 | .004 | .023 | .881 | .000 |
| Quadrant * Cold Pressor * Condition | 2.75,137.9 | 5.390 | 1.882 | .140 | .036 |
| Quadrant * Cold Pressor * Condition * Sex | 3,150 | 1.514 | .575 | .633 | .011 |
| Valence * Condition | 1,50 | .019 | .013 | .911 | .000 |
| Valence * Condition * Sex | 1,50 | .005 | .003 | .956 | .000 |
| Quadrant * Valence * Condition | 2.66,133.4 | 16.475 | .394 | .734 | .008 |
| Quadrant * Valence * Condition * Sex | 3,150 | 14.353 | .385 | .764 | .008 |
| Cold Pressor * Valence * Condition | 1,50 | .030 | .020 | .889 | .000 |
| Cold Pressor * Valence * Condition * Sex | 1,50 | .010 | .007 | .934 | .000 |
| Quadrant * Cold Pressor * Valence * Condition | 3,150 | 15.144 | 1.606 | .190 | .031 |
| Quadrant * Cold Pressor * Valence * Condition * Sex | 3,150 | .791 | .084 | .969 | .002 |

*Table 4*
*Estimated Marginal Means for Quadrant*

| *Quadrant* | *Mean* | *Std. Error* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|
| 1 | 3.254 | .220 | 2.812 | 3.697 |
| 2 | 4.178 | .195 | 3.787 | 4.569 |
| 3 | 3.123 | .207 | 2.707 | 3.540 |
| 4 | 4.412 | .223 | 3.964 | 4.860 |

*Table 5*
*Pairwise Comparisons for Quadrant*

| *Quadrant* | *Quadrant* | *Mean Diff.* | *Std. Error* | *Sig.* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|---|---|
| *1* | 2 | -.924 | .392 | .134 | -2.000 | .153 |
| | 3 | .131 | .256 | 1.000 | -.574 | .835 |
| | 4 | -1.158* | .393 | .029 | -2.236 | -.079 |
| *2* | 1 | .924 | .392 | .134 | -.153 | 2.000 |
| | 3 | 1.055* | .344 | .021 | .108 | 2.001 |
| | 4 | -.234 | .242 | 1.000 | -.900 | .432 |
| *3* | *1* | -.131 | .256 | 1.000 | -.835 | .574 |
| | *2* | -1.055* | .344 | .021 | -2.001 | -.108 |
| | *4* | -1.289* | .408 | .016 | -2.408 | -.169 |
| *4* | 1 | 1.158* | .393 | .029 | .079 | 2.236 |
| | 2 | .234 | .242 | 1.000 | -.432 | .900 |
| | 3 | 1.289* | .408 | .016 | .169 | 2.408 |

*Table 6*
*Interaction Effects of Quadrant versus Condition*

| *Quadrant* | *Condition* | *Mean* | *Std. Error* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|---|
| 1 | 1 | 2.930 | .352 | 2.222 | 3.637 |
| | 2 | 3.579 | .176 | 3.225 | 3.932 |
| 2 | 1 | 4.546 | .316 | 3.911 | 5.182 |
| | 2 | 3.809 | .155 | 3.498 | 4.121 |
| 3 | 1 | 2.533 | .309 | 1.912 | 3.153 |
| | 2 | 3.714 | .180 | 3.353 | 4.075 |
| 4 | 1 | 4.912 | .329 | 4.252 | 5.572 |
| | 2 | 3.912 | .188 | 3.534 | 4.290 |

*Table 7*
*Descriptive Statistics – Intragroup Spatial Variables for Males*

| *Variable* | *Mean* | *Standard Deviation* | *N* |
|---|---|---|---|
| Left-Dist-Pre-Pos-Word | 2.41 | 3.104 | 17 |
| Left-Dist-Pre-Pos-Face | 3.24 | 2.728 | 17 |
| Left-Dist-Pre-Neg-Word | 2.47 | 3.243 | 17 |
| Left-Dist-Pre-Neg-Face | 3.94 | 2.839 | 17 |
| Left-Dist-Post-Pos-Word | 2.06 | 3.132 | 17 |
| Left-Dist-Post-Pos-Face | 3.00 | 2.693 | 17 |
| Left-Dist-Post-Neg-Word | 2.41 | 3.355 | 17 |
| Left-Dist-Post-Neg-Face | 3.82 | 3.226 | 17 |
| Left-Prox-Pre-Pos-Word | 4.24 | 4.280 | 17 |
| Left-Prox-Pre-Pos-Face | 2.24 | 2.195 | 17 |
| Left-Prox-Pre-Neg-Word | 6.47 | 5.051 | 17 |
| Left-Prox-Pre-Neg-Face | 5.41 | 2.717 | 17 |
| Left-Prox-Post-Pos-Word | 3.41 | 4.317 | 17 |
| Left-Prox-Post-Pos-Face | 2.76 | 2.705 | 17 |
| Left-Prox-Post-Neg-Word | 6.88 | 5.207 | 17 |
| Left-Prox-Post-Neg-Face | 5.24 | 3.093 | 17 |
| Right-Dist-Pre-Pos-Word | 3.18 | 4.812 | 17 |
| Right-Dist-Pre-Pos-Face | 4.76 | 3.649 | 17 |
| Right-Dist-Pre-Neg-Word | 2.12 | 3.120 | 17 |
| Right-Dist-Pre-Neg-Face | 2.53 | 2.625 | 17 |
| Right-Dist-Post-Pos-Word | 2.88 | 4.910 | 17 |
| Right-Dist-Post-Pos-Face | 4.88 | 3.407 | 17 |
| Right-Dist-Post-Neg-Word | 1.94 | 2.585 | 17 |
| Right-Dist-Post-Neg-Face | 2.82 | 2.744 | 17 |
| Right-Prox-Pre-Pos-Word | 5.12 | 5.110 | 17 |
| Right-Prox-Pre-Pos-Face | 4.76 | 2.990 | 17 |
| Right-Prox-Pre-Neg-Word | 3.82 | 3.557 | 17 |
| Right-Prox-Pre-Neg-Face | 3.12 | 2.736 | 17 |
| Right-Prox-Post-Pos-Word | 6.65 | 5.873 | 17 |
| Right-Prox-Post-Pos-Face | 4.35 | 3.239 | 17 |
| Right-Prox-Post-Neg-Word | 3.76 | 4.070 | 17 |
| Right-Prox-Post-Neg-Face | 3.12 | 2.891 | 17 |

*Table 8*
*Within-Subjects Effects for Males*

| *Source* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta Squared* |
|---|---|---|---|---|---|
| Quadrant | 1.602,25.627 | 178.238 | 3.551 | .053 | .182 |
| Cold Pressor | 1,16 | .017 | 1.895 | .188 | .106 |
| Valence | 1,16 | .002 | .190 | .668 | .012 |
| Condition | 1,16 | .017 | 1.895 | .188 | .106 |
| Quadrant*ColdPressor | 3,48 | 1.208 | .698 | .558 | .042 |
| Quadrant*Valence | 3,48 | 157.320 | 2.300 | .089 | .126 |
| ColdPressor*Valence | 1,16 | .002 | .190 | .668 | .012 |
| Quadrant*ColdPressor*Valence | 3,48 | 1.360 | .164 | .920 | .010 |
| Quadrant*Condition | 1.615,25.832 | 118.561 | 4.794 | .023 | .231 |
| ColdPressor*Condition | 1,16 | .017 | 1.895 | .188 | .106 |
| Quadrant*ColdPressor*Condition | 3,48 | 3.472 | 1.713 | .177 | .097 |
| Valence*Condition | 1,16 | .002 | .190 | .668 | .012 |
| Quadrant*Valence*Condition | 3,48 | 5.801 | .375 | .771 | .023 |
| ColdPressor*Valence*Condition | 1,16 | .002 | .190 | .668 | .012 |
| Quadrant*ColdPressor*Valence*Condition | 3,48 | 5.526 | 1.284 | .291 | .074 |

*Table 9*
*Interaction Effects for Quadrant versus Condition*

| *Quadrant* | *Condition* | *Mean* | *Std. Error* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|---|
| 1 | 1 | 2.338 | .602 | 1.063 | 3.614 |
| | 2 | 3.500 | .322 | 2.817 | 4.183 |
| 2 | 1 | 5.250 | .520 | 4.148 | 6.352 |
| | 2 | 3.912 | .236 | 3.412 | 4.412 |
| 3 | 1 | 2.529 | .620 | 1.216 | 3.843 |
| | 2 | 3.750 | .327 | 3.058 | 4.442 |
| 4 | 1 | 4.838 | .660 | 3.438 | 6.238 |
| | 2 | 3.838 | .226 | 3.360 | 4.317 |

*Table 10*
*Descriptive Statistics – Intragroup Spatial Variables for Females*

| *Variable* | *Mean* | *Std. Deviation* | *N* |
|---|---|---|---|
| Left-Dist-Pre-Pos-Word | 3.94 | 5.302 | 35 |
| Left-Dist-Pre-Pos-Face | 4.17 | 4.169 | 35 |
| Left-Dist-Pre-Neg-Word | 3.20 | 4.079 | 35 |
| Left-Dist-Pre-Neg-Face | 3.23 | 3.059 | 35 |
| Left-Dist-Post-Pos-Word | 3.34 | 4.940 | 35 |
| Left-Dist-Post-Pos-Face | 3.77 | 3.473 | 35 |
| Left-Dist-Post-Neg-Word | 3.60 | 4.279 | 35 |
| Left-Dist-Post-Neg-Face | 3.46 | 3.184 | 35 |
| Left-Prox-Pre-Pos-Word | 4.37 | 5.168 | 35 |
| Left-Prox-Pre-Pos-Face | 2.63 | 3.273 | 35 |
| Left-Prox-Pre-Neg-Word | 3.54 | 3.988 | 35 |
| Left-Prox-Pre-Neg-Face | 4.51 | 3.100 | 35 |
| Left-Prox-Post-Pos-Word | 4.00 | 5.058 | 35 |
| Left-Prox-Post-Pos-Face | 3.43 | 4.354 | 35 |
| Left-Prox-Post-Neg-Word | 3.46 | 3.988 | 35 |
| Left-Prox-Post-Neg-Face | 4.26 | 3.165 | 35 |
| Right-Dist-Pre-Pos-Word | 2.69 | 3.724 | 35 |
| Right-Dist-Pre-Pos-Face | 4.09 | 4.196 | 35 |
| Right-Dist-Pre-Neg-Word | 2.11 | 3.008 | 35 |
| Right-Dist-Pre-Neg-Face | 3.26 | 2.694 | 35 |
| Right-Dist-Post-Pos-Word | 2.43 | 3.500 | 35 |
| Right-Dist-Post-Pos-Face | 4.06 | 4.151 | 35 |
| Right-Dist-Post-Neg-Word | 2.91 | 3.617 | 35 |
| Right-Dist-Post-Neg-Face | 3.31 | 3.075 | 35 |
| Right-Prox-Pre-Pos-Word | 4.31 | 5.460 | 35 |
| Right-Prox-Pre-Pos-Face | 4.54 | 4.730 | 35 |
| Right-Prox-Pre-Neg-Word | 5.60 | 5.123 | 35 |
| Right-Prox-Pre-Neg-Face | 3.77 | 3.309 | 35 |
| Right-Prox-Post-Pos-Word | 5.09 | 5.474 | 35 |
| Right-Prox-Post-Pos-Face | 3.69 | 4.398 | 35 |
| Right-Prox-Post-Neg-Word | 4.94 | 5.567 | 35 |
| Right-Prox-Post-Neg-Face | 3.94 | 3.404 | 35 |

*Table 11*
*Within-Subjects Effects for Females*

| *Source* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta Squared* |
|---|---|---|---|---|---|
| Quadrant | 2.365,74.985 | 116.095 | 4.680 | .008 | .121 |
| Cold Pressor | 1,34 | .089 | 2.482 | .124 | .068 |
| Valence | 1,34 | 2.232 | 2.203 | .147 | .061 |
| Condition | 1,34 | .357 | 1.337 | .256 | .038 |
| Quadrant*ColdPressor | 3,102 | 1.135 | .457 | .713 | .013 |
| Quadrant*Valence | 3,102 | 10.896 | .144 | .933 | .004 |
| ColdPressor*Valence | 1,34 | 2.800 | 2.820 | .102 | .077 |
| Quadrant*ColdPressor*Valence | 3,102 | 5.940 | .560 | .643 | .016 |
| Quadrant*Condition | 3,102 | 54.550 | 5.040 | .003 | .129 |
| ColdPressor*Condition | 1,34 | .089 | .329 | .570 | .010 |
| Quadrant*ColdPressor*Condition | 3,102 | 2.749 | .941 | .424 | .027 |
| Valence*Condition | 1,34 | .032 | .015 | .905 | .000 |
| Quadrant*Valence*Condition | 3,102 | 32.425 | .683 | .565 | .020 |
| ColdPressor*Valence*Condition | 1,34 | .057 | .026 | .873 | .001 |
| Quadrant*ColdPressor*Valence*Condition | 3,102 | 12.993 | 1.098 | .354 | .031 |

*Table 12*
*Pairwise Comparisons for Quadrant*

| *Quadrant* | *Quadrant* | *Mean Diff.* | *Std. Error* | *Sig.* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|---|---|
| 1 | 2 | -.186 | .438 | 1.000 | -1.413 | 1.041 |
| | 3 | .482 | .280 | .563 | -.302 | 1.266 |
| | 4 | -.896 | .411 | .218 | -2.049 | .256 |
| 2 | 1 | .186 | .438 | 1.000 | -1.041 | 1.413 |
| | 3 | .668 | .350 | .390 | -.313 | 1.649 |
| | 4 | -.711 | .310 | .169 | -1.579 | .157 |
| 3 | 1 | -.482 | .280 | .563 | -1.266 | .302 |
| | 2 | -.668 | .350 | .390 | -1.649 | .313 |
| | 4 | -1.379* | .424 | .016 | -2.567 | -.190 |
| 4 | 1 | .896 | .411 | .218 | -.256 | 2.049 |
| | 2 | .711 | .310 | .169 | -.157 | 1.579 |
| | 3 | 1.379* | .424 | .016 | .190 | 2.567 |

*Table 13*
*Estimated Marginal Means for Quadrant*

| *Quadrant* | *Mean* | *Std. Error* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|
| 1 | 3.589 | .240 | 3.102 | 4.077 |
| 2 | 3.775 | .224 | 3.319 | 4.231 |
| 3 | 3.107 | .208 | 2.685 | 3.530 |
| 4 | 4.486 | .242 | 3.994 | 4.978 |

*Table 14*
*Interaction of Quadrant versus Condition*

| *Quadrant* | *Condition* | *Mean* | *Std. Error* | *Lower Bound CI* | *Upper Bound CI* |
|---|---|---|---|---|---|
| 1 | 1 | 3.521 | .395 | 2.719 | 4.324 |
| | 2 | 3.657 | .189 | 3.273 | 4.041 |
| 2 | 1 | 3.843 | .361 | 3.108 | 4.577 |
| | 2 | 3.707 | .183 | 3.335 | 4.079 |
| 3 | 1 | 2.536 | .309 | 1.908 | 3.164 |
| | 2 | 3.679 | .194 | 3.284 | 4.074 |
| 4 | 1 | 4.986 | .329 | 4.318 | 5.654 |
| | 2 | 3.986 | .237 | 3.504 | 4.468 |

*Table 15*
*Descriptive Statistics for Physiologic Analyses*

| *Variable* | *Counterbalance* | *Mean* | *Std. Deviation* | *N* |
|---|---|---|---|---|
| SBP Baseline 1 | Words | 121.68 | 10.367 | 25 |
| | Faces | 121.75 | 10.892 | 24 |
| SBP Post 1 | Words | 122.32 | 10.746 | 25 |
| | Faces | 120.67 | 11.849 | 24 |
| SBP Baseline2 | Words | 120.88 | 8.691 | 25 |
| | Faces | 119.50 | 12.311 | 24 |
| SBP Post2 | Words | 123.12 | 10.596 | 25 |
| | Faces | 122.13 | 11.156 | 24 |
| DBP Baseline1 | Words | 77.12 | 7.518 | 25 |
| | Faces | 75.33 | 8.509 | 24 |
| DBP Post1 | Words | 77.72 | 6.573 | 25 |
| | Faces | 76.75 | 8.828 | 24 |
| DBP Baseline2 | Words | 78.80 | 7.000 | 25 |
| | Faces | 77.33 | 8.801 | 24 |
| DBP Post2 | Words | 78.76 | 8.182 | 25 |
| | Faces | 78.04 | 8.913 | 24 |
| HR Baseline1 | Words | 77.20 | 14.151 | 25 |
| | Faces | 70.46 | 13.420 | 24 |
| HR Post 1 | Words | 74.84 | 11.887 | 25 |
| | Faces | 71.92 | 10.249 | 24 |
| HR Baseline 2 | Words | 77.80 | 13.913 | 25 |
| | Faces | 73.79 | 8.220 | 24 |
| HR Post 2 | Words | 74.76 | 12.577 | 25 |
| | Faces | 72.79 | 9.682 | 24 |

*Table 16*
*Physiologic Variable Multivariate Omnibus Analyses*

| Effect | | Test | Value | F | Hypothesis df | Error df | Sig. | Partial Eta. Squared |
|---|---|---|---|---|---|---|---|---|
| Between Subjects | Intercept | Pillai's Trace | .996 | 3448.659b | 3.000 | 45.000 | .000 | .996 |
| | Counterbalance | Pillai's Trace | .039 | .614b | 3.000 | 45.000 | .609 | .039 |
| Within Subjects | Trial | Pillai's Trace | .411 | 3.022b | 9.000 | 39.000 | .008 | .411 |
| | Trial*CB | Pillai's Trace | .088 | .419b | 9.000 | 39.000 | .917 | .088 |

*Table 17*
*Within-Subjects Effects for Physiologic Analyses*

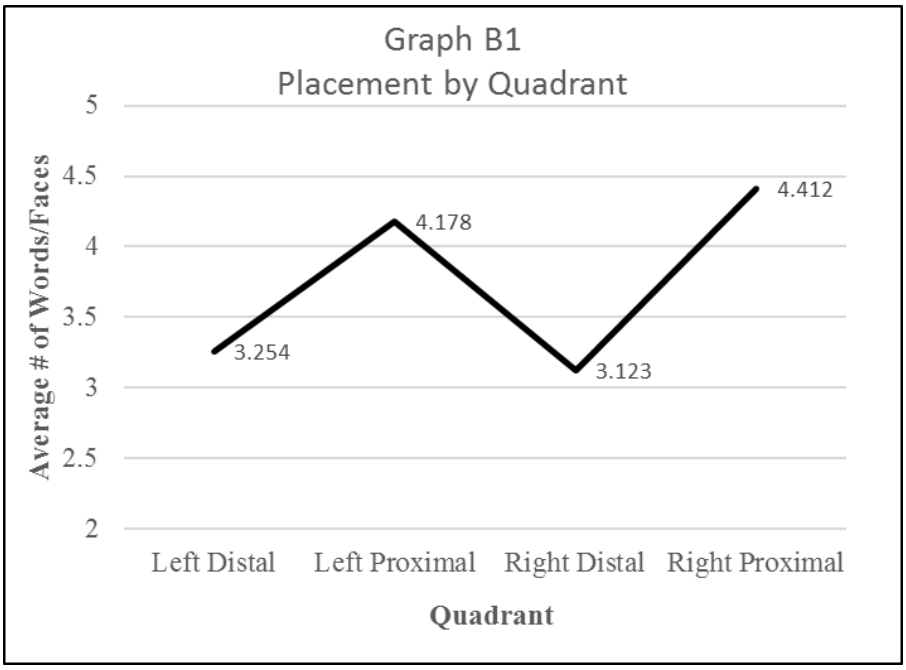
| *Source* | *Measure* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta²* |
|---|---|---|---|---|---|---|
| Trial | SBP | 3 | 49.343 | 1.831 | .144 | .038 |
| | DBP | 2.612 | 52.942 | 4.059 | .012 | .080 |
| | HR | 1.966 | 88.178 | 1.533 | .222 | .032 |
| Trial*CB | SBP | 2.708 | 7.759 | .260 | .835 | .005 |
| | DBP | 2.417 | 3.522 | .250 | .819 | .005 |
| | HR | 1.966 | 79.551 | 1.383 | .256 | .029 |

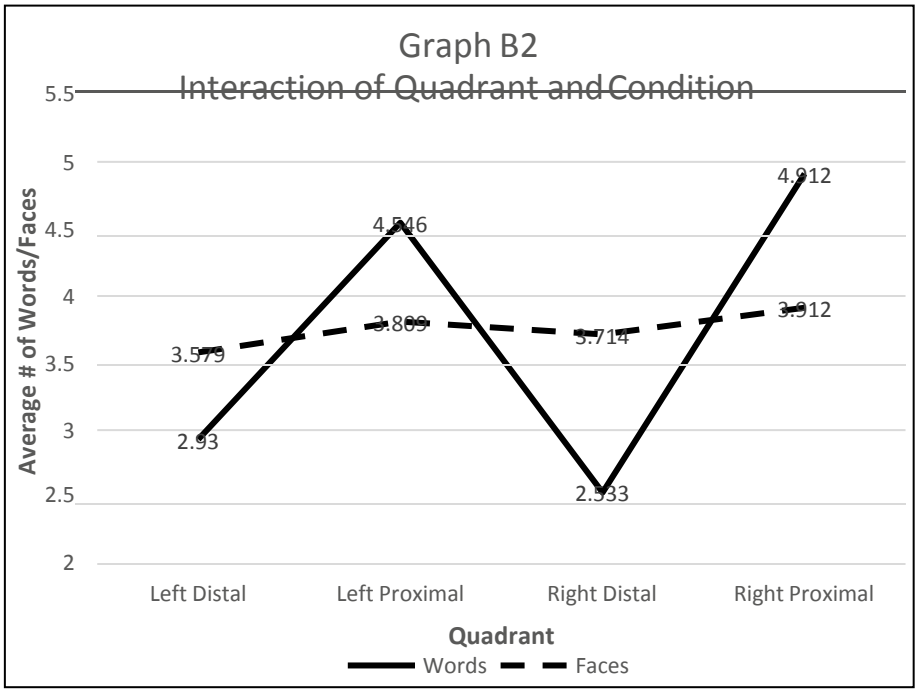
*Table 18*
*Within-Subjects Contrasts for Physiologic Analyses*

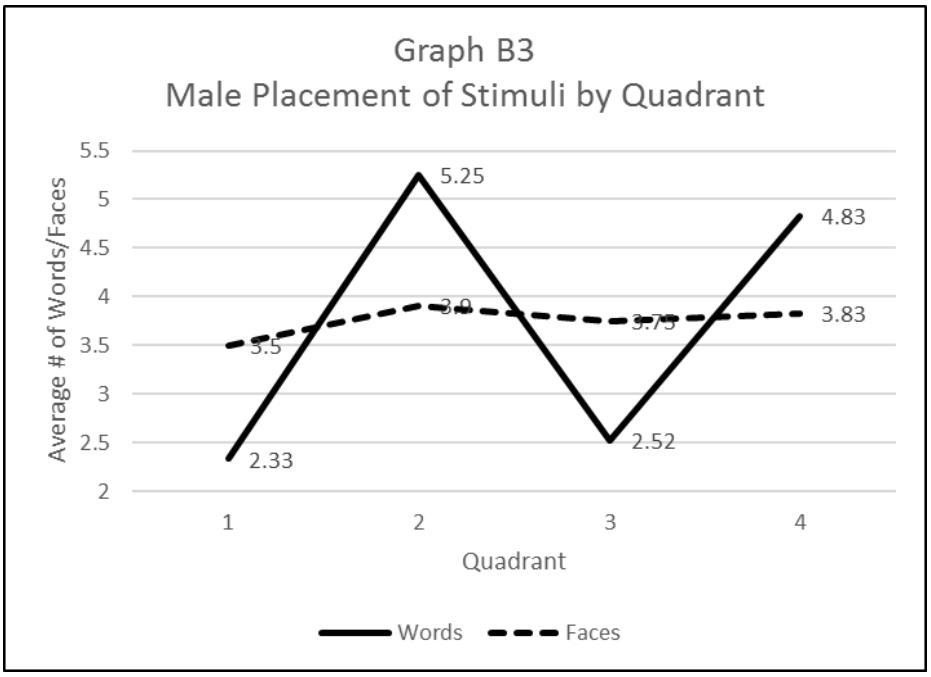
| *Source* | *Measure* | *Trial* | *df* | *Mean Square* | *F* | *Sig.* | *Partial Eta²* |
|---|---|---|---|---|---|---|---|
| Trial | SBP | Linear | 1 | 4.932 | .208 | .650 | .004 |
| | | Quadratic | 1 | 86.260 | 3.392 | .072 | .067 |
| | | Cubic | 1 | 56.837 | 1.792 | .187 | .037 |
| | DBP | Linear | 1 | 132.450 | 7.532 | .009 | .138 |
| | | Quadratic | 1 | 5.565 | .661 | .420 | .014 |
| | | Cubic | 1 | .252 | .031 | .860 | .001 |
| | HR | Linear | 1 | 12.481 | .229 | .634 | .005 |
| | | Quadratic | 1 | 30.150 | .801 | .375 | .017 |
| | | Cubic | 1 | 130.715 | 6.216 | .016 | .117 |
| Trial*CB | SBP | Linear | 1 | 5.226 | .221 | .641 | .005 |
| | | Quadratic | 1 | 13.607 | .535 | .468 | .011 |
| | | Cubic | 1 | 2.175 | .069 | .795 | .001 |
| | DBP | Linear | 1 | 4.491 | .255 | .616 | .005 |
| | | Quadratic | 1 | .014 | .002 | .967 | .000 |
| | | Cubic | 1 | 4.007 | .497 | .484 | .010 |
| | HR | Linear | 1 | 107.244 | 1.970 | .167 | .040 |
| | | Quadratic | 1 | 9.681 | .257 | .614 | .005 |
| | | Cubic | 1 | 39.462 | 1.877 | .177 | .038 |

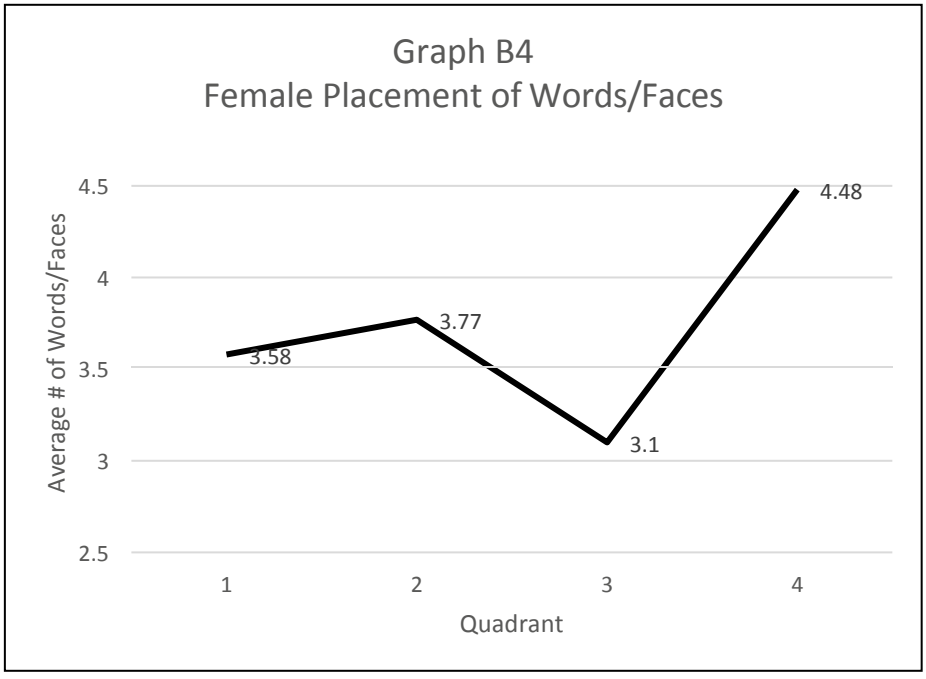
## Appendix B

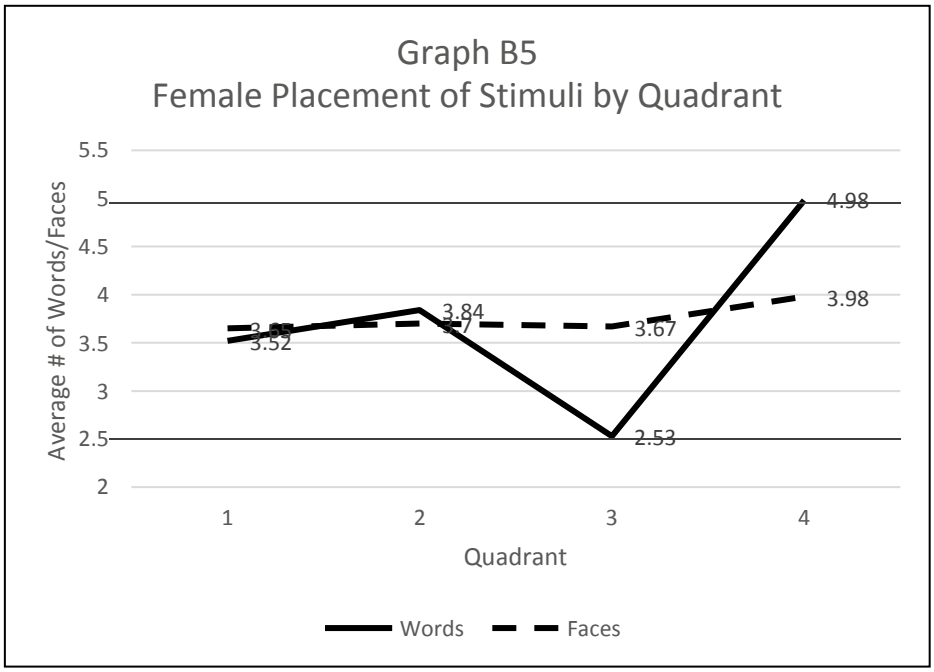
## Graphs and Figures

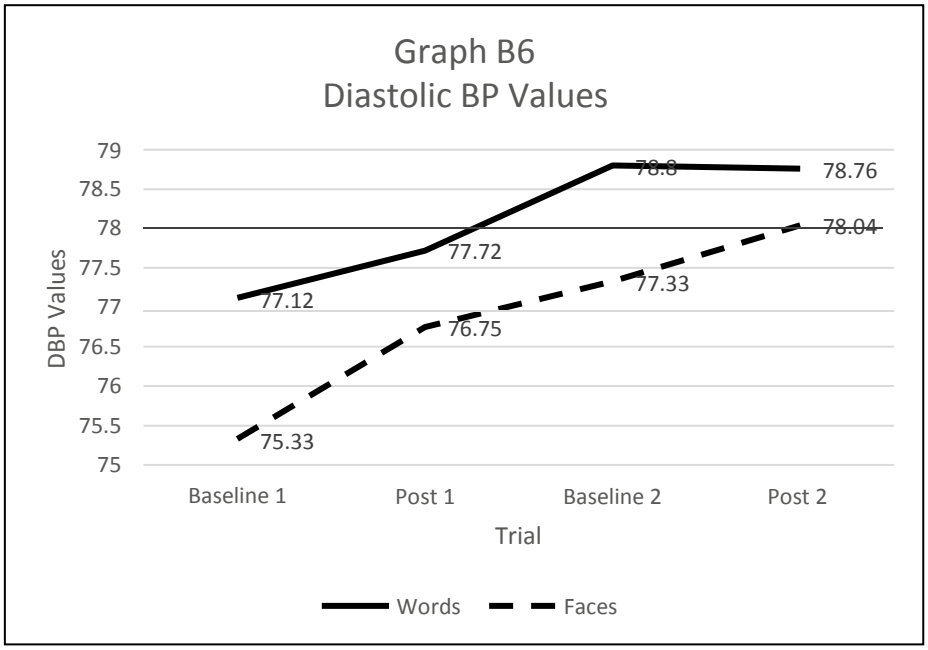



Graph B3
Male Placement of Stimuli by Quadrant
Average # of Words/Faces
5.5
5
4.5
4
3.5
3
2.5
2
5.25
4.83
3.5
3.83
2.33
2.52
1
2
3
4
Quadrant
Words
Faces


Graph B4
Female Placement of Words/Faces
Average # of Words/Faces
4.5
4
3.5
3
2.5
4.48
3.77
3.58
3.1
1
2
3
4
Quadrant


Graph B5
Female Placement of Stimuli by Quadrant
Average # of Words/Faces
5.5
5
4.5
4
3.5
3
2.5
2
1
2
3
4
Quadrant
3.52
3.84
2.53
4.98
3.67
3.98
Words
Faces


Graph B6
Diastolic BP Values
DBP Values
79
78.5
78
77.5
77
76.5
76
75.5
75
Baseline 1
Post 1
Baseline 2
Post 2
Trial
77.12
77.72
78.8
78.76
75.33
76.75
77.33
78.04
Words
Faces

# Appendix C
## Materials

*Demographics Questionnaire*

Name:

Age:

Month/Year of Birth:

Gender:

Race/Ethnicity:

Years of Education:

Place of Origin:

Professional/Employment Status:

*Medical History Questionnaire*

1. Have you ever lost consciousness for more than 5 minutes? Yes No
2. Do you have a history of head injury? Yes No
3. Have you ever suffered a head injury resulting in a hospital stay longer than 24 hours? Yes No
4. Have you ever experienced fainting spells or blackouts? Yes No
5. Have you ever undergone neurological surgery? Yes No
6. Do you have a history of neurological disorder(s)? Yes No
7. Do you have a history of epilepsy or seizures? Yes No
8. Do you have a history of respiratory problems or conditions? Yes No
9. Do you have a history of respiratory or cardiac arrest or hypoxia (lack of oxygen)? Yes No
10. Do you have a history of limb injury? Yes No
11. Do you have a history of congenital or developmental problems? Yes No
12. Do you have a history of learning disability or educational difficulties? Yes No
13. Are you able to read, write, and spell without difficulty? Yes No
14. Do you have any history of cardiovascular disease? Yes No
15. Do you have any history of hyper- or hypotension (high- or low blood pressure)? Yes No
16. Do you have any history of hyper- or hypothyroidism? Yes No
17. Do you have any sensory impairments (vision and hearing)? Yes No
18. Do you wear glasses or use corrective lenses or contacts? Yes No
19. Do you have a history of alcohol, drug, or other substance abuse or dependence? Yes No
20. Do you consume more three or more alcoholic beverages more than two nights a week? Yes No
21. Do you use tobacco products? Yes No
22. Do you have a history of sleep disorder(s)? Yes No
23. Do you have a history of movement problems

or musculoskeletal disorder? Yes No

24. Do you have a history of psychological or psychiatric disorder(s)? Yes No
25. Have you ever received treatment for a psychiatric condition (i.e therapy or medication)? Yes No
26. Are you currently prescribed any psychiatric medications? Yes No
27. Are you currently taking any prescription medications? Yes No
28. Do you have a history of chronic pain? Yes No
29. Do you have any history of cardiac or cardiovascular problems? Yes No
30. Do you have any diagnosed medical conditions or current illness? Yes No
31. Have you ever been prescribed and used a long-term medication of any kind? Yes No

Medications currently prescribed (and taken):

_____
_____
_____
_____

If you answered Yes to any of the previous questions, please specify and explain below:

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

*Coren, Porac, and Duncan Laterality Questionnaire*

| *Circle the appropriate number after each item:* | Right | Left | Both |
|---|---|---|---|
| With which hand would you throw a ball to hit a target? | 1 | -1 | 0 |
| With which hand do you draw? | 1 | -1 | 0 |
| With which hand do you use an eraser on paper? | 1 | -1 | 0 |
| With which hand do you remove the top card when dealing? | 1 | -1 | 0 |
| With which foot do you kick a ball? | 1 | -1 | 0 |
| If you wanted to pick up a pebble with your toes, which foot would you use? | 1 | -1 | 0 |
| If you had to step up onto a chair, which foot would you place on the chair first? | 1 | -1 | 0 |
| Which eye would you use to peep through a keyhole? | 1 | -1 | 0 |
| If you had to look into a dark bottle to see how full it was, which eye would you use? | 1 | -1 | 0 |
| Which eye would you use to sight down a rifle? | 1 | -1 | 0 |
| If you wanted to listen to a conversation going on behind a closed door, which ear would you place against the door? | 1 | -1 | 0 |
| If you wanted to listen to someone's heartbeat, which ear would you place against their chest? | 1 | -1 | 0 |
| Into which ear would you place the earphone of a transistor radio? | 1 | -1 | 0 |

# of Right + # of Left = Total Score
_____ +_____= _____

Is your mother left or right hand dominant? _

Is your father left or right hand dominant? __

*Cold Pressor Assessment*

Please circle the most appropriate answer to each of the following questions:

1. How stressful was putting your hand in the ice water?

   (1 = not stressful at all, 4 = moderately stressful, 7 = extremely

   stressful) 1 2 3 4 5 6 7

2. What level of pain did you experience when you put your hand in the ice water? (1 = not painful at all, 4 = moderately painful, 7 = extremely painful)

   1 2 3 4 5 6 7

*Recruitment and Consent Information*

Recruitment Information

Recruitment for this in-lab study will take place through SONA. The SONA system is available to all members of the Virginia Tech community. This study will be on the list of SONA projects available for students and individuals will be able to sign-up for a date and time to participate in the in-lab session via this SONA system.

SONA Descriptions:

The purpose of this study is to examine brain function, dysfunction, and their relationship to emotion regulation and spatial representation systems within the right cerebral hemisphere. This is being done in order to gather more information on some of the neural mechanisms underlying several neuropsychological syndromes that result from neurological damage (e.g. stroke or tumor).

This experiment will take place within the Behavioral Neuroscience Laboratory in the Department of Psychology. You will initially be asked to complete some self-report questionnaires about your feelings and beliefs, some of which may be health related and of a sensitive nature. After this you will have some physiological variables (heart rate and blood pressure) measured with the use of a biophysiological acquisition system that will be connected to you. The system is non-invasive and only consists of a blood pressure cuff around your arm and some electrocardiographic leads attached to your wrist and ankle. Measurements will be taken and you will be asked to perform some spatial tasks that only require you to remain seated and follow instructions. You will also be asked to place your hand in cold water for a short period of time. This may cause some discomfort but there are no risks associated with this procedure. Following these tasks, you will be asked to fill out some more questionnaires at the end. This study should take no longer than 45-60 minutes, after which you will be debriefed and allowed to leave.

There are no anticipated risks associated with this study. You may experience transient discomfort associated with the placement of your hand in cold water. However, this is a procedure that has been used in research studies for several decades and is considered safe. The potential benefits to science and humankind that may result from this study are a greater understanding of the brain and the role of various brain systems in regulating emotion and spatial awareness. Additionally, data from this study may shed light on some of the underlying mechanisms of several prominent neuropsychological disorders. No promise or guarantee of benefits has been made to encourage you to participate.

Please note that there may be circumstances under which the investigator may determine that a subject should not continue as a subject.

Should you withdraw or otherwise discontinue participation, you will be compensated for the portion of the project completed in accordance with the Compensation section of this document. Participants will be awarded 1.5 credits for participation. Participants will be screened for

eligibility on the basis of medical history and associated questionnaires.

*Informed Consent*

# VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY

**Informed Consent for Participants**
**in Research Projects Involving Human Subjects**

**Title of Project:** Neuropsychological Investigation of Space and Emotion in Brain Function

**Principle Investigator:** David W. Harrison, Ph.D dwh@vt.edu 540-231-4422

**Investigator(s):** Ransom W. Campbell, M.A rcamp17@vt.edu 423-645-5537

## I. Purpose of this Research Project

The purpose of this study is to examine specific aspects of brain function as they relate to things like emotion and behavioral tasks. This is being done in order to gather more information on some of the neural mechanisms underlying some common neuropsychological disorders. The results from this study may be published or presented in a professional scientific format.

The following is a list of exclusionary criteria for participation in this study: left-handedness, a history of neurologic injury or disease, major medical or systemic illness, and current use of psychotropic or neurotropic medications.

## II. Procedures

This experiment will take place within the Behavioral Neuroscience Laboratory in the Department of Psychology. You will initially be asked to complete some self-report questionnaires about your feelings and beliefs, some of which may be health related and of a sensitive nature. After this you will have some physiological variables (heart rate and blood pressure) measured with the use of a biophysiological acquisition system that will be connected to you. The system is non-invasive and only consists of a blood pressure cuff around your arm and some electrocardiographic leads attached to your wrist and ankle. Measurements will be taken and you will be asked to perform some spatial tasks that only require you to remain seated and follow instructions. During these tasks you will be asked to place some stimuli in different locations while remaining seated. You will also be asked to place your hand in ice water (32-35 degrees Fahrenheit) twice during this study for 45-seconds each time. This procedure will cause temporary discomfort and pain (see below risks). Following these tasks you will be asked to fill out some more questionnaires at the end. This study should take no longer than 45-60 minutes, after which you will be debriefed and allowed to leave.

## **III.** Risks

The risks associated with this study involve exposure to pain. You will be placing your hand in ice water (32-35 degrees Fahrenheit) for 45-seconds and you should expect this to cause discomfort and pain. The pain experienced may be at the threshold of what you can normally tolerate. You will be asked to do this twice during the study. However this is a safe procedure that has routinely been used in our laboratory studies and the pain is temporary. You will be able to withdraw your hand from the water at any time if needed and can discontinue participation at any time. There is no risk of permanent damage associated with this procedure. Any expenses accrued for seeking or receiving medical or mental health treatment will be the responsibility of the subject and not that of the research project, research team, or Virginia Tech.

## **IV.** Benefits

The potential benefits to science and humankind that may result from this study are a greater understanding of the brain and the role of various brain systems in regulating emotion and spatial awareness. Additionally, data from this study may shed light on some of the underlying mechanisms of several prominent neuropsychological disorders. No promise or guarantee of benefits has been made to encourage you to participate.

## **V.** Extent of Anonymity and Confidentiality

Your name and contact information (email address) will be gathered for the purposes of ensuring you are awarded credit through the SONA system once you have adequately completed the study. Identifying information will be coded and stored in a locked file cabinet within a locked room in our laboratory. Only researchers associated with this study will have access to the data. At no time will the researchers release identifiable results of the study to anyone other than individuals working on the project without your written consent. The Virginia Tech (VT) Institutional Review Board (IRB) may view the study's data for auditing purposes. The IRB is responsible for the oversight of the protection of human subjects involved in research.

Note: in some situations it may be necessary for a researcher to break confidentiality. For the purposes of this study, if the researchers have reason to suspect that a child is abused or neglected, or that a person poses a threat of harm to others or him/herself, the researcher is required by Virginia State law to notify the appropriate authorities.

## **VI.** Compensation

There is no compensation for participation in this study. However, participants will be awarded credits via the SONA experiment management system for participation that may correspond to course credit or extra course credit elsewhere. You will receive 1.0 credits for each 30 minutes of participation. If you are ineligible to participate following the questionnaires, you will receive prorated credit for your time spent. Compensation

following voluntary withdrawal from the study will also be prorated based upon time spent.

## **VII.** Freedom to Withdraw

It is important for you to know that you are free to withdraw from this study at any time without penalty. You are free not to answer any questions that you choose or respond to what is being asked of you without penalty.

Please note that there may be circumstances under which the investigator may determine that a subject should not continue as a subject.

Should you withdraw or otherwise discontinue participation, you will be compensated for the portion of the project completed in accordance with the Compensation section of this document.

## **VIII.** Questions or Concerns

Should you have any questions about this study, you may contact one of the research investigators whose contact information is included at the beginning of this document.

Should you have any questions or concerns about the study's conduct or your rights as a research participant, or need to report a research-related injury or event, you may contact the Virginia Tech Institutional Review Board at irb@vt.edu or (540) 231-3732.

## **IX.** Subject's Consent

I have read the Consent Form and conditions of this project. I have had all my questions answered. I hereby acknowledge the above and give my voluntary consent:

_____Date_____

Subject signature

_____

Subject printed name

---

*Condition Dependent Instructions to Participants*

***Words Instructions***

Baseline Recording
*"Recordings will now be taken which include your heart rate and blood pressure, so please remain still with your feet flat on the floor and arms resting on the chair."*

Baseline Placement
*"In front of you is a collection of individually laminated words. When instructed please take individual words from the collection, read each one to yourself, and place them however you wish on the board in front of you. Please place the words until you have them all on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."*

Cold Pressor Stress
*"When instructed, please place your left hand in the water to a point about 1 inch above the wrist. You will be asked to hold your hand in the water for 45-seconds after which you will be told to remove it. This will be difficult due to some discomfort, but please try and to keep your hand in the water until instructed to remove it. (Ready the stopwatch to time) Please place your hand in the ice water."*

Post-Stress Spatial Placement
*"As before, when instructed you will begin taking words from the collection in front of you, reading each one to yourself, and placing them however you wish on the board. Please place the words until you have them all on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."*

Post-Stress Physiologic Recording
*"Please remain seated for another recording of your heart rate and blood pressure."*

***Faces Instructions***

Baseline Recording
*"Recordings will now be taken which include your heart rate and blood pressure, so please remain still with your feet flat on the floor and arms resting on the chair."*

Baseline Placement
*"In front of you are several cards with faces on them. When instructed please take each face from the collection, look at each one, and place them on the board however you wish so that each face is visible. Please continue until you have placed all the faces on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."*

Cold Pressor Stress

*"When instructed, please place your left hand in the water to a point about 1 inch above the wrist. You will be asked to hold your hand in the water for 45-seconds after which you will be told to remove it. This will be difficult due to some discomfort, but please try and to keep your hand in the water until instructed to remove it. (Ready the stopwatch to time) Please place your hand in the ice water."*

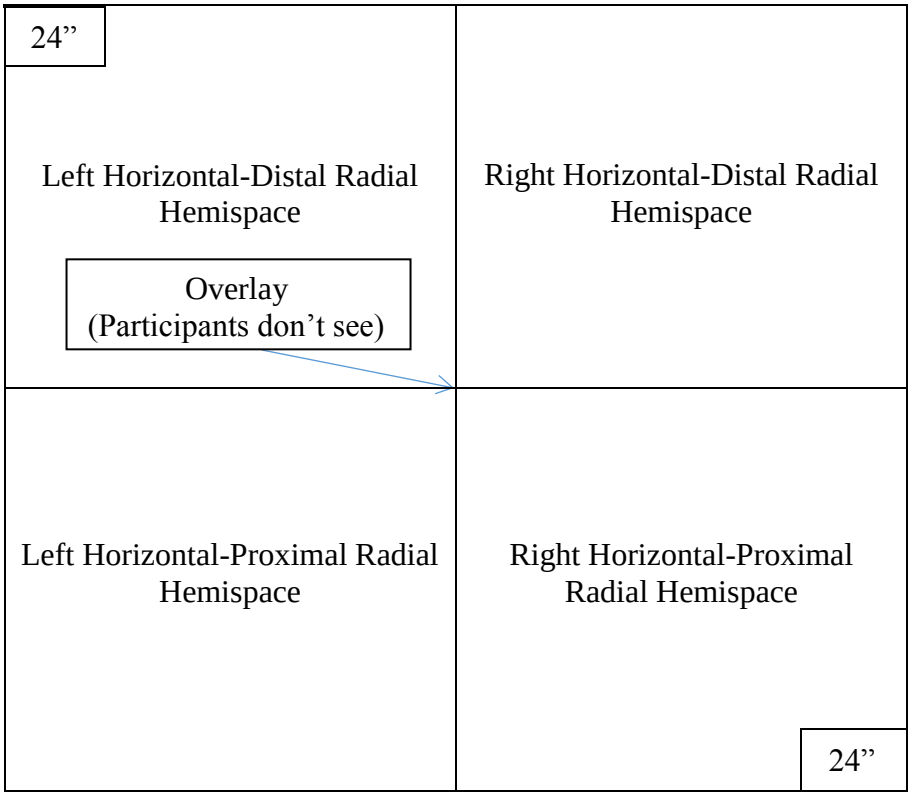
Post-Stress Spatial Placement

*"As before, when instructed please take each face from the collection, look at each one, and place them on the board however you wish so that each face is visible. Please continue until you have placed all the faces on the board. You will have approximately 3 minutes to do this. Let us know when you are done. (When ready) Please go ahead."*

Post-Stress Physiologic Recording

*"Please remain seated for another recording of your heart rate and blood pressure."*

*Overlay Diagram*



## Appendix D

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