Lateralized Induction of Cardiovascular Responses: Exploring Asymmetric Autonomic Regulation

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ABSTRACT

There is clear evidence that the autonomic nervous system (ANS) is lateralized at both the peripheral as well as the central levels of the nervous system. Both the vagus and the sympathetic ganglia asymmetrically innervate the sino-atrial node and the myocardium of the heart. This lateralization has also been observed in afferent as well as efferent projections to nuclei in the brainstem, hypothalamus, and amygdala. Where laterality has not been as clear is in regions of the frontal lobe dedicated to the regulation of autonomic nervous system responses. This study addressed that issue via the implementation of lateralized autonomic response-evoking tasks. With the use of cardiovascular and electrodermal measures, the present study indexed autonomic responses to lateralized stimuli. This study also explored the role of lateralization within sex as well as in relation to reported gender identity. The findings lend support to the right hemisphere as serving a dominant role in regulating sympathetic nervous system activity, while lending less conclusive support for lateralization of parasympathetic nervous system regulation. Men demonstrated greater lateralization for sympathetic nervous system responses across several different metrics of autonomic indices. The exploration of gender variables in relation to lateralization of autonomic responses was generally not supported.

DEDICATION

I dedicate this document to my entire family, both immediate and extended. For some bizarre reason they have always had unwavering faith in my capabilities.

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Introduction

It has long been understood that the brain serves an important role in regulating and responding to somatic and visceral activity in the body (Darwin, 1999, pp. 71–72, originally published in 1872). A substantial body of evidence has supported the view that specific regions in the frontal lobe regulate autonomic nervous system (ANS) activity (Critchley et al., 2000; 2003; Gianaros, 2008). There is also evidence that the regulation of each branch of the ANS is largely lateralized to being preferentially regulated in one hemisphere (Craig, 2005; Foster, Drago, Ferguson, & Harrison, 2008; Thayer & Lane, 2009).

Much evidence through behavioral, pharmacological, and imaging research has implicated the right hemisphere as having a greater role in regulating sympathetic nervous system (SNS) activity. These findings are further supported by other laterality models that posit behavioral and psychological processes to be housed in the same hemisphere which mostly rely on SNS activation. The processing of negative emotions as well as the initiation and maintenance of defensive behaviors have been observed to largely be regulated by the right hemisphere (Hugdahl & Westerhausen, 2010). Regulation of parasympathetic nervous system (PNS) activity is less clear in terms of lateralized function. Some empirical work has supported a larger role of the right hemisphere in regulating PNS activity (Wittling et al. 1990), while other research has supported the left (Lane et al., 1989; Ahern et al., 2001). Currently two competing models exist for explaining the preferential lateralization of PNS processes (Foster, Drago, Ferguson, & Harrison, 2008; Thayer & Lane, 2009).

Although several studies and clinical observations have contributed to the topic of lateralized regulation of the ANS branches, few have explored sex differences in lateralization. This void is curious considering how there is a storied literature founded upon basic differences

in lateralization of structures and functions in men compared to women (McGlone, 1980; Hugdahl & Westerhausen, 2010). In terms of preferential handling of information such as prosodic, linguistic, sequential, and spatial processing, men have been shown to demonstrate greater hemispheric lateralization (Voyer, 1996).

The present study addresses both topics of ANS and sex differences in brain lateralization. Lateralized stimuli were used in an attempt to largely direct afferent information to a selected hemisphere. The cold pressor task, which has long been used to elicit large SNS responses (Hines, 1936), and a lateralized modification of the facial cooling task, which typically induces a reflexive PNS response (Friedman, Thayer, & Tyrell, 1996; Wolf, 1965), were implemented on both the left and ride sides of the body. The physiological responses elicited from the assumedly contralateral afferent projections were compared.

Frontal Regulation of ANS Activity

Physiological activity, reactivity, and recovery serve as important processes for maintaining homeostatic levels in the body. Responding to thermoregulatory changes, maintaining fluid and nutrient balances, and responsiveness to noxious stimuli are just of few of the challenges that are handled by these nervous system processes. Reflexive responses are executed through fast acting autonomic-somatic coupling, are evolutionarily old, and are important for basic survival purposes. However, with the evolutionary development of the prefrontal cortex, complex regulatory capacity has become possible. This regulation often still takes place in non-conscious format, but cognitive and emotional appraisals provide greater on-line assessment and reaction to afferent information from both external and internal events.

Over the last two decades, several models have been formulated which map out the intricate networks involved in central nervous system (CNS) regulation of ANS activity (Thayer

& Lane, 2009; Critchley et al., 2011; Gianaros, 2008). Much of the early evidence supporting these models arose from animal studies as well as sparse contributions from clinical observations of dysfunctional or damaged areas of the nervous systems. With the advent of spatially improved imaging technologies, these models have received greater structural and functional support within human samples. With the concurrent recording of brain imaging and physiology, direct changes in autonomic activity have been coupled with corresponding changes in CNS recruitment. These particular studies have further supported specialized regional specificity in the brain that largely serves in attending to bodily changes (Thayer et al., 2011).

Although there is a small amount of variability between the brain regions posited by these models, a brief summary of overlapping areas will be summarized. Specific regions in the prefrontal cortex serve largely inhibitory roles over subcortical regions of the brain. Regions of the medial prefrontal cortex (mPFC) and specifically the ventral portion (vmPFC) as well as the orbitofrontal cortex (OFC) have been implicated in inhibitory functions over subcortical regions of the brain and brainstem in humans as well as animals (Roy et al., 2009; Ozdemi & Hachinski, 2008). Gathered from a large literature of work performed with rats, monkeys, and humans, the medial regions of the PFC have generally been accepted as having a largely regulatory role in the 'viscero-motor system' via subcortical pathways directed through the amygdala, hypothalamus and brainstem (Ongur & Price, 2000).

Just posterior to the aforementioned prefrontal regions are the anterior insula (aINS) and the anterior cingulate cortex (ACC) which have been implicated in ANS regulating roles such as interoception (Craig, 2002; 2009), homeostatic regulation (Craig, 2003), and general error detection (Carter et al., 1998) which has been implicated in the decision-making phase of whether to allot resources for mobilization or not (De Neys, Moyens, & Vansteenwegen, 2010).

Communication from the aINS and the ACC can generally travel to subnuclei of either the amygdala or the hypothalamus for the mobilization of resources to address the appraised situation (Craig, 2005; Gianaros, 2008).

The central nucleus of the amygdala (CeA) has been thoroughly established as a key structure in forming a link between higher cortical regions of the brain and effector centers of the lower regions of the brain that have more direct afferent and efferent communication with the ANS (Saha, 2005). Therefore, the CeA plays a critical role in both the integration and coordination of cardiovascular responses. The CeA is an important output nucleus of the amygdala that receives neural information from both lateral and basolateral nuclei of the amygdala, but also receives highly processed sensory information from various sensory cortices. It in turn projects to regions of the hypothalamus and brainstem leading to either excitatory or inhibitory efferent responses.

One important connection of the CeA is with the nucleus of the solitary tract (NTS) in the brainstem. Studies using both retrograde and anterograde tracers have demonstrated the communication between these two groups of nuclei (Wallace, Magnuson, & Gray, 1992). The NTS is located in the dorsal region of the medulla and is the primary endpoint of afferent fibers transmitting information from several visceral organs. It also receives information from baroreceptors in the carotid arteries and aortic arch which communicate blood pressure status. The NTS projects to at least three other sub-nuclei in the brainstem: the dorsal vagal motor nucleus (DVN) and the nucleus ambiguus (NAm) which preferentially handle vagal activity through cholinergic neurons, and the caudal ventrolateral medulla (CVLM) which tonically inhibits the rostral ventrolateral medulla (RVLM). The RVLM is tonically active with sympathoexcitatory neurons and therefore its inhibition leads to general suppression of SNS

response (Guyenet, 1990). The RVLM has important baroreceptor sensitive neuronal connections in the spinal cord which ultimately project to the heart as well as other organs (Dampney, 1994).

Activation of the NTS via baroreceptor feedback stimulates inhibitory neurons in the CVLM which serve to suppress excitatory output from the RVLM (Chalmers et al., 1994). This activity directly affects blood pressure activity, with RVLM suppression leading to blood pressure decreases (and RVLM activation leading to blood pressure increases). Ultimately, the CeA serves to tonically inhibit the NTS via GABAergic connections which consequently leads to the systematic suppression of excitatory neurochemical activity during resting states (Saha, Batten & Henderson, 2000). However, efferent signaling to the CeA from either cortical or subcortical regions can lead to disinhibition of the CeA, which can produce excitatory neurochemical activity through both NTS activation and disinhibition of the RVLM. While mapping out the directional pathways of the CeA, it must also be noted that a small amount of fibers exiting the CeA have direct communication with the RVLM and can lead to direct excitation of noradrenergic neurons (Wallace, Magnuson, & Gray, 1992).

The next step in efferent communication from the CNS is excitation to the heart, which must travel through the stellate ganglion which originates in the intermediolateral cell column of the spinal cord. However, any inhibitory cholingergic activity of the heart travels through efferent fibers of the vagus nerve which have a more direct path from regulatory nuclei in the brainstem such as the NAm. These efferent fibers communicate directly to the sino-atrial (SA) node of the heart and provide tonic suppression of heart rate (HR) For further reference of CeA's role in regulating cardiovascular activity, see Saha, 2005.

Enter Laterality

Improvements in research and clinical technology have led to a thorough mapping of these pathways. However, with the development of models to explain this activity, little attention has been paid to the lateralized role that many structures in the aforementioned pathways may serve in handling this information. Considering the gross amount of empirical work based in structural and functional lateralization before the popular usage of imaging equipment, there is an obvious call for re-attending to laterality distinctions that may be present in these often bilateral structures.

It has been suggested that neuroscientists no longer like to discuss the divided nature of the brain (McGilchrist, 2011). Lateralized functionality of the brain rose to popularity in the 60s and the 70s with the widespread recognition of split-brain studies, but has since fallen out of mainstream neuroscience interest. This is unfortunate considering the vast literature contributing to the psychological and behavioral implications of lateralized processes. The following paragraphs will discuss the role of lateralization in the previously defined pathways. However any informed conversation on laterality must first discuss the role of the corpus callosum.

The corpus callosum is a wonderfully thick and dense connection of axonal fibers that primarily serve to communicate information from one hemisphere to the other. It consists of approximately 200-400 million axons (Banich, 1995). A review of existing evidence has shown that the while the corpus callosum primarily serves an excitatory role in interhemispheric information transference, it also has a notable role in the inhibition of neural signaling (Bloom & Hynd, 2005). The premise underlying interhemispheric inhibition is important because of the implications it holds for allowing the functions of a given hemisphere to predominate in signal processing and consequential behavioral execution. Alterations with the structure of the corpus

callosum have been related to many types of psychiatric and developmental disorders (Schaefer & Bodensteiner, 1999; Preis et al., 2000).

Important for the current investigation, the corpus callosum has direct and diffuse connections between anterior regions of the cortex for both hemispheres (Banich, 1995). This segment of the corpus callosum is called the genu. The function of the middle segment of the corpus callosum which connects the motor and somatosensory regions of the hemispheres is also of interest. There are two types of fibers that generally make up the corpus callosum. There are large diameter fibers that transmit motor and sensory information while other, smaller diameter fibers primarily transmit information from the association areas. These smaller fibers are thought to serve a larger role in the process of inhibition (Bloom & Hynd, 2005; Yazgan et al., 1995). GABA is the most prevalent neurotransmitter in the brain and it is primarily inhibitory, and it serves an important role in cross-hemisphere inhibition (Irlbacher, Brocke, Mechow, & Bandt, 2007). However, evidence also supports the view that the corpus callosum actually consists of several pathways that can communicate independently, so inhibition may take place in one part and excitation in another (Banich, 1995).

The role of the corpus callosum is relevant considering the consequences of its inhibitory capabilities and for hemispheric lateralization of function. Primarily, the role of hemispheric lateralization at the functional level suggested here is that activation of one hemisphere generally leads to compensatory deactivation of the opposite hemisphere. Theories purporting this view have long been in existence; notably the functional cerebral systems theory (Kinsbourne, 1975) and the homotopic inhibition theory (Cook, 1984). Kinsbourne brought attention to the dynamic between the two hemispheres being in constant inhibitory conflict with each other, which allows one hemisphere to be active while inhibiting the other. Empirical support exists for this theory,

largely through studies employing dichotic listening tasks (e.g., Bryden, 1988). Cook extended (or narrowed) this theory to focus on inhibition of a homologous structure with the excitation of the other. Tucker has also contributed extensively to this theory (1981). The balance theory is based upon another laterality model that embraces the functional significance of inhibition of the opposing hemisphere (Foster, Drago, Ferguson, & Harrison, 2008). This theory has been supported by a variety of empirical work (Snyder, Shenal, & Harrison, 1998). Generally speaking, these theories suggest that stimuli transmitted to a particular hemisphere are assumed to be mostly processed in that hemisphere since the other hemisphere will simultaneously be expected to decrease its activity. Before venturing further into a discussion on brain lateralization, the literature suggesting lateralization in the periphery should be visited. Therefore, a review of evidence supporting both structural and functional lateralization starting at the level of peripheral wiring and then moving up to specific sub-regions of the frontal lobe that serve regulatory roles in ANS activity will be presented.

Autonomic Laterality

Communication between the ANS and the CNS is bidirectional, involving constant feedback between the two systems. The vagus nerve serves an integral role in this communication. The vagus is traditionally thought of for its efferent functions, but it is made up of approximately 80% afferent fibers (Porges, 1998). With this information noted, comprehension of laterality at the peripheral level may be just as informative as at the cortical level when trying to comprehend complex phenomena such as an organism's behavior (Berntson, Sarter, & Cacioppo, 2003).

Asymmetry in peripheral innervation of the heart. Autonomic control of cardiac activity appears to be asymmetrical at the peripheral level. At the SA node, most of the sympathetic

innervation takes place in fibers carried by the right stellate cardiac nerves. The same holds for the parasympathetic innervations with most SA node innervations coming from the right vagus (Levy & Martin, 1979). These right-sided innervations appear to mostly regulate cardiac chronotropic activity. Conversely, ANS control of inotropic and dromotropic effects as mediated by sympathetic and parasympathetic pathways to the AV node are more strongly regulated by left side innervations (see Wittling, 1995 for a review).

Autonomic asymmetry in the brainstem. The three components of cardiac activity also seem to be mostly lateralized at the level of the brainstem. Evidence supporting this was provided by injection of a retrograde tracer into the cardiac ganglion, which showed three times as many cells in the left NAm than in the right ventrolateral NAm (Massari, Johnson, & Gatti, 1995). Considering the role that the cardiac ganglion plays in regulating AV conduction, it can be presumed that dromotropic and intotropic regulation are largely lateralized to the left NAm. Other research suggests that the right side of the ventrolateral medulla (VLM) plays a larger role in chronotropic control. Unilateral injection of GABA into sympathoexcitatory nuclei of the VLM showed a marked decrease in myocardial contractility when injected to the left side, while injection to the right side showed suppressive effects on HR (Shapoval, Sagach, Pobegailo, 1991).

To summarize, cardiac activity at the level of the brainstem appears to be lateralized in the same organization as it is at the peripheral level. Chronotropic activity, which has both vagal and sympathetic contributions, is regulated by mostly right-sided neural structures. Dromotropic and inotropic activity, which are determined by sympathetic contributions, are mostly regulated by left-sided structures (see Wittling, 1997 for a review). However this lateralized organization of regulating cardiac activity at the peripheral and brainstem levels does not appear to apply to

organization in more evolutionarily recent regions of the brain. Instead of lateralizing specific components of cardiac activity, the temporal and frontal lobes seem to show a preference for regulating the branches of the ANS; although this lateralization of ANS regulation has been much less clear in the literature (Ahern, et al., 2001; Oppenheimer, Gelb, Girvin, & Hachinski, 1992).

Lateralization persists in the amygdala. However after reviewing 54 studies which assessed differences in amygdalar processing between the left and right amygdalae, a clear pattern had not emerged (Baas, Aleman, & Kahn, 2004). It has been suggested that the right amygdala serves a larger role in rapid stimulus detection while the left amygdala serves a larger role in sustained evaluation of information (Wright et al., 2001). Regardless of stimulus type or task instructions, it appears that the left amygdala has shown greater levels of activity in both duration and magnitude than the right amygdala (Baas et al., 2004). A meta-analysis on neuroimaging findings in emotion processing showed that the left amygdala was more frequently activated, especially in the context of negative emotion (Wager et al., 2003). In terms of laterality of the amygdalae in autonomic control, one previous investigation failed to find any laterality differences (Healy & Peck, 1997), while others have inferred that tachycardia or bradycardia elicited from insular lobe stimulation also evokes an amygdalar response considering their ipsilateral connectivity (Cechetto & Gelb, 2001; Oppenheimer, 2001). One study of note found sex differences in amygdala lateralization while simultaneously recording skin conductance. (Williams, Barton, Kemp, Liddell, Peduto, Gordon, & Bryant, 2005). Women were found to have bilateral amygdalar response to fear signals, while men only demonstrated right amygdalar response. The study also showed that the right amygdala and skin conductance responses attenuated faster for men while women maintained a more tonic level of "arousal".

Overall, it must be noted that there is a paucity of research that has looked at amygdala laterality in terms of ANS activity.

Currently, there are two opposing models that represent how prefrontal regions of the brain are differentially lateralized in processing SNS and PNS activity. According to both models, the right hemisphere has largely been implicated as serving a dominant role in regulating SNS activity (Wittling, 1997). This has been supported through studies employing a variety of methods. However, the regulation of PNS activity is currently less clear. The right hemisphere has been posited by some to largely regulate both SNS and PNS activity and has been supported by various methods of research (Ahern et al., 2001; Lane et al., 1989). However, these findings are faced with conflicting empirical work. There is a competing theory that couches the regulation of PNS activity in the left hemisphere and also has a body of research to support these claims (Craig, 2005). Using both human and animal models, many empirical investigations have been conducted that were either designed explicitly to assess lateralized ANS regulation, or minimally provide information about this basic organization by assessing related phenomena. These investigations have varied greatly in the tools and methods implemented to address the issue at hand. Several key studies will be sampled from this literature.

Review of studies assessing lateralized regulation of the ANS

Unilateral Brain Damage/Stroke Studies. A small body of work has contributed information for hemispheric regulation of the ANS based upon studies conducted in patients with unilateral brain damage. Using stroke and traumatic brain injured (TBI) patients with unilateral hemispheric damage while recording HR and SC responses, Andersson and Finset (1998) found significantly reduced autonomic reactivity to mathematical stressors in right hemisphere injured patients when compared to left hemisphere damaged patients. Another group of researchers used

emotional slides to elicit SC responses in patients with left and right hemisphere damage. They found that patients with left hemisphere damage showed greater SNS responses than those with right hemisphere damage. Classifying damage to the "dominant" or "non-dominant" hemisphere, Morrow et al. (1981) showed that patients with dominant hemisphere damage had decreased SC responses to emotional stimuli, while non-dominant hemisphere damage tended to suppress SC reactivity altogether. The right hemisphere served as the "non-dominant" hemisphere for all but one of the subjects. These results suggest that the right hemisphere serves a larger role in producing SNS responses as well as in processing emotional stimuli. Another study looking at unilateral brain-damaged patients' responses to emotional stimuli also showed increased SC responses with left hemisphere damage, but no significant SC changes in right hemisphere damaged patients (Zoccolotti, Scabini, & Violani, 1981). Overall, these studies have provided mixed results (with little information about parasympathetic activity), are often underpowered, and suffer from many uncontrolled variables such as: volume of structural damage and time since injury (and consequent plasticity of function). Also, the main elicitor of ANS reactivity is often limited to emotional stimuli and the main measure employed is usually SC, which does not provide information as to the role of parasympathetic activity during the task.

Epilepsy and the Wada Test. Some of the most insightful research on the issues at hand has come from observations of differential ANS responses after deactivation of one hemisphere via intracarotid sodium amobarbital (ISA) injections in clinical trials (Zamrini et al., 1990; Lane et al., 1989; Ahern et al., 2001). These "studies" are usually clinical observations of epileptic patients undergoing preoperative evaluation for whether surgery is required. The ISA injections are able to fundamentally cause transient deactivation of the targeted frontal lobe while leaving

the subcortical and posterior regions of that hemisphere functionally intact. These studies have produced slightly discrepant findings in terms of cardiac changes. One of the earlier investigations using this approach found HR to increase with left hemisphere inactivation and HR to decrease after right hemisphere inactivation (Yoon et al., 1997). Using only eight subjects in presurgical evaluation of temporal lobe epilepsy, the authors used spectral analysis of heart rate variability (HRV) and assumed the low frequency/high frequency (LF/HF) ratio as an indicator of sympatho-vagal balance. Right side inactivation provided nonsignificant results, but left side inactivation showed a clear increase in LF/HF ratio, suggesting an increase in sympathetic activity, a decrease in parasympathetic activity, or both happening simultaneously. Ahern et al. (2001) used a much larger sample size (n=73) and found that HR increased from deactivation of either hemisphere, but was greater for right hemisphere deactivation. They also found the high frequency (HF) spectral component of HRV decreased during deactivation of either hemisphere, but these decreases only reached significance levels for right hemisphere deactivation. The discrepant findings in these studies may be products of varying sample size, the use of clinical populations, and the inconsistent metrics used for measurement of cardiovascular activity.

Other Clinical Populations. Using a clinical sample consisting of Parkinson's patients with either left or right hemi-body onset of symptoms, Foster and colleagues (2011) measured HR and blood pressure (BP) at resting levels. Although resting HR was higher with right hemi-body onset patients as expected, resting BP was higher with left hemi-body onset patients which was opposite of the authors' expectations. Another clinical study looked at laterality in terms of ANS responses to unilateral-onset migraines. ECG recordings over a 24-hour period showed that cluster headaches were related to low HRV only in right-sided migraines (Micieli et al., 1993).

EEG in asymmetry. A few studies have utilized electroencephalography (EEG) during resting states and have measured asymmetrical bandwidth power while simultaneously measuring cardiovascular variables. One study found a negative correlation between SBP and alpha magnitude in the right temporal lobe (Foster & Harrison, 2004). They also observed a positive relationship between left frontal activity and beta wave magnitude. Another study from this lab found that the level of alpha wave magnitude in the left frontal lobe was positively correlated with heart rate, while the right frontal found an opposite relationship (Foster & Harrison, 2006). Two studies assessed resting cardiovascular activity with EEG activity and found an asymmetrical relationship across the frontal lobes. Lower HR was correlated with right frontal alpha activity, while higher HR was correlated with left frontal alpha activity (Foster & Harrison, 2006). These findings suggest that individuals with tonic right-frontal activation have elevated sympathetic activity, although, they do not inform regarding parasympathetic influence on HR.

Neuropsychological Tests. It should also be noted that tests designed for neuropsychology evaluations, such as the Rey Auditory Verbal Learning Test (RAVL; Rey, 1964), have been used as hemispheric stressors (Snyder, Harrison, & Shenal 1998). This test has proven to elicit affective responses and cause blood pressure responses. Another test, the Ruff Figural Fluency Test (RFFT; Ruff, Light, & Evans, 1987), has also been used to stress right frontal lobe functioning (Foster, Williamson, & Harrison, 2005). The RFFT has proven to elicit large sympathetic responses, particularly in high hostile individuals, who have been known to have larger tonic levels of right frontal activity, which puts them at risk for sympathetic over-responsiveness to right hemisphere stress.

Lateralized stimulus presentation. Several studies have implemented some variation of lateralized stimulus presentation or motoric execution. The premise underlying these studies is

that the sensory information is predominantly transmitted to the contralateral hemisphere and therefore is more likely to be preferentially processed by the receiving hemisphere. Depending on the location on a limb, somewhere between 70 and 90% of afferent and efferent sensory and motor fibers project to the contralateral hemisphere (Andreassi, 2006). These types of studies can assess differences in autonomic responsiveness as indirect measures of cortical regulation via corresponding changes in activity of the contralateral hemisphere (Stuss & Benson, 1984). Examples of these would be hemispheric activation by lateralized presentation of visual stimuli. For example, positive films have been shown to elicit larger BP responses when presented to the right hemisphere than when presented to the left hemisphere (Wittling, 1990).

A recent investigation using a passive lateralized vibro-tactile stimulation demonstrated a relative decrease in HR from right hand stimulation and a relative increase in HR from left hand stimulation (Foster et al., 2012). However, in this study parasympathetic activity was assumed through a decrease in HR and was only seen in 10 of the 19 subjects (half of which also experienced HR decreases from left hand stimulation).

Insula Stimulation. Another method used to explore ANS laterality has been intraoperative insular stimulation, which is traditionally used for seizure control (Oppenheimer et al., 1992). This procedure allows for the observation of cardiac reactivity after direct stimulation of the left and right insular cortices. Stimulation of right insula produced a tachycardia response, while stimulation of the left insula produced a bradycardia response. These results provide further support for the right hemisphere's role in sympathetic regulation and support the role of the left hemisphere in parasympathetic control.

Research out of This Laboratory. The cold pressor task has a long history of being used in research as a physiological stressor (Hines, 1936). It reliably elicits large blood pressure

responses and often a modest increase in HR (Knepp & Friedman, 2008). The task usually involves submersion of either a hand or a foot in ice water for an extended period of time (Durel et al., 1993). Due to the mostly contralateral projection of sensory afferents from the distal portions of the limbs, the cold pressor task is well suited to be used as an assessment of lateralized responsiveness. The Mind-Body Laboratory has produced two pilots that have provided strong evidence for right hemisphere regulation of SNS activity largely through blood pressure responses to the cold pressor task. . A pilot of 19 male and female subjects using a lateralized cold pressor task showed significantly greater BP responses to left hand submersion compared to right hand submersion (Friedman, Vella, & Lozier, 2006). A more recent pilot using 29 male undergraduates demonstrated the same lateralized effect with significantly larger systolic and diastolic blood pressure responses elicited by left hand submersion (McGinley et al., 2011).

Another task that has been reliably used in laboratory settings for eliciting a patterned autonomic response is the facial cooling task (Friedman, Thayer, & Tyrrell, 1996). This task can vary from application of a cool mask to a participant's forehead to full submersion of face into a container of cold water. The task has been shown to elicit an evolutionarily old response termed the "dive reflex". This reflex has been observed in less complex organisms than humans and is suggested to serve a role in preservation of oxygen while the organism is under water (Andersen, 1963; 1965). The reflexive bradycardia response elicited by the cold stimulus largely functions through afferent stimulation of the trigeminal nerves in the face (Eckberg, Mohanty, & Raczkowska, 1984). The largest effects are typically seen with the upper two branches of the cranial nerve, the ophthalmic and the maxillary, however, stimulation of just the mandibular branch has also shown to elicit a mild bradycardia response (Khurana, et al., 1980). The upper

two branches of the trigeminal nerve mostly project to the ipsilateral hemispheres (Morecraft et al., 2001), however, the mandibular branch's projections are largely contralateral instead of ipsilateral (Meyer, Wehahn, Rothwell, Roericht, & Fauth, 1994). The afferents are not as contralaterally distributed as afferents from the distal portions of the limbs, however, a strong enough elictor of afferent stimulation may produce a contralateral response.

In summary of findings from this varied collection of research methods, activity related to the SNS has largely been associated with the right hemisphere. This has been well-supported by many different experimental techniques. However, the role of parasympathetic activity has varied considerably depending on methods for elicitation. Also, few of these studies have used direct quantification of parasympathetic activity which is most easily measured by spectral or time-based measures of heart rate variability. There appear to be few studies that have been able to directly elicit parasympathetic responses, particularly in a way that the information is lateralized to processing within a specific hemisphere.

Sex Differences in Laterality

Few of the aforementioned studies exploring asymmetric autonomic regulation have assessed the variable of sex differences in this asymmetric functional arrangement. Considering the vast literature that has found sex differences in the degree of lateralization across a variety of tasks and behaviors (McGlone, 1980; Hugdahl & Westerhausen, 2010), it is reasonable to suspect that men may demonstrate greater lateralization than women in autonomic regulation when presented with lateralized stimuli. The only known work exploring this topic is a pilot from the Mind-Body lab (Friedman, Lozier, & Vella, 2006). In this pilot, women displayed comparable levels of systolic (SBP) and diastolic blood pressure (DBP) reactivity to both the left and right hand, but men were more reactive during left hand submersion (Friedman, Lozier, &

Vella, 2006). Left hand submersion resulted in decreases in RMSSD (a measure of vagal activity) which implies vagal withdrawal during the task. Right hand submersion did not show this same effect. The findings of this pilot suggest greater functional lateralization in men.

Although not in the realm of laterality differences, research has found sex differences in autonomic responses. Women tend to possess greater protection than men against cardiovascular disease, hypertension, and myocardial infarctions (Jorgensen & Houston, 1981). In laboratory settings, women have been shown to be less autonomically responsive to both physical and mental stressors (Convertino, 1998; Hinjosa-Laborde, Chapa, Lange, & Haywood, 1999; Kring and Gordon, 1998). Men have also been shown to respond to stress with greater increases in blood pressure, heart rate, and catecholamine levels in plasma comparative to women (Hinjosa-Laborde, Chapa, Lange, & Haywood, 1999). Another physiological difference is that the reflex bradycardia response to increased blood pressure is diminished in women compared to men (Convertino, 1998). Although likely intertwined with hormonal differences, it is possible that these differences may be partly due to women's more diffuse distribution of ANS regulatory control.

One study explored asymmetry in HR modulation by sex, but did not obtain any measure of frontal lobe activity (Kirchner, Pauli, Hilz, Neundorfer, & Stefan, 2002). This study used patients with unilateral temporal lobe epilepsy to observe HR increases during seizures. They observed greater increases in HR for right-sided seizures compared to left hemisphere seizures and also found the degree of lateralization to be greater in males than females.

Sex differences in functional asymmetries are likely due to differences in cerebral organization. Women have consistently evidenced greater bilateral representation of functions for both verbal and nonverbal abilities (Ecoyer-Dab & Robert, 2004; Hines, Chiu, McAdams,

Entler, & Lipcamon, 1992). Conversely, men have typically shown greater hemispheric specialization for both verbal and nonverbal abilities. A meta-analysis of 396 significance levels across a variety of studies showed that men tend to also have greater functional asymmetries than women in visual and auditory modalities (Voyer, 1996).

Considering the vast amount of literature on lateralization differences between men and women, there appears to be a dearth of literature investigating sex differences in hemispheric lateralization in regard to ANS functioning. The pilot from this lab, along with the literature implicating functional asymmetries between men and women, suggests that exploring sex differences in lateralized autonomic reactivity is an area worth investigating.

Although the last few decades have produced a plethora of studies that demonstrate sex differences in lateralization, it has been noted that this distinction may not be so clear. Through a meta-analysis of verbal abilities, it has been noted that intra-sex variance is much greater than inter-sex variance (Hyde & Lin, 1988). This assertion may direct investigations towards locating factors other than biological sex, which may lend to lateralization differences. Some literature has brought question to the causes for these alleged sex differences in lateralization. Therefore, it may be important to further investigate any mechanisms, whether psychological or biological in origin, which may contribute to these differences. Gender role identification may be one of these mechanisms.

Gender Contributions

Although there is little information that explores gender identity as a moderating factor in patterns of autonomic responsiveness to stressors, there is evidence to support the view that functional lateralization may be related to variables other than biological sex. This investigation examined the relationship of right-handed men, sex role identity, and functional cerebral

lateralization (Kozaki & Yasukouchi, 2005). The findings suggested that men with higher masculinity in their sex role identity may have greater functional lateralization. Building upon this study and other literature that looks at gender identification as an important factor for phenotypic development during maturation infers that sex role identification may be an important factor in functional lateralization.

Aims

Much of psychological research has been directed towards investigating the relationship between genetic and environmental factors in biological, psychological, and behavioral development. The current study sought to investigate interacting elements of all three. The design of this study addressed asymmetric regulation of ANS activity as well as sex and gender differences in functional arrangement (i.e. lateralization).

The primary aim of this study was to investigate hemispheric lateralization for regulating autonomic nervous system activity. The literature is still inconclusive for which hemisphere serves a more substantial role in regulating parasympathetic activity. Recent publications demonstrate the still ongoing disagreement for which hemisphere serves a more prominent role in regulating parasympathetic activity (Foster, Drago, Ferguson, & Harrison, 2008; Thayer & Lane, 2009). Preliminary evidence from this laboratory demonstrated the usefulness of using the cold pressor as a lateralized task for assessing hemispheric specialization in regulating the cardiovascular components of ANS activity (McGinley et al., 2011). It is hypothesized that the left sided tasks will elicit larger SNS responses. Specifically, the left-sided cold pressor task will elicit larger blood pressure, heart rate, and skin conductance responses than the right-sided cold pressor task. It is unclear whether the PNS is predominantly lateralized to the right or the left hemisphere, so it is hypothesized that the vagal responses of the facial cooling task will support

one of the two models presented here. Therefore, it is expected that there will be a larger vagal-mediated HRV response for the left-sided facial cooling task which would support the Thayer and Lane (2009) model, or that the vagal response elicited from the right-sided facial cooling task will be greater than the left and support the Harrison (Foster et al., 2005) and Craig (2005) model.

Since it is challenging to employ a task that can elicit predominantly parasympathetic activity in a lateralized manner, a modified version of the facial cold pressor task served as an exploratory endeavor. Although standard versions of the facial cooling task have repeatedly demonstrated increases in parasympathetic activity as indexed by a bradycardia response and an increase in HRV, there is no knowledge of it being used in a lateralized manner.

A secondary aim of this investigation was in discovering whether laterality differences in ANS regulation exist between men and women. Although some meta-analyses have shown that the research on sex differences between men and women may not be as pronounced as commonly believed (Hyde & Lin, 1988; Hyde, 1990), preliminary evidence from this laboratory has indicated that lateralization differences may hold true for ANS activity (Friedman, Vella, & Lozier, 2006). Therefore, one of the primary aims of this investigation was to further explore this relationship between sex and lateralization via autonomic responsivity. It was anticipated that the trend observed in this laboratory would subsist and men would demonstrate greater lateralization. Therefore it is hypothesized that the left-side cold pressor will elicit a larger lateralized blood pressure and heart rate increase for men, while women will demonstrate either a smaller degree of lateralization or bilateral representation of SNS regulation. It is also hypothesized that the measurements of vagally-mediated HRV will demonstrate a greater degree of lateralization in men compared to women.

This investigation also held an exploratory hypothesis. Most of the literature investigating laterality differences between sexes has not accounted for sex role identity. Therefore, this study explored the relationship between sex role identity and lateralization of ANS responses. It was hypothesized that women who strongly identify with masculine roles would be more lateralized in their autonomic responses, while men who strongly identify with feminine roles would be less lateralized.

Method

Subjects

Seventy-three college students (37 female; mean age = 19.77, SD=1.76) were recruited for this study through Virginia Polytechnic and State University psychology department's SONA online research system to serve as subjects in the study. Eligibility requirements were posted on the advertisement page of the SONA site. The requirements were as follows: right-handed, aged 18-26, non-smokers, with no history of neurological and cardiovascular disease. The study took place as a one-part laboratory session. As offered by various psychology classes at the University, the subjects were provided with extra credit for completing the session. The subjects were also instructed to abstain from alcohol for twenty-four hours, caffeine for twelve hours, food for one hour, and vigorous exercise for two hours before their laboratory visit. Institutional review board (IRB) approval was attained from Virginia Tech in order to conduct this study. The IRB approval code for the protocol was #11-485.

Questionnaires

Several questionnaires were given to the subjects after the electrodes and leads were attached to their body but before they performed the study's tasks:

Health History Questionnaire: Gathers information on health problems that could potentially conflict with the results of study (Appendix C).

Mind-Body Laboratory Recent Health History Questionnaire: Gathers information on recency of caffeine and alcohol consumption, recency of exercise, as well as the last time the subject ate (Appendix D).

Laterality Questionnaire (Coren & Porac, & Duncan, 1979): May affect subjects' tendencies towards preferential lateralization (Appendix E).

Bem Sex-Role Inventory (BSRI; Bem, 1974): Assesses masculinity and femininity as two separate dimensions, thereby making it possible to characterize a person as masculine, feminine, or androgynous (Appendix F).

Pain Assessment Questionnaire: assesses self-reported pain experienced during each task (Appendix H)

Self Assessment Manikin (SAM; Morris, 1995): assesses self-reported affect experienced during each task (Appendix I)

Materials

Equipment

Electrocardiography (ECG), and electrodermal activity (EDA) were collected using CONMED disposable, pre-gelled stress-testing spot electrodes. EDA was measured with two electrodes placed on the 2nd and 3rd fingers of the left and right hands in accordance with placement recommendations of Fowles et al.(1981). ECG was collected by two thoracic electrodes (Appendix G). The ECG signals were amplified through an ECG 100C system (BIOPAC Systems Inc, Goleta, CA). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded using a MedWave Fusion non-invasive BP monitoring system (MedWave Inc., Danvers, MA). SBP and DBP were recorded using a BP monitor cuff with a sensor that measured pulse oxymetry. There were three different cuffs (child, adult, and extra large)

available for appropriate sizing. The sensors were placed over the radial artery for maximizing signal detection.

The signals from ECG and BP were interfaced through an MP150 system (BIOPAC Systems Inc, Goleta, CA). The EDA was amplified and interfaced through an MP36 system (BIOPAC Systems Inc, Goleta, CA). The analog data from the MP150 was then sent to a Mac computer in the adjoining room. This Mac computer recorded the incoming physiological data on a software program, Biopac Acqknowledge 4.1(BIOPAC Systems, Inc, Goleta, CA). The physiological data from the MP36 was sent to a Dell laptop which recorded the data on a software program, Biopac Student Lab Pro 3.7.7 (BIOPAC Systems, Inc, Goleta, CA). All raw signals were digitized at 1,000 Hz. Artifact detection was performed by visual inspection and with software assistance using Biopac Acqknowledge 4.1 and Biopac Student Lab Pro 3.7.7.

Autonomic Measures

Cardiovascular measures in this study were derived from ECG and from BP signals. The inter-beat interval (IBI) and heart rate variability (HRV; the difference in time between successive R-spikes) were derived from the ECG signal. Since HRV is often assessed in both temporal and frequency domains, so both were derived from the ECG signal and analyzed in this study. Spectral frequency bands were derived from Fast Fourier Transformation, and calculated for two of the frequency bandwidths: the high-frequency (HF) component of the waveform (0.15-0.50 HZ) was of specific interest as an indicator of parasympathetic influence on the heart (Task Force, 1996), while the low frequency (LF) band was of interest for changes in sympathetic activity and blood pressure modulation. HF is generally understood to be the respiratory component of HRV. LF, however, is less well understood. There is controversy over whether it is a purely sympathetic frequency, whether it contains some vagal presence, or as to

how large of a role the Mayer waves of blood pressure contribute to the signal (e.g. Hopf et al., 1995). A recent review of pertinent research indicates that LF power indexes baroreflex-modulated cardiac ANS outflow (Goldstein et al., 2011).

Only one time domain metric of HRV was analyzed. The root mean square of successive differences (RMSSD) is strongly related to vagal modulation (Penttila, et al., 2001). It assesses beat-to-beat changes in heart rate and can be quantified as:

$$RMSSD = (\sum (IBIj+1 - IBIj)2)\text{^}1/2.$$

$\sum$ (IBIj+1 – IBIj)^2 averages the squared successive differences between consecutive R spikes. All time-based and spectral-based metrics of HRV were analyzed and extracted from the software program, Kubios HRV v2.0 (Biosignal Analysis and Medical Imaging Group, Kuopio, Finland). SBP, DBP, and mean arterial pressure (MAP) were taken from the blood pressure readings. MAP was calculated from SBP and DBP; MAP = 2/3 DBP + 1/3 SBP (Nyklicek et al., 1997; Razminia et al., 2004).

Laboratory Design

Procedure

Each subject was provided with a brief explanation of the equipment and then informed about the study's sequence of events. The subjects then provided informed consent to participate in the study. In preparation for the foot cold pressor task, subjects were asked to remove their footwear in order to normalize foot temperature to the room. Then either the researcher or a research assistant applied the ECG electrodes and the corresponding leads to the subject.

The subjects were then asked to fill out four questionnaires (Appendices C, D, E, and F) that were displayed on Qualtrics, an internet survey provider on a desktop computer. After completion of the questionnaires, the subject had both hands set up for the EDA electrode

arrangement, as well as the BP wrist sensor. The research assistant (or the researcher) then initiated the first of twelve tasks. Each of the tasks was three minutes in duration, except for the facial cooling tasks which were two minutes in length. The tasks took place as follows:

Phase 1:

(1) Baseline task: In accordance with previous findings which demonstrated slightly greater cardiovascular stability by employing mildly engaging baseline tasks instead of traditional basal baseline tasks, the study employed "vanilla baseline" tasks (Jennings, Kamarck, Stewart, Eddy, & Johnson, 1992). The subject was instructed to relax and watch the video that appeared on the computer monitor directly in front of them. The video displayed a picture slide composed of images rated low on arousal and medium on valence as rated by the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2001).

(2) Left side facial cooling: the researcher entered the room with a bag filled with cold water. The temperature for the facial cooling task was 9.7ºC (SD 1.03). The researcher then stood behind the subject while pressing the bag on the left side of the subject's face. The bag covered the lower portion of the face, covering the cheek and below the eye. The researcher stayed in the room for 2 minutes.

(3) Recovery period: this third task involved the subject sitting in a still position while attempting to be quiet and minimizing movement. This task lasted 3 minutes and then the researcher reentered the room for the fourth task.

(4) Baseline task 2: the subject was once again be instructed to relax and watch another, similar baseline video composed of neutral images as rated by the IAPS. The researcher exited the room after beginning the video, and then reentered three minutes later for the commencement of the fifth task.

(5) Right side facial cooling: the researcher entered the room with a bag filled with cold water. The temperature for the facial cooling task was 9.8ºC (SD 0.98). The researcher then stood behind the subject while pressing the bag on the right side of the subject's face. The bag covered the lower portion of the face, covering the cheek and below the eye. The researcher stayed in the room for 2 minutes.

(6) Recovery period 2: this task was a repetition of the third task. The subject was instructed to sit in a still position for 3 minutes while attempting to be quiet and minimizing movement.

Phase 2:

(7) Baseline 3: the subject watched a third baseline video of neutral IAPS images for 3 minutes. The researcher reentered the room and placed a cooler filled with ice water (9.5ºC, SD 1.12) on the floor next to the subject's foot .

(8) Left foot cold pressor: the subject submerged his/her left foot into the cooler of ice water and was requested to keep it submerged for the duration of the task. The researcher left the room and reentered at the end of the three minute task. He then requested that the subject remove his foot from the ice water which signified the beginning of the recovery task. The researcher then picked up the cooler of water and left the room.

(9) Recovery 3: the subject was asked to stay seated and attempt to reduce bodily movements for 3 minutes.

(10) Baseline 4: the subject was asked to remain seated and watch another IAPS neutral video.

(11) Right foot cold pressor: the subject submerged his/her right foot into the cooler of ice water (9.7ºC, SD 1.14) and kept it submerged for the duration of the task. After instruction, the researcher exited the room.

(12) Recovery 4: the subject was asked to remain seated and watch another IAPS neutral video.

The order of tasks was varied across subjects. A quasi-counterbalancing scheme was used to mitigate the effects that maintaining the same task order would present. In order to avoid subject discomfort and time spent re-calibrating equipment, eight orders were used.

Task Ordering:

The facial cooling and cold pressor tasks were separated into two phases which were randomized across subjects. Phase 1 presented first and employed the two facial cooling tasks. Phase 2 presented second and employed the two foot cold pressor tasks. Using the facial cooling tasks first was preferable considering the quick withdrawal effects of parasympathetic activation comparative to the slower withdrawal effects of sympathetic activation. In order to account for differences that may arise from collecting BP from one arm and not the other, an eight-block design was implemented. It was quasi-randomized: arm which BP is collected from, side of the face that is first cooled, and foot that is first submerged. The order of tasks was as follows:

(1) Phase 1: right side facial cooling, left side facial cooling| Phase 2: right cold pressor, left cold pressor| Blood pressure cuff right arm
(2) Phase 1: left side facial cooling, right side facial cooling| Phase 2: right cold pressor, left cold pressor| Blood pressure cuff right arm
(3) Phase 1: right side facial cooling, left side facial cooling| Phase 2: left cold pressor, right cold pressor| Blood pressure cuff right arm
(4) Phase 1: left side facial cooling, right side facial cooling| Phase 2: left cold pressor, right cold pressor| Blood pressure cuff right arm
(5) Phase 1: right side facial cooling, left side facial cooling| Phase 2: right cold pressor, left cold pressor| Blood pressure cuff left arm

(6) Phase 1: left side facial cooling, right side facial cooling| Phase 2: right cold pressor, left cold pressor| Blood pressure cuff left arm

(7) Phase 1: right side facial cooling, left side facial cooling| Phase 2: left cold pressor, right cold pressor| Blood pressure cuff left arm

(8) Phase 1: left side facial cooling, right side facial cooling| Phase 2: left cold pressor, right cold pressor| Blood pressure cuff left arm.

Upon completion of each of the facial cooling and foot pressor tasks, the researcher acquired ratings of pain and valence for the task (Appendix H and I). After completion of all of the tasks, the researcher provided an opportunity for the subject to ask any questions about the study. After any lingering questions were answered, the subject was thanked for their participation and given permission to leave.

Data Analysis

The first hypothesis required a within-subjects comparison for physiological responses to left vs. right side presentation of the FC and CP tasks. The second hypothesis also utilized a within-subjects comparison for physiological responses to left vs. right side tasks within men and women. Therefore, the data were analyzed by a Repeated Measures 2x2 ANOVA (task x side):

Task	Task Side	
FC	LEFT	**FC_LEFT**
	RIGHT	**FC_RIGHT**
CP	LEFT	**CP_LEFT**
	RIGHT	**CP_RIGHT**

The dependent variables were the physiological responses: RMSSD, HF power, LF power, LF/HF ratio, IBI, MAP, SBP and DBP. Since the SC recordings were taken from both hands, the data were analyzed in a 2 x 2 x 2 Repeated Measures AVOVA (task x side x hand):

Task	Hand	Task Side	
FC	Right	LEFT	**FC_LEFT_RH**
		RIGHT	**FC_RIGHT_RH**
	Left	LEFT	**FC_LEFT_LH**
		RIGHT	**FC_RIGHT_LH**
CP	Right	LEFT	**CP_LEFT_RH**
		RIGHT	**CP_RIGHT_RH**
	Left	LEFT	**CP _LEFT_LH**
		RIGHT	**CP _RIGHT_LH**

The mean scores for each autonomic variable were calculated for each lateralized task (i.e. FCrt, FClft, CPrt, CPlft) and for each preceding baseline task. The mean scores of each physiological variable for the baseline tasks were then subtracted from the lateralized tasks (i.e. task – baseline) creating change scores. These change scores for the right and left tasks were then compared using repeated measures ANOVA to test for significant differences. The calculation of change scores has proven to be preferable over analyzing residual scores when assessing the generalizability of responses across a variety of tasks. The delta change presents fewer limitations with post hoc contrasts (Lllabre, Spitzer, Saab, Ironson, & Schneiderman, 1991).

All analyses were executed with Statistical Software Package for the Social Sciences (SPSS) v 19.0. The default error term specified by SPSS for repeated measures ANOVAs is "pooled within". Pooled within is suggested as the appropriate default error term to use in repeated measures designs (Roberts & Russo, 1999). Therefore, the default mode of pooled within was used.

The third hypothesis, which was exploratory, looked at masculinity and femininity scores as predictors for lateralization differences. Lateralization scores were created by subtracting the previously created right-side scores from the left-side scores. Masculinity and femininity scores were created by calculating mean values of responses across each subscale of the BSRI. Basic exploration was conducted by means of bivariate correlations between the laterality scores with the masculinity and femininity scores.

There are some data points missing due to equipment malfunction and other experimental issues. The results had slightly uneven N values seen across the dependent variables. Therefore pairwise deletion was used in cases of missing data. Three subjects lost ECG for the entirety of the study due to issues resulting from poor attachment of the ECG leads. Due to malfunctions with calibrating the blood pressure monitor, one subject did not have blood pressure readings for the entirety of the study. Six subjects did not have EDA recorded because of poor calibration between the amplifier and the recording software. Occasional tasks are missing data for either blood pressure or SCR due to excessive movement or excessive sweat production, respectively. It should also be noted that the SCR variables as well as the HF power and LF power variables were log transformed to correct for their non-normal distributions.

Ethical Considerations

In order to ensure privacy for each of the subjects, the physiological data collected during each session were stored on a password protected computer in the Mind Body Laboratory (MBL) in Williams Hall at Virginia Polytechnic Institute and State University. The self-reported questionnaires were stored in a locked cabinet in the same room. The data were only viewed and handled by members of the MBL. No information was collected which would allow the subject to be connected to his or her data. Each subject's file was saved under a file name which contained no personally identifying information.

Results

In order to assess whether self-report responses to the lateralized tasks differed, pairwise t-tests were performed on both affect and pain ratings between left and right-sided tasks. If ratings for one side were significantly different than the other side, it is possible that the autonomic responses to the lateralized tasks may partially influenced by greater metabolic recruitment in response to task perception, instead of only being related to lateralized regulation. However, the t-tests between right- and left-sided tasks for the PAQ and the SAM were all non-significant (See Table 1).

Other non-physiological variables were explored for systematic relationships with physiological responses at baselines and task periods. Bivariate correlations were conducted between these physiological and non-physiological variables. Body mass index (BMI) was significantly correlated with several blood pressure variables at different tasks in the study, but it was not correlated with any of their change scores at $p<.1$ and therefore was not considered in further analyses. Lifetime use of caffeine was negatively correlated with BP at several time periods, but also was not correlated with any change scores at $p<.1$ and therefore was not

considered in further analyses. Recent use of caffeine was not significantly correlated with any physiological variables. No other self-report data were systematically correlated with physiological responses and thus were ruled out as contributing factors to ANS responses.

In the following HRV analyses for the FC tasks, only averages over the first minute of the task were used. The increase in vagal activity during the tasks was only significant in the first minute and mostly dissipated by, or during, the second minute of the task for both FCrt ($F(1,69)=.093$, $p>.1$) and FClft ($F(1,68)=.007$, $p>.01$). This seems consistent with the relatively short bradycardia response typically seen in this task (Khurana et al., 1980). Although longer time periods are traditionally recommended for the spectral and time-series analyses for HRV, the Task Force for HRV (1996) stated that approximately one minute is needed to assess the HF (i.e. vagally-mediated) component of HRV.

Effectiveness of the Manipulations

The cold pressor task was expected to elicit large cardiovascular responses as demonstrated by increases in blood pressure and decreases in IBI (i.e. the inverse of heart rate), while decreasing vagally-mediated measures of HRV. Therefore, repeated measures ANOVAs were conducted comparing the baseline values to the task values for each physiological variable. Both the right and left cold pressor tasks elicited significant blood pressure and IBI changes from baseline to task (see Table 2 for blood pressure changes and Table 4 for cardiac changes). SBP change was significant for CPrt ($F(1,66)=52.965$, $p<.001$) and CPlft ($F(1,68)=114.181$, $p<.001$), as was DBP change for CPrt ($F(1,67)=39.709$, $p<.001$) and CPlft ($F(1,69)=70.593$, $p<.001$). The decrease in IBI was significant for both CPrt ($F(1,69)=50.231$, $p<.001$) and CPlft ($F(1,68)=60.985$, $p<.001$). RMSSD showed a modest decrease for both CPrt ($F(1,69)=5.668$, $p<.05$) and CPlft ($F(1,68)=6.636$, $p<.05$), but HF power did not for either CPrt ($F(1,69)=2.432$,

p>.1) or CPlft (F(1,68)=2.998, p>.05). SC responses for both left and right hands increased significantly to both CP tasks at p<.001 (see Table 6).

For the facial cooling tasks, changes in DBP and MAP were non-significant at p>.05. SBP showed a modest increase for FCrt (F(1,69)=5.302, p<.05), but a non-significant response to FClft (F(1,69)=2.821, p>.05). Both facial cooling tasks elicited significant bradycardia responses as evidenced by an increase in IBI for FCrt (F(1,69)=29.259, p<.001) and FClft (F(1,68)=50.38, p<.001). This is further supported by the vagal measures of RMSSD and HF power. RMSSD was significant for FCrt (F(1,69)=8.02, p<.01) and FClft (F(1,68)=19.577, p<.001). HF power was significant for both FCrt (F(1,69)=4.645, p<.05) and FClft (F(1,68)=11.448, p=.001). SC responses significantly decreased for both hands during each facial cooling task at p<.01 (see Table 6).

Right vs. Left Hemisphere ANS Regulation

For laterality comparisons, change scores were created for physiological variables for both right and left sided tasks by subtracting the values from the preceding baselines. Therefore, the corresponding change scores only captured the physiological change represented by the effects of each task. Blood pressure responses showed greater increases to left foot submersion compared to right foot submersion (see Table 3). Change scores computed from the blood pressure variables showed SBP for CPlft to be significantly greater than CPrt (F(1,66)=5.414, p<.05). DBP (F(1,67)=4.561, p<.05) and MAP (F(1.66)=5.488, p<.05) were also in the same direction. There was also a significant decrease in IBI in CPlft compared to CPrt (F(1,68)=3.989,p=.05). No measures of vagal activity displayed lateralized decreases from either cold pressor task (all p<.1; see Table 5 for cardiac laterality scores). CPlft elicited significantly larger SC responses for the right hand (F(1,62)=5.273, p<.05), and trended towards

a significantly greater increase for the left hand ($F(1,62)=3.72$, $p=.058$). The SCR laterality scores can be found in Table 7.

The change scores for the FC task did not elicit task differences in cardiac variables when the sample was analyzed as a whole. The vagal measures were in the direction of larger response from FClft, but neither RMSSD ($F(1,68)=1.798$, $p>.1$) nor HF power ($F(1,68)=1.921$, $p>.1$) reached significance levels (see Table 5). The increase in IBI was also in the direction of larger FCrt response ($F(1,68)=.992$, $p>.1$), but was not significant.

For within-task SC values, repeated measures ANOVAs were conducted comparing left hand baseline-to-task change with right hand baseline-to-task change. Within-task, but between-hand, SC analyses showed non-significant comparisons for FClft ($F(1,62)=.327$, $p>.1$) and for CPlft ($F(1,62)=.603$, $p>.1$). However, right sided tasks elicited more meaningful contrasts with a significant decrease in left hand reactivity compared to right hand reactivity for FCrt ($F(1,62)=4.573$, $p<.05$) and CPrt demonstrated a trend towards greater left hand response compared to right hand response ($F(1,64)=3.385$, $p=.07$). See Table 8 for between-hand SC comparisons.

Sex Differences in Reactivity

Sex differences in reactivity were measured by comparing baseline to task physiological variables in a repeated measures ANOVA. This was conducted for both men and women, separately. The cold pressor tasks elicited significant increases in all blood pressure measurements for both men and women ($p<.001$). However, the only significant blood pressure response for the facial cooling tasks within men or women was a greater SBP response to FCrt ($F(1,35)=5.396$, $p<.05$) which was seen only in women. However, DBP for the same task was

non-significant ($F(1,35)=.393$, $p>.1$). See Table 9 for within-sex blood pressure responses to CP and FC tasks.

Sex Differences in Laterality

For addressing the second hypothesis regarding the magnitude of laterality differences between men and women, repeated measures ANOVAs were separately run on each dependent physiological variable within each sex. Therefore, change scores were created by subtracting baseline from task values for both men and women. For BP measurements during CP tasks, men showed greater DBP responses for CPlft compared to CPrt ($F(1,33)=4.27$, $p<.05$), but only trended towards significance for SBP ($F(1,33)=2.926$, $p=.097$) and MAP ($F(1,33)=3.948$, $p=.055$). Although always in the direction of left-side preference, women did not reach significance levels in BP reactivity for CPlft compared to CPrt for SBP ($F(1,32)=2.6$, $p=.117$), DBP ($F(1,33)=1.166$, $p=.288$), or MAP ($F(1,32)=1.979$, $p=.169$). Differences in IBI decreases were in the predicted direction for both sexes but did not reach significance levels for men ($p>.1$) or women ($p>.1$). See table 10 for within-sex blood pressure responses to FC and CP tasks. See table 12 for cardiac laterality changes within each sex.

Men demonstrated RMSSD increases from baseline to facial cooling tasks for both FCrt ($F(1,35)=8.456$, $p<.01$) and FClft ($F(1,35)=10.625$, $p<.01$). Although women also displayed an RMSSD increase to FClft ($F(1,32)=10.194$, they did not display a significant increase for FCrt ($F(1,33)=.37$, $p>.1$). These findings were further supported by HF power for both men and women. Women displayed a significant increase in HF power for FClft $(1,32)=4.973$, $p<.05$), but not for FCrt ($F(1,33)=.474$, $p>.1$). These cardiac changes to task can be found in table 11. The only cardiac variable that was significant when laterality scores were created from subtracting right-side task change from left-side change was the greater RMSSD response for

FClft ($F(1,32)=5.345$, $p<.05$). The HF power difference was non-significant ($F(1,32)=2.132$, $p>.1$). It should be noted that the task force assembled to standardize HRV analyses (1996) recommends that spectral measures be relied upon for shorter time periods. These cardiac laterality analyses can be found in table 12. It should also be noted that although men did not show significant laterality differences for any of the more purely PNS measures, they did show a trend towards a decrease in the LF/HF ratio ($F(1,35)=3.943$, $p=.055$) for FClft compared to FCrt which suggests a larger vagal response compared to sympathetic withdrawal. Women did not show this same laterality difference ($F(1,32)=1.066$, $p>.1$).

Women demonstrated greater SC reactivity for both hands across all of the tasks in this study (see table 13 for SC changes from baseline to task for each sex). Women showed a significant increase in SC for both hands to both CPrt and CPlft at $p<.001$. Men showed more modest increases specifically to the CPrt task for right hand reactivity ($F(1,33)=5.197$, $p<.05$) as well as left hand reactivity ($F(1,33)=5.522$, $p<.05$). Women showed significant decreases in SC for both hands to both FCrt and FClft at $p<.01$ or greater. Men only showed a significant decrease in SC response to the left hand of FCrt ($F(1,34)=6.277$, $p<.05$). They showed non-significant decreases for left hand response to FClft ($F(1,34)=1.338$, $p>.1$), right hand response to FCrt ($F(1,34)=2.423$, $p>.1$) and only a trend towards significance for right hand response to FClft ($F(1,34)=4.091$, $p=.051$). Even though women were more reactive to all of the tasks, they were not significantly lateralized for any left-side compared to right-side tasks (all $p>.1$). Men demonstrated greater lateralization for CPlft compared to CPrt, for right hand reactivity ($F(1,31)=5.441$, $p<.05$), but not for left hand reactivity ($F(1,34)=.442$, $p>.1$). These within-hand, but between-task, laterality scores can be found in table 14. Analyses looking at between-hand

responses in each task showed a significantly greater SC decrease for FCrt ($F(1,34)=4.982$, $p<.05$) for men only. Women had no significant differences at $p<.1$ (see table 15).

Gender Identity Contributions to Laterality

Self-reported masculinity and femininity scores can be found in Table 16. Basic exploration into the relationship of gender variables with laterality was conducted using bivariate correlations. The gender variables were correlated with laterality scores that were created by subtracting right side physiology change scores from left side change scores. Masculinity and femininity did not significantly predict laterality differences for BP responses to the CP tasks ($p>.1$). The only significant correlation with masculinity was the laterality score with MAP, $r= -.372$, $p<.05$ suggesting that greater masculinity in females predicts less lateralization in MAP. The only significant correlation for femininity was with the laterality change score for RMSSD between FClft and FCrt, $r= .396$, $p<.05$, indicating greater laterality. This relationship disappeared when explored within sex.

Discussion

This study sought to examine lateralized regulation of the two branches of the ANS. The findings from this study lend further support to the role of the right hemisphere as serving a more dominant role in regulating SNS activity (Foster, Drago, Ferguson, & Harrison, 2008; Lane et al., 1989). Although there was not a pure cardiovascular measure of SNS activity as could be derived from impedance cardiography, the significant differences in several indices of BP, IBI, and SCR strongly implicate the right hemisphere as serving a larger role in SNS activity. Although there are vagal contributions to the BP and IBI signals, the observed cardiovascular changes were most likely the products of an increase in both alpha- and beta-adrenergic SNS activity. The lateralized SC responses lend further support to the SNS response by an increase in

cholinergic receptor activation in addition to the adrenergic responses involved in heart rate and blood pressure changes. Most of the studies that have previously explored this asymmetric relationship have used various cardiovascular indices as markers. The support lent from the SC responses further implicates the right hemisphere as serving a more global role in SNS regulation. Also, the CP task has a long history of use as a task employed for eliciting large SNS responses (Hines, 1936). The right hemisphere model of SNS regulation is also supported by the FCrt task which showed a larger decrease in sympathetic response for the left hand compared to the right hand during a largely parasympathetic dominant task.

The attribution of lateralized hemispheric regulation for PNS activity is still not clearly discernible. Group-level analyses indicate no significant differences in PNS activity between the two sides. Even when analyzed only within sex, there does not appear to be a significant parasympathetic increase when using the most appropriate metric for assessing HRV at such a short interval. Most of the vagally-mediated measures of HRV are in the direction suggesting greater right hemisphere regulation of PNS activity, but the findings are not robust enough to argue for that assumption. The lateralized facial cooling tasks were admittedly not powerful enough to elicit robust laterality differences in vagal response, however, it must be strongly considered that regulation of the PNS may not be lateralized to a particular hemisphere. An inherent limitation of theories supporting the lateralization of parasympathetic activity is the assumption of inhibition of the contralateral hemisphere during activation. Theories that support functional lateralization are often built upon foundational ideas of minimizing metabolic costs by causing compensatory attenuated activity in the other hemisphere (Kinsbourne, 1975). However, parasympathetic activity usually serves as the vehicle for restorative and energy-conserving processes and therefore may not necessitate compensatory contralateral deactivation. Also, from

a functional, energy-efficient perspective it would be logical for both hemispheres to have adequate access to elicit efficient energy-saving modulation of behavior and resources. Since parasympathetic activity has fast-acting capabilities on metabolically costly processes such as cardiac output, then quick access to the de-regulating abilities of vagal modulation would be beneficial for either hemisphere to access regardless of the type of behavioral or cognitive process enacted. Also, large increases in PNS activity are often phasic and do not require sustained, concentrated processing from a particular hemisphere. Therefore it is possible that there is no need for contralateral inhibition for an often short-lived and energy efficient metabolic process. Indeed, a review of research looking at imaging in tandem with HRV has reported no laterality differences (Thayer et al., 2011).

Put into simple terms: just because there are two hemispheres and two branches of the ANS does not mean that these pairs require a 1-to-1 differentiation of structural housing. Theories steeped in the need for lateralization of apparently oppositional processes may be limited by the tendency to functionally (and consequently, anatomically) separate the opposing processes. However, there are many states in which PNS and SNS activity can take place simultaneously, reciprocally, and in various conditions lying between these two dichotomized poles (Berntson, Cacioppo, & Quigley, 1991; 1993). These conditions support the position that both branches can be housed within one hemisphere and leaves room open to the possibility of bilateral hemispheric regulation. Also considering how research has generally supported that many functions attributed to PNS regulation have evolved much more recently than basic SNS processes (Porges, 1998; 2007), it seems logical that PNS activity would not be as clearly rendered to the functional role of one hemisphere. Laterality has been observed in even

relatively simple organisms (Halpern et al., 2005) and therefore may precede the later evolution of some PNS functions.

Implications for other Psychological Laterality Models

Positive and Negative Emotionality

There is still an active debate pertaining to the autonomic specificity of basic emotions. Although there is relatively well-founded empirical research demonstrating distinct patterns of autonomic activity for particular emotions (Stephens, Christie, & Friedman, 2010), there remains dissenting perspectives (Cacioppo et al., 2000; Barrett, 2011). Regardless of the specificity of individual emotions, there are more discernible distinctions in dimensional contrasts in emotions. Research from Bob Levenson and Barbara Fredrickson suggests that emotions on these dimensions can largely be dependent on larger dominance in PNS activity for positive emotions and SNS activity for negative emotions (Levenson, 2003; Garland et al., 2010). When reframed in laterality models of ANS activity this would on the surface appear to support a dominant role of the left hemisphere in regulating PNS activity (Craig, 2005; Demaree, Everhart, Youngstrom, & Harrison, 2005). However, there is also research with unilateral brain-damaged patients that clearly demonstrates the role of the right hemisphere in the expression and display of positive emotion (Borod, 1993). The potential bilateral recruitments of PNS activity in positive emotion further supports to the need for circuitry involved in PNS regulation readily available in both hemispheres.

Approach (appetition) and Avoidance (aversion)

It has been suggested in previous literature that approach-oriented behaviors and temperament are associated with a more parasympathetic dominant underlying system (Porges, 1996).

The opposite relationship pertaining to avoidance/aversion responses associated with more SNS activity has also been relatively well-demonstrated in both animals and human studies (Sutton & Davidson, 1997; Beauchaine, 2001; Konarska, Stewart, & McCarty, 1990). Approach and avoidance behavior have often been linked to the left and right hemispheres, respectively (Demaree, Everhart, Ferguson, & Harrison, 2005; Harmon-Jones, 2010). This separation supports parasympathetic and sympathetic nervous system regulation again, but according to the evaluative space model proposed by Cacioppo and Berntson (1994; Norris, Berntson, & Cacioppo, 2010), complex organisms occasionally are required to perform avoidant behaviors during goal-pursuit or engage in approach-oriented behaviors to rid of a threat. These situations of dual engagement may require more complex architecture of autonomic flexibility for appropriate responding. The Polyvagal Theory uniquely distributes the functions of the autonomic nervous system into three hierarchical tiers that have evolved with organismic complexity (Porges, 2007). Instead of necessary frontal lobe lateralization of ANS activity, the theory purports that two different branches of the vagus are differentially engaged during states dependent on perceptions of environmental safety. In this theory there is not necessarily just a global state of parasympathetic activation that would be suggested by asymmetric activation of a hemisphere, but there are distinct behavioral manifestations of the two branches that differentially respond to states of threat or during social facilitation.

Other Lateralized Models:

Although a thorough addressing is outside the scope of the current topic, it should be noted that other psychological and behavioral phenomena that have been associated with asymmetric hemispheric regulation may also serve to be better understood by the implications of lateralized ANS regulation. Such models could be anxiety (Blackhart, Minnix, & Kline, 2006),

depression (Allen, Urry, Hitt, & Coan, 2004), hyperactivity (Oades, 1998), or the oppositional constructs of dominance and submission (Demaree, Everhart, Ferguson, & Harrison, 2005). There has already been considerable support lent to the larger role of SNS in the right-hemisphere dominant high-hostile population (Demaree & Harrison, 1997; Everhart & Harrison, 1995). Other laterality models implicated with behavioral and psychological processes may be better informed when conceptualized in light of an ANS laterality framework.

Sex Differences

The second main hypothesis of this study dealt with the relationship of sex and lateralization of ANS regulation. The results for sex differences in laterality produced significant results, but the results were not robustly demonstrated across all autonomic indices. Men demonstrated significant right hemisphere lateralization for DBP, but only trended towards significance for SBP and MAP. Women did not show significant laterality differences for any of the BP metrics. IBI differences were not significant for either sex and only right hand reactivity for CPlft compared to CPrt was significant for men. No significant laterality differences in EDA were observed for women.

PNS lateralization provided even less of a convincing story. There were no significant laterality differences in vagal measures for the CP task. There were significant increases in vagal activity in the FC tasks on both sides for men, but they were not significantly different from each other. Only FClft displayed a significant increase in vagal change from baseline for women. Therefore, it proved to be a significantly greater increase than when compared to FCrt, although the increase was still smaller than for the vagal response for men on either side. Also, this finding was only significant for RMSSD and not for the spectral analysis measure of HF power. Considering that one measure of vagal activity was significantly related, but another was not,

suggests that the difference is not a robust one. It should also be noted that the Task Force assembled to standardize HRV measurement (1996) stated that frequency domain methods should be preferred over time-based measurements in cases of short recording periods. Therefore, if those recommendations are followed, then there is a non-significant HRV laterality difference for vagal response to the FC tasks. The time-based measures such as RMSSD are ideal for studies involving longer durations. The difference in significance across the two vagal measures is curious considering their generally high correlation with each other.

Although structural and functional differences in laterality have been demonstrated between men and women, these findings are often small to moderate-sized effects. In terms of hemispheric connectivity which suggests functional lateralization, sex differences have been observed in ratios of gray matter to white matter and in corpus callosum density, however it has been recommended that generalizations of functional differences be carefully extrapolated from these findings (Allen, Damasio, et al., 2003). These findings suggest greater lateralization for SNS regulation in men, but it is cautioned that intra-sex variability is likely a more informative research area than inter-sex variability.

The Role of Gender Identity

Self-reported sex roles as determined by the BSRI did not predict reliable differences in laterality responses. However, several things should be noted when taking these analyses into consideration. The BSRI was originally published close to four decades ago and may no longer be a reliable assessment of masculine and feminine roles in modern culture. Also, the self-reported scores in this sample may not be representative of the college populations (Prince & Casey, 2010). Notably, women scored higher on masculinity than men on average, and men displayed typically lower masculinity scores than in recent reports (Perlta, et al., 2010).

Limitations and Future Directions

Although the increase in metrics of BP, IBI, and SCR support the right hemisphere's role in SNS regulation, this association cannot be confidently be made without a more pure measure of cardiovascular sympathetic activity, which this study lacked. The role of the investigator being present for the FC task may have introduced error variance which is not possible to control for in the analyses. This potential social stressor may have served a role in attenuating the individual differences in the bradycardia responses to FC. Reliable HRV measures are traditionally collected over long periods of time, but this study was limited by the relatively phasic bradycardia response elicited by the "dive reflex". The implications of the HRV findings would be better supported if a vagal response elicited for a longer duration had taken place. Conversely, the SNS activity in the cold pressor task may have been more informative if the time segments had been broke into smaller segments. Several subjects reported a peak of self-reported discomfort during the first half of the task and reported the latter half to be less aversive. This change may have been apparent in each subject's physiology and the greatest variability in task physiology may have been most apparent during the middle of the task.

The most obvious deficiency with the current study is the lack of direct measurements of brain activity. This research would benefit from having future studies incorporate the use of EEG or brain imaging. Although the original transference of afferent sensory information can be assumedly preferentially handled by the hemisphere that is contralateral to the stimulus induction, no assumption can be reliably upheld that the receiving hemisphere is continually serving a larger role in regulating that information over the duration of a task spanning several minutes. A more powerful elicitor of parasympathetic activity could also better serve to inform this enterprise. The elicitor used in the current study may simply not have induced a large

enough parasympathetic response to assess individual differences in asymmetric regulation. Another way to modify the task would be to collect autonomic information from the hand cold pressor while recording skin conductance from the feet.

Conclusion

The present study addressed the issues of lateralized regulation of autonomic nervous system activity. The findings lend considerable support to the greater role of the right hemisphere in regulating sympathetic nervous system activity. This is in line with prior research supporting this hypothesis. The lateralized regulation of parasympathetic nervous system activity was not clearly demonstrated. There is weak support for a greater role of the right hemisphere in regulating vagal activity, however it is suggested that this issue be conceptually reassessed with the possibility that both hemispheres serve active roles its regulation. Framed in this light, it may be intuitive to consider the bi-hemisphere representation of PNS regulation since decades of research have continually demonstrated mixed results. The study also addressed whether sex differences in lateralization of regulation of the autonomic nervous system exist. The findings lend some support to a greater lateralization of sympathetic activity in men, but these findings are not robust or distributed across many different measures of autonomic activity. Exploration into whether gender identification moderated the relationship in lateralization proved ultimately non-significant. Future studies should increase power in addressing these questions as well as find a more powerful elicitor of lateralized parasympathetic activity.

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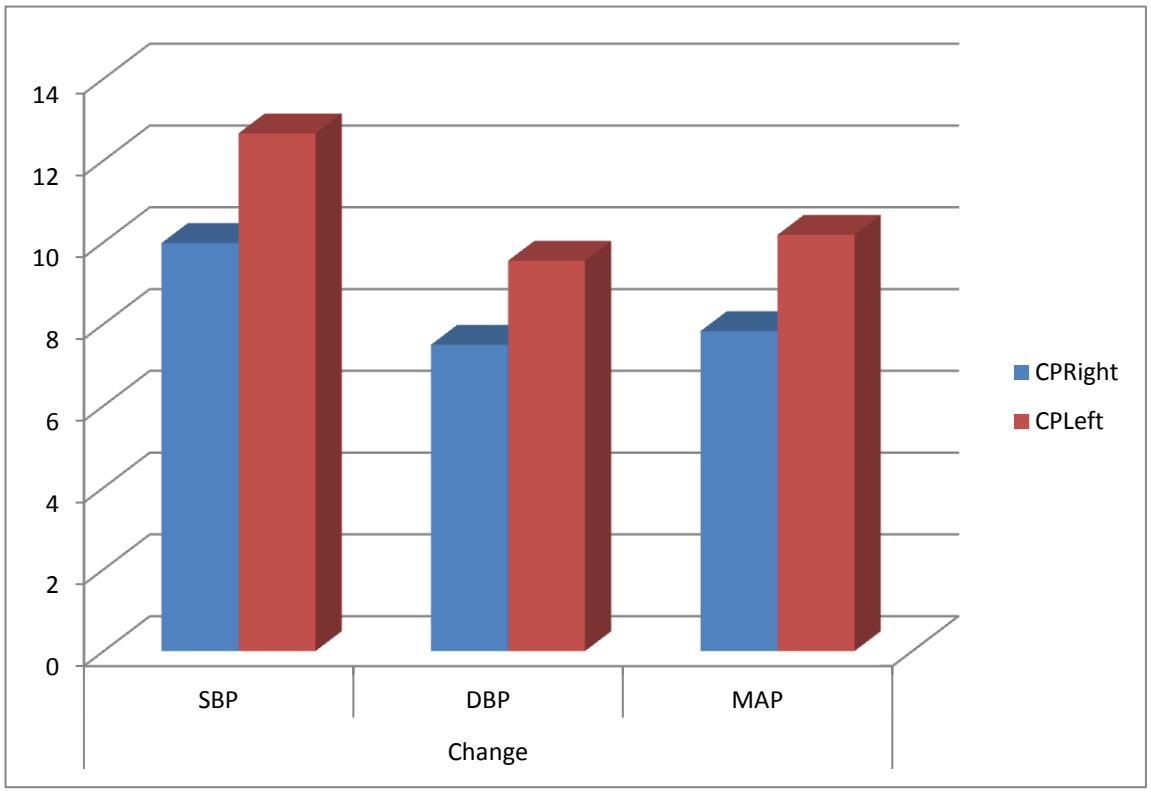
Appendix A

Figures

Figure 1

Metrics of blood pressure change from baseline to cold pressor tasks



Appendix B

Tables

Table 1

Subjects' self-reported affect and pain for each of the tasks.

	Cold Pressor Right		Cold Pressor Left				
	Mean	SD	Mean	SD	t-value	df	sig
Pleasantness	1.82	0.71	1.83	0.83	-0.108	71	0.915
Painfulness	3.26	1.07	3.38	1.07	-1.436	71	0.156
	Facial Cooling Right		**Facial Cooling Left**				
	Mean	SD	Mean	SD	t-value	df	sig
Pleasantness	2.75	0.67	2.83	0.55	-1.771	72	0.081
Painfulness	1.64	0.83	1.52	0.76	1.696	72	0.094

Table 2

Blood pressure (in mmHG) change from baseline to tasks (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared).

Measure	Task	Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	FCrt	1.305	4.74	5.302	69	**0.024**	0.071
	FClft	0.823	4.098	2.821	69	0.098	0.039
	CPrt	9.978	11.222	52.965	66	**0.0001**	0.445
	CPlft	12.657	9.893	114.181	68	**0.0001**	0.627
DBP	FCrt	-0.167	3.785	0.134	68	0.715	0.002
	FClft	-0.1162	3.271	0.087	68	0.769	0.001
	CPrt	7.492	9.805	39.709	67	**0.0001**	0.372
	CPlft	9.544	9.504	70.593	69	**0.0001**	0.506
MAP	FCrt	0.3198	3.985	0.444	68	0.507	0.006
	FClft	0.2082	3.459	0.25	68	0.619	0.004
	CPrt	7.824	8.067	63.022	66	**0.0001**	0.488
	CPlft	10.181	7.995	111.8971	68	**0.0001**	0.622

Table 3

Blood pressure (in mmHG): change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	CP (L-R)	2.43	8.54	5.414	66	**0.023**	0.076
DBP	CP (L-R)	1.86	7.18	5.965	66	**0.017**	0.083
MAP	CP (L-R)	2.13	7.45	5.488	66	**0.022**	0.077

Table 4

Cardiac changes for baseline to task periods (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

		Mean	SD	F-value	df	p-value	Partial Eta Sq.
IBI (ms)	FCrt	37.071	57.34	29.259	69	**0.0001**	0.298
	FClft	44.056	51.562	50.38	68	**0.0001**	0.426
	CPrt	-66.149	78.089	50.231	69	**0.0001**	0.421
	CPlft	-84.536	89.919	60.985	68	**0.0001**	0.473
RMSSD	FCrt	8.008	23.658	8.02	69	**0.006**	0.104
	FClft	11.404	21.411	19.577	68	**0.0001**	0.224
	CPrt	-6.588	23.153	5.668	69	**0.02**	0.076
	CPlft	-9.696	31.267	6.636	68	**0.012**	0.089
HF Power	FCrt	0.07	0.28	4.645	69	**0.035**	0.063
	FClft	0.12	0.28	11.448	68	**0.001**	0.144
	CPrt	-0.09	0.35	2.432	69	0.123	0.034
	CPlft	-0.12	0.460	2.998	68	0.088	0.042
LF Power	FCrt	-0.17	0.43	10.163	69	**0.002**	0.128
	FClft	-0.17	0.49	8.505	68	**0.005**	0.111
	CPrt	-0.001	0.37	0.003	69	0.954	0
	CPlft	-0.05	0.44	0.721	68	0.399	0.01
LF/HF Ratio	FCrt	-0.3761	1.55	4.123	69	**0.046**	0.056
	FClft	-0.7447	2.109	8.607	68	**0.005**	0.112
	CPrt	0.5622	2.025	5.395	69	**0.023**	0.073
	CPlft	1.054	4.112	4.532	68	**0.037**	0.062

Table 5

Cardiac changes: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

		Mean	SD	F-value	df	p-value	Partial Eta Sq.
IBI (ms)	FC (L-R)	6.03	50.28	0.992	68	0.323	0.014
	CP (L-R)	-16.95	70.52	3.989	68	**0.05**	0.055
RMSSD	FC (L-R)	3.28	20.3	1.798	68	0.184	0.026
	CP (L-R)	-3.15	25.22	1.075	68	0.304	0.016
HF Power	FC (L-R)	0.05	0.29	1.921	68	0.17	0.027
	CP (L-R)	0.03	0.44	.327	68	.569	.005
LF Power	FC (L-R)	-0.003	0.51	0.003	68	0.96	0
	CP (L-R)	-0.04	0.49	.548	68	.462	.008
LF/HF Ratio	FC (L-R)	-0.35	2.5	0.836	68	0.364	0.012
	CP (L-R)	0.48	4.11	0.884	68	0.35	0.013

Table 6

Mean skin conductance response changes for both hands from baseline to task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FCrt	-0.04	0.11	9.469	62	**0.003**	0.132
	FClft	-0.05	0.11	12.399	62	**0.001**	0.167
	CPrt	0.06	0.11	18.071	64	**0.0001**	0.22
	CPlft	0.09	0.11	42.699	62	**0.0001**	0.408
SCR Left Hand	FCrt	-0.06	0.14	13.121	62	**0.001**	0.175
	FClft	-0.04	0.12	7.78	62	**0.007**	0.111
	CPrt	0.07	0.13	21.429	64	**0.0001**	0.251
	CPlft	0.1	0.12	44.86	62	**0.0001**	0.42

Table 7

Mean skin conductance response changes for each hand, between tasks: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Hand	Task	Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FC (L-R)	-0.01	0.16	0.056	62	0.813	0.001
	CP (L-R)	0.03	0.11	5.273	62	**0.025**	0.078
SCR Left Hand	FC (L-R)	0.02	0.21	0.607	62	0.439	0.01
	CP (L-R)	0.025	0.104	3.724	62	0.058	0.057

Table 8

Mean skin conductance response changes within each task, between hands: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared

		Mean	SD	F-value	df	p-value	Partial Eta Sq.
FCrt	L-R	-0.021	0.078	4.573	62	**0.036**	0.069
FClft	L-R	0.004	0.058	0.327	62	0.569	0.005
CPrt	L-R	0.013	0.055	3.385	64	0.07	0.05
CPlft	L-R	0.006	0.061	0.603	62	0.441	0.01

Table 9

Within sex blood pressure (in mmHG) change from baseline to tasks (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	FCrt	0.56	4.18	0.619	33	0.437	0.018
	FClft	0.93	3.91	1.917	33	0.175	0.055
	CPrt	9.4	9.36	34.337	33	**0.0001**	0.51
	CPlft	11.49	8.95	56.103	34	**0.0001**	0.63
DBP	FCrt	-0.84	3.07	2.458	32	0.127	0.071
	FClft	-0.18	3.29	0.102	32	0.752	0.003
	CPrt	5.3	7.65	26.363	33	**0.0001**	0.444
	CPlft	8.22	8.71	46.418	33	**0.0001**	0.584
MAP	FCrt	-0.39	3.28	0.457	32	0.504	0.014
	FClft	0.21	3.4	0.13	32	0.721	0.004
	CPrt	7.02	7.17	32.538	33	**0.0001**	0.496
	CPlft	9.2	7.3	54.011	33	**0.0001**	0.621
Women		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	FCrt	2.01	5.18	5.396	35	**0.026**	0.134
	FClft	0.72	4.32	1.007	35	0.323	0.028
	CPrt	10.57	12.99	21.847	32	**0.0001**	0.406
	CPlft	13.79	10.64	58.727	34	**0.0001**	0.633
DBP	FCrt	0.45	4.29	0.393	35	0.535	0.011
	FClft	-0.06	3.3	0.102	35	0.92	0
	CPrt	8.94	10.89	20.249	33	**0.0001**	0.38
	CPlft	11.22	9.74	34.226	35	**0.0001**	0.494
MAP	FCrt	0.97	4.49	1.672	35	0.204	0.046
	FClft	0.2	3.56	0.118	35	0.733	0.003
	CPrt	8.65	8.93	30.991	32	**0.0001**	0.492
	CPlft	11.13	8.62	58.457	34	**0.0001**	0.632

Table 10

Blood pressure (in mmHg) laterality differences within each sex: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	CP (L-R)	2.09	7.11	2.926	33	0.097	0.081
DBP	CP (L-R)	2.92	6.6	6.453	32	**0.016**	0.168
MAP	CP (L-R)	2.18	6.4	3.948	33	0.055	0.107
Women		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SBP	CP (L-R)	2.78	9.89	2.6	32	0.117	0.075
DBP	CP (L-R)	1.49	8.06	1.166	33	0.288	0.034
MAP	CP (L-R)	2.08	8.49	1.979	32	0.169	0.058

Table 11

Within sex cardiac changes from baseline to tasks (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men		Mean	SD	F-value	df	p-value	Partial Eta Sq.
IBI	FCrt	37.62	58.9	14.685	35	**0.001**	0.296
	FClft	42.72	48.92	27.452	35	**0.0001**	0.44
	CPrt	-56.02	73	19.135	35	**0.0001**	0.353
	CPlft	-71.93	99.81	18.179	34	**0.0001**	0.348
RMSSD	FCrt	14.39	29.69	8.456	35	**0.006**	0.195
	FClft	13.89	25.57	10.625	35	**0.002**	0.233
	CPrt	-4.04	23.99	1.125	35	0.296	0.031
	CPlft	-10.45	40.42	2.34	34	0.135	0.064
HF Power	FCrt	0.11	0.29	5.032	35	**0.031**	0.126
	FClft	0.14	0.33	6.453	35	**0.016**	0.156
	CPrt	0.02	0.28	0.28	35	0.6	0.008
	CPlft	0.03	0.470	0.175	34	0.678	0.005
LF Power	FCrt	-0.11	0.49	1.793	35	0.189	0.049
	FClft	-0.21	0.52	5.724	35	**0.022**	0.141
	CPrt	0.08	0.36	1.518	35	0.226	0.042
	CPlft	0.11	0.45	2.29	34	0.139	0.063
LF/HF Ratio	FCrt	-1.73	2.65	0.405	35	0.528	0.011
	FClft	-0.85	0.79	16.268	35	**0.0001**	0.317
	CPrt	2.84	2.37	4.978	35	**0.032**	0.125
	CPlft	3.27	4.84	1.398	34	0.245	0.039
Women							
IBI	FCrt	38.48	56.18	14.173	33	**0.0001**	0.3
	FClft	45.52	55.02	22.583	32	**0.0001**	0.414
	CPrt	-79.48	81.67	32.2	33	**0.0001**	0.494
	CPlft	-97.51	77.81	53.391	33	**0.0001**	0.618
RMSSD	FCrt	1.29	12.18	0.37	33	0.547	0.011
	FClft	8.69	15.64	10.194	32	**0.003**	0.242
	CPrt	-9.13	22.67	5.52	33	**0.025**	0.143
	CPlft	-8.92	18.16	8.203	33	**0.007**	0.199
HF Power	FCrt	0.03	0.26	0.474	33	0.496	0.014
	FClft	0.1	0.26	4.937	32	**0.033**	0.134
	CPrt	0.16	0.4	5.71	33	**0.023**	0.147
	CPlft	0.21	0.440	7.958	33	**0.008**	0.194
LF Power	FCrt	0.24	0.34	13.155	33	**0.001**	0.285
	FClft	0.13	0.45	2.778	32	0.105	0.08

	CPrt	0.08	0.37	1.789	33	0.19	0.051
	CPlft	0.03	0.43	0.129	33	0.722	0.004
LF/HF Ratio	FCrt	0.87	0.9	8.979	33	**0.005**	0.214
	FClft	1.25	2.28	0.48	32	0.493	0.015
	CPrt	2.36	2.02	1.143	33	0.293	0.033
	CPlft	2.75	2.87	5.201	33	**0.029**	0.136

Table 12

Cardiac laterality differences within each sex: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men		Mean	SD	F-value	df	p-value	Partial Eta Sq.
IBI	FC (L-R)	5.1	52.61	0.339	35	0.564	0.01
	CP (L-R)	-15.91	75.17	1.569	34	0.219	0.044
RMSSD	FC (L-R)	-0.5	21.47	0.019	35	0.89	0.001
	CP (L-R)	-6.41	25.92	2.144	34	0.152	0.059
HF Power	FC (L-R)	0.03	0.31	0.326	35	0.572	0.009
	CP (L-R)	.014	0.43	0.039	34	0.845	0.002
LF Power	FC (L-R)	-0.1	0.52	1.22	35	0.277	0.034
	CP (L-R)	-0.03	0.47	0.141	34	0.707	0.004
LF/HF Ratio	FC (L-R)	-0.96	2.38	3.943	35	0.055	0.101
	CP (L-R)	0.27	4.9	0.328	35	0.57	0.009
Women							
IBI	FC (L-R)	7.04	48.4	0.698	32	0.41	0.021
	CP (L-R)	-18.02	66.5	2.497	33	0.124	0.07
RMSSD	FC (L-R)	7.4	18.38	5.345	32	**0.027**	0.143
	CP (L-R)	0.21	24.41	0.003	33	0.959	0
HF Power	FC (L-R)	0.07	0.28	2.132	32	0.154	0.062
	CP (L-R)	-0.05	0.45	0.357	33	0.554	0.011
LF Power	FC (L-R)	-0.11	0.47	1.859	32	0.182	0.055
	CP (L-R)	-0.06	0.52	0.423	33	0.423	0.52
LF/HF Ratio	FC (L-R)	0.31	2.49	1.066	33	0.309	0.031
	CP (L-R)	0.69	3.15	0.787	33	0.381	0.023

Table 13

Mean skin conductance response changes within sex for both hands from baseline to task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Mean		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FCrt	-0.026	0.098	2.423	34	0.129	0.067
	FClft	-0.041	0.121	4.091	34	0.051	0.107
	CPrt	0.028	0.07	5.197	33	**0.029**	0.136
	CPlft	0.0569	0.082	15.475	31	**0.0001**	0.333
SCR Left Hand	FCrt	-0.0483	0.114	6.277	34	**0.017**	0.156
	FClft	-0.026	0.133	1.338	34	0.255	0.038
	CPrt	0.041	0.101	5.522	33	**0.025**	0.143
	CPlft	0.067	0.1	13.766	31	**0.001**	0.308
Women		Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FCrt	-0.064	0.123	7.621	27	**0.01**	0.22
	FClft	-0.056	0.089	10.856	27	**0.003**	0.287
	CPrt	0.096	0.141	14.433	30	**0.001**	0.325
	CPlft	0.13	0.129	31.638	30	**0.0001**	0.513
SCR Left Hand	FCrt	-0.056	0.089	6.971	27	**0.014**	0.205
	FClft	-0.065	0.11	9.974	27	**0.004**	0.27
	CPrt	0.108	0.143	17.529	30	**0.0001**	0.369
	CPlft	0.134	0.125	35.178	30	**0.0001**	0.54

Table 14

Between task, within hand, skin conductance laterality changes: change score from left task – change score from right task (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men	Task	Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FC (L-R)	-0.016	0.158	0.346	34	0.560	0.010
	CP (L-R)	0.032	0.077	5.441	31	**0.026**	0.149
SCR Left Hand	FC (L-R)	0.022	0.203	0.442	34	0.52	0.012
	CP (L-R)	0.025	0.103	1.902	31	0.178	0.058
Women	Task	Mean	SD	F-value	df	p-value	Partial Eta Sq.
SCR Right Hand	FC (L-R)	0.009	0.17	0.074	27	0.787	0.003
	CP (L-R)	0.034	0.144	1.762	30	0.194	0.055
SCR Left Hand	FC (L-R)	0.018	0.216	0.193	27	0.664	0.007
	CP (L-R)	0.026	0.107	1.766	30	0.194	0.056

Table 15

Sex differences within task, but between hand skin conductance changes: change score from left hand – change score from right hand (means, standard deviations, Repeated Measures ANOVA, and Partial Eta Squared)

Men		Mean	SD	F-value	df	p-value	Partial Eta Sq.
FCrt	L-R	-0.023	0.06	4.982	34	**0.032**	0.128
FClft	L-R	0.015	0.063	2.088	34	0.158	0.058
CPrt	L-R	0.013	0.044	3.13	33	0.086	0.087
CPlft	L-R	0.009	0.046	1.173	31	0.287	0.036
Women		Mean	SD	F-value	df	p-value	Partial Eta Sq.
FCrt	L-R	-0.019	0.097	1.071	27	0.31	0.038
FClft	L-R	-0.01	0.049	1.102	27	0.303	0.039
CPrt	L-R	0.012	0.066	0.98	30	0.33	0.032
CPlft	L-R	0.003	0.075	0.053	30	0.82	0.002

Table 16

Masculinity and femininity scores for men and women

		Mean	S.D.
Men	Masculinity	4.72	0.83
	Femininity	4.59	0.64
Women	Masculinity	4.86	0.71
	Femininity	5.12	0.45

Appendix C

Mind-Body Laboratory Health History Questionnaire

A very brief medical history must be obtained as part of the experimental protocol. It is very important that you be completely honest. This information will be kept strictly confidential.

1. What is your age, height, weight, and gender?

Age: _____ years

Height: _____ feet, _____ inches

Weight: _____ pounds

Sex: ___M ___F

2. Since birth, have you ever been hospitalized or had any major medical problems?

___ Yes ___ No

If Yes, briefly explain:

3. Have you ever experienced a concussion or lost consciousness due to a blow to the head?

___ Yes ___ No

If Yes, briefly explain:

4. Have you ever had problems that required you to see a counselor, psychologist, or psychiatrist?

___ Yes ___ No

If Yes, briefly explain:

5. Do you use tobacco products of any kind?

___ Yes ___ No

If Yes, describe what kind how often/much:

6. Have you ever been diagnosed with a psychological disorder?

___ Yes ___ No

If Yes, briefly explain:

7. Do you currently have or have you ever had any of the following?

___ Yes ___ No Strong reaction to cold weather

___ Yes ___ No Circulatory problems

___ Yes ___ No Tissue disease

___ Yes ___ No Skin disorders (other than facial acne)

___ Yes ___ No Arthritis

___ Yes ___ No Asthma

___ Yes ___ No Lung problems

___ Yes ___ No Cardiovascular disorder/disease

___ Yes ___ No Diabetes

___ Yes ___ No Hypoglycemia

___ Yes ___ No Hypertension (high blood pressure)

___ Yes ___ No Hypotension (low blood pressure)

___ Yes ___ No Hepatitis

___ Yes ___ No Neurological problems

___ Yes ___ No Epilepsy or seizures

___ Yes ___ No Brain disorder

___ Yes ___ No Stroke

If you responded Yes to any of the above conditions, briefly explain:

8. Have you ever been diagnosed as having:

___ Yes ___ No Learning deficiency or disorder

___ Yes ___ No Reading deficiency or disorder

___ Yes ___ No Attention deficit disorder

___ Yes ___ No Attention deficit hyperactivity disorder;

9. Do you have:

___ Yes ___ No Claustrophobia (extreme fear of small closed spaces)

___ Yes ___ No Blood phobia (extreme fear of needles or blood)

___ Yes ___ No Phobia of any type (if Yes, briefly explain:)

___ Yes ___ No Generalized anxiety disorder

___ Yes ___ No Anxiety disorder of any type (if Yes, briefly explain:)

If you responded Yes, briefly explain here:

10. List any over-the-counter or prescription medications you are currently taking:

11. List the symptoms that these drugs are treating

12. List any other medical conditions that you have or have had in the past:

13. What is your average daily caffeine consumption (approximate number of cups/glasses of coffee, tea, or caffeinated soda)?

14. What is your average weekly alcohol consumption (approximate number of alcoholic beverages)?

15. How many hours of sleep do you average per night?

Appendix D

Mind-Body Laboratory Recent Health History Questionnaire

A very brief medical history must be obtained as part of the experimental protocol. It is very important that you be completely honest. This information will be kept strictly confidential.

1. When was the last time that you have had any alcohol before the study began?

2. When was the last time you have had a caffeinated beverage before the study began?

3. When was the last time that you are before the study began?

4. What phase of the menstrual cycle are you currently in (beginning, middle, or end)?

5. How many hours of sleep did you get last night?

6. Did you engage in vigorous exercise within the last 2 hours?

Appendix E

Handedness Questionnaire

Most people are either right-handed or left-handed. However, there are different "degrees" of handedness. Some people use one hand for jobs that require skill and the other hand for jobs that involve reaching. Other people use the same hand for these different jobs. Use this "Handedness Questionnaire" to measure the strength of handedness. Place a mark in a box for each question that describes you best.

	LEFT Hand	RIGHT Hand	EITHER Hand
1. Which hand do you use to write?			
2. Which hand do you use to draw?			
3. Which hand do you use to throw a ball?			
4. Which hand do you hold a tennis racket?			
5. With which hand do you hold a toothbrush?			
6. Which hand holds a knife when you cut things?			
7. Which hand holds a hammer when you nail things?			
8. Which hand holds a match when you light it?			
9. Which hand holds an eraser when you erase things?			
10. Which hand removes the top card when you deal from a deck?			
11. Which hand holds the thread when you thread a needle?			

12. Which hand holds a fly swatter?			
TOTAL			

How to Determine your Score

1. Count the number of LEFT, RIGHT and EITHER responses.
2. Multiply the number of RIGHT responses by 3. This number = R
3. Multiply the number of EITHER responses by 2. This number = E
4. Add R + E + (number of LEFT responses). This sum is your score.

Here is a table to help:
Number of RIGHT responses x 3 = ____
Number of EITHER responses x 2 = ____
Number of LEFT responses = ____
TOTAL = _____

How to Interpret Your Score

Score Handedness
33 to 36 = Strongly Right-Handed
29 to 32 = Moderately Right-Handed
25 to 28 = Weakly Right-Handed
24 = Ambidextrous
20 to 23 = Weakly Left-Handed
16 to 19 = Moderately Left-Handed
12 to 15 = Strongly Left-Handed

(This questionnaire was adapted from the handedness questionnaire by Stanley Coren, *The Left-Hander Syndrome: The Causes and Consequences of Left-Handedness*, Free Press, New York, 1992.)

Appendix F

BEM SEX ROLE INVENTORY

Rate yourself on each item, on a scale from 1 (never or almost never true) to 7 (almost always true). When you have completed the inventory, transfer your ratings to the inventory score sheet.

1. self reliant
2. yielding
3. helpful
4. defends own beliefs
5. cheerful
6. moody
7. independent
8. shy
9. conscientious
10. athletic
11. affectionate
12. theatrical
13. assertive
14. flatterable
15. happy
16. strong personality
17. loyal
18. unpredictable
19. forceful
20. feminine
21. reliable
22. analytical
23. sympathetic
24. jealous
25. leadership ability
26. sensitive to other's needs
27. truthful
28. willing to take risks
29. understanding
30. secretive
31. makes decisions easily
32. compassionate
33. sincere
34. self-sufficient
35. eager to soothe hurt feelings
36. conceited
37. dominant
38. soft spoken
39. likable
40. masculine
41. warm
42. solemn
43. willing to take a stand
44. tender
45. friendly
46. aggressive
47. gullible
48. inefficient
49. acts as a leader
50. childlike
51. adaptable
52. individualistic
53. does not use harsh language
54. unsystematic
55. competitive
56. loves children
57. tactful
58. ambitious
59. gentle
60. conventional

Inventory Score sheet

Enter your ratings in the appropriate columns

Column 1	Column 2	Column 3
1	2	3
4	5	6
7	8	9
10	11	12

13	14	15
16	17	18
19	20	21
22	23	24
25	26	27
28	29	30
31	32	33
34	35	36
37	38	39
40	41	42
43	44	45
46	47	48
49	50	51
52	53	54
55	56	57
58	59	60

- Add up your ratings in column 1 and divide total by 20. This is the masculinity score.

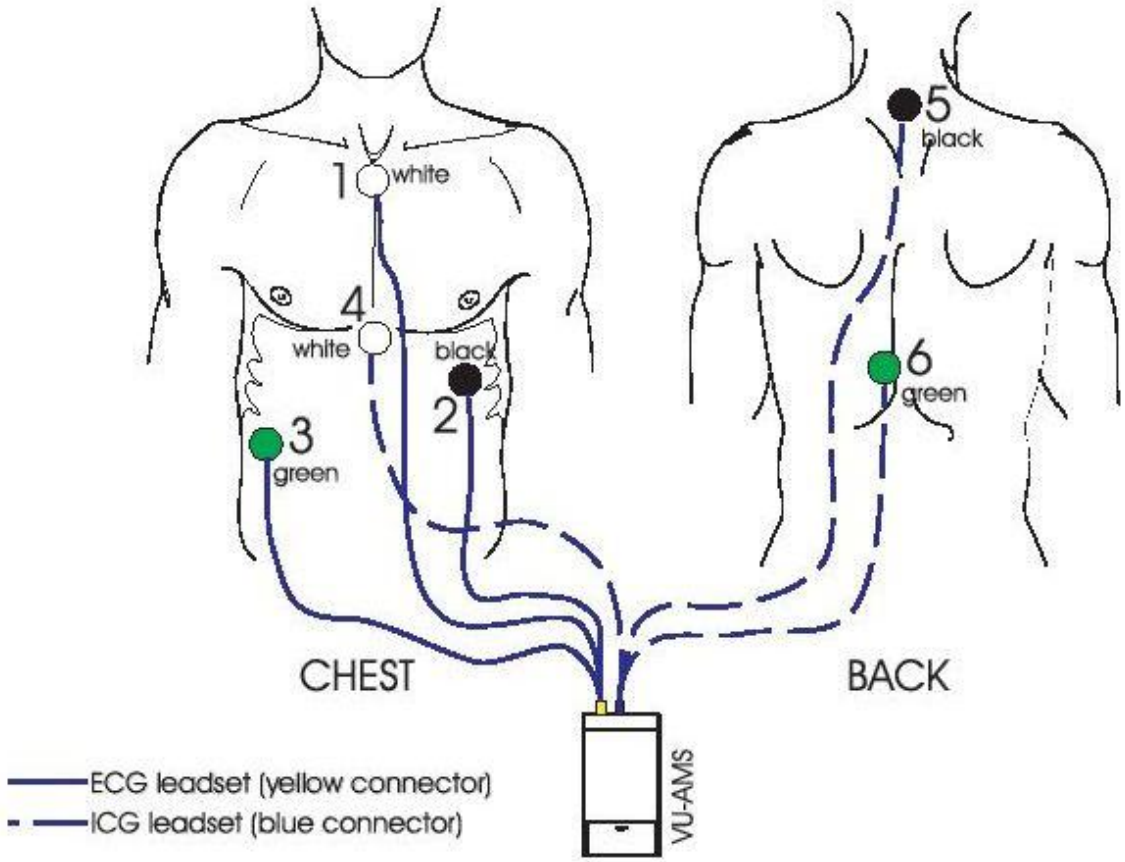
- Add up your ratings in column 2 and divide total by 20. This is the femininity score.

- Add up your ratings in column 3 and divide total by 20.

If your masculinity score is above 4.9 (the approximate median for the masculinity scale) and your femininity score is above 4.9 (the approximate femininity median), then you would be classified as androgynous on Bem's scale.

Appendix G

Electrode Placement Diagram



Appendix H

Pain Assessment Questionnaire

(1) Rate your pain on the left foot cold pressor task

1	2	3	4	5
Not Painful		Painful		Extremely Painful

(2) Rate your pain on the right foot cold pressor task

1	2	3	4	5
Not Painful		Painful		Extremely Painful

(3) Rate your pain on the left side facial cooling task

1	2	3	4	5
Not Painful		Painful		Extremely Painful

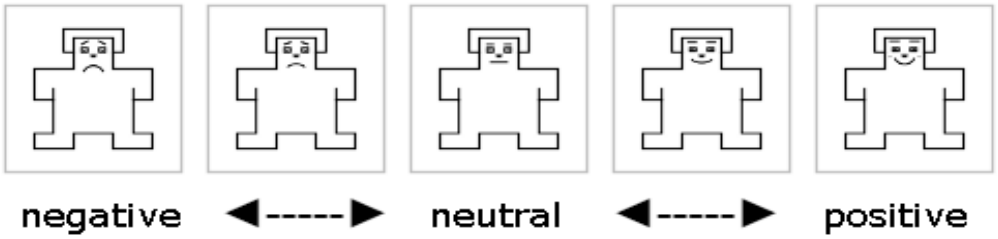
(4) Rate your pain on the right side facial cooling task

1	2	3	4	5
Not Painful		Painful		Extremely Painful

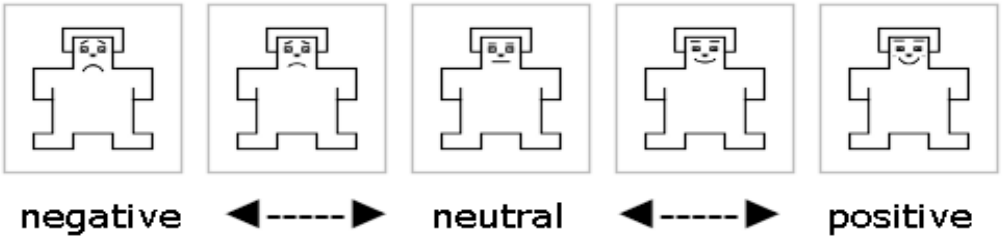
Appendix I

Self Assessment Manikin

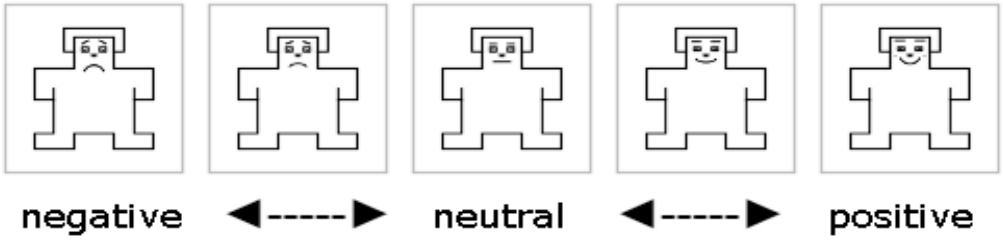
Right Side Facial Cooling



Left Side Facial Cooling



Right Foot Cold Pressor



Left Foot Cold Pressor