The Acute GABAergic Effects of Mindfulness Meditation in the Motor Cortex of University Students

Saam Azargive

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Abstract -

Background: Previous research demonstrated the cortical silent period (CSP) protocol, a measure of $GABA_B$ related cortical inhibition, to reliably reflect differences between psychiatric populations and healthy controls. Furthermore, cognitive behaviour therapy (CBT) and mindfulness meditation programs have been shown to affect CSP positively. In this pilot study, we assessed acute effects of mindfulness meditation by measuring pre-post differences in participants with minimal experience with meditation.

Methods: The CSP protocol was employed to measure cortical inhibition before and after a single 40 minute guided meditation session. Furthermore, involvement with the practice before and after the appointment was used to determine if experience affected the degree of change in cortical inhibition and whether this change could predict a participant's likelihood of attending weekly meditation tutorials. Finally, increases were expected to be correlated with 5 measures of self-reports of anxiety, depression, and mindfulness.

Results: Significant pre-post differences were found after 40 minutes of mindfulness meditation in 67 students with minimal experience with meditation ($t_{(66)} = 2.334$, $p = 0.011$). Students who had no prior meditation experience (< 2 hours) exhibited significant increases in CSP ($\Delta\bar{x} = 0.014$ s) compared to those with more experience ($F_{(1, 1)} = 5.388$, $p = 0.024$, $\eta^2 = 0.079$). Change in CSP did not predict likelihood of continued attendance ($F_{(1, 1)} = 1.242$, $p = 0.269$). Finally, baseline CSP measures were found to be negatively correlated with self-reports of negative automatic thoughts ($r = -0.303$, $p = 0.008$, $n = 63$).

Discussion: Findings indicated improved cortical inhibition in minimally experienced mindfulness meditation practitioners after 40 minutes of meditation and that experience plays a role in the effectiveness of a single guided mindfulness meditation session. Furthermore, the degree of change in CSP was predicted by the severity of self-reported automatic thoughts possibly as a result of the decreased difficulty of staying focused with fewer intrusive thoughts allowing for a more equanimous meditation session. This evidence suggests GABAergic neurotransmission may prove to be involved in a neurophysiological mode of action and that automatic thoughts may be a psychological variable involved in a cognitive mechanism underlying the health benefits associated with mindfulness meditation.

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List of Abbreviations

ANOVA - Analysis of variance
ANT - Attention network task
APB - *Abductor pollicis brevis*
ASI - Anxiety sensitivity index
ATQ - Automatic thoughts questionnaire
BDI - Beck depression inventory
BOLD - Blood-oxygen dependent
CBT - Cognitive behavioural therapy
CES-D - Center for Epidemiological studies - Depression
CI - Cortical inhibition
CSP - Cortical silent period
DEQ-SC - Depressive experiences questionnaire - Self criticism
ECT - Electroconvulsive therapy
EEG - Electroencephalography
EMG - Electromyography
FA - Focused attention
OM - Open monitoring
FEF - Frontal eye fields
FPN - Frontoparietal network
GABA - Gamma aminobutyric acid
IFG - Inferior frontal gyrus
IPS - Intraparietal sulcus
KIMS - Kentucky inventory of mindfulness skills
LICI - Long interval cortical inhibition
MBCT - Mindfulness based cognitive therapy
MBSR - Mindfulness based stress reduction
MDD - Major depressive disorder
MM - Mindfulness meditation
MP - Maladaptive perfectionists
MW - Mind wandering
RMT - Resting motor threshold
RT - Reaction time
SD - Standard deviation
SEM - Standard error of the mean
SICI - Short interval cortical inhibition
SMG - Supramarginal gyrus
SPL - Superior parietal lobule
SW - Shapiro-Wilk
TMS - Transcranial magnetic stimulation
TPJ - Temporoparietal junction
URPP - Undergraduate research participation pool
VFC - Ventral frontal cortex

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1. **Introduction** –

1.1. Cortical Inhibition

Several lines of neurophysiological evidence suggest meditation has effects on excitation and inhibition in the human cortex. For example, increases in prefrontal cortical activity have been associated with meditation, thereby increasing the production-delivery of glutamate (Lutz, et al., 2008) and stimulating the thalamus to deliver inhibitory signals to the lateral posterior and geniculate nuclei (Gazzaniga, 2000; Cornwall and Phillipson, 1988). Increases in inhibitory neurotransmitters have been shown to affect selective inhibition in the visual cortex (Andrews, et al., 1997) and posterior superior parietal lobe (Bucci, et al., 1999), enabling improved abilities to selectively target and disregard unimportant stimuli (Newberg and Iversen, 2003). This is believed to occur in meditation through the effects of cortical inhibition (CI).

CI refers to the tempering of cortical output through mechanisms, that are still unclear but nonetheless, highly associated with inhibitory neurotransmitter γ-aminobutyric acid (GABA) subtypes and their associated receptor mediated interneuron activity (Iversen et al., 1971; Krnjevic, 1974; McCormick, 1989). Research on human CI has revealed that higher levels are associated with normal healthy brain functions and downstream cognitive processes such as working memory (Daskalakis, et al., 2008b) and arithmetic calculations (Palva, et al., 2005). Several psychiatric conditions, such as depression and schizophrenia, have been found to correlate with deficiencies in CI as measured with transcranial magnetic stimulation (TMS) protocols (Daskalakis et al., 2002b, c; Fitzgerald, et al., 2002, Fitzgerald, et al., 2004).

TMS can be used to measure GABAergic networks by affecting the activity of different subtypes of GABA, i.e. $GABA_A$ or $GABA_B$. Three protocols exist that vary in terms of how many pulses are delivered, and the interval of time between these pulses, with all protocols using electromyography (EMG) to measure the muscle activity that results. Short interval cortical inhibition (SICI) and long interval cortical inhibition (LICI) are two examples of paired-pulse paradigms used to measure CI (Sanger, et al., 2001) while the third example, the cortical silent period (CSP), exemplifies single-pulse paradigms (Radhu et al. 2012). Although recent evidence suggests that TMS measures of CI may actually be inversely related with glutamate-glutamine activity (Tremblay, et al., 2013), thereby linking SICI, LICI, and CSP with the neurotransmitter responsible for regulating excitatory neurotransmission. This complementary hypothesis, which suggests that glutamate-glutamine activity is responsible for changes in CI measured by TMS rather than GABA levels, is possible but requires more research in order to challenge and reverse the putative paradigm described below.

$GABA_A$ receptor-induced neurotransmission, which occurs within a short time span (~1-25 ms) (Sanger, et al, 2001; Wang and Buzsaki, 1996), can be measured by SICI (Ziemann et al. 1996a) as evidenced from its modulation by lorazepam (Ziemann et al. 1996b). The physiological mechanism of this neurotransmitter's inhibitory effects involves the activation of anion-permeable channels ($GABA_AR$) leading to a rapid synaptic inhibitory synaptic potential (Isaacson and Scanziani, 2011). SICI works by delivering a paired-pulse via transcranial magnetic stimulation to the motor cortex with short intervals (1-25 ms) – the first pulse (conditioning pulse) is delivered at a subthreshold intensity and the second pulse (test pulse) is at a suprathreshold intensity. The subsequent muscle activity is measured via electromyography.

Conversely, $GABA_B$ receptors induce inhibitory potentials that exist within a relatively longer time interval (~100-200 ms) (McCormick 1989) which LICI and CSP also occupy (Radhu et al. 2012). This neurotransmitter exerts its slower effects through the activation of downstream K^+ channels signalled by its respective receptor ($GABA_BR$) (Lüscher, et al., 1997). $GABA_B$

activity has been measured in psychiatrically diagnosed patients (compared with healthy controls) via CSP duration which has been found to be negatively correlated with condition severity in schizophrenia, depression, and bipolar disorders (Daskalakis et al., 2002; Daskalakis et al., 2007; Levinson, et al., 2010; Levinson et al., 2007; Liu et al., 2009). The correlation between LICI and CSP (Farzan et al. 2010) as well as the changes induced by baclofen, a $GABA_B$ receptor agonist, (McDonnell, et al., 2006; Sanger, et al., 2001; Siebner et al. 1998; Werhahn et al. 1999) indicate that these measures could be used to detect the longer acting changes in CI that might result from effective interventions.

The clinical evidence associating CSP with $GABA_B$ activity stems from studies observing a lengthened CSP from direct intrathecal infusion of baclofen, a $GABA_B$ agonist (Siebner, et al., 1998). Concurrently, clozapine and other antipsychotic medications are noted as lengthening CSP when compared to unmedicated patients (Daskalakis, et al., 2008a; Liu, et al., 2009). While both of these studies were cross-sectional and based on patients with conditions severe enough to necessitate clozapine use, a longitudinal study confirmed this causal relationship after 6 weeks of clozapine treatment (p = 0.014) (Kaster, et al., 2015. Electroconvulsive therapy (ECT) and the therapeutic benefits associated with it in MDD patients has correlated emotional regulation-dysregulation with CI and changes in $GABA_B$ levels. For example, 10 MDD patients underwent 10 sessions of ECT, after which point CSP was observed to have increased by a mean of 40.5 ms (Bajbouj, et al., 2006). Magnetic resonance spectroscopy measurements after ECT in MDD patients also demonstrated an increase in GABA concentration (Sanacora, et al., 2003) in addition to direct measures of serum GABA (Esel, et al., 2008). Although these represent the more extreme examples of mental illness and intervention changing CI, $GABA_B$, and the CSP, other studies have suggested the possibility that less extreme, less invasive, and less expensive circumstances can induce observable changes in the above mentioned variables.

Interestingly, changes in CI may occur at significant levels outside of clinical diagnostic levels (Radhu, et al., 2012; Guglietti, et al., 2013). Sub-clinical changes in CSP may indicate a greater sensitivity to mental health that can be exploited for better understanding how these psychiatric predispositions develop into full-blown disorders. If this practice proves accurate, early dysfunctions of CI and psychiatric well-being as well as the effects of their treatment, such as CBT (Radhu, et al., 2012) or their management, such as meditation (Guglietti, et al., 2013) may be measurable. This brings us to the goal of this study which is to better understand the underlying mechanisms of how mindfulness meditation (MM) generates its purported mental health benefits through the use of a sensitive neurophysiological measure. It is our intention to help lay the foundations for a better understanding of MM, namely the dose-response relationship and its interactions with the psychological subcomponents of the mental health disorders that are arguably the most prevalent and are known to be affected by MM, namely anxiety and depression.

1.2. Vipassana and Mindfulness Meditation

Vipassana (pronounced **Vih-PAH-san-ah** or **Vi-PASH-an-ah**) is a form of meditation that fosters concentration and mindfulness, is associated with physical and psychological well-being, and is often referred to as mindfulness meditation (MM). Although there is some disagreement as to whether Vipassana is a derivative of MM or vice versa (Ahir, 1999; Lutz, et al., 2008), the former is, historically, the older of these two descriptors. Translated from the Buddhist tradition of Therevada, Vipassana is Pali for “insight.” It represents a basic meditative technique that cultivates observation of the present moment objectively and without emotional reaction, summarized as a “presence of mind” (Chiesa et al., 2011b) or “mindfulness” (Chiesa, et al., 2011b; Kabat-Zinn, 1994 p. 4; Bishop, et al., 2004; Lutz, et al., 2008). Therefore, despite the historical differences of their conception, MM and Vipassana are relatively similar methods in the context of meditative practices aimed at developing mindfulness.

1.3. Relevant forms of meditation

Meditation exists in many other forms, each with associated definitions, techniques, and belief systems or worldviews. Accordingly, a reductionist approach is often employed to delineate the specific effects of each practice. Because the aim of the current study is to describe methods for improving mental health through mindfulness practice, the descriptive categories used in the largest review to date of clinical trials on meditation in health care were employed to categorize MM under the umbrella term of “meditation” (Ospina et al, 2008). Ospina and colleagues classify each trial reviewed within one of 5 different categories of meditation (with 2 additional categories devoted to mixed methods of meditation and those that do not clearly define the related technique). The 5 fundamental categories include: MM, Mantra meditation, Qigong meditation, T’ai Chi, and Yoga.

A discussion of MM is aided by a brief comparison with Mantra meditation, a structurally similar and highly studied practice. Ospina and colleagues define mantra meditation as practices that focus on repeating a *mantra*, a word, term, sentence, sound, or symbolic expression (2008). As will be further discussed, Mantra meditation aims for a form of meditation that is purely concentrative, whereas MM or Vipassana incorporate random events through its open monitoring of sensations and thoughts. Mantra meditation arguably represents one of the currently most frequently studied forms of meditation in clinical settings with 141 trials being conducted as of 2008 (Ospina et al, 2008). Common forms include Acem meditation, Transcendental Meditation

(TM™), and *Kundalini*. The specific practices involve passive observation of breath with simultaneous focus on a sequence of words, such as *sat nam* (translated simply to Truth Name) in *Kundalini*. The instructions involve sustained attention on the mantra with any departures or mind-wandering (MW) events responded to with a refocusing on the mantra. Similar to other forms of meditation that incorporate focused meditation, including MM, different forms of mantra meditation appear to activate areas of the hippocampus (Engström, et al., 2010), indicating a possible mode of action for the observed effects on memory and spatial awareness (Slagter, et al., 2007; Hodgins and Adair, 2010).

1.4. Mindfulness

Within the mindfulness category, Ospina and colleagues include MM, Vipassana, and Zen as notable examples (2008). Vipassana is the ancient Buddhist form of MM that, modified for clinical treatment programs, has been referred to as mindfulness-based stress reduction (MBSR) and mindfulness based cognitive therapy (MBCT) programs. Generally, the instructions for MM have been summarized as: 1) focusing attention on the present moment 2) with openness and without judgement. This two-component explanation was popularized by Kabat-Zinn as "paying attention in a particular way, on purpose, in the present moment, and non-judgementally" (Kabat-Zinn, 1994, p. 4) and has been echoed by many researchers who have aimed to study and define it (Bishop et al., 2004; Jha et al., 2007; Chiesa and Serretti, 2011; Awasthi, 2013). Bishop and colleagues argued that MM uses both (1) self-regulated attention of the present moment (awareness) and (2) an attitude of openness, acceptance, and curiosity (equanimity) (2004) although they maintain an open interpretation not limited to these 2 points. Lutz and colleagues attempted to categorize meditative practices along a spectrum of meditative practices where mindfulness meditation would distinctively fall between what they call focused attention (FA) and open monitoring (OM) forms (2008). Although these authors have contributed to better understandings of MM, a consensus for an operational definition is still lacking, with significant discrepancies among the most recent operationalizations requiring reconciliation (Ospina et al., 2008; Chiesa et al., 2011b; Hölzel et al., 2011; Awasthi, 2013).

Nonetheless, instructions for MM can be described as follows: (Kabat-Zinn, 1994; Bishop, et al., 2004; Lutz, et al., 2008) it is typically performed seated in a straight posture, with closed eyes; initial awareness is brought to current sensations (e.g. "feel your feet against the ground, the chair against your back, and the air against your skin") followed by a focusing of attention on breathing sensations (e.g. "pay attention to the air flowing through your nose, your chest rising and falling"). Up to this point, the instructions mimic that of a form of focused attention meditation known as Anapana. In practice, Anapana is sometimes used as an introductory technique as new practitioners learn MM or Vipassana. This focus on the breath is continued until a MW is noticed by the practitioner, which is followed by an attentional shift back to the sensations of breathing. The goal is to acknowledge the MW event non-judgementally with minimal attachment. Often, beginners benefit from the guidance of a leader who meditates while simultaneously offering verbal instructions.

1.5. Focused Attention and Open Monitoring

MM instructions assume the practitioner will experience spontaneous instances of MW despite continued efforts to maintain the focus of attention on the sensation of one's breath in the present moment. The breath is therefore the centre of the meditator's awareness and serves to anchor attention in the present moment. The 'focus' is a concept present in almost all forms and instructions of meditation that incorporate focal attention and can range from internally derived stimuli, external stimuli, autonomously generated stimuli (i.e. mantra), etc. Any internal or external event, stimuli or sensations, or automatic thoughts or cognitions that pulls the practitioner's attention away from the present moment and/or the breath is considered a distraction, and is acknowledged as such, before a return of attention to the breath. These distractions can involve a train of cognitions that are completely removed from the focus, and constitute a MW away from the present moment.

MW is a term used to refer to the above described phenomenon and exists in the neuroscience literature to represent a variety of generally unfocused cognitions (Christoff, et al., 2011; Mason, et al., 2007). In MM, MW is arguably the true target of the practitioner`s attention as he/she must remain vigilant to its presence (or more accurately, vigilant to the *absence* of awareness of the present moment) through meta-cognitions. Thus, it is the subjects' task to identify this target event and return attention back to 'the focus.' Although MM also aims to establish a greater awareness of the nature of these MW events via OM, which can help the practitioner choose how to respond as opposed to automatically reacting, FA represents the foundation upon which OM is practiced. Thus, FA must be better understood in scientific terms before OM can be properly discussed, and visual neurosciences offer a useful avenue to this understanding.

Target detection in visual systems has been a topic of interest for researchers trying to understand how the brain orients resources in response to new or distracting stimuli for stimulus-driven attention (LaBar, et al., 1999; Rushworth, et al., 2001; Giesbrecht, et al., 2006; Sylvester, e al., 2007). Physiological and imaging evidence has led to the identification of 2 anatomically distinct cortico-cortical networks necessary for attending to environmental stimuli (Corbetta and Shulman, 2002). The dorsal frontoparietal network (FPN), with core regions in the intraparietal sulcus (IPS), superior parietal lobule (SPL), dorsal frontal cortex and frontal eye fields (FEF), and the ventral FPN, with core regions in temporoparietal junction (TPJ), the ventral supramarginal gyrus (SMG), ventral frontal cortex (VFC), the middle frontal gyrus (MFG), inferior frontal gyrus (IFG), frontal operculum, and anterior insula, constitute these neuroanatomical regions (**Figure 1.1**) (Corbetta, et al., 2008). Functionally, the *dorsal* FPN is thought to regulate motivated control of attention in a focused task, ignoring extraneous stimuli that would normally be considered noise, and this is consistent with evidence associating the same structures with conflict monitoring (Carter, et al., 1998; Ridderinkhof, et al., 2004; Carter et al., 2005), selective attention (Corbetta and Shulman, 2002) and sustaining attention (Coull, 1998; Posner and Rothbart, 2007). The *ventral* FPN, on the other hand, is responsible for the attentional shift of attention to a relevant environmental stimulus, acting as a 'circuit-breaker' and reorienting the dorsal FPN towards this information (Downar, et al., 2001; Kincade, et al., 2005); it can therefore inhibit and/or facilitate the *dorsal* FPN.

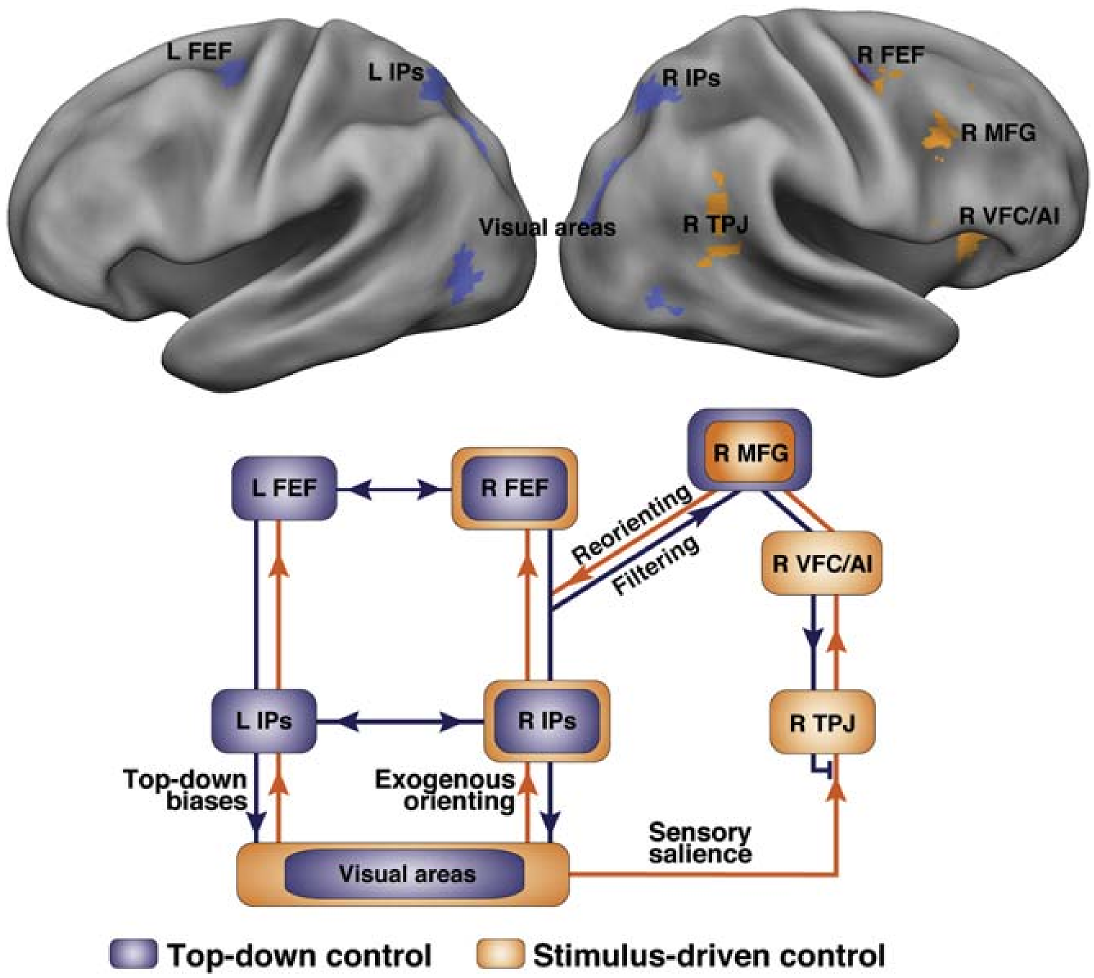


Figure 1.1 – Defined anatomical regions of the dorsal (blue) and ventral (orange) frontoparietal networks (FPN). The dorsal FPN is involved in top-down control of focused attention, including central motivations, planning, and anticipation. The ventral FPN is involved in the attentional shift when relevant (and possibly salient) stimuli are presented (Corbetta, et al., 2008).

Evidence of the FPNs involved in auditory modalities (Driver & Spence, 1998; Downar et al., 2001; Mayer et al., 2006) suggests that it may represent a generalized network of attentional regulation, reinforcing the call for investigation of these networks in stimulus-neutral conditions such as meditation. Hasenkamp and colleagues have given evidence for activation of these FPN networks by using MW as the internal event of interest (Hasenkamp, et al., 2012), shifting the locus of the stimulus to internal rather than external events. While more research is required to establish whether these findings are reliable and whether the activation of these networks are as robust as Corbetta and Hasenkamp claim, they present intriguing evidence that these attentional networks may be central to regulating attention universally and may not be limited to visual and/or environmental stimuli.

In contrast to FA, OM is characterized by acknowledging and encountering [sensations], cognitions, and emotions. This experience is often described as ‘witnessing’ the experience of these stimuli moment-to-moment, allowing the practitioner to have an increased distance from the events and allowing for a more thoughtful response whether there is a passive or active response (Lutz, et al., 2008). This is the aspect of MM that is concerned with non-judgemental awareness and is thought to improve awareness of patterns in automatic thoughts, emotional states, and typical reactions to external stimuli (Lutz, et al., 2008). It lacks a concrete ‘focus’ and is a specialized group of techniques for better attending to unexpected stimuli (Valentine and Sweet, 1999). OM has also been shown to engage the anterior insula and somatosensory cortex during a body perception component of MBSR, when compared to a group of controls (Farb, et al., 2007), signifying it as a stimulus-driven approach to the self-evaluation of physical *and* mental states.

1.6. Psychological, Cognitive, and Health-Related Benefits of Meditation

Recently, interest in meditation has spurred increased discussion and subsequent research into the scientific nature of its effects and mechanisms. As is true for most young fields, there was weakness in the beginning, with limited definitions, control groups/conditions, and scientific rationale (Ospina, et al., 2008). This has led to calls for improvements in design, rigour, and rationale, a challenge which has arguably been heard with subsequent improvements in the general quality of meditation-related research studies (Gotink, et al., 2015). Nonetheless, major improvements are still required in terms of scientific rigour (i.e. randomization and sample size), especially as more data on the beneficial outcomes of meditation accumulate. However, with conservative inclusion criteria and objective review, psychological (Chiesa, et al., 2011a, 2009), cognitive (Chiesa and Serretti 2011b), and physiological (Chiesa 2010, 2011a; Ospina 2008) findings have emerged.

Psychological stress and anxiety have been found to be affected by mindfulness-based therapies. For example, Shapiro and colleagues found results consistent with reduced levels of stress and increased levels of forgiveness in N = 15 female undergraduate students in a Roman Catholic University (2008). Despite the limitations of self-report measures, a single-gender sample, and not including a comparison group (e.g. MBCT), this study is noteworthy for the positive changes that persisted 8 weeks following the intervention; a correlation between meditation practice and psychological benefit was found. Rumination was measured in 2 studies using the Reflection Rumination Questionnaire where the MBSR group showed significant decreases and the control group did not (Trapnell and Campbell, 1999; Jain, et al., 2007). This finding was also distinguished from a relaxation training group, suggesting MBSR possessed a more specific effect than solely relaxation. Other studies have reported similar improvements in positive affect and reductions in perceived stress and hostility (Beauchamp-Turner and Levinson, 1992), increases in positive self-concept, self-esteem, self-worth, benevolence, and self-acceptance (Nystal and Garde, 1997; Sridevi and Rao, 1998; Emavardhana and Tori, 1997), and improvements in interpersonal skills (Tloczynski and Tantriella, 1998). These findings were confirmed and extended in another study that determined that MBSR was effective in reducing stress in female nursing students, with N = 16 subjects showing significant improvements in mean stress ($p < 0.05$) (Beddoe and Murphy, 2004). Lastly, stress levels before and after a 10-day Vipassana retreat decreased significantly at levels that were maintained 3 months post-retreat in N = 53 ($p < 0.001$) (Ostafin et al., 2006).

Mindfulness-based therapies have also been shown to have efficacy in reducing the effects of identified psychopathological processes. Davidson et al. observed decreased trait anxiety and negative affect (Davidson, et al., 2003). Other researchers have demonstrated decreases in measures of distress, automatic thoughts, anxiogenic cognitions, and depressive symptoms in clinical populations of patients with depression (Brown, et al., 2007; Greeson, 2008; Klainin-Yobas, et al., 2012) and anxiety (Chen, et al., 2012; Galante, et al., 2012). In clinical contexts, MBCT is used as a treatment option for depression although its efficacy in major depressive disorder seems to offer no significant difference when compared with anti-depressants (Chiesa, et al., 2011a). However, MBCT has been shown to affect patients with 3 relapses or more, reducing the risk for the next episode by 43% when compared to treatment as usual (Coelho, et al., 2007). This contrasts with traditional treatments that have a stymied efficacy after multiple relapses, signifying MBCT as a specific tool for mitigating the risk for relapse and sustaining good mental health (Godfrin and van Heeringen, 2010; Bondolfi, et al., 2010; Fjorback, 2011). Research is needed to properly understand how the improvements in inhibition from mindfulness-based interventions can improve obsessive-compulsive disorder and attention deficit hyperactivity disorder. A recent review by Gotink, et al., explores standardized mindfulness-based interventions as they relate to mental illness and chronic diseases (2015).

Cognitive and neuropsychological effects have also been studied in order to determine whether MM affects aspects of attention, executive function, and memory. Changes in sustained attention due to MM were observed (Ren, et al., 2011) when a meditation condition was compared to being wait-listed (control) in undergraduate students in a Beijing university (N = 48) with a pre-post-test of problem-solving. They further sub-divided the meditation condition into an ‘M10’ and ‘M100’ with participants reporting (counting) every 10 or 100 breaths, respectively. M10 demonstrated higher post-test scores relative to M100 which was higher relative to control. This indicated that practicing with higher frequencies of alertness and vigilance resulted in better problem-solving scores. Another study on sustained attention found improvements in the Digit Span backward (and forward) of the Wechsler Adult Intelligence Scale. Participants who participated in a 10-day Vipassana retreat improved their reaction times (RT) in the internal switching task between T1 to T2, while controls did not ($p < 0.04$), with this improvement only apparent in the affective condition as opposed to the emotionally neutral condition ($p < 0.005$) (Chambers et al., 2008). These effects support a previous study by Jha and colleagues who noted a significant difference ($p < 0.001$) of RT in the attention network test (ANT) between T1 and T2 for newly trained meditators as opposed to controls (Jha, et al., 2007). Other studies using the ANT have also shown decreased RT and error rates (Tang, et al., 2007; van den Hurk, et al., 2010a) but, these effects were not observed in other studies with smaller MM interventions (in terms of intensity and length of time) (Tang et al., 2007; Polak, 2009) suggesting the existence of a dose-response relationship between MM and sustained attention.

When observing selective and executive attention, notable differences seem to be observable mainly in long-term meditators. When meditation experience was calculated by minutes per day, a relationship was found associating increased experience with faster RTs in the Global local letters task ($p < 0.05$) (Chan and Wollacott, 2007). Similar findings were observed by Jha et al., (2007), Hodgins and Adair (2010), van den Hurk et al., (2010b) and Moore and Malinowski (2009), associating more meditation experience with better selective and executive attention. Using the Stroop task, significant improvements in executive attention were measured within a randomized mindfulness intervention with arousal levels controlled for (Wenk-Sormaz, 2005). This indicates that selective and executive attention may be rigid constructs in the context of meditation that require more work to change significantly - 'the more you put into it, the more you get out.' However, given self-selection biases (with the exception of Wenk-Sormaz in 2005), these observations may be a reflection of the intrinsic characteristics of those populations sampled that are more interested in learning meditation.

The intersection of attention and memory is also a cognitive area on which MM seems to affect. Slagter et al. (2007) used the attentional blink paradigm (Raymond et al., 1992) to observe significant differences in a group who participated in a 3 month Vipassana retreat when compared to control ($p < 0.001$) with differences that were correlated with reduced brain resource allocation (based on p3b amplitude). A similar test of attention and working memory called the Change blindness flickering text was used to observe similar differences between experienced meditators and non-meditators (Hodgins and Adair, 2010). These studies demonstrate the utility of examining higher MM doses, with studies looking exclusively at working memory confirming this idea. After their 10-day Vipassana retreat (Chambers et al., 2008), participants demonstrated significant working memory improvements tested by the digit span backward and forward of the Wechsler Adult Intelligence Scale, whereas a 4-day retreat found no effects (Zeidan et al., 2010a).

Effects in memory specificity can also be interpreted in the context of psychopathology as depression has been shown to impact the recall of autobiographical memories (Kuyken and Howell, 2006; Williams, et al., 2007). As a result, MM effects in depressed patients may be associated with effects on memory specificity; Williams et al. (2000) and Hargus et al. (2010) showed these effects with preliminary studies under controlled circumstances but lacking proper randomization. Although Heeren et al. (2009) performed a randomized controlled trial and confirmed these findings, further research is required to replicate these observations.

Ren and colleagues affirmed their above mentioned cognitive findings of more vigilant and alert meditation resulting in improved problem-solving abilities, by using EEG recordings measures of relaxation (alpha and i-22) and alertness (i-35) (2011) to indicate neurophysiological effects suggesting differences in brain function resulting from meditating. Effects on the immune system have also been noted in virus-challenge and cytokine studies (Davidson, et al., 2003; Pace, et al., 2010) which may have a potential mechanism through recently discovered lymphatic networks through the brain (Louveau, et al., 2015). Other brain-related findings have been found using fMRI. Although the number of reliable studies is scant, two separate experiments have found increased BOLD activation in FPNs during practice of FA (Ives-Deliperi et al., 2011; Hasenkamp et al., 2012). This indicates the altered use of these attention-governing neural networks with meditation, opening up the field to the possibility that meditation could affect the biology of the nervous system. Other neuroimaging studies have found that MM can have long term effects on the thickness of subcortical grey matter within the hippocampus (Lazar et al., 2000; Lazar et al., 2005; Hölzel, et al., 2011) where increased grey matter volume and density were found, suggesting that the skills learned through MM may have had a physical effect on structures responsible for memory consolidation and awareness of spatial constructs (Hölzel, et al., 2011). These structural changes are similar to the changes associated with learning other complex skills from naïve/novice to experienced levels (Gaser and Schlaug, 2003; Draganski, et al., 2004; Dragnanski, et al., 2006; Maguire, et al., 2006; Bezzola, et al., 2011; Hüfner, et al., 2011). Given the neuropsychological effects MM has been shown to have with memory, it is reasonable to suggest that these structural changes may be responsible for improved working memory and memory specificity.

1.7. Behavioural CI Studies Using CSP

A study using CSP (Radhu, et al., 2012) demonstrated that maladaptive perfectionists (MP), when randomly allocated to a cognitive behaviour therapy (CBT) intervention, exhibited significantly longer CSP, and significantly improved self-reported measures of mood, anxiety, and negative cognitions in comparison to MP wait-list controls. In light of other intervention studies showing similar effects, more research is needed to delineate the isolated effects of mindfulness meditation on CI, particularly in relation to improved mental health. This research aims to acquire evidence for changes in GABAergic inhibitory neurotransmission as a mechanism in mental health improvement, and contribute support for mindfulness meditation as a stress-reduction practice with neurophysiological benefits.

Practice of transcendental meditation has been shown to lead to an increase in central GABAergic neuronal activity (Elias and Wilson, 1995; Elias et al., 1995) which includes the motor cortex. Other research has used self-identified meditators who have accumulated varying quantities of meditation practice hours and demonstrated acute meditation-related increases in the CSP (Guglietti et al. 2013). To evaluate differences, meditators were compared with age- and sex-matched controls engaged in a routine non-meditating activity (i.e., watching a standard emotionally neutral video clip) for a comparable duration of time (Guglietti, et al., 2013). CSP was measured before and after manipulation, where there was observed an increase in the meditation group and no change in control with a significant group by time interaction ($p < 0.02$), demonstrating a measurable effect of meditation on $GABA_B$ activity, but not $GABA_A$ as measured by SICI.

These findings must be replicated and extended them by testing a different population with substantially less meditation experience and with a smaller dose. The aim of this research would be to determine if these effects can be observed under less intense conditions in order to determine the lower levels of intensity by which the effects of meditation can be induced. Answering this question would be in line with a larger goal in the meditation literature regarding the determination of a dose-response relationship. In addition, this may help an implicit objective of making MM more accessible, easier to approach, and possible to apply in existing everyday routines.

1.8. Mental Health of University students

Previous research has shown a higher prevalence of poor mental health, psychological distress, depression and suicidal ideation in post-secondary students (Bieling, Israeli, Smith, & Antony, 2004; Hamilton & Schweitzer, 2000; Hoff & Muehlenkamp, 2009). Furthermore, our research has shown that students at York University either suffer from higher rates of depression at 57.1% (CES-D score > 16) (Pirbaglou, et al., 2013), or that these rates are increasing, especially when compared to approximately 11.7% in a small university population 7 years prior (Price, et al., 2006). This indicates an increased need for improved mental health care on University campuses for students. Because counselling and psychotherapy are expensive limited resources, open drop-in sessions of MM that are free of charge have proven popular (Fashler, 2015). These 'mindfulness tutorials' were offered to students at York University through a student-led club known as the Healthy Student Initiative (HSI), creating an opportunity to study the effects of MM in a novice population of University students. Students were offered guided MM tutorials available every day of the week during the normal academic year, beginning in September of 2013.

1.8.1. Results of a Pilot Study on Newly Trained Meditators

A pilot study, which sampled 31 students who attended these sessions during the 2013-2014 academic year, indicated that after accruing an average of 13 hours of self-reported meditation experience, participants exhibited a significant change in CSP after 40 minutes of guided MM ($p < .005$). No tests were conducted at baseline, however, when participants would be considered naïve to the practice. Although relationships were observed relating baseline CSP to measures of self-reported tension (POMS), automatic thoughts (ATQ), and anxiety sensitivity (ASI), the sample size was too small to examine if these measures could predict the extent to which CSP could change. These shortcomings represent the areas of interest for the present study, as we are interested in how these measures behave in a naïve population where prior meditation experience lies at a theoretical zero-point. Furthermore, we intended to include self-report measures of depression as the research literature indicates a possible relationship.

1.9. Goals of the Current Study

The objectives in this study fall into two broad categories with several sub-components: 1) how CI interacts with the practice of meditation and 2) how psychological measures of well-being predict changes in CI.

The primary objective was accomplished by examining how 40 minutes of guided MM affected CI in a pre-post design. In a post hoc analysis, we also analyzed how CI interacts with the degree of a participant's involvement with the practice of MM. Participant's past and future practice were reported and tracked (with assistance by the HSI) in the following way: A) separating participants into a naïve and novice group and comparing relative differences and B) using changes in CI to predict behavioural adherence to attending the MM tutorials.

The secondary objective was to determine if any change could be predicted by baseline measures of self-reported mindfulness and depressive symptomology in addition to automatic thoughts and anxiety sensitivity. In order to achieve this, a larger sample size was collected when compared to previous pilot studies based on sample size estimates. We aimed to detect differences in CI change as they relate to the above mentioned psychological constructs.

Therefore, the objectives can be outlined as: 1) to measure the changes in CI before and after a guided meditation session; 2) to determine the effects of A) previously accrued hours of experience in changing CI and B) the predictability of accruing further hours of experience based on observed changes in CI; and 3) to quantify the relationship between measures of psychological well-being and the ability to change CI with meditation.

1.10. Hypotheses

The above mentioned objectives are predicted to behave in in the following ways:

1) CI, as measured by CSP, will increase after a 40-minute guided meditation session compared to baseline.
2) Larger positive changes in CI, as measured by CSP:
    a. will occur in participants with more previous exposure to meditation, as measured by hours of experience (the equivalent of two full tutorials, or ≥ 2 hours), compared to naïve participants.
    b. will predict increased future exposure to meditation by participants, as measured by hours of tutorial attendance after the experiment (≥ 2 tutorials).
3) Higher scores in automatic thoughts, anxiety sensitivity, self-criticism, and depression, and a lower score in mindfulness will predict larger positive changes in CI, as measured by CSP.

2. Methods

2.1. Recruitment

Participants were currently enrolled students at York University in Toronto, Ontario, Canada during the academic year of 2014-2015. Students were recruited through in-class announcements as well as email and poster advertisements. York University's Undergraduate Research Participation Pool (URPP) was also used for recruitment, which incentivizes undergraduate participation in research studies on campus by offering a small amount of extra credit in a variety of psychology courses.

Interested individuals contacted the research team through email and were screened for eligibility. Email follow-ups were conducted systematically, tracking each participant's progress through the study. Appointment scheduling emails were sent out after screening interviews conducted by telephone or in person where convenient. Following the appointment, a thank-you and debriefing email with relevant information was sent.

Informed consent was obtained with a digital signature from each participant. This study was approved by the research and ethics boards for York University, Toronto, ON (Certificate # 170-2012).

2.2. Subject criteria

Inclusion criteria for this study required that participants were students enrolled in York University at the time of recruitment. They were required to be fluent in English, able to competently provide voluntary consent, and be between 18-35 years of age.

Participants were also required to be free of psychopathology with the exception of students with clinically diagnosed anxiety or depression, including those prescribed anti-depressants, based on self-report. Because the aim of this program was ultimately to better understand how providing free and easily accessible guided mindfulness meditation tutorials could benefit the mental health of a population of University students, excluding participants who would be expected to gain the most from the practice (i.e. those with anxiety and depression) (Fjorback, et al., 2011) was considered counter-productive, and there is no current evidence of additional risk posed by mindfulness meditation activity to individuals with these conditions.

2.3. Procedures

Participants were asked to complete a demographic battery including age, ethnicity, education level, and prior meditation experience. Calculations for previous exposure used years, average hours per week, and attendance in the following equation:

Hours of experience = ((Average hours per week x 52) x Years practicing) + Previous Attendance

The aim was to ensure that those included were relatively inexperienced or naïve with regards to the practice, although complete naiveté to mindfulness meditation was not a requirement for this study.

2.4. Psychometric Instruments (Appendix)

2.4.1. Automatic Thoughts Questionnaire

The Automatic Thoughts Questionnaire (ATQ; Hollon and Kendall, 1980) is a 30-item questionnaire designed to assess the frequency of negative automatic cognitions. This questionnaire was primarily developed in the context of depression to evaluate four dimensions of personal negative statements: 1) personal maladjustment and desire for change; 2) negative self-concepts and negative expectations; 3) low self-esteem; and 4) helplessness. Ranging from a score of 30 to 150, the ATQ has an internal reliability of .95-.96 as determined by Cronbach's alpha (Dobson and Breiter, 1983). Validated in college and clinical populations with anxiety and depression (Hollon and Kendall, 1980; Dobson and Breiter, 1983; Hollon, Kendall, and Lumry, 1986), this 5-point Likert scale questionnaire asks how frequently each thought occurred in the preceding week and includes items such as, "What's wrong with me?" and "I feel like I'm up against the world" with responses ranging “Not at all” (1), “Sometimes” (2), “Moderately often” (3), “Often” (4), and “All the time” (5) (**Appendix)**.

2.4.2. Anxiety Sensitivity Index

The Anxiety Sensitivity Index (ASI; Reiss et al., 1986) is a 16-item questionnaire designed to delineate the magnitude of participants’ fear of anxiety symptoms. In the context of trait anxiety, this measure exists as a distinct measurement tool that differentiates trait anxiety from anxiety sensitivity. Three factors form the structure for measuring global anxiety sensitivity concerns: 1) physical; 2) psychological; and 3) social (Stein, Jan, and Livesley, 1999). Scoring within a range of 0 to 64, Reiss and colleagues report the validity of the measure when comparing controls and those with general anxiety disorders to those with agoraphobia specifically and high levels of test-retest reliability (.75) (Reiss, et al., 1986). This 4-point Likert scale index asks the participant how much they agree each question, including items such as, “It is important for me not to appear nervous,” and “When my throat feels tight, I worry that I could choke to death” with responses “Very little” (0), “A little” (1), “Some” (2), “Much” (3), and “Very much” (4) (**Appendix**).

2.4.3. Kentucky Inventory of Mindfulness Skills

The Kentucky Inventory of Mindfulness Skills (KIMS; Baer et al., 2004) is a 39-item questionnaire designed to measure skills commonly associated with mindfulness on four dimensions: 1) observing; 2) describing; 3) acting with awareness; and 4) accepting without judgement. Scoring within a range of 9 and 45, Baer et al. report reliability with Cronbach's alpha levels of .91, .86, .83, and .87 for the above mentioned dimensions, respectively. This reverse scored 5-point Likert scale includes items such as, "I notice changes in my body, such as whether my breathing slows down or speeds up," and "I tend to evaluate whether my perceptions are right or wrong" with responses “Never or very rarely true” (1), “Rarely true” (2), “Sometimes true” (3), “Often true” (4), and “Very often or always true” (5) (**Appendix**).

2.4.4. Depressive Experiences Questionnaire – Self Criticism

The Depressive Experiences Questionnaire (DEQ; Blatt, et al., 1976) is a 66-item questionnaire designed to measure affect regarding participants’ relationships and concept of self with 3 factors: 1) Dependency, 2) Self-Criticism, and 3) Efficacy. The second factor, self-criticism (SC), has previously been shown to be the most sensitive factor to actual vulnerability characteristics in the DEQ (Rudich, et al., 2008) which, in combination with the impracticality of using the entire 66-item questionnaire, has led the current study to only include the items of the DEQ associated with SC. Scoring within a range of 6 to 42, this modified 7-point Likert scale questionnaire has a reliability score as measured by Cronbach’s alpha of .73 (Rudich, et al., 2008). Items include “I find it hard to accept my weaknesses,” and “I compare myself often to standards or goals” with responses ranging from “Strongly agree” (7) to “Strongly disagree” (1) and a midpoint for neutral or undecided opinions (4) (**Appendix**).

2.4.5. Center for Epidemiological Studies Depression Scale

The Center for Epidemiological Studies Depression scale (CES-D; Radloff, 1977) is a 20-item scale designed to measure depressive feelings and behaviours within the last 7 days. As it focuses on current levels of depressive symptomatology, it is particularly tuned to measuring the result of a triggering event such as that associated with preterm delivery during pregnancy (Li, et al., 2009). With a range of 0 to 60 scores, with a reported alpha of .85 in the general population and .90 in their patient sample (Radloff, 1977). This reverse-scored 4-point Likert scale asks how frequently each thought occurred in the preceding week and includes items such as, "I felt depressed," and "I enjoyed life" with responses "Rarely or none of the time (less than 1 day)" (1), "Some or a little of the time (1-2 days)" (2), "Occasionally or a moderate amount of time (3-4 days)" (3), and "Most or all of the time (5-7 days)" (4) (**Appendix**).

2.5. Transcranial Magnetic Stimulation Procedure

The experiment was conducted in two separate rooms, with an additional waiting room for holding waiting participants. Informed consent and psychometric questionnaires were obtained collected in Room 1, following by a 40 minute meditation period seated in a chair with their eyes closed in Room 2, a small, darkened space which allowed isolation and quiet. CI assessments included a baseline measurement before meditation and another measurement after meditation, both conducted in Room 3. Each individual CI measurement was divided into three steps: 1) localization of M1, 2) determination of resting motor threshold (RMT), and 3) measurement of CSP.

Before localization of M1, the equipment and participant were prepared as follows: a transcutaneous electrode was placed on the skin superficial to the right *abductor pollicis brevis* (APB) muscle after the skin was scrubbed and lightly washed with isopropyl alcohol 70% v/v. A 'ground' electrode (Kendall 5400 Diagnostic Tab Electrode, Covidien) was placed on the surface of the skin, superficial to the right medial posterior ulna with an attached alligator clip after treating the skin with the same protocol. Muscle activity was recorded with this electrode using an electromyograph (EMG) and input into Signal version 5 (Cambridge Electronic Design Ltd., 2011) with EMG amplification set to 10,000 times.

Localization of M1 began with the participant relaxing their right hand. TMS was applied using a 70 mm diameter figure-of-eight magnetic coil powered by a 1.5 T Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, Wales) at 5 second intervals. The output intensity of the first magnetic pulse was set to 50% of the maximum power output. The starting location of stimulation was at the junction of the left frontal and parietal bones (coronal suture), 45 degrees laterally from the midline targeting the hand area of the left motor cortex (**Figure 2.1.**). TMS pulses were applied in a spatially exploratory manner until a local maximum for the amplitude of APB muscle contraction was found and landmarked with washable ink.

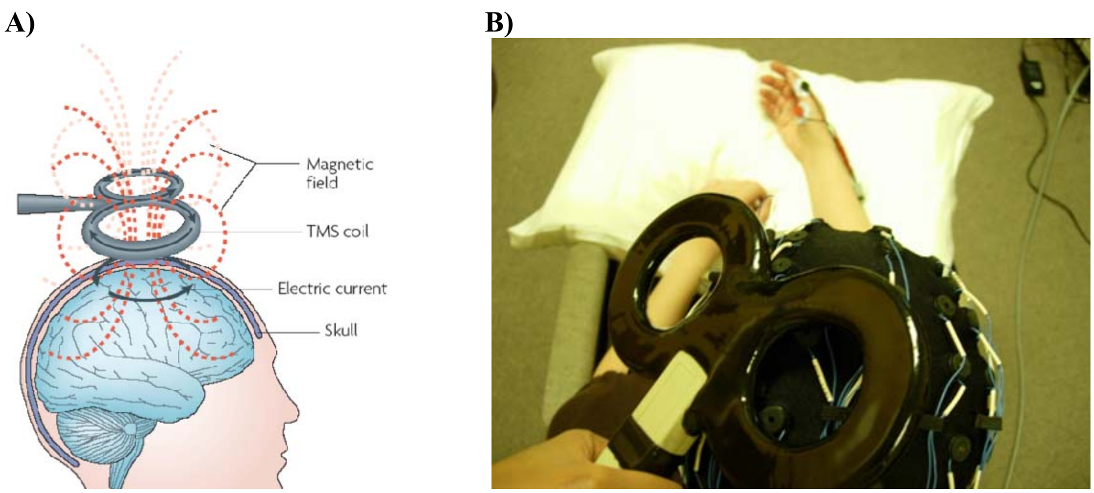
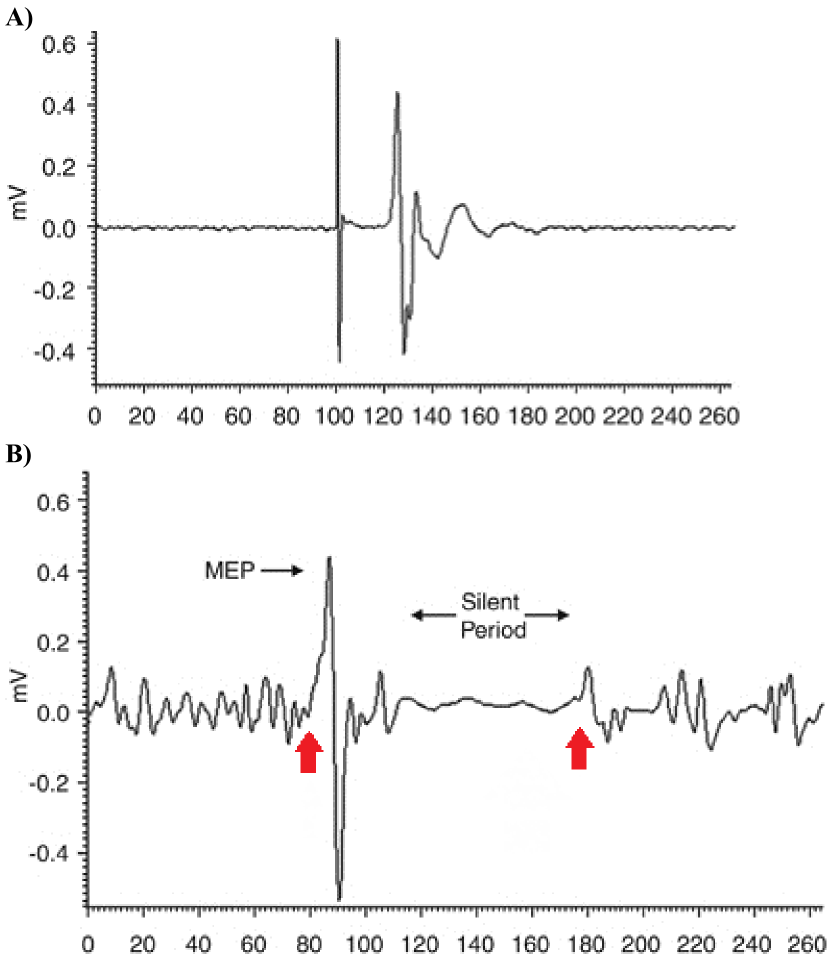


Figure 2.1. Stimulation of the motor cortex by transcranial magnetic stimulation shown in **A)** a schematic diagram (Ridding and Rothwell, 2007), and **B)** a photograph with a live participants from the experimenters point of view (Unknown source).

After M1 was localized, the participant's RMT was determined. While the participant maintained a relaxed APB, TMS was applied to the marked location and the power output modulated until an intensity was found that generated a motor evoked potential (MEP) of >50 μV in 5 of 10 trials (Kujirai et al., 1993). The percentage of maximum power output was set as the RMT or 100% of the intensity required to depolarize the motor cortex enough to generate a measureable MEP and was recorded.

After determining RMT, CSP was measured as follows: EMG amplification was set to 1,000 times. The measurement begins with the participant holding a strength gauge between their right thumb and index finger. They are asked to maintain 20% of their maximum pinch strength throughout the measurement using the gauge as a guide after determining their maximum strength capacity. The TMS power output was set to 140% of RMT in order to deliver 10 high intensity stimulations to the marked M1 location at 7.1 second intervals (140.8 mHz). This high-intensity excitatory magnetic pulse and MEP is visible as a spike in EMG activity followed by a period of motor inactivity. Using the average waveform of 10 trials, the CSP duration was defined as the time from the MEP onset to the return of any voluntary EMG activity (absolute CSP) ending with a deflection in the EMG waveform (Tergau, Wanschura, and Canelo 1999) (**Figure 2.2.**).



<u>Figure 2.2.</u> - A surface electromyogram recording (x = time (ms), y = electric potential (mV)) of the *abductor pollicis brevis* muscle responding to single pulse suprathreshold TMS **A)** while relaxed without active contraction and **B)** during voluntary tonic contraction. The cortical silent period can be observed as cessation of voluntary muscle activity and is measured from the onset of the motor evoked potential to the return of voluntary motor activity (indicated by the arrows, respectively) (Fitzgerald, et al., 2009).

2.6. Statistical Analysis

A paired samples t-test was used to determine if there were any changes in CSP after the normality and homogeneity of the dataset was tested. Before hypothesis testing could be conducted, the normality of the sample was tested. The Shapiro-Wilk (SW) test returned pre-meditation CSP ($W_{(67)} = 0.99$, $p = 0.88$) and post-meditation CSP ($W_{(67)} = 0.983$, $p = 0.503$) distributions that confirm the null-hypothesis, indicating the data did not significantly deviate from normal distribution. The SW test is a statistical test of normality where the null-hypothesis indicates the population sampled from is normally distributed with 95% certainty. No assumptions about the homogeneity of the variances were made as each variable was compared to its pair.

For ANOVA testing, the distribution was deemed statistically normal by the WS test (W = 0.923, p = 0.453). Homogeneity for ANOVA was tested using Levene's test of equality of error variances (pre-meditation - F = 2.710, p = 0.052; post-meditation – F = 0.434, p = 0.729). To understand changes in CSP after 40 minutes of meditation (*time*) in the context of participants' previous involvement with practicing meditation as well as predicting continuation of practice after experimentation, we created 2 factors. The first compared those who had been previously exposed to meditation to those who were naïve to the practice (*experience*), and the second compared those who continued participation in the meditation tutorial program through tutorial attendances to those who did not (*attendance*). Therefore, the repeated measures ANOVA was conducted with two between-subjects factors, *experience* (Naïve versus Novice defined by a cut-off of 2 hours of experience) and *attendance* (No Attendance versus Attended defined by a cut-off of attending 2 tutorials) with a within-subjects factor, *time* (Pre meditation versus Post meditation), resulting in a 2 (Time) x 2 (Experience) x 2 (Attendance) ANOVA with time as a within-subjects factor and experience and attendance as the between-subjects factors. Our intention was to examine the two 2-way interactions, Time x Experience and Time x Attendance, in order to understand how involvement with the practice of MM interacted with the observed changes in CI, as measured by the CSP.

Pearson correlations were used to assess associations between percent change in CSP between pre- and post-meditation measurements and mean scores on the ATQ, the ASI, the

KIMS, the DEQ-SC, and the CES-D, after applying a Bonferroni correction ($\alpha = 0.01$). In order to collapse the repeated measure of CSP in the Pearson correlations, percent change was used as post meditation CSP is dependent on baseline pre meditation CSP. All data was analyzed using SPSS version 20 (IBM, New York). Sample size estimates were based on G*Power (Faul, et al., 2007) with effect size ($\eta^2 = 0.07$), alpha = 0.05, and power = 0.95 taken from the 2013 study by Guglietti and colleagues (2013), resulting in a minimum sample of N = 64 to detect a statistical difference.

3. Results

3.1. Demographics

One hundred and two individuals expressed interest in participating and were screened for eligibility. Thirteen individuals were deemed ineligible due to being diagnosed with an excluded medical or psychiatric illness or having magnetic contraindications such as metal implants, and 1 was dismissed as their CSP could not be obtained (RMT was above the possible range for testing). Fourteen individuals were lost to follow up and 2 withdrew from the study due to being uncomfortable with the TMS procedure. This resulted in 72 individual students being tested. One individual's data was excluded from analysis due to deviations from CSP protocol and 4 were excluded due to being outside of the age range indicated for inclusion.

In total, sixty seven individuals (24 male, 43 female) with a mean age of 20.45 years (SD = 2.32, range = 10) participated in the study. Previous meditation experience was calculated as having a mean of 49.8 hours (SD = 254.67, range = 1823.00), a median of 0.0 hours, and a range of 1,823.0 hours, and being highly skewed with kurtosis = 6.204. Two outliers account for a majority of the skewness with 1,047 and 1,823 hours of experience, that when excluded, caused the mean to be 7.2 hours of experience - their data was not excluded as these subjects were not noted as differing in any other variable and, when tested post hoc, did not significantly affect the results of the analysis.

Table 3.1. - Participant Characteristics

Demographics	**n (%)**
Sex	
Male	24 (32.0)
Female	43 (57.3)
Ethnicity	
White	29 (38.7)
South Asian	17 (22.7)
West Asian	5 (6.7)
Black - African	4 (5.3)
Chinese	4 (5.3)
South East Asian	2 (2.7)
Latin American	2 (2.7)
Black - Caribbean	2 (2.7)
Korean	1 (1.3)
Hispanic	1 (1.3)
Program of Study	
Kinesiology	28 (37.3)
Psychology	17 (22.7)
Biomedical Science	4 (5.3)
Biology	2 (2.7)
Child Studies	2 (2.7)
Undecided	1 (1.3)
Other	13 (17.3)
Mean Hours Accrued – Hours (SD) = 49.8 (254.67)	
<2	49
2-10	5
10-50	7
>50	6

3.2. Comparison of CSP Before and After 40 min of MM

Mean differences in CSP increased from 0.1471 s to 0.1522 s (a change of 0.0051 s) after 40 minutes of guided MM and these changes were statistically significant ($\Delta\bar{x}$ = 5.1 ms, $t_{(66)}$ = 2.334, p = 0.012) (**Figure 3.1.**). This shows that the group as a whole significantly increased their CSP after 40 minutes of meditation.

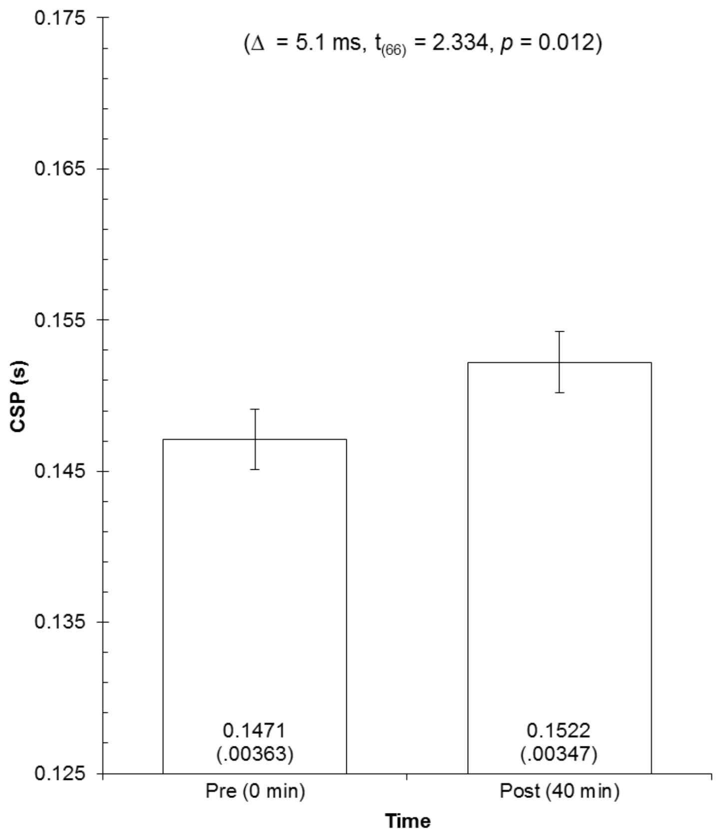


Figure 3.1. - Mean cortical silent period (CSP) duration in seconds in 67 participants. Values represent means (standard errors). Students demonstrated significant increases in CSPs after 40 minutes of guided mindfulness meditation ($p = 0.011$).

3.3. Past and Future Practice and CSP Change

Consistent with the above t-test, there was a significant main effect of **Time** [$F_{(1, 1)} = 6.887$, $p = 0.011$, $\eta^2 = 0.099$] as predicted by Hypothesis 1, that CSP would increase after 40 minutes of meditation. There were significant interaction effects of **Time x Experience** [$F_{(1, 1)} = 5.388$, $p = 0.024$, $\eta^2 = 0.079$] but no **Time x Attendance** interaction [$F_{(1, 1)} = 1.242$, $p = 0.269$] (**Figure 3.2.**). This shows that, for each group, experience can predict CSP increase after 40 minutes but this increase cannot predict subsequent attendance. There was a significant **Time x Experience x Attendance** interaction [$F_{(1, 1)} = 5.352$, $p = 0.024$, $\eta^2 = 0.078$]. The simple effects are summarized in **Table 3.3.**

Table 3.2. - Multivariate simple effects of 40 minutes of guided mindfulnes meditation, with observed mean differences in cortical silent period (CSP) in 67 participants. The zero-experience (naïve) group demonstrated significant differences (p = 0.001) compared to novice meditators. A significant change in CSP predicted increased attendance (p = 0.029) when compared to those who attended no tutorials.

Effects	F	*p*-value	η^2
Time	6.887*	.011	.099
Time x Experience	5.388*	.024	.079
Time x Attendance	1.242	.269	.019
Time x Experience x Attendance	5.352*	.024	.078

* p < 0.05

Table 3.3. - Multivariate simple effects of 40 minutes of guided mindfulnes meditation, with observed mean differences in cortical silent period (CSP) in 67 participants. The zero-experience (naïve) group demonstrated significant differences (p = 0.001) compared to novice meditators. A significant change in CSP predicted increased attendance (p = 0.029) when compared to those who attended no tutorials.

Grouping Factor		Mean Difference (s)	*p*-value	Std. Error
Experience	Naive (n=49)	-0.014***	.001	0.004
	Novice (n=18)	-0.001	.838	0.004
Attendance	No Attendance (n=53)	-0.004	.171	0.003
	Attended (n=14)	-0.01*	.029	0.005

* p < 0.05
** p < 0.01
*** p < 0.001

3.3.1. CSP Change in Novice and Naïve Participants (Time x Experience)

Participants with previous meditation exposure (18 novice participants) averaged a 1 ms increase in CSP, while participants with no prior experience with meditation (49 naïve participants) averaged a 14 ms increase (**Figure 3.2.**) which was a significant group by time interaction (**Table 3.2.**). There was a significant within-groups effect for naïve meditators [$F_{(1, 63)} = 13.359$, $p = 0.001$, $\eta^2 = 0.175$] but not for novice meditators [$F_{(1, 63)} = 0.042$, $p = 0.838$] (**Table 3.3.**). This shows that naïve meditators increased their CSP after 40 minutes of meditation but novice meditators did not. An independent samples t-test indicated baseline measures (pre-meditation CSP) were not significantly different between novice meditators and naïve meditators [$t_{(65)} = -0.406$, $p = 0.343$].

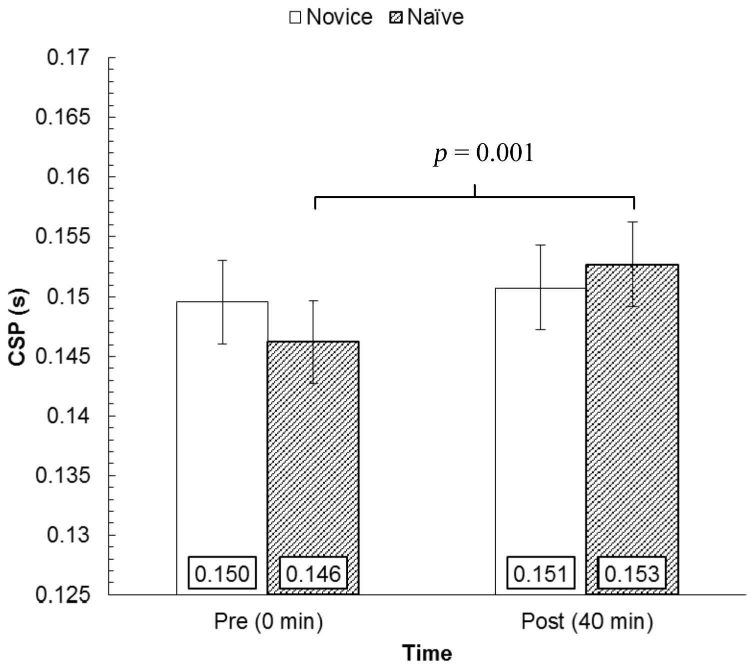


Figure 3.2. - Mean cortical silent period (CSP) duration in seconds in 67 participants. Values represent means (standard errors). Students who had no prior meditation experience (n = 49) exhibited significant increases in CSP ($\Delta\bar{x}$ = 0.014 s, $p = 0.001$) whereas those who did have previous meditation experience (n = 18) did not ($\Delta\bar{x}$ = 0.001 s, p = 0.838).

3.3.2. Between Participants Who Attended or Did Not Attend (Time x Attendance)

Participants who attended sessions after their measurement appointment (14 attended) averaged a 10 ms increase in CSP, while those who did not attend any sessions after their measurement appointment (53 with no attendance) averaged a 4 ms increase (**Figure 3.3.**) which was not a significant group by time interaction (**Table 3.2.**). There was a significant within-groups effect for CSP on Attended [$F_{(1,\ 63)} = 4.971$, $p = 0.01$, $\eta^2 = 0.073$] but not for No Attendance [$F_{(1,\ 63)} = 1.919$, $p = 0.171$] (**Table 3.3.**), however this difference did not pass the test of significance in the above mentioned ANOVA. An independent samples t-test indicated baseline measures (pre-meditation CSP) were not significantly different between participants who attended and participants who did not [$t_{(65)} = 0.927$, $p = 0.179$].

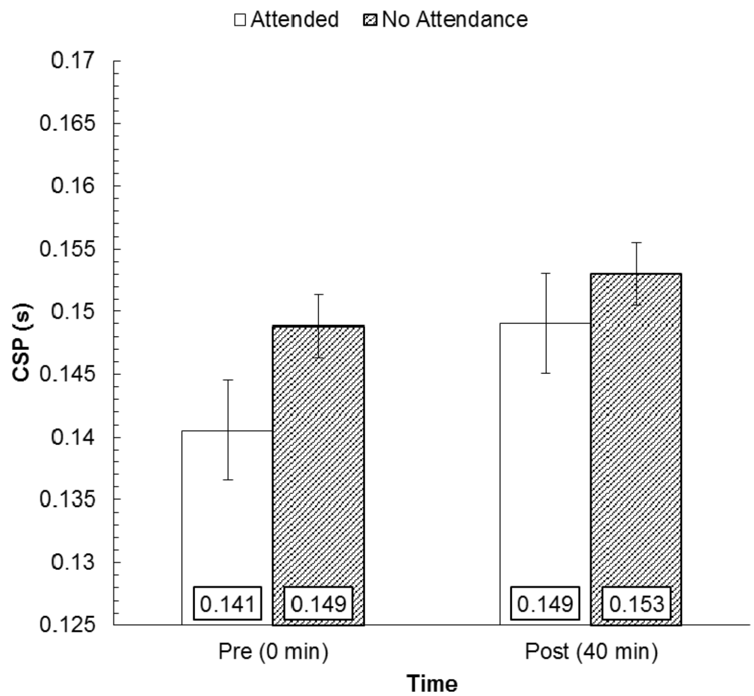
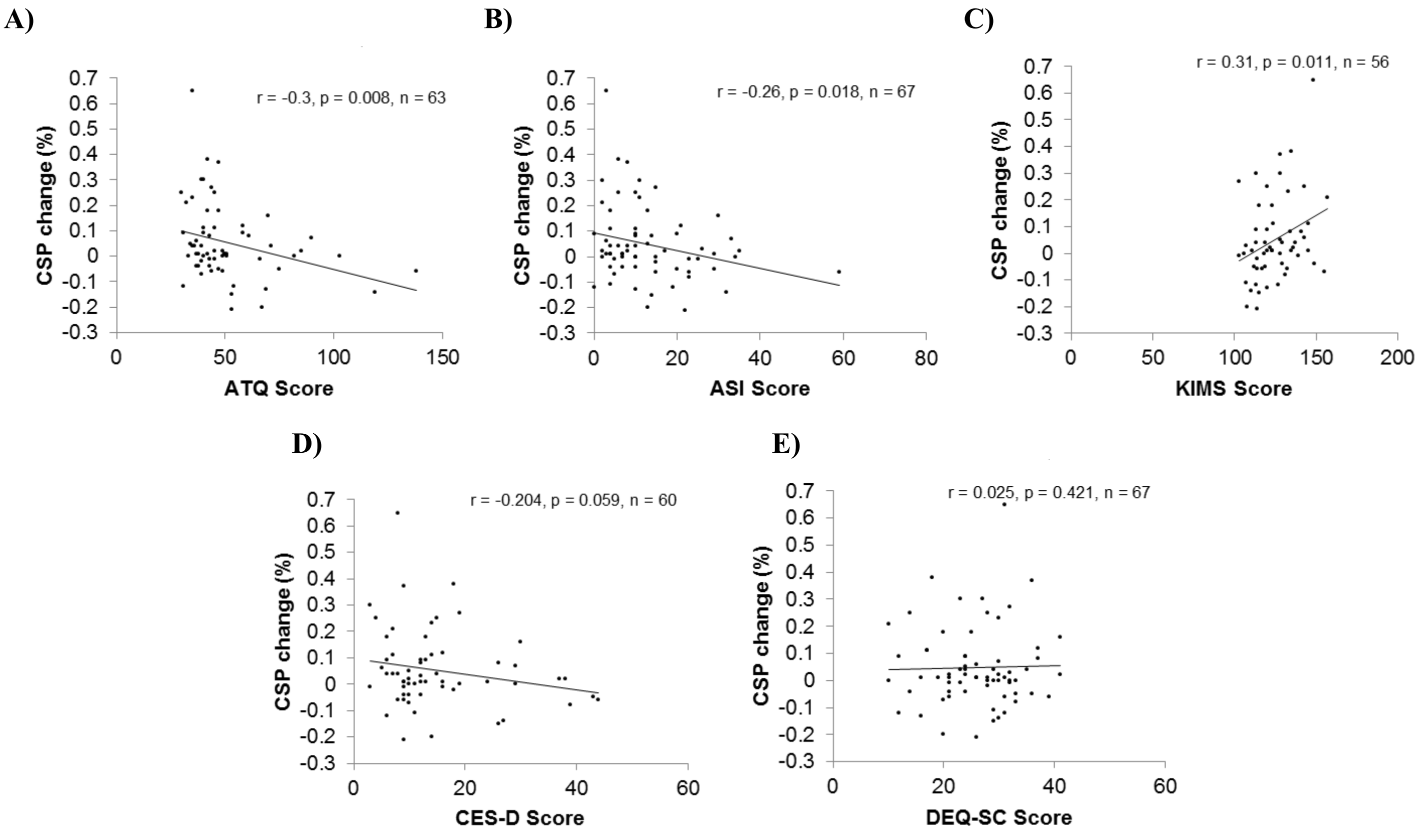


Figure 3.3. - Mean cortical silent period (CSP) duration in seconds in 67 participants. Values represent means (standard errors). Students who attended tutorials (n = 14) exhibited significant increases in CSP ($\Delta\bar{x}$ = 0.010 s, $p = 0.029$) whereas those who did not attend any tutorials (n = 53) did not exhibit significant changes in CSP ($\Delta\bar{x}$ = 0.004 s, $p = 0.171$).

3.4. Correlation of CSP Change with Measures of Psychological Well-Being

After applying a Bonferroni correction to the α-level, Pearson correlations between percent change in CSP and five self-report measures of psychological well-being were computed ($\alpha = 0.01$). A significant relationship with a moderate negative correlation was found for participants' percent change in CSP and their mean scores on the **A)** ATQ ($r = -0.303$, $p = 0.008$, $n = 63$). Although not significant, similar trends were found for mean changes in participants' CSP with a negative relationship with mean scores on the **B)** ASI ($r = -0.256$, $p = 0.018$, $n = 67$) and a positive relationship with mean scores on the **C)** KIMS ($r = 0.306$, $p = 0.011$, $n = 56$). No significant correlations were found between mean changes in participants' CSP with mean scores on the **D)** DEQ-SC (r = 0.025, *p* = 0.421, n = 67) and mean scores on the **E)** CES-D (r = -0.204, *p* = 0.059, n = 60). This indicates that scores on the ATQ taken before a meditation session can be used to predict the change in CSP after 40 minutes of MM.



<u>Figure 3.4.</u> - Mean cortical silent period (CSP) percent change in seconds versus **A)** ATQ (r = -0.303, p = 0.008, n = 63), **B)** ASI (r = -0.256, p = 0.018, n = 67), **C)** KIMS (r = 0.306, *p* = 0.011, n = 56), **D)** DEQ-SC (r = 0.025, p = 0.421, n = 67), and **E)** CES-D (r = -0.204, p = 0.059, n = 60).

4. Discussion

4.1. Hypothesis 1 - CI will increase after a 40 minute guided meditation session compared to baseline.

The mean CSP of the 67 participants measured increased significantly after 40 minutes of guided mindfulness meditation (**Figure 3.1.**). If the assumption that $GABA_B$ governs CSP is accepted, these results confirm MM can increase $GABA_B$ receptor mediated neuroinhibitory neurotransmission. This is the first finding to suggest that those with minimal exposure to MM training are capable of experiencing acute neurophysiological effects from a single 40 minute session.

These apparent changes in $GABA_B$ activity likely reflect the effects of MM on the pyramidal cells of the cortex, as they are responsible for responding to inputs with modulations in cortical oscillations (Markram, et al., 2004; Pouille and Scanziani, 2001; Rossignol, 2011; Wehr, 2003). By extension, this effect on CI should have a simultaneous effect on cortical excitation based on studies on the interconnectivity of inhibitory interneurons of the cortex (van Vreeswijk and Sompolinsky, 1996; Litvak, et al., 2003; Bereshpolova, et al., 2011) and observations of their synchronicity during spontaneous activity (Okun and Lampl, 2008).

Because $GABA_B$ acts as a broad inhibitory neurotransmitter with metabotropic effects, effects on its activity may have downstream effects on cognitive processes (Daskalakis, et al., 2008b; Palva, et al., 2005) and psychological constructs (Daskalakis et al., 2002b, Daskalakis, et al., 2002c; Fitzgerald, et al., 2002, Fitzgerald, et al., 2004) linked to CI. The slow, enduring hyperpolarizations, resulting from the G-protein coupled receptor activation of $GABA_B$ receptors (Franek, et al., 2004), have been proposed as the components of this neurotransmitter's activity that are responsible for the effects observed by the above mentioned authors.

Furthermore, alpha activity has been found to be correlated with states of meditation when synchronized (Hebert, et al., 2005; Travis, et al., 2004; Travis and Wallace, 1999), which is also associated with increased levels of CI (Klimesch, et al., 2007). Therefore, the mechanism for the cognitive and psychological effects of MM may be neurophysiological in origin.

Limitations: It should be noted that as no control group was included, no conclusions concerning causality are appropriate. Nonetheless, a correlation with 40 minutes of MM was found with CSP change. However, Guglietti and colleagues included a control group in their study on the acute effects of meditation on CSP (2013). It is therefore important to note that while a control group will be included in future studies, the current study was a valuable extension of the Guglietti et al. (2013) study as it offered useful information about minimally trained meditators. Furthermore, because there was an apparent explanatory correlation with psychometric indices that were predicted to interact with MM practice, there is reason to believe that these observed effects were not Type I errors. Further research with a control group will be necessary to determine causality, nonetheless.

Despite this, no study has been done to determine whether sitting quietly with eyes closed can affect CSP in a significant way. Thus, the observed CSP changes may have resulted from sitting quietly with eyes closed or due to some other 3rd variable. This weakness was also present in the above mentioned study (Guglietti, et al., 2013) and must be addressed in future studies before conclusions regarding the active component of MM can be made.

These observations were measured in a sample with 49.8 hours of previous meditation experience with 2 extreme outliers in this respect. When removed, the average hours of experience became 7.2 but the observed change in CSP remained with approximately the same significance level ($p = 0.0011$). We expected exposure to MM to affect an individual's ability to modulate their CSP with MM such as with experienced meditators (Guglietti, et al., 2013) and also expected the modulation of CSP resulting from early experiences with MM to affect a participants likeliness for future exposure to MM.

4.2. Hypothesis 2 - Changes in CI will be predicted by experience and will predict attendance

Previous MM exposure was measured by self-report and attendance to the in-person HSI tutorials *before* the date of the experiment and future MM exposure was measured by attendance to the in-person HSI tutorials *after* the date of the experiment. These comparisons were therefore made post hoc based on the results of the above mentioned data.

Calculations for previous exposure used years, average hours per week, and attendance in the following equation:

Hours of experience = ((Average hours per week x 52) x Years practicing) + Previous Attendance

Comparing those who accrued less than 2 hours of meditation practice (naïve) with those who had greater than or equal to 2 hours of meditation practice (novice) revealed a significant experience by time interaction ($p = 0.011$) (**Figure 3.2.**). However, the directionality of this relationship was counter to the hypothesis that more experienced participants (novice group) would have a larger CSP change when compared to participants with less experience (naïve group). CSP for naïve participants was found to increase by an average of 14 ms which is in contrast to novice participants who averaged a 1 ms increase (**Figure 3.2.**). These results were not significantly affected by the exclusion of the 2 outliers in meditation experience and so they were included in the total sample size.

The potentiation of $GABA_B$ in naïve participants is unexpected as they lacked the experience to confidently meditate in the expected manner. However, the degree of this potentiation (14 ms) is less than what has been previously shown in experienced meditators (Guglietti, et al., 2013). The difference between naïve and novice participants may therefore reflect something within the novice group or the protocol itself. Based on informal reports by participants, increased exposure to MM is associated with more independent practice with less guidance. As a result, following the strict instructions that were provided for the 40 minutes of MM may have been an unusual session for more experienced participants. Therefore, the protocol itself may be most appropriately used in naïve populations who have no ability to meditate on their own for the first time. Future studies should investigate the effects of guidance on the quality of a meditation session and the subsequent neurophysiological effects.

Limitations: this analysis was done post hoc, resulting in a non-random sample for each group. Self-selection may have caused expectations and anticipations of the participants, resulting in a biased set of samples. However, this quality is difficult to control for as life-time experience is often by self-selection. A wait-list control starting with two groups of naïve participants may be a potential method for improving this design and mitigating this limitation. A similar placebo effect to the previous hypothesis test is likely to have had an effect, bringing attention to the need for the use of an appropriate 'sham' control in meditation studies (Zeidan, et al., 2010b).

Recording attendance for future exposure from in-person HSI sessions was accomplished with sheets of paper signed by participants at the end of each session. These were recorded and tracked throughout the remainder of the school year. Comparing those who attended less than 2 in-person meditation tutorials (No Attendance) with those who attended greater than or equal to

2 in-person meditation tutorials (Attended) revealed no significant attendance by time interaction ($p = 0.269$). This did not confirm our hypothesis that those who experienced significant changes in CSP would be more likely to fall into the group that attended tutorials.

Therefore, significant CSP change could not predict whether a participant would continue to attend sessions or not. A high quality meditation session in neurophysiological terms, assumed to be reflected by significant increases in CSP, does not appear to influence the behaviour to attend sessions in that meditative practice. This is important to consider since the variables that govern a person's likelihood to continue with a new behavioural habit do not include whether the preliminary exposure to that behaviour were successful (Dunn, et al., 2004; Jordan, et al., 2002). However, this experience may have the potential to affect readiness or openness to change (Ryan, et al., 2011). Therefore, readiness and openness to change measures should be included in future iterations of this study model.

With the above limitations in mind, and the understanding that our *a priori* intention was to evaluate two 2-way interactions, a 2x2x2 ANOVA may not have offered the most useful statistical analysis. Different statistical tests should be used in future explorations of the same constructs. We propose a separate 2x2 ANOVA should be used to analyze the interaction between Time and Experience. However, due to the nature of the unequal variances, as measured by Levene's test ($p < 0.01$), a non-parametric equivalent should be used. We suggest an extension of the Kruskel-Wallis test known as the Scheirer-Ray-Hare test to accomplish this, as test well known in the biology literature (McAffee & Morgan, 1996; Tolimieri et al., 2000; Hitchmough, 2003). To analyze the interaction of Time x Future Attendance, we propose a linear regression in order to properly interpret the effect of a meditation session, as measured by CSP, on future interaction with and attendance of MM tutorials.

4.3. Hypothesis 3 - Automatic thoughts, anxiety sensitivity, self-criticism, and depression, and mindfulness will predict changes in CI

Average percent change in CSP was found to correlate with scores on the ATQ (r = -0.3, $p < 0.01$) (**Figure 3.4a.**). Scores on the ASI and the KIMS were also found to trend with percent CSP change in the hypothesized directions (r = -0.26, $p = 0.018$ and r = 0.3, $p = 0.011$) (**Figure 3.4b. & c.**). Assuming the ATQ is an accurate tool for measuring current rates of negative automatic thoughts, this result suggests that automatic thoughts may influence a person's ability to potentiate $GABA_B$ through meditation.

When the 2 participants with outlying hours of meditation experience were excluded, this relationship remained significant. Furthermore, one of the two trending associations between CSP and psychometrics (ASI and KIMS) changed to become significant. The KIMS was found to have a significant relationship with percent change in CSP when the 2 experienced participants were removed from the sample.

The confirmation of this hypothesis offers a valuable insight into a potential candidate for a cognitive mechanism underlying MM. Negative automatic thoughts have the propensity to A) have intrusive properties (Clark and de Silva, 1985; Beckmann, 1998), b) be emotionally charged (Hollon and Kendall, 1980), and correlate with increased rates of depression (Harrell and Ryon, 1983; Nishikawa, et al., 2013). Thusly, staying focused on the breath would prove more difficult if intrusive cognitions are occurring more frequently. Further, non-judgemental appraisals and separating emotion from cognition would occur with less ease. It therefore follows that having less intrusive thoughts would result in a more focused and equanimous meditation. If we presume that the observations of Hypothesis 1 and those tested by Guglietti and colleagues in 2013 are true, that the quality of a MM session is reflected neurophysiologically in $GABA_B$

potentiation and CSP increase, then increased frequency of negative automatic thoughts should correlate with a smaller increase, or a decrease, in CSP with meditation. Although typically used in cases of extreme CI changes, CSP appears to be sensitive to smaller changes in CI reflecting subtle and potentially sub-clinical changes in CI (Radhu, et al., 2012; Guglietti, et al., 2013). This finding further suggests that small, sub-clinical dysfunctions of psychiatric well-being may be measurable with CSP and acute CSP change resulting from an intervention like MM.

No effect was found in measures of clinical depression, which may indicate that there is either no effect of depressive symptomology on CI in the sample we measured, or that these measures were not sensitive enough to detect sub-clinical subtleties. Future studies may wish to replicate with different measures of depression, such as the Beck Depression Inventory (BDI; Beck, et al., 1988) or the Hamilton Psychiatric Rating Scale for Depression (HRSD; Hamilton, 1960).

Firstly, each measure of psychological well-being was conducted by self-report, making them susceptible to social desirability and fakeability effects. Furthermore, many of these scores refer to the week prior to testing (i.e. ATQ and CES-D), causing inaccuracies to result from distorted memories and a bias towards how participants are feeling at the time of testing. Secondly, despite the ATQ (and possibly the ASI and KIMS) suggesting predictive power in regards to percent change in CSP, these results are correlative and cannot give insight into the causal relationship between psychiatric constructs and CSP.

4.4. Limitations

In addition to the specific limitations described above, the study as a whole included several limitations. The cortical silent period is an indirect measure of $GABA_B$ activity and cortical inhibition, which therefore requires that these findings be validated with more direct measures such as that observed in serum GABA (Esel, et al., 2008). Tangential to this is the putative understanding that the effects of meditation are not specifically associated with the part of the frontal lobe controlling motor output (motor cortex). A greater effect size and a more accurate observation of CI changes from meditation may be best done with CI measurements of the prefrontal cortex (Davidson, et al., 2003; Creswell, et al., 2007; Newberg, et al., 2001).

Further limitations include the lack of baseline or control groups as this experiment emerged from a campus-based mindfulness initiative. Conclusions about the causality of MM in regards to its effects on CI require a comparison group. Future studies should also include accurate measures of practice duration and frequency required to evoke a change in CSP modulation (dose-response), such as in the form of shorter and longer meditation sessions (i.e., 10, 20, 40, and 60 minute sessions).

Although a sample of 67 is relatively high for a TMS study on CI, the sample characteristics are not ideal as it was conducted through convenience sampling. Generalizations to university populations, with predominantly White and South Asian ethnicities, and an educational focus on the sciences, prevents conclusions from being made to the general population. There is also a moderate bias towards sampling females. Furthermore, participants were recruited with the knowledge that they would be included in a study on meditation, allowing for a selection bias and leaving out those who may have a disinterest in the practice. This therefore limits the conclusions regarding *anyone* with limited meditation experience to be able to affect their GABAergic activity as effort, motivation, and interest may have played a part.

In conclusion, the findings herein suggest that a single 40 minutes session of guided MM is correlated with increases in CSP in an inexperienced group of university students, suggesting an increased GABAergic tone in the motor cortex. Changes were significant among those who were naïve to the practice, but not those who had been previously exposed and were novices. Lastly, negative automatic thoughts were negatively correlated with increases in CSP in our sample, suggesting a facet of the cognitive mechanism associated with the neurophysiological benefits of practicing MM. As these results are limited in the above mentioned regards, it is important to refrain from over-generalizations. The stigma associating MM with less conventional treatments is beginning to diminish. This is evidenced by the impact of recent publications and its incorporation into hospitals, possibly signalling a trend for MM becoming more 'mainstream' instead of an exclusively 'alternative' treatment. With cautious optimism, we call for more research using controlled designs with rigorous experimentation and shrewd interpretation to conservatively maximize any potential benefit and effectively minimize any possible harm.

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Appendix

The Automatic Thoughts Questionnaire (ATQ; Hollon and Kendall, 1980)

Instructions: Listed below are a variety of thoughts that pop into people's heads. Please read each thought and indicate how frequently, if at all, the thought occurred to you over the last week. Please read each item carefully and fill in the appropriate answer in the following fashion:

1 = Not at all
2 = Sometimes
3 = Moderately often
4 = Often
5 = All the time

	1	2	3	4	5	Prefer not to answer
1. I feel like I'm up against the world	☐	☐	☐	☐	☐	☐
2. I'm no good	☐	☐	☐	☐	☐	☐
3. Why can't I ever succeed?	☐	☐	☐	☐	☐	☐
4. No one understands me	☐	☐	☐	☐	☐	☐
5. I've let people down	☐	☐	☐	☐	☐	☐
6. I don't think I can go on	☐	☐	☐	☐	☐	☐
7. I wish I were a better person	☐	☐	☐	☐	☐	☐
8. I'm so weak	☐	☐	☐	☐	☐	☐
9. My life's not going the way I want it to go	☐	☐	☐	☐	☐	☐
10. I'm so disappointed in myself	☐	☐	☐	☐	☐	☐
11. Nothing feels good anymore	☐	☐	☐	☐	☐	☐
12. I can't stand this anymore	☐	☐	☐	☐	☐	☐
13. I can't get started	☐	☐	☐	☐	☐	☐
14. What's wrong with me?	☐	☐	☐	☐	☐	☐
15. I wish I were somewhere else	☐	☐	☐	☐	☐	☐
16. I can't get things together	☐	☐	☐	☐	☐	☐
17. I hate myself	☐	☐	☐	☐	☐	☐
18. I'm worthless	☐	☐	☐	☐	☐	☐
19. I wish I could just disappear	☐	☐	☐	☐	☐	☐
20. What's the matter with me?	☐	☐	☐	☐	☐	☐

	1	2	3	4	5	Prefer not to answer
21. I'm a loser						
22. My life is a mess						
23. I'm a failure						
24. I'll never make it						
25. I feel so helpless						
26. Something has to change						