

The Determinants of Reaction Times: Influence of Stimulus Intensity

by

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A thesis

presented to the University of Waterloo

in fulfilment of the

thesis requirement for the degree of

Master of Science

in

Kinesiology

Waterloo, Ontario, Canada, 2015

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AUTHOR'S DECLARATION

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

I understand that my thesis may be made electronically available to the public.

Scott Theodore Janssen

ABSTRACT

The central nervous system has the ability to generate very rapid ‘temporally urgent’ sensory motor reactions in response to stimuli under certain conditions. For example, temporally urgent reactions have been shown to occur during control of protective responses, such as regaining balance after a perturbation or reacting rapidly to a startling auditory stimulus. Two different mechanisms have been proposed to the observation of rapid reaction times; 1) different (shorter) pathway for those reactions with very rapid reactions and/or 2) increased synaptic excitability to reduce the time required at each site of synaptic convergence leading to a reduction in total reaction time. The overarching hypothesis of this work is that the occurrence of rapid reactions is mediated by the facilitation of pathways through stimulus driven and/or central facilitation leading to significant reduction in reaction time. The current work is delimited to a focus on the determinants of reaction time in response to auditory stimuli. Two studies were conducted to determine the relationship between stimulus intensity and behavioural and neurological responses. Study one focused on influence of stimulus intensity on simple and choice reaction time performance. Choice reaction time is distinguished by need for higher level cortical processing for decision making. Stimulus induced changes in choice reaction time would be most likely accounted for by pathway facilitation. Results from study one showed an overall decrease in choice reaction time to an increase in stimulus intensity with no difference in errors suggesting an increase in stimulus intensity results in increase synaptic facilitation. Study two focused on electrophysiological events associated with auditory stimuli. It was proposed that evidence of more rapid electrophysiological events and increased amplitude would support a model of synaptic facilitation with increases in auditory stimulus intensity. Results from study

two showed decreased peak latencies with high stimulus amplitudes as well as increased cortical activity prior to motor responses further suggesting reductions in reaction time to increases in stimulus intensity are a result of increased synaptic facilitation. Overall this thesis is focussed on developing a further understanding of stimulus intensity as a determinant of reaction time so that in the future one may better understand the factors that contribute to slowing in older adults and those with neurological impairment.

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Dr. Bill McIlroy, for his guidance and wisdom throughout the completion of this thesis as well as my committee members for their insight. Thanks to all the members of the NiMBaL lab for all their great support, ideas, and friendship. Thank you to my family back home, for their loving support and everyone else who helped along the way.

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LIST OF ABBREVIATIONS

AEP	Auditory Evoked Potential
ANS	Autonomic Nervous System
CNS	Central Nervous System
CRT	Choice Reaction Time
EEG	Electroencephalography
EMG	Electromyography
ERP	Event Related Potential
GSR	Galvanic Skin Response
LATER	Linear Approach to Threshold with Ergodic Rate
LC	Locus Coeruleus
PET	Positron Emission Tomography
TA	Tibialis Anterior
TMS	Transcranial Magnetic Stimulation

CHAPTER 1: BACKGROUND

1.1 Rationale & Importance of Rapid Reactions

The ability to monitor, identify, process and rapidly respond to an unpredictable environment is an important aspect of natural behaviour. Healthy individuals are proficient at generating appropriate, rapid responses in response to stimuli associated with potentially dangerous situations. These responses are referred to as temporally urgent reactions (Lakhani et al. 2010) and are characterized by the ability to generate an extremely rapid and spatially precise movement in the face of urgency. Examples include corrective reactions to maintain balance, protective reactions when driving or in the event of a potentially harmful stimuli.

Healthy individuals can elicit responses with very rapid reaction times while still maintaining superior motor control such as those associated with balance control (Maki & Whitelaw, 1993; Carpenter et al., 2004; Coombes et al., 2009a). Unexpected balance perturbations are perhaps the most reliable and complex examples of controlled rapid responses. Experimentally investigated in both the upper and lower limb, whole-body balance perturbations generate onset latencies as low as 90ms while still maintaining control and adapting to the surrounding environment (Maki & McIlroy, 1997; Maki et al., 2001; Maki & McIlroy, 2006). The combination of complexity of the control and still very rapid reactions is highlighted from the control of reach to grasp reactions (van Ooteghem et al. 2014; Gage et al. 2009).

However such temporally urgent reactions are not only evident in balance control reactions. Another example of temporal urgent reactions is response to high intensity auditory stimuli, also known as the “startle” response. The startle response is elicited following presentation of an unexpected intense auditory stimulus (Valls-Solle et al., 1995; 1999; Davis 1984). With onset latencies comparable to balance perturbations, many authors argue that the

neurological processing of the startle response uses a shorter, subcortical pathway to achieve shorter latencies.

In situations requiring temporal urgency, appropriate responses are vital to ensure the safety of the individual as well as others. However, the ability to generate such rapid reactions can become impaired and delayed with aging (Spirduso, 1980; Kail, 1986; Salthouse, 2000; Kolev et al., 2006) or neurological deficits and injuries (Fridman et al., 2004; Miller, 1970; Stuss et al., 1989; Kaizer et al., 1988; Kurtzer et al., 2013). Although the importance of these reactions is paramount in the safety in these susceptible populations, little is currently understood regarding the neurological mechanisms that result in delayed reactions or rapid reactions associated with healthy adults. The overarching goal is to identify features of both the stimulus and the CNS network that may influence speed of processing. Of specific focus in the present study is the reaction time to auditory stimuli. In the current study auditory stimulus were used to probe factors that influence reaction times with a specific focus on the influence of intensity of stimulation. This is specifically interesting due to the link between high intensity stimulus and very fast reactions (startle responses) (Valls-Solé et al., 1995; Carlsen et al., 2004; 2007). The focus of the current work is to explore the link between stimulus intensity and reaction time to afford insight into the possible factors that determine CNS processing.

In summary, there are times when there is a need to perform reactions to stimuli very rapidly and preserve a high level of control. What remains unclear is the mechanisms by which the CNS is able to preserve such rapid reactions and control. While the long term application will be to focus on temporally urgent reactions in naturally occurring behaviours, the current study is delimited to a focus on better understanding the determinants of speeded reactions

within the CNS. More specifically the current work will focus on auditory evoked reactions and advancing understanding of the specific potential for reducing reaction times.

1.2 Reaction Time Definition

The reaction time method has been used extensively since the mid-nineteenth century in the investigation of speed of processing (Donders, 1969). Reaction time (or premotor time) is the central processing time between the stimulus and onset of a reaction (Donders, 1969; Sternberg, 1969). It is measured as the amount of time elapsed between the presentation of a stimulus and the onset of a response. In contrast, response time reflects the time between onset of stimulus and the completion of the associated movement and movement time is the duration of the movement phase of a response. There does exist some confusion that revolves around the measurement of reaction time. Ideally the onset of reaction is measured as the onset of muscle activity (measured using electromyography). However, many studies rely on the onset of movement (eg button press) or force change. Such measures, while estimating reaction time, actually include delays associated with time to generate force (including electromechanical delay time) (Cavanagh & Komi, 1979). For the specific purpose of this study, and consistent with the formal definition of reaction time (Donders, 1969; Sternberg, 1969), the term reaction time is specially associated with the CNS processing times as measured from onset of stimulus to the onset of muscle activity.

When delimited to time between stimulus onset and onset of electrical activity of muscle, the elements that contribute to reaction time include: 1) sensory activation, 2) conduction times and 3) synaptic delays. When using a suprathreshold stimulus intensity, and maximizing time to activate sensory receptors, the dominant contributions to reaction time are: 1) conduction times

(axon distance x conduction velocities) and 2) synapse time (number of synapses and synaptic delay time). Arguably, in spite of differences in conduction velocities, these likely remain relatively constant across specific reaction time studies relying on similar sensory/motor pathways. For example the large myelinated median nerve has been shown to travel between 50-60 metres/sec for both sensory inputs and motor outputs (Letz & Gerr, 1994). As a result, the main factors that will contribute to changes in reaction time are: 1) path length (axon lengths and number of synapses) and 2) synapse delay.

1.2.1 Simple Reaction Time

A simple reaction time task requires a single response from a single stimulus. The simplicity of a simple reaction time task allows the response to be programmed prior to the onset of the stimulus with fewer processes taking place between the stimulus presentation and the onset of the response (Klapp, 1996). Therefore the processing that takes place during a simple reaction time task include: 1) identification of the stimulus and 2) preprogrammed response execution. More complex tasks have been associated with longer reaction times, thus it has been suggested that more complex tasks require longer processing times leading to increased reaction times (Henry & Rogers, 1960).

1.2.2 Choice Reaction Time

In a choice reaction time paradigm, the neurological processes that take place are more complex than a simple reaction time paradigm. Before a response is produced, there is a greater demand on CNS processing that necessarily increases the reaction time. These processes have

been summarized into 3 unique stages: stimulus identification, response selection and response programming (Schmidt & Lee, 1999).

1.2.2.1 Stimulus Identification

Donders (1969) was among the first to investigate the time course of each stage of choice reaction time that he believed to be independent of one another and to occur in a specific order. To accomplish this, he would design 3 different reaction time tasks. The A-Reaction was a simple reaction time task involving a single response (pressing a key), upon the presentation of a single stimulus (a light). The B-Reaction was a choice reaction time task requiring a different response (pressing a key with the right hand versus the left hand) to the presentation of 2 different stimuli (a red light versus a blue light). Finally the C-Reaction was a go/no-go task in which the single response key press was required, but still involved 2 separate stimuli (red light = press key, blue light = do not press key). The argument being that the differences between these reaction time tasks reflect the differences in the serial components of speed of processing. The results indicated that choice reactions require complex cognitive processing. In a simple reaction time task there is little to no response selection required due to the one possible response. Furthermore, pre-programming could take place prior to the stimulus presentation and therefore executed in advance. Thus, stimulus identification is the only reaction time process required.

When a reaction time task involves more than one response the individual must select the correct response. Since the appropriate response is not known in advance, extra processing time is required and therefore the response must be selected and programmed following the stimulus

identification. In other words, in a choice reaction situation the response selection processes and response programming process must take place within the reaction time interval.

1.2.2.2 Response Selection

In a choice reaction time paradigm, more response selections exist. Reaction time intervals are thought to increase in a choice reaction time paradigm owing to the need to discriminate between the correct response and any incorrect responses. In Hick's (1952) study participants reacted to the lighting of pea lamps by pressing corresponding keys. The number of choices was manipulated by both increasing in a regular manner as well as randomizing numbers of choice alternatives. The results showed that as the number of response alternatives increased so too did reaction time. However, the increase seen was not linear, but in fact logarithmic. Each time the number of response alternatives double, reaction time increased by a relatively constant amount (~150 ms). Hick suggested that the Log_2 of the number of response alternatives represented the number of "bits" of information that need to be coded within the reaction time interval before the response is carried out with each bit representing a constant amount of time. Therefore, each time a new "bit" of information is added a constant amount of extra processing time is required to solve the motor problem. This evidence supports that in a choice reaction time paradigm, central processing is required to select the correct response within the reaction time interval.

Schluter et al. (1998) studied the cortical components of choice reactions and found that transcranial magnetic stimulation (TMS) was effective in interfering with the response selection process in a visual choice reaction time task. In a series of 3 experiments, TMS was applied over primary motor cortex, premotor cortex and primary somatosensory motor cortex at varying

latencies following the visual stimulus. The first experiment explored the contralateral stimulation during a choice reaction time task and found that stimulation of the dorsal premotor cortex, 140 ms after the visual cue, was effective in delaying the response. Furthermore, primary motor cortex stimulation was also effective at delaying the response, albeit at longer latencies (Schluter et al., 1998). The author suggests that the delays in motor response from TMS are due to interference with the response selection process. The second experiment used the same protocol as the first, however this time using the ipsilateral side from the response hand. Results showed that only stimulation over the left premotor cortex was effective at delaying response time while right side stimulation had no effect. Therefore TMS stimulation over the left premotor cortex interfered with response times on both the right and left sides. The final experiment used TMS stimulation of the ipsilateral premotor cortex during both simple and choice reaction time tasks. Results again showed that stimulation over the left premotor cortex at 100 ms following the visual stimulus was effective at delaying response times in the choice reaction time task. Furthermore, TMS stimulation had no effect on delaying the simple reaction time task. Thus, it was concluded that the left premotor cortex plays a dominant role in response selection (Schluter et al., 1998).

Positron emission tomography (PET) was then used to study the cortical dominance in response selection (Schluter et al., 2001). Participants performed a simple or choice reaction time task and PET scans were observed. Results showed significantly more activity in the left prefrontal, premotor and intraparietal areas during the choice reaction time task, regardless of which hand was used to respond (Schulter et al. 2001). These findings support the earlier work that TMS disrupts response selection in a choice reaction time task when applied over the left premotor cortex (Schulter et al. 1998). The authors suggest that in order to complete the choice

reaction time task, participants must visually discriminate between the various stimuli and select the appropriate response. Furthermore, because left premotor and parietal areas were unlikely to be involved in visual discrimination, response selection was concluded as the reason for the activation (Schulter et al. 2001). Evidence suggests that response selection is a cortical event occurring in higher order neural centres within the reaction time interval.

1.2.2.3 Response Programming

In a simple reaction time task the response is known in advance and therefore can be preprogrammed prior to the stimulus presentation. Contrary, in tasks requiring a response not known before hand, such as a choice reaction time paradigm, the response cannot be programmed in advance of the stimulus. Therefore, in a choice reaction time paradigm the programming of an appropriate response must take place within the reaction time interval. Previous literature has shown that more complex responses lead to longer reaction time intervals (Klapp, 1996). In a task involving the pronunciation of either one syllable or two syllable words, reaction time proved significantly longer for words containing two syllables. This occurred because the appropriate response was not known before hand and programming was not possible until after the stimulus was presented. The more complex responses take longer to program (Henry & Rogers, 1960) and therefore lead to longer reaction times (Klapp, 1996). Because response complexity had no effect on simple reaction time (Klapp, 1996), it was argued that the response could be preprogrammed in advance. A choice reaction time cannot be preprogrammed in advance and the increase in the reaction time interval can be attributed to the motor programming stage of the 3-stage model of information processing.

1.3 Determinants of Reaction Time Latency

Humans have the ability to evoke very fast reactions under some conditions. Lakhani (2013) demonstrated that whole body balance perturbations can generate upper limb onset latencies of approximately 157 ms. These trials were paired with a 60 dB auditory tone and after only conditioning with 20 paired stimulus trials, participant's executed the task with the same onset latencies as the auditory tone. Both intensity and stimulus modality where changed following the paired trials and the participants were still able to maintain the perturbation latencies. This raises the question, what are the CNS mechanisms responsible for such rapid reaction time latencies?

There are an extensive number of potential modifiers that can affect reaction time including gender (Der & Deary, 2006), physical fitness (Spirduso, 1980; Bunce et al., 1993); Davranche et al., 2006), fatigue (Welford & Brebner, 1980), practice (Klapp, 1995; Mowbray & Rhoades, 1959) and limb dominance (Dane & Erzurumluoglu, 2003). However, these modifiers have been unable to demonstrate the significance reductions in reaction time as those associated with temporally urgent reactions. The factors cited below have shown the ability to reduce the reaction time latencies significantly and may be primarily involved in the control of temporally urgent reactions.

1.3.1 Stimulus Characteristics

There are 3 primary modalities used for sensorimotor integration with reaction times differing based on the anatomy of entering the sensory organ and being coded by the appropriate neurological area. Auditory stimuli tend to evoke the quickest responses at 140-160ms, followed

by somatosensory sensory stimuli at 150-160ms and then visual stimuli at 180-200ms (Galton, 1890).

Stimulus intensity has been revealed as a strong modulator of reactions time. As the intensity of the stimulus increases the response latencies will decrease (Woodworth, 1935). This trend has been expressed in auditory (Carlsen et al., 2007), visual (Bell et al., 2006; Carreiro et al., 2011) and somatosensory (Grisolia & Wiederholt, 1980; Huttunen, 1995). Furthermore, a stimulus that is perceived as threatening (ie extreme intensity), such as the reactions seen in compensatory balance reactions to prevent a fall, has a profound effect on reaction time (Lakhani et al., 2011). Carlsen et al. (2004) have divided sensorimotor processing time into pre-motor and motor reaction times finding that pre-motor reaction time is significantly reduced at extreme auditory stimulus intensity, while reaction time remains unchanged. This suggests that sensory information and cortical areas may play an important role in integration of stimulus intensity to produce a motor command.

1.3.2 Arousal

In situations that are perceived as threatening, higher cortical centres seem to have a greater involvement in the control of movement (Llewellyn et al., 1990). Measurements of galvanic skin response (GSR) during balance perturbation trials vary based on amplitude and complexity (Sibley et al., 2010a). GSR is a research tool used to measure arousal levels quantifying the skins sweat response in response to a given stimuli. It is typically measured on the middle phalynx of the 3rd and 4th digits but can be recorded from the toes. However, causality between GSR and threatening stimuli has not been demonstrated. One hypothesis is autonomic nervous system pathways could provide a neurological representation of stimulus

characteristics in addition to being processed by sensory systems (Sibley et al., 2010b).

Conversely, high amplitude GSR output following a balance perturbation task may be caused by the unexpected stimulus and represent an error signal. Further research is required regarding the causal effect between autonomic nervous system pathways and sensory motor processing.

1.3.3 Attention

Attention, functionally described as “the preferential allocation of processing resources to signals and signal domains that pertain most strongly to the goals of the system,” is a complicated factor of reaction time (Posner, 2011). In reaction time studies, attention has been divided into 2 aspects; involuntary attention and voluntary attention (Wundt, 1897; Posner et al., 1980). Involuntary attention refers to an automatic response regardless of the correct predicted outcome, whereas voluntary attention refers to the optimal allocation of sensory inputs to correctly predict a task outcome (Prinzmetal et al., 2005). Research has demonstrated that reaction time latencies are significantly reduced when participants are aware of a visual stimuli location (Posner et al., 1980). Although reaction time could be reduced with elevated attention, accuracy could remain constant, thus focused attention may have the ability to undermine the speed-accuracy trade-off, a feature uniquely demonstrated in situations requiring rapid responses.

1.3.4 Pre-cueing

An individual’s reaction time is significantly reduced with the ability to anticipate an incoming stimulus. However, ‘real world’ scenarios requiring rapid reactions, such as a slip and fall, may not provide the external cues necessary for anticipation of an impending stimulus. Nevertheless, laboratory experiments have revealed a significant level of pre-stimulus cortical

activity when the participants are able to predict a stimulus (Nachev et al. 2008; Mochizuki et al., 2009). However, if the timing of an impending stimulus was known in a choice reaction time task, the individual would still be able to produce a rapid response, but would only be correct in their choice 50% of the time (Frith & Done, 1986). This finding suggests that prior warning of a stimulus only appears to be useful in a lab setting and may not be applicable to the environmental stimuli of the 'real world'.

1.4 General Model of Rapid Reactions

Currently, theoretical models exist to explain the mechanisms responsible for assessing sensory information and selecting an appropriate response within a reasonable timeframe. Of particular interest are models that reduce reaction times in the presence of a stimulus requiring temporal urgency. There are 2 possible ways to accelerate reaction time within the central nervous system; 1) complete the reaction using a shorter pathway or 2) augment the processing time within existing pathways (see Figure 1-1).

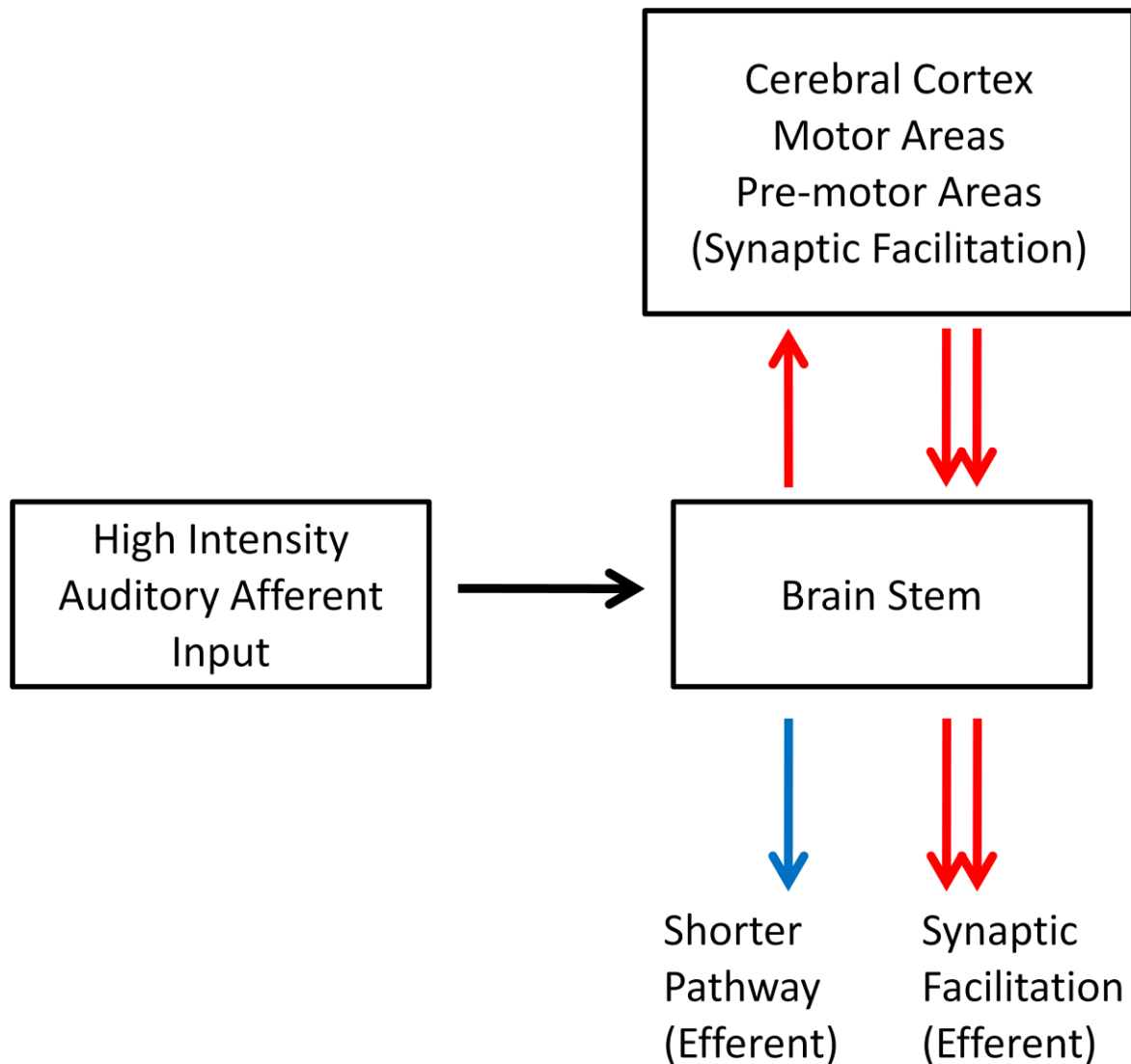


Figure 1-1: Pathway selection versus synaptic facilitation theoretical model. Speed of processing can increase at high auditory stimulus intensities in one of 2 ways. Auditory afferents travel to the brainstem and can either: 1) activate descending motor pathway nuclei resulting in a shorter pathway (BLUE) or 2) travel to cerebral motor and pre-motor areas where synaptic facilitation results in faster efferent outputs (RED).

1.4.1 Pathway Length

In the presence of urgency, the CNS must utilize a network of processing centres to efficiently and safely produce appropriate movements. One possible solution for completing these movements is to rely on a different movement pathway and utilize a shorter pathway to

complete these movements. A shorter neurological pathway equates to faster processing time which may explain the decrease in response latency. This is well demonstrated by the latency of different responses evoked by muscle stretch. Stretch reflex applied to ankle dorsiflexors elicit 3 separate bursts of activity (labelled M1, M2 and M3) that had average onset latencies of 44, 69 and 95 ms (Petersen et al., 1998). The M1 burst of activity reflects the short spinal monosynaptic stretch reflex, while the M3 represents the much longer polysynaptic transcortical processing revealing the relationship between latency and pathway length and number of synapses.

The startle response has been hypothesized to be a protective response consisting of a characteristic set on muscle actions in response to a sudden intense stimulus (Davis, 1984; Yeomans & Frankland, 1996). Moreover, an unexpected acoustic, tactile or vestibular stimulus (Scott et al., 1999; Yeomans & Frankland, 1996) leads to a general flexion response in mammals, although antagonistic extensor contraction has also been observed (Brown et al., 1991a). The startle response also consists of an increase in central nervous system and autonomic nervous system activity (Thackray, 1972). Several authors suggest that reactions to startling auditory stimuli utilize a shorter, subcortical pathway (Carlsen et al., 2004). Evidence suggests that processing of intense auditory stimuli activates the midbrain reticular formation which is able to access a motor program that has been prepared for the volitional act (eg. Simple reaction) and triggers it without control from higher cortical structures (Davis et al., 1982). In this way it has been proposed that it is possible to evoke very rapid pre-planned reactions using startle-like stimulus.

1.4.2 Pathway Facilitation to Augment Processing Speed

However, just as there is evidence of different latencies for different pathways there is also considerable evidence for the influence of synaptic modulation to influence reaction time. Assuming that such a high degree of sophisticated movement execution in response to complex stimuli (eg choice reactions) requires high-level processing, then increasing the speed of processing would require facilitation inputs along the synapses of the existing pathway. Augmented processing is described in the linear approach to threshold with ergodic rate (LATER) model (Reddi & Carpenter, 2000). The model states that for any given reaction there is a decision signal that rises at a linear rate. The rate at which the signal rises represents the rate of neuronal firing that when altered, changes the speed of the reaction. Both the baseline neuronal activity and the rate of neuronal information have an impact on reaction time.

One of the main hypotheses for influencing pathway facilitation is the autonomic nervous system (Sibley et al. 2014). Several studies have demonstrated elevated levels of galvanic skin response (GSR) activity, used as a proxy of autonomic nervous system activity, following high intensity somatosensory stimuli (ex balance disturbance) (Maki & Whitelaw, 1993; Maki & McIlroy, 1996; Adkin et al., 2002; Sibley et al., 2008; 2009; Lakhani et al., 2013). These studies provide evidence indicating that the ANS likely assists in the generation of reactions to high intensity stimuli. Furthermore, it is evident that these high intensity balance reactions require cortical contributions (Maki et al., 2001; Sibley et al., 2008; 2009; Lakhani et al., 2011; 2012; 2013), therefore influences from the ANS likely take place at the synaptic level.

Stimulus anticipation can influence baseline neural activity and thus a profound effect on reaction time (Carpenter & Williams, 1995). Furthermore, in decision making tasks, evidence had shown a build-up of neural activity prior to the movement in cortical areas, including the

lateral intraparietal area (Roitman & Shadlen, 2002) and the prefrontal cortex (Kim & Shadlen, 1999). The LATER model identifies baseline neural activity and rate of information accumulation as important factors that influence reaction time that may contribute to reduced processing time in existing processing pathways.

Stimulus context has also been known to influence reaction time. Reduced reaction times have been identified following presentation of fear inducing visual stimuli (Hajcak et al., 2007; Coombes et al., 2009b; Finucane & Power, 2010). The authors hypothesize that cortical structures may focus attention on the fear induced stimuli as well as block out irrelevant information in order to generate a faster response.

1.4.3 Stimulus Intensity

Stimulus intensity has long been known to reduce reaction time. Simple reaction time has been revealed to decrease as stimulus intensity increases (Pins & Bonnet, 1996). It has been suggested that visual processing of intensity is independent of more complex neural processing and rapid latencies could be generated in a choice reaction time task. Evidence supports the idea that reaction time is a function of stimulus intensity regardless of task complexity (Pins & Bonnet, 1996).

Lakhani et al. (2013) suggested that the very rapid reactions associated with perturbation were associated with stimulus intensity, proposing that a balance perturbation represents very large volume of somatosensory drive. In contrast studies that focus on simple reaction times have suggested the CNS utilizes an independent, subcortical pathway to generate a pre-planned motor response, contributing to the shorter onset latency (Valls-Sole et al. 1999; 2008; Carlsen et al., 2007). However, others have demonstrated the critical involvement of the cortex within

temporally urgent reactions (Bolton et al., 2012; Lakhani et al., 2012; 2014; Dietz & Berger, 1984; Dietz et al., 1985; Ackermann et al., 1986; Quant et al., 2004).

Lakhani et al. (2011) conducted an experiment to test the underlying control of compensatory and voluntary reach-to-grasp reactions. Participants responded to both whole body balance perturbations and 60 dB auditory tones in 3 different conditions. After presentation of either a balance disturbance or auditory tone participants would 1) reach-to-grasp to a fixed handle providing balance recovery, 2) reach-to-grasp to a free handle that was movement relevant but consequence irrelevant, or 3) plantar flex, which provided no balance recovery. Results showed no difference in reaction times across task conditions. The only significant difference was the reaction times between the auditory tone (190 – 210 ms) and the balance perturbation (90 – 100 ms). These results suggest that the stimulus characteristics, rather than the motor actions, are driving the speed of process (Lakhani et al., 2011). However, there are two differences in the stimulus characteristics: 1) stimulus modality and 2) stimulus intensity. Therefore the following studies will focus on auditory stimuli.

1.5 Auditory Reactions

As previously mentioned, the focus of this thesis will be on reactions to auditory stimuli, specifically with respect to the influence of stimulus intensity on speed of processing. Evidence that suggests that very intense auditory stimuli lead to a startle response, of which the onset latencies appear to be elicited distinctly faster than lower intensity stimuli (Carlsen et al., 2004). This capacity to rapidly increase simple reaction time by simply altering the intensity of stimulation provides an intriguing model to explore the generalizability of this phenomenon. Additionally, auditory stimuli allows for precise control over the stimulus properties including

intensity level (ie. dB level) and frequency (Hz) while still being able to achieve intensities utilized in the startle response.

1.5.1 Auditory Processing

Sound is produced when surround air pressure changes, causing vibrations that can be transduced into neural impulses by the hair cells of the inner ear. This sound information, including amplitude and frequency are then transferred via neural connections to the primary auditory cortex (Kelly, 1991). The human ear is sensitive to sound frequencies from 20 Hz to 20000 Hz. Furthermore, the amplitude of sound frequencies, measured in decibels (dB), is related to a specific reference pressure (Kelly, 1991). For reference, normal human conversation is about 60 dB, while a siren is 120 dB and a jet engine or firearm is 140 dB (American Speech-Language-Hearing Association).

Sound waves travel through the auditory canal and cause the tympanic membrane (eardrum) to oscillate. The oscillation is then transmitted to the inner ear via the auditory ossicles. The auditory ossicles are made up of three small bones; the malleus, the incus and the stapes. The stapes makes contact with the oval window of the cochlea and transmits the oscillations of the sound waves to the cochlea's fluid filled compartments. The fluid waves throughout the cochlea and causes movement of the basilar membrane and the organ of Corti, the apparatus used for sensory transduction (Kelly, 1991).

The sensory receptors of the inner ear, hair cells, are facilitated or inhibited with movement of the basilar membrane. Movement of the organ of Corti with respect to the overlying tectorial membrane results in mechanical bending of the stereocilia, mobile region of the hair cell, with respect to the body of the hair cell. Bending of the stereocila in one direction

results in depolarization of the cell and increased release of neurotransmitter, while bending in the other direction leads to hyperpolarization of the cell and a decreased release of neurotransmitter (Kelly, 1991). The cochlea portion of the vestibulocochlear nerve, made up of spiral ganglion cells fire in response to neurotransmitter release from the hair cells. Thus, oscillations in the cochlea and basil membrane lead to hair cell oscillations, which cause the oscillatory neurotransmitter release and ultimately oscillatory firing of the vestibulochochlear nerve. The amplitude of the sound wave (ie loudness) is coded from the firing rate of the hair cell neurons (Kelly, 1991).

The central auditory pathway begins from the projections of the eighth cranial nerve that terminate in the ventral cochlear nucleus in the brainstem at the level of the medulla (Kelly, 1991; Yeomans & Frankland, 1996). Some neurons from the cochlear nucleus will project bilaterally to the superior olivary nuclei (one on each side of the brainstem), which include information on sound localization. Axons then project bilaterally to the inferior colliculus of the midbrain, via the lateral lemniscus pathway, where they will join direct projections from the cochlear nuclei. Postsynaptic cells of the inferior colliculus project ipsilaterally to the medial geniculate nucleus of the thalamus. These neurons will then project and terminate in the ipsilateral primary auditory cortex (Kelly, 1991). Evoked potential experiments have suggested that the neural signaling produced from an auditory stimulus reaches the primary auditory cortex with a latency of about 35ms (Erwin & Bushwald, 1986).

1.5.2 The Acoustic Startle Response

As noted the startle response has been hypothesized to be a protective response consisting of a characteristic set of muscle actions in response to a sudden intense stimulus (Davis, 1984; Yeomans & Frankland, 1996).

In experimental conditions a fine balance must be struck between using a sufficiently intense stimulus to elicit a startle response and minimizing the risk of damage to the auditory sensory apparatus of the participant. Many studies have had success eliciting a startle response utilizing a stimulus between 115 and 130 dB (Abel et al., 1998; Brown et al., 1991a; Valls-Sole et al., 1999). However, prolonged exposure to sound levels above 120 dB is cautioned against by authors. Evidence also suggests that startle can be elicited at all frequencies in the audible range (Pilz, Schnitzler & Menne, 1987) it is argued that the frequency of the startle stimulus is not a critical consideration (Li & Yeomans 1999).

Electromyography (EMG) is the primary measurement of startle response due to the reliability of the response (Brown et al., 1991a) and the practicality of the method (Jones & Kennedy, 1951). Brown et al. (1991a) found that muscle activity in the orbicularis oculi (OOc) was always observed in response to the acoustic stimulus. EMG latencies increased with increasing segmental distance from the brainstem, with facial muscles being the first to activate, followed by neck, upper arm, lower arm, trunk and finally leg muscles (Brown et al. 1991a). Sternocleidomastoid (SCM) activity was the first EMG response after the eye blink, was found to be the most consistent after the eye blink and the last to disappear due to repeated startle stimulation (habituation) (Brown et al., 1991a).

The blink reflex has been seen as a response to loud auditory stimuli in many experiments (Blumenthal, 1996; Brown et al., 1991a; 1991b; Miwa, Nohara, Hotta, Shimo &

Amemiya, 1998; Saring & von Cramon, 1981; Valls-Sole et al., 1995; 1999) and therefore used as an indicator that startle has occurred (Blumenthal, 1996; Brown et al., 1991a; Valls-Sole et al., 1995; 1999). However, Brown et al. (1991a) demonstrated that the eye blink continued to occur even when the participants were no longer being startled and the EMG profile of OOc was much longer in duration when a true startle was elicited (prior to habituation) concluding that the 2 blink responses are physiologically separate.

The auditory blink reflex pathway is similar to the general auditory pathway described above. However, the auditory blink reflex deviates from the primary auditory pathway after the synapse in the inferior colliculus. Lesion studies have shown axons project from the inferior colliculus to the midbrain reticular formation (Hori, Yasuhara, Natio & Yasuahra, 1986). From the midbrain reticular formation, axons then synapse at the facial nucleus (Hienrichson & Watson, 1983; Hori et al., 1986) and then continue through the facial nerve (CN VII) to innervate OOc (Brown et al., 1991a).

Given the assumption that the acoustic blink reflex and the acoustic startle response are physiologically separate, the two reactions must also differ in neurological pathways (Brown et al. 1991a). In contrast to the midbrain reticular formation pathway described in the acoustic blink reflex, studies have reported that the pontine reticular formation is of central importance in the startle circuit (Davis, 1984). It is hypothesized that an acoustic startle stimulus is transduced by the ears and the signal is passed along 3 or more pathways. One pathway leads to the midbrain reticular formation which leads to a short latency blink reflex. A second pathway leads to the pontine reticular formation, which activates the neurons of the nucleus reticularis pontis caudalis (RPC), leading to a generalized startle response activating motor pathways. Muscle reactions occur at longer latencies as segmental distance from the brainstem

increases (Brown et al. 1991a). Furthermore, the cranial nerves are activated in a caudal to rostral direction, first activating SCM (CN XI), then activating OOc (CN VII), followed by activation of masseter (CN V) (Brown et al., 1991a). A third pathways with then follow the normal auditory pathway to the primary auditory cortex. Normal auditory processing to the primary auditory cortex has important implications within the following studies. The hypothesis is that afferent input from the auditory nerve follows the traditional auditory processing pathway, however, in order to increase reaction time the information is facilitated at the synaptic level further along the sensory motor pathway.

1.5.3 Factors Affecting the Acoustic Startle Response

In the previous section, the response effects of the acoustic startle response were discussed, yet there are many factors such as external environment and prior experience, which may affect the startle response. These may also lead to differences in startle response latency, amplitude or both. Some of these factors will be discussed below.

1.5.3.1 Habituation

Habituation to a startle stimulus involves a gradual decrease in response amplitude as exposure to the stimulus is repeated. With respect to EMG responses resulting from startling stimuli, habituation affects EMG amplitude, but does not affect EMG onset latency (Schicatano & Blumenthal, 1998). Many components of the startle response are no longer seen in humans after 2 to 6 random startle stimuli presentations, indicating that the participants eventually have no obvious response to the stimulus (Brown et al., 1991a). With repeated exposure the response

tends to decline in amplitude (Abel et al., 1998) and disappear in peripheral regions first (Davis & Heninger, 1972).

A reduction effect on habituation of the startle response was observed in participants who were prepared to react to a 'go' signal (Valls-Sole et al., 1997). Participants were exposed to startling stimuli in each of 4 different conditions; 1) resting quietly, 2) resting in a busy environment, 3) preparing to react in a reaction time task, or 4) focusing on an upcoming visual stimulus. Results showed that the rate of habituation was significantly decreased when participants were startled in conjunction with a visual 'go' signal in a reaction time task. In this condition, EMG amplitude in both the SCM and masseter muscles did not decrease below 60% of initial amplitude. Furthermore, all other conditions showed EMG amplitude falling below 20% of the initial values by the fifth presentation of the startle stimulus. The authors suggest that the focus of completing the motor task reduced the cortical inhibition of the startle response resulting in decreased habituation (Valls-Sole et al., 1997). Likewise, no habituation of the startle response was observed over 14 trials, in which a startling stimulus (124 dB) replaced the imperative stimulus in a reaction time task (Siegmund et al., 2001). No significant changes in muscle onset latency or amplitude were shown with repeated startling stimulus exposure. These results further support Valls-Sole et al. (1997) conclusion that readiness to perform a motor task is most likely the reason for decreased habituation (Siegmund et al., 2001).

1.5.3.2 Pre-pulse Inhibition

A pre-pulse, which is characterized as a small change in the sensory environment that precedes a startle inducing stimulus, has effects on the startle response. A short time frame pre-pulse (5-10ms) prior to the startle stimulus presentation has been shown to reduce startle

latencies (Graham, 1975). A pre-pulse at longer intervals (15 – 2000ms) prior to the startle stimulus has been shown to decrease startle amplitude, with a decaying effect as the pre-pulse interval lengthens (Graham, 1975). This type of modification has become known as pre-pulse inhibition (PPI) of startle (Davis, 1984; Hoffman, 1984; Lehmann et al., 1999). PPI has been suggested to reflect the ability of higher cortical areas to filter sensory information (Abel et al., 1998; Blumenthal, 1996; Zhang et al., 1998).

Conversely, evidence has shown that at pre-pulse latencies of greater than 2000ms, startle response latencies are reduced (Lipp et al., 2000). Furthermore, the effects can occur even when the sensory modalities of the pre-pulse and startle stimulus differ (e.g. visual pre-pulse followed by an auditory startle) (Lipp et al., 2000; Zhang et al., 1998). However, enhancement effects of a pre-pulse are most prominent when the pre-pulse and the startle occur within the same sensory modality (Balaban, Anothony & Graham, 1985). The implication of PPI to the current thesis is that the sensory environment must be kept sufficiently constant throughout all task conditions. Therefore, reaction times elicited are due to only properties of the presented stimulus.

1.5.3.3 Other Considerations

Although the major contributors to the differences seen in the startle response have been reviewed, there are several other factors that may interact in a complex way to influence the startle response. As complex interactions form between factors such as arousal levels, attention and environment, their individual contributions to influencing startle response latencies becomes less clear.

Several studies have investigated the possibility of gender differences in startle responses. Evidence from these studies however suggests that there is no difference in startle response latencies between sexes (Abel et al., 1998).

Although one might assume that as arousal increases, the startle response latencies would decrease accordingly, however the literature has shown that contradictory results (Davis, 1984). One method leading to increased levels of arousal is having participants ingest caffeine (Andrews et al., 1998). Startle response latencies have been revealed to be similar between subjects who were given caffeine and subjects given a placebo (Andrews et al., 1998; Schicatano & Blumenthal, 1998). However, what the currently literature has lacked and what the following studies will focus on is startling tones affect on arousal levels within the CNS.

Attention has also been shown to have an effect on the startle response. If attention is directed at a stimulus in the same modality as the startling stimulus, the startle response elicited results in a shorter latency, whereas attention directed towards a different sensory modality had no effect on the startle response (Richards, 2000). Furthermore, when subjects who were instructed to attend to a startle stimulus, a visual task, or given no instruction on attention allocation, results showed that only when attention was focus on the visual cue did the startle response have a longer latency, whereas no difference in latency was found between attending to the startle response or no instruction (Schicatano & Blumenthal, 1998). Participants in the following studies will not be instructed to allocate their attention to any particular stimulus.

Another factor that has been shown to have an effect on the startle response is the background noise in the external environment. When background noise was increased from 65 to 75 dB, the startle response increased however, startle response returned to baseline when background noise increased to 90 dB (Ison & Hammond, 1971). Therefore, the following

studies will ensure that background noise is kept at a constant level as to ensure consistent reaction time latencies.

1.6 Auditory Stimulus Intensity & Reaction Time

The relationship between auditory stimulus intensity and simple reaction time has been well established within the literature. As auditory stimulus intensity increases reaction time latencies decrease (Miller et al., 1999; Carlsen et al., 2007). Experiments regarding increases in decibel (dB) levels (30-90dB) can reduce reaction times (370-250ms, respectively) (Kohfeld, 1971).

Experiments involving pre-cueing have shown decreases in reaction time from approximately 120 to 100 ms when intensity was increased from 83 dB to 123 dB respectively (Carlsen et al., 2007). Although latencies within these experiments were much shorter, participants were aware and able to anticipate when the stimulus would be presented.

Although the relationship between simple reaction time and stimulus intensity has a well established reduction in latency to an increase in intensity, choice reaction time to auditory stimulus intensity has traditionally been overlooked, especially at high intensity levels. One experiment reported a reduction in choice response time from approximately 610 ms to 560 ms when auditory stimulus intensity was increased from 55 dB to 90 dB, respectively (Miller et al., 1999). Although a reduction in the reaction time latency may have taken place, a more comprehensive insight into choice reaction time is required, particularly evidence at higher stimulus intensities.

Choice reaction time has significant implications in determining how our CNS increases speed of processing to greater intensity stimuli. Choice reaction time requires response

programming in order to make the correct reaction (Klapp, 1996), whereas a pre-programmed response is provided to participants in simple reaction time tasks. Intuitively, we can assume that in order to make the correct response in a choice reaction time task the CNS must maintain following the same processing pathway regardless of intensity levels. Therefore, if we demonstrate the same decrease in reaction time to high intensity auditory stimuli (commonly seen in simple reaction time) in choice reaction, we will provide evidence of pathway facilitation at the synaptic level.

1.7 Cortical Activity Associated with Auditory Stimulation

Cortical potentials associated with auditory stimulus presentation are well documented within the literature. Early latency waves are present in the first 10 ms following the stimulus and include both receptor potentials from the cochlea and responses arising from the auditory nerve and low midbrain structures, whereas middle latency waves occur between 10 – 80 ms and are less mappable but are thought to include brainstem and thalamic potentials (Kraus & Nicol, 2009). However, the primary focus of electrophysiological correlates for this thesis will focus on the late latency auditory potentials.

Late latency auditory evoked potentials (AEPs) occur beyond 80 ms following the stimulus and are the first potentials associated with cortical activity and are larger in amplitude and lower in frequency relative to the early or middle latency waves (Kraus & Nicol, 2009). The relationship between auditory stimulus intensity and auditory potentials has not been extensively researched. However, studies have demonstrated larger N1 late latency amplitudes and slightly shorter N1 latencies to higher intensity tones (Picton et al., 1974; Jaskownki et al., 1994). However, research has been limited to auditory tones consisting of 100 dB or less. The focus of

this thesis will be on the shortened latency and increased amplitude of the N1 wave up to 120 dB to provided insight on pathway facilitation to high intensity auditory stimuli.

1.8 Relationship between Autonomic Nervous System & Reaction Time

Although there is no direct causation between the autonomic nervous system and reaction time there appears to be a definite association. When experimentally monitoring arousal levels within the CNS researchers use galvanic skin response (GSR) as a proxy measure of ANS activity (Sibley et al., 2014).

There are a number of studies indicating that the ANS likely assists in generating rapid reaction times associated with the high stimulus intensity of balance perturbations (Sibley et al., 2008; 2009). Previous work has also established that the GSR is a summation of both sensory inputs (i.e. a whole body balance disturbance) and motor outputs (i.e. reaching to grasp a handle) and that the amplitude of the GSR is severely attenuated if either the sensory or motor output is not present in the response (Sibley et al., 2009). Furthermore, it has been demonstrated that a large magnitude GSR can be temporarily evoked in the absence, but expectation, of the appropriate sensory input, indicating potential cognitive relationships to the GSR (Lakhani et al., 2013). Sibley et al. (2010b) demonstrated dissociation between the level of cortical excitability and GSR following whole body balance disturbances and concluded that although cortical and GSR response amplitudes are changed with the introduction of a perturbation, the variables may not be related. It is important to note that the long onset latency of the sweat response used to generate the GSR results in the inability to draw conclusions regarding the temporal profile of the GSR with respect to the latency of the EMG onset. However, it appears that the GSR can be

driven by the mere expectation of a temporally unpredictable high intensity stimulus, coupled with the initiation of the appropriate motor outflow.

This work with GSR has important implications to this thesis as we will only be focusing on one stimulus modality (auditory) and modifying stimulus intensity. GSR amplitudes to increasing auditory stimulus intensity are unknown and may provide insight into a possible mechanism for modulation of reaction times to increasing levels of stimulus intensities.

1.9 Study Objectives

The primary objective of this thesis is to determine the relationship between auditory stimulus and reaction time for simple and choice reaction times. The rationale was to provide insight into the potential mechanisms that may be associated with increased reactions times at very high stimulus intensities that may simulate temporally urgent conditions. The thesis focussed on two complementary studies to determine the relationship between stimulus intensity and reaction time reflecting facilitation of a 'common' pathway or, as proposed from the startle literature, reflected engagement of different neural pathways. The overall hypothesis is that the increasingly rapid reactions to auditory stimulus intensity, even within the range of acoustic startle, reflect facilitation of a common pathway rather than involvement of different pathways (e.g. cortical versus subcortical). The first study set out to determine if the well described relationship between auditory stimulus intensity and simple reaction time can be seen for choice reaction time tasks. It was proposed that if the effect of auditory intensity was facilitation of pathway excitability then the influence of reaction time should be common for both simple and choice reaction times. Since the latter are most likely cortically mediated it was proposed that such pathway excitability, and lower reaction times, should also be observed by increased

cortically activity to large amplitude auditory stimuli. As a result the second study adopted a complementary approach of measuring event related potentials during auditory evoked simple reaction time tests to determine if increased stimulus intensity was associate with change in latency and amplitude of cortical events that were likely mediating the sensory motor response. Collectively this thesis set out to provide evidence of pathway facilitation to an increase in stimulus intensity. A secondary objective for the two studies was to explore the possible association between stimulus intensity, autonomic nervous system activity and reaction time. Evidence of the autonomic nervous systems involvement in high intensity situations remains unclear (Lakhani et al. 2011; Sibley et al., 2008; 2009) but may provide a plausible rationale for facilitating speed of processing within the current CNS pathways, thus, the role of the autonomic nervous system in high intensity situations will be explored.

CHAPTER 2: REACTION TIME TO HIGH INTENSITY AUDITORY STIMULI: SIMPLE & CHOICE REACTION TIME

2.1 Introduction

Rapid reactions are required in everyday situations. For example, the reactions we make while driving to avoid accidents in the face of unexpected stimuli or the reactions that take place following a balance disturbance. These temporally urgent movements are executed with precise motor control and utilized to protect ourselves from harm. However, the ability to generate such rapid reactions can become impaired and delayed with aging (Spirduo, 1980; Kail, 1986; Salthouse, 2000; Kolev et al., 2006) or neurological deficits and injuries (Fridman et al., 2004; Miller, 1970; Stuss et al., 1989; Kaizer et al., 1988; Kurtzer et al., 2013). Despite the importance of temporally urgent reactions, little information is known about the underlying CNS mechanisms that are responsible for achieving such rapid motor latencies.

There are two primary ways that one can observe a faster response to a specific stimulus: 1) facilitate the speed of processing by reducing synaptic delays via facilitation of pathway CNS pathway with fewer synapses or 2) recruit a different pathway with shorter axon lengths and fewer synapses. For example, a wink and a blink are similar in their motor movement; however they require different neurological processing (Miles, 1931; Peterson, 1931).

One class of temporally urgent reactions is the acoustic startle response. The startle response has been hypothesized to be a protective response consisting of a characteristic set of muscle actions in response to a sudden intense stimulus (Davis, 1984; Yeomans & Frankland, 1996). Furthermore, it has been suggested that an unexpected startling acoustic stimulus activates pontine reticular formation nuclei leading to motor pathway activation and rapid onset latencies that increase as segmental distance from the brainstem increases (Brown et al., 1991a). A number of researchers have demonstrated reduced reaction time latencies in response to unexpected startling stimuli that significantly differ from non-threatening stimuli (Valls-Sole et

al. 1999; 2008; Carlsen et al., 2003; 2004; 2007). Under such an argument the rapid reactions associated with the startling stimulus are proposed to arise due to differences in pathway (brain stem path) as opposed simply facilitation of the pathway mediating any response to an auditory stimulus. The rationale for rapid reactions relying on a 'shorter' pathway merges from the historical reaction time data from visual or auditory stimuli which reveal much longer central processing delays for cortically mediated reactions (Brown et al., 1991a; Davis 1984).

In contrast there is an emerging body of literature that suggests even the most complex of sensorimotor processing involves a distributed network, including the cortex, that can be associated with very rapid reactions. For example, compensatory balance reactions, shows a profound decrease in reaction time onset latency (~90ms) to whole-body instability, compared to voluntary control triggered by a non-threatening stimulus (McIlroy & Maki, 1995b; Adamovich et al., 1997; Gage et al., 2007). These whole-body balance control reactions were shown to be every bit as sophisticated as voluntary control reactions, including movement characteristics and control challenges, and yet, were executed much faster. Because whole-body balance reactions are extremely complex it was hypothesized that this class of temporally urgent reactions requires cortical contributions. Similarly, studies looking at cortically mediated corrections to perturbations reveal very rapid reactions to stimuli in spite of the level and sophistication of processing (Nashed et al., 2014).

Recent evidence from Lakhani et al. (2012) suggests that the rapid reactions seen in whole-body balance reactions are not due to changes in somatosensory processing, but rather the motor output. Electroencephalography data shows increased motor potentials prior to the motor output of the participants following a balance perturbation (Lakhani et al. 2012). In a follow up study, using continuous theta burst stimulation, participants who attenuated to the stimulation

showed biologically significant increases in reaction time following high intensity median nerve stimulation (Lakhani et al. 2014). This evidence further supports the involvement of the motor cortex in response to high intensity somatosensory stimuli.

Although there is evidence to support both temporally urgent paradigms, the mechanisms are still debated. Do both classes of temporally urgent reactions use the same neural network? If so, does it represent a cortical or subcortical network? Or perhaps the acoustic startle response is a unique class of temporally urgent movements that appears to violate the traditional voluntary reaction paradigm.

The overarching purpose of this study is to determine if stimulus intensity similarly modulates the reaction time for both simple and choice reaction time conditions. Such evidence would indirectly support the idea that it is possible to achieve very rapid reactions through modulation of pathway excitability and cannot be simply associated with changes in the involved pathway (e.g. subcortical involvement). Current literature has shown as intensity of auditory stimuli increase, simple response latencies decrease (Carlsen et al., 2007). We will be using an auditory choice reaction time task, a task that requires cortical contributions (Donders, 1969), and modeling it against the simple reaction time task. Our primary hypothesis is choice reaction time will decrease, in the same fashion as simple reaction time, as stimulus intensity increases up to and including sound levels (~120 dB) that have been shown to evoke a startle response (Abel et al., 1998; Brown et al., 1991a; Valls-Sole et al., 1999). A secondary hypothesis is that the autonomic nervous system plays a role in the facilitation of these rapid reactions to each impending stimulus, thus galvanic skin response will be collected as a measurement of autonomic nervous system activity during the simple and choice reaction time tasks.

2.2 Methods

2.2.1 Participants

Twelve healthy adults (26 ± 5 ; 6 males; 6 females) participated in this study. None of the participants had any neurological, musculoskeletal or hearing impairment that may have affected their ability to complete all reaction time tasks. All participants provided informed consent and the study was approved by a research ethics committee at the University of Waterloo.

2.2.2 Protocol

Stimuli

Participants were instructed to “react as fast as possible” (in both the simple and choice reaction time tasks described below) upon detection of an auditory tone. The auditory stimulus consisted of 3 different intensity levels, 80 dB, 100 dB and 120 dB and 2 frequencies, one high (1000 Hz) and one low (700Hz). A custom LabView program generated the auditory tone and was then amplified using a Bryston ST series amplifier. After the signal was amplified, presentation occurred through a speaker located behind approximately 30 cm from the participant’s ears (posterior). The auditory stimuli intensities were measured using a precision level sound meter (B+K Precision Sound Level Meter).

Simple Reaction Time Task

During the simple reaction time task the participants responded with dorsiflexion of a single foot for the duration of the trials. One group of trials consisted of responding to the auditory tone of the lower frequency (700 Hz) and responding with only the left foot, while the other group consisted of responding to the auditory tone of the higher frequency (1000 Hz) and responding with only the right foot.

Choice Reaction Time Task

During the choice reaction time task the participants responded with dorsiflexion of the right or left foot, depending on the stimulus frequency. Participants responded with dorsiflexion of the left foot for the low frequency (700 Hz) auditory tone and with dorsiflexion of the right foot for the high frequency (1000 Hz) auditory tone.

Task Order & Trials

All tasks were organized into 4 blocks that were randomized for presentation order, each consisting of 48 trials. The order of the task conditions within each block was also randomized. The trials for each task were performed as a group within a block to avoid switching between task conditions. For example within block 1 there were 3 task conditions (SRT to three different stimulus intensities). The order of the task conditions was randomized and all 16 trials for each task condition were completed sequentially. Block 2 was completed in the same way as block 1. Within block 3 there were 6 task conditions (three different stimulus intensities at two different frequencies). The frequency presented determined the appropriate response and the order of the task conditions were randomized and all 8 trials for each task condition were completed sequentially. Block 4 was completed in the same way as block 3.

Table 2-1: Stimulus intensities and number of trials for each of the trial conditions and blocks. Blocks were performed in random order and all trials within each block were performed in pseudorandom order. Block #1 consisted of only high frequency tones and participants responded with right foot dorsiflexion only, whereas Block #2 consisted of only low frequency tones and participants responded with left foot dorsiflexion only. Block #3 & #4 consisted of both high and low frequency tones and participants were told to respond with their left foot for low frequency tones and with their right foot for high frequency tones.

Block #1		Block #2		Block #3				Block #4			
Simple RT		Simple RT		Choice RT				Choice RT			
1000 Hz		700 Hz		High Frequency		Low Frequency		High Frequency		Low Frequency	
Task 1	80 dB (n=16)	Task 1	80 dB (n=16)	Task 1	80 dB (n=8)	Task 4	80 dB (n=8)	Task 1	80 dB (n=8)	Task 4	80 dB (n=8)
Task 2	100 dB (n=16)	Task 2	100 dB (n=16)	Task 2	100 dB (n=8)	Task 5	100 dB (n=8)	Task 2	100 dB (n=8)	Task 5	100 dB (n=8)
Task 3	120 dB (n=16)	Task 3	120 dB (n=16)	Task 3	120 dB (n=8)	Task 6	120 dB (n=8)	Task 3	120 dB (n=8)	Task 6	120 dB (n=8)

2.2.3 Data Acquisition

Electromyography (EMG) was collected from the right tibialis anterior (rTA), left tibialis anterior (lTA) and right sternocleidomastoid (SCM). EMG electrode sites were shaved (if necessary) and cleaned with abrasive cream and alcohol. Silver/silver-chloride electrodes were fixed 2 cm apart over each muscle belly. EMG signals were amplified by a magnitude of 1000 and stored for offline processing.

Galvanic skin response (GSR) was collected using two electrodes placed on the middle phalanges of the third and fourth digits of the participant's left hand. The electrodes were filled with a conductive paste and the sites were cleaned with abrasive gel and alcohol. The signal was pre-amplified and low-pass filtered and stored for offline processing.

A synchronization pulse, at the time of the auditory stimulus presentation was sent to the collection computer and used as the stimulus onset for each trial.

2.2.4 Signal Processing

Stimulus onset time was determined by the initial presentation of the auditory tone and noted by a square-wave at different volts to identify the type of stimulus (ie intensity and frequency). Motor response timing was determined relative to the stimulus onset.

EMG signals were digitally filtered from 20-250 Hz, using a 2nd order dual pass butterworth filter and conditioned by removing and DC offset bias and by full wave rectification of the signal. EMG onset latency was defined as the time when the EMG amplitude exceeded five standard deviations of the mean of a 100ms baseline value taken prior to the stimulus onset. Amplitude of the EMG signal was calculated as the total integrated EMG activity (iEMG) for 100 ms following the EMG onset. EMG duration was determined by visually placing an EMG offset cursor after the rectified signal returned to baseline and calculating the elapsed time between the EMG onset and offset cursor.

GSR data was filtered offline with a 2nd order low pass filter at 5 Hz. The phasic GSR onset latency was defined as the time when a positive, sustained increase in slope, occurring between 0.5 and 5 seconds following the auditory stimulus. GSR amplitude was calculated as the difference between the onset amplitude and the peak amplitude. GSR time to peak was calculated as the difference between the peak amplitude time occurrence and the GSR onset.

2.2.5 Statistical Analysis

The primary statistical analysis focused on the effect of stimulus intensity and type of reaction time task on EMG onset. A two-way repeated measures ANOVA was conducted on the mean reaction times across subjects and stimulus intensity, type of reaction time task as well as their interaction effect. Significance level was set at 0.05.

Secondary statistical analysis focused on the effect of stimulus intensity and type of reaction time task on GSR amplitude. A two-way repeated measures ANOVA was again conducted on the mean GSR amplitudes across subjects and stimulus intensity, type of reaction time task as well as their interaction effect. Significance level was set at 0.05.

2.3 Results

All participants successfully completed all trials in all conditions. Results are summarized in **Table 2-2**. Due to no significant difference between high frequency and low frequency, reaction times were collapsed across frequencies.

Table 2-2: Overall mean (and standard deviations) for reaction time (ms) and galvanic skin response (GSR) for the different task and stimulus intensities. Mean error rates (% incorrect) are provided for choice reaction time tasks.

	Simple Reaction Time			Choice Reaction Time		
	80 dB	100 dB	120 dB	80 dB	100 dB	120 dB
Tibialis Anterior (Latency, ms)	335.1 ± 68.5	306.0 ± 53.0	294.2 ± 44.4	597.3 ± 152.7	542.9 ± 128.1	508.1 ± 113.6
GSR Amplitude (mS)	2.4 ± 2.9	4.1 ± 4.6	6.3 ± 6.0	3.1 ± 4.2	5.7 ± 5.8	8.1 ± 7.3
Error %	N/A	N/A	N/A	11.39% ± 11.76%	12.14% ± 11.05%	11.86% ± 10.93%

2.3.1 Reaction Time

Simple reaction time was significantly faster than choice reaction time at all intensity levels ($F_{[1,11]}=103.30$, $p < 0.05$). The greater the intensity of the auditory stimulus the faster the reaction time for both simple ($F_{[2,11]}=14.73$, $p < 0.05$) and choice ($F_{[2,11]}=17.65$, $p < 0.05$) reaction time tasks. There was also a significant difference between reaction time and the interaction of intensity and type of task ($F_{[2,11]}=4.45$, $p = 0.0238$) (See **Figure 2-1**). Therefore, an increase in intensity had a greater effect on the choice reaction time task. **Figure 2-6** and **Figure 2-7** show an individual example of reaction times across stimulus intensity for participant 2 for SRT and CRT respectively. Participant 2 is a good representation of the mean showing a gradual decrease in reaction time with increasing stimulus intensity.

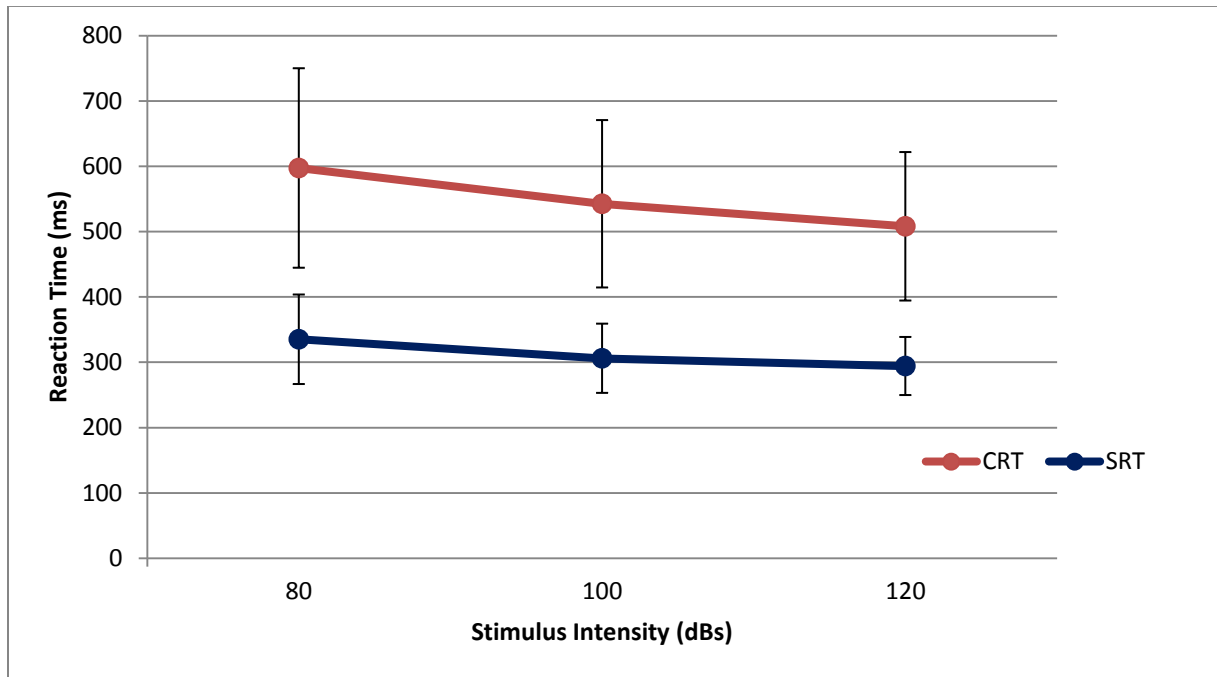


Figure 2-1: Mean reaction times and standard deviations to all stimulus intensities for simple and choice reaction time tasks averaged across subjects. SRT was significantly faster than CRT ($F_{[1,11]}=103.30$, $p < 0.05$). The greater the intensity of the auditory stimulus the faster the reaction time: SRT ($F_{[2,11]}=14.73$, $p < 0.05$), CRT ($F_{[2,11]}=17.65$, $p < 0.05$).

Further analysis on the distribution of means across subjects was computed to determine the cause in reduction of reaction time with an increase in stimulus intensity. Results are summarized in **Table 2-3**. **Figure 2-4** and **Figure 2-5** show all reaction times across participants for SRT and CRT respectively.

The median simple reaction time was significantly faster than choice reaction time at all intensity levels ($F_{[1,11]}=114.77, p <0.05$). The greater the intensity of the auditory stimulus the faster the median reaction time for both simple and choice reaction time tasks ($F_{[2,11]}=25.49, p <0.05$). Furthermore, there was no significant difference in skewness ($F_{[2,11]}=0.74, p 0.49$), standard deviation ($F_{[2,11]}=2.73, p 0.09$) or kurtosis ($F_{[2,11]}=0.41, p 0.67$) between intensities for both simple and choice reaction time tasks.

Table 2-3: Distribution of means, medians, skewness, standard deviations, kurtosis, minimums and maximums across simple and choice reaction time (ms) for all stimulus intensities.

	Simple Reaction Time			Choice Reaction Time		
	80 dB	100 dB	120 dB	80 dB	100 dB	120 dB
Mean	335.1	306.0	294.2	597.3	542.9	508.1
Median	329.9	298.9	288.7	577.6	536.0	501.5
Skewness	1.12	0.85	0.93	1.05	0.52	0.80
Standard Deviation	54.0	48.5	44.5	126.1	100.0	121.4
Kurtosis	2.67	1.47	2.17	2.66	1.69	2.73
Minimum	255.4	228.2	220.2	389.3	364.3	310.8
Maximum	499.3	435.3	418.4	941.9	810.8	847.4

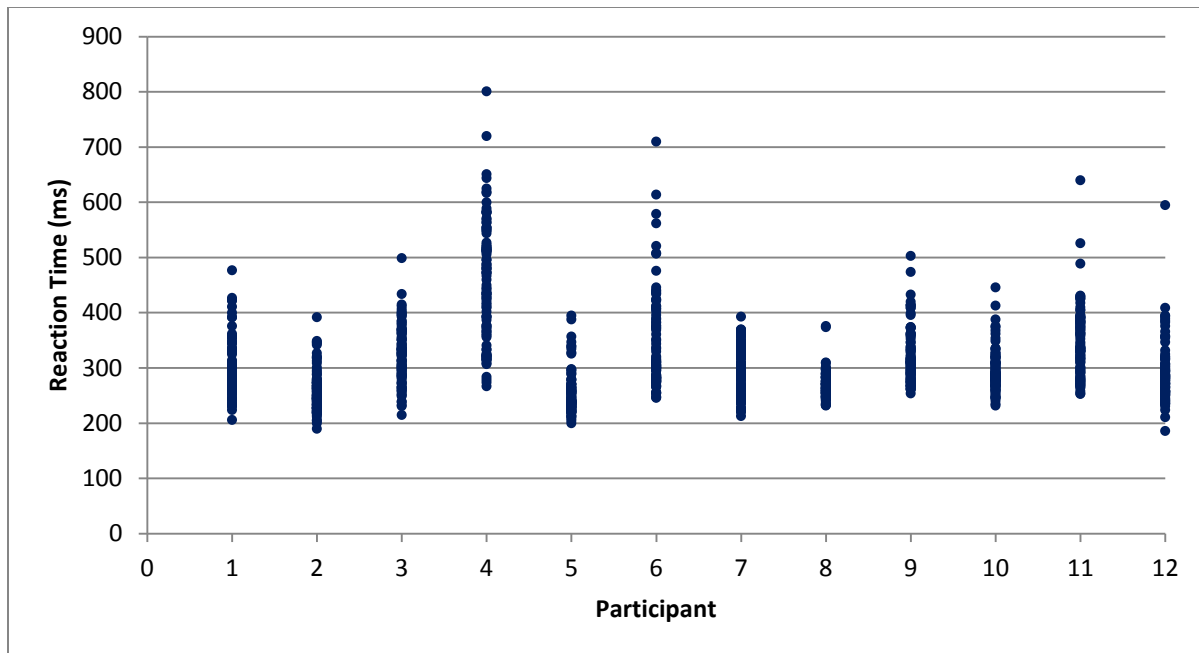


Figure 2-4: Distribution of reaction times for each participant in simple reaction time tasks collapsed across stimulus intensity.

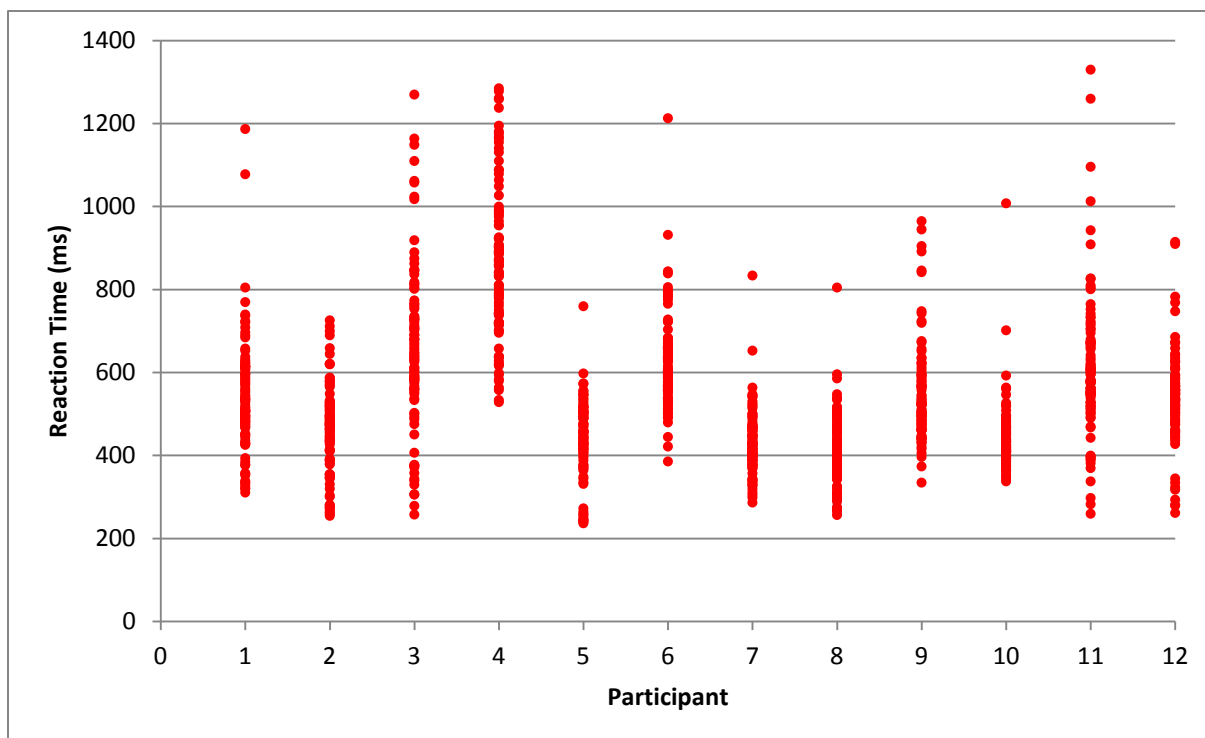


Figure 2-5: Distribution of reaction times for each participant in choice reaction time tasks collapsed across stimulus intensity.

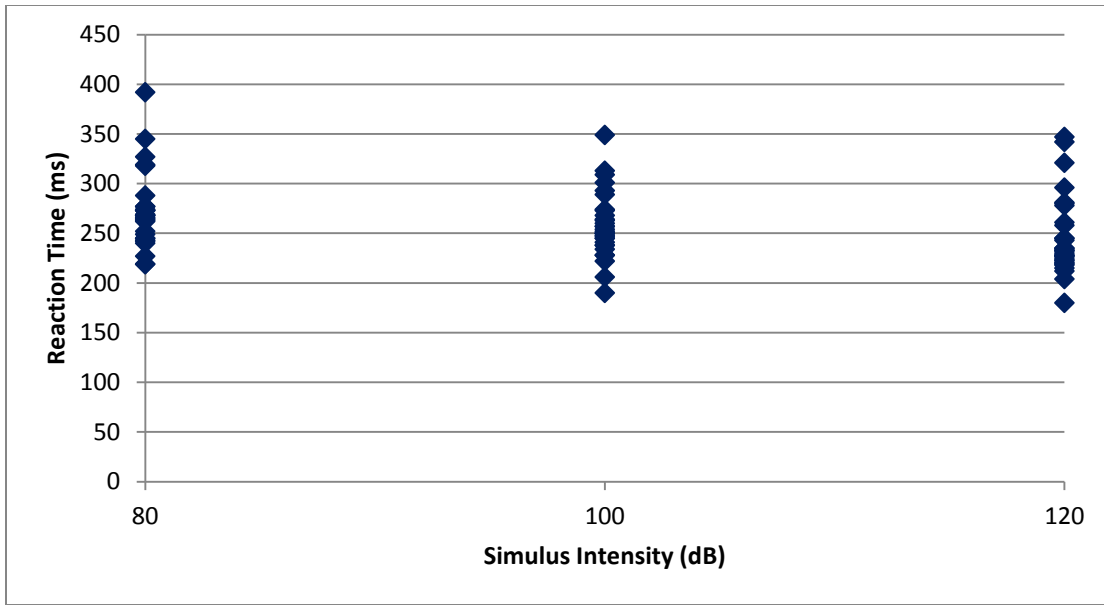


Figure 2-6: Distribution of reaction times for participant 2 in simple reaction time tasks across stimulus intensity.

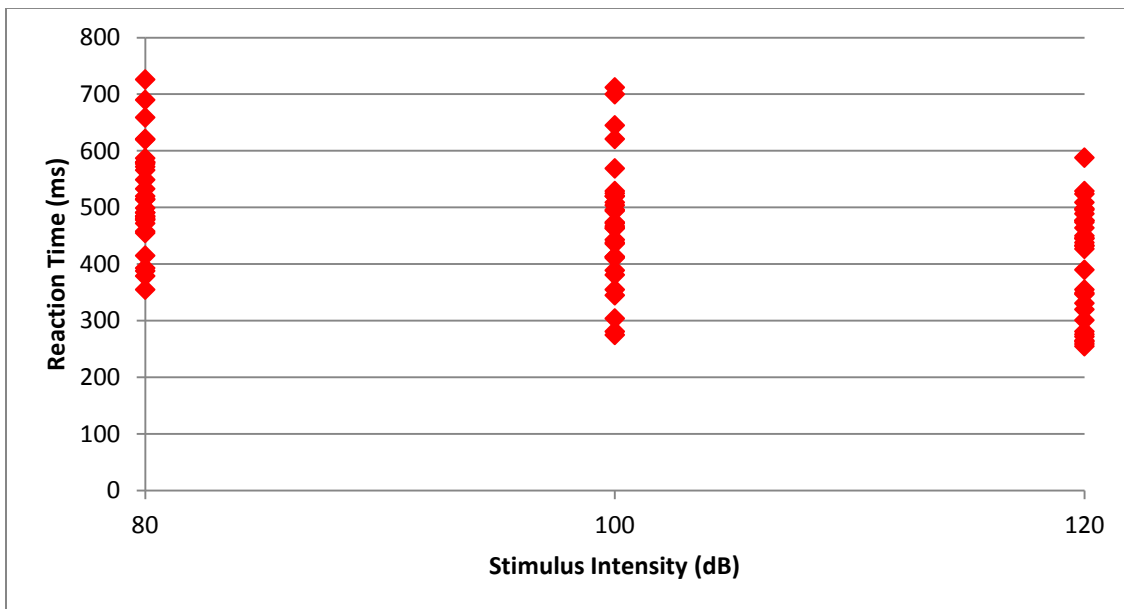


Figure 2-7: Distribution of reaction times from participant 2 for choice reaction time trials plotted for each stimulus intensity.

2.3.2 Galvanic Skin Response

There was no significant difference in GSR amplitude comparing between simple and choice reaction time ($F_{[1,11]}=2.47, p=0.14$). However, the greater the intensity of the stimulus the greater the GSR amplitude for both simple ($F_{[2,11]}=11.93, p <0.05$) and choice reaction time tasks ($F_{[2,11]}=18.61, p <0.05$). The mean values increased progressively from 80 to 120 dB. There was significant difference between GSR amplitude and the interaction of intensity and type of task ($F_{[2,11]}=4.13, p <0.05$) (See **Figure 2-2**). Therefore, the GSR amplitude was greater for choice reaction time tasks versus simple reaction time tasks, specifically at higher amplitude of stimulation.

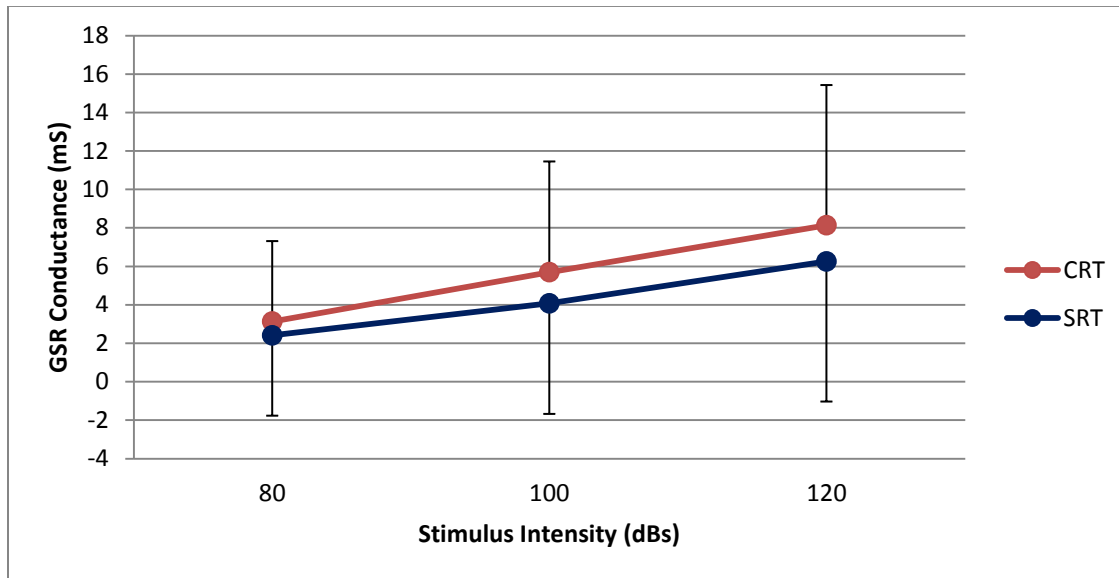


Figure 2-2: Mean peak GSR conductance values and standard deviations averaged across subjects for all stimulus intensities for simple (SRT) and choice (CRT) reaction time tasks. The greater the intensity of the stimulus the greater the GSR amplitude for both SRT ($F_{[2,11]}=11.93, p <0.05$) and CRT ($F_{[2,11]}=18.61, p <0.05$).

2.3.3 Error Rate

There was no significant difference in rate of errors made during choice reaction time tasks across all stimulus intensities; 80 dB (11.39% \pm 11.76%), 100 dB (12.14% \pm 11.05%), 120 dB (11.86% \pm 10.93%) ($F_{[2,11]}=0.06$, $p=0.939$) (See **Figure 2-3**). While error rates across subjects varied (1.0% to 39.2%) the variability across tasks within subjects was much smaller. For example, participant 6 made very few errors to 120 dB tones (3.13%) and no errors to 80 or 100 dB trials, whereas participant 4 made many errors (80 dB = 34.38%, 100 dB = 43.75%, 120 dB = 39.39%).

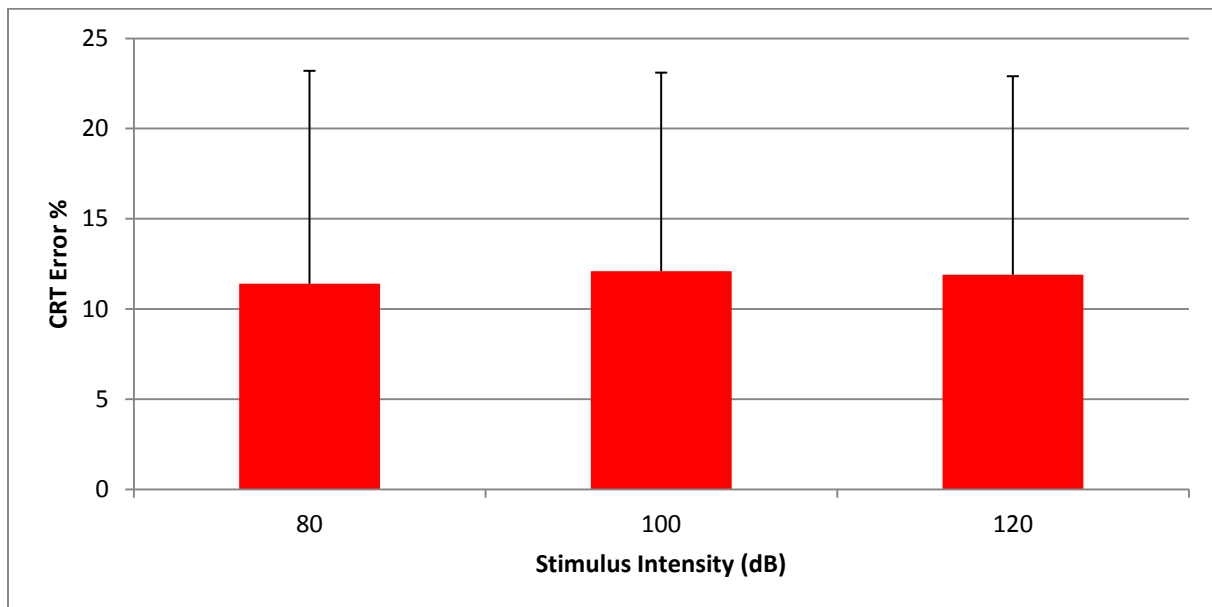


Figure 2-3: Mean error rate (%) and standard deviations for each intensity for choice reaction time tasks averaged across subjects. There was no statistical difference in error rate comparing between stimulus intensities ($p>0.05$).

2.3.4 SCM Activity

Only 5 of the 12 participants collected within the current study showed SCM activity in response to an auditory tone. Within those 5 participants there were a total of 31 trials that presented SCM activity. **Table 2-4** shows the mean reaction times, number of trials and task

condition breakdown of the trials that contained SCM activity. Overall, the trials tended to occur at higher stimulus intensity (none occurred at 80 dB). It is difficult to make conclusions on such a low sample size, however, the reaction times seen within the SCM trials are variable ranging from 238 ms to 376 ms in the SRT trials and 420 ms to 479 in the CRT trials.

Table 2-4: Mean reaction times (ms) (and total number of trials) when SCM activity occurred. Only 5 participants are presented as the remaining 7 showed no SCM activity.

Participant	SRT			CRT		
	80 dB	100 dB	120 dB	80 dB	100 dB	120 dB
P05	n/a	n/a	238 (1)	n/a	n/a	n/a
P07	n/a	308 (2)	276 (7)	n/a	479 (2)	448 (1)
P08	n/a	341 (2)	258 (1)	n/a	n/a	n/a
P10	n/a	n/a	376 (1)	n/a	n/a	420 (8)
P12	n/a	n/a	n/a	n/a	477 (3)	449 (3)

2.4 Discussion

The primary goal of this study was to determine if reaction times for simple and choice tasks were similarly influenced by the intensity of auditory stimuli. The current study did support the hypothesis that increasing stimulus intensity decreased the reaction time of both simple and choice reaction times. The amplitude of the stimulus effect resulted in approximately a 40 ms average reduction in simple reaction time and a 90 ms average reduction in choice reaction time between the low and high amplitude stimulation. These differences in reaction times in the choice reaction associated with the increase in stimulus intensity were not associated with an increase in errors. As a result the current work support the view that stimulus intensity could facilitate speed of processing for stimulus reaction control even when mediated by higher level cortical decision making regions. In addition, the current study revealed differences in autonomic reactivity, measured using GSR that scaled with the amplitude of perturbation. This

latter observation, as discussed later in the discussion, may be associated with a potential mechanism contributing to increased speed of processing to increased stimulus intensity.

The rationale of the study was to explore influence of stimulus intensities at levels that would approach those that evoke startle reactions as was reported by Carlsen et al. (2007). In spite of the intense stimulation (ie 120 dB) there was no consistent activity evoked in neck muscles that would be indicative of a startle reaction (Brown et al., 1991a; Carlsen et al., 2007). Sternocleidomastoid activity only occurred in 5 subjects for a total of 31 trials. In addition, the current study presented reaction times that were not as fast as reported in previous work (Carlsen et al., 2007). Carlsen et al., (2007) demonstrated reaction times of approximately 120 ms for 83 dB tones and 100 ms for 103 and 123 dB tones. These reaction times were much faster than the reaction times presented in the current study leading to the view that these responses were unlikely a classic startle response, even though they were more likely to occur at higher intensities. However, Carlsen et al., (2007) utilized pre-cueing within their experimental protocol, where participants were presented with a warning tone that informed them that the stimulus would be presented exactly 2500 ms later. Laboratory experiments have revealed significantly faster reaction times and a significant level of pre-stimulus cortical activity when the participants are able to predict a stimulus (Nachev et al. 2008; Mochizuki et al., 2009). As a result this would account, in part, for the differences in reaction times between the work of Carlsen et al. (2007) at high intensities and the current study. That said the reaction times in the current study were typically much longer than report in other studies using auditory simple reaction times.

2.4.1 Choice reaction time decreases with increasing stimulus intensity

Many studies have demonstrated that an increase in stimulus intensity leads to a decrease in simple reaction time across all modalities (Carlsen et al., 2007; Bell et al., 2006; Carreiro et al., 2011; Grisolia & Wiederholt, 1980; Huttunen, 1995). Furthermore, some reaction time studies have shown a decreasing trend in simple reaction time up to and including a high intensity auditory startle stimulus (Carlsen et al., 2007). However, attempts to show choice reaction time over an increasing auditory stimulus, including startling intensities, could potentially uncover new information regarding CNS processing. The current study demonstrated no interaction effect between stimulus intensity and type of reaction time task (SRT or CRT). In other words, simple and choice reaction time both decreased with an increasing in stimulus intensity to a proportional degree. Choice reaction time utilizes, in part a cortical network pathway to identify the stimulus, decide on the proper reaction, and then execute said reaction (Schmidt & Lee, 1999). Considering that continuous nature of the influence of stimulus intensity on speed of processing and the absence differences in error rate it is hypothesized that the large reduction in onset latencies seen in the choice reaction time task are a result of synaptic facilitation. The potential mechanisms are discussed in subsequent sections.

2.4.2 Number of errors across intensities was consistent

Arguably, one possible explanation for more rapid reactions in the choice reaction time tasks is individuals adopting a strategy in which they trade off accuracy for speed. The basic principle of the speed-accuracy trade-off is grounded in the inverse relationship between the time required to complete a movement and the accuracy of the resulting movement. One must accumulate information about a particular situation to make an accurate decision, which requires

time (Schouten & Bekker, 1967; Wickelgren, 1977). Intuitively, the reduction in reaction time in the present study could have been the result of reducing accuracy in order to increase speed; however this was not the case as there were no statistical differences in error rates across stimulus intensity. In addition, in spite of the more rapid reactions (average reduction of 90 ms), the error rates were relatively low (approximately 11%) and were similar for all stimulus intensities. Similar to the results of Carlsen et al. (2007), these error results suggest that the speed-accuracy trade off appears to be violated during high intensity auditory stimuli. This finding also supports, indirectly, the idea that increased speed of processing is a product of pathway facilitation rather than an alternate pathway.

Another example of violation of the speed-accuracy trade off is responses to unexpected balance perturbations. These particular movements share a number of kinematic and kinetic properties analogous to non-urgent movement; the only difference being the striking reduction in onset latencies (Gage et al., 2007). Many have demonstrated the involvement of higher level cortical processing in the control of balance reactions (Dietz & Berger, 1984; Dietz et al., 1985; Ackermann et al., 1986; Duckrow et al., 1999; Quant et al., 2004; Dimitrov et al., 1996). Perhaps higher level cortical processing is required to maintain the accuracy of actions in response to balance perturbations as well as high intensity auditory stimuli.

2.4.3 Potential Mechanisms

In light of the fact that differences were observed in both simple and choice reaction time and that the influences were related to the amplitude of stimulation it is hypothesized that there are two potential and related mechanisms that may contribute to increased speed of processing. Increase in stimulus intensity leads to a greater recruitment and increased firing rate of auditory

afferents which: 1) increases post-synaptic excitation due to temporal and spatial summation reducing synaptic delays (LATER) and 2) increases engagement of autonomic nervous systems which, via parallel pathways, may augment facilitation.

The linear approach to threshold with ergodic rate (LATER) model proposes that following stimulus presentation there is a decision signal which rises linearly from an initial level at a certain rate and once the threshold is reached a response is triggered (Reddi & Carpenter, 2000). Neurophysiologically, the rate at which the signal rises represents the rate of neuronal firing which alters the slope (speed) required to reach the threshold to produce the reaction. The LATER model can be applied to the current study and may explain, at least in part, the reductions in reaction time. As auditory stimulus intensity levels increased they would: increase post-synaptic facilitation and the rate at which the synaptic decision signal rises, decreasing the amount of time to threshold, ultimately increasing post-synaptic excitation across many synapses contributing to more rapid processing times by reducing synaptic delays.

The current study also revealed increased arousal levels occurring during trials with higher stimulus intensities. There are several studies that have revealed the relationship between stimulus intensity and autonomic reactivity (Sibley et al., 2008; 2009; Lakhani et al., 2013). Increase autonomic nervous system activity may be a possible mechanism that may augment process speed in response to increased stimulus intensity. If in fact increased ANS activity can influence excitability of the ongoing reaction it must do this via a parallel pathway. One of the possible mechanisms is via activation of sympathetic pathways that may contribute to concurrent facilitation of pathways involved in sensorimotor control. A possible example is excitation of the locus coeruleus (LC) neurons in the brainstem which lead to release of nor-epinephrine with diffuse innervations of the CNS including the cerebral cortex and spinal cord (Jones & Yang

1985; Jones & Moore 1977). The high intensity auditory tones may activate LC neurons which send projections, via parallel pathways to motor and pre motor cortical areas influencing motor response and decreasing reaction time (Bouret & Sara, 2002; Lecas, 2004). Further research is required to determine if there is increased LC activity following high intensity auditory tones. The limitation of the use of GSR as a measure of autonomic reactivity is the dependence on skin conductance and the associated delay in responses. This leads to an inability to determine the precise timing of the responses with respect to onset of stimulation. As a result there remains no direct evidence of the potential role for pathway facilitation via activation of a parallel autonomic pathway on to the sensorimotor pathways.

2.5 Conclusion

The current study set out to determine if reaction times for both simple and choice tasks were influenced by stimulus intensity. It was demonstrated that simple and choice reaction times were similarly influenced by increasing levels of auditory stimulus intensity, leading to faster reaction times to highly intense tones. Additionally, autonomic nervous system activity increased with an increase in auditory stimulus intensity. This work has potential implications to the factors that influenced processing speed evoked by external stimuli. The potential that stimulus intensity and associated autonomic reactivity may influence speed of processing has potential implications to possible reasons accounting for slowing in older adults. While the current study revealed more rapid reactions it was not clear where in the processing pathway the modulation of processing speed occurred. The subsequent study 2 was conducted in order to reveal the evidence of the changes in timing of electrophysiological events at the cortex in responses to changes in stimulus amplitude.

CHAPTER 3: ELECTROPHYSIOLOGICAL CORRELATES OF CHANGES IN REACTION TIME BASED ON AUDITORY STIMULUS INTENSITY

3.1 Introduction

Reaction time methodology has been used extensively to uncover speed of processing components within the CNS (Galton, 1890; Donders, 1969). Reaction time is a vital tool used to probe neurological pathway information and overall CNS health based on the elapsed time required to stimulate muscle activity (Stuss et al., 1989; Hetherington et al., 1996). Because of this, a large body of literature has explored a wide variety of factors that affect speed of processing, including age (Luchies et al., 2002; Welford, 1976), gender (Noble et al., 1964; Adam et al., 1999), anticipation (Welford & Brebner, 1980), stimulus modality (Galton, 1890; Welford & Brebner, 1980), arousal (Vaez Mousavi et al., 2009), task urgency (Thobois et al., 2007; Gage et al., 2007; Maki and McIlroy, 1997) and stimulus intensity (Kohfeld, 1971; Pins & Bonnet, 1996).

Of particular interest in the present study are the possible factors that contribute to very rapid reactions such as those seen in response to stimuli that demand temporal urgency. In the face of temporal urgency, humans are able to execute extremely fast reactions, such as those following a balance perturbation (~100 ms) (Gage et al., 2007). These reactions serve to protect us from harm (Thobois et al., 2007; Lakhani et al., 2011a) however, 'temporally urgent' reactions can become compromised with aging (Spiriduso, 1980; Kail, 1986; Salthouse, 2000; Kolev et al., 2006) or neurological deficits and injuries (Fridman et al., 2004; Miller, 1970; Stuss et al., 1989; Kaizer et al., 1988; Kurtzer et al., 2013; Kutukcu et al., 1999; Hetherington et al., 1996). In order to identify methods to reduce/improve processing time the mechanisms of speed of processing of such reactions must first be understood.

There are two main ways our CNS can influence reaction time. The first are physical characteristics of the neurological network. These characteristics can include axon length,

conduction velocity and the number of intervening synapses. One theory of rapid onset reactions is in the face of urgency our CNS takes a shorter (ie less synapses / shorter axons). Evidence suggests that reaction times to startling auditory stimuli results in rapid onset latencies that differ from non-threatening stimuli (Valls-Sole et al. 1999; 2008; Carlsen et al., 2003; 2004; 2007). The authors hypothesize that startling auditory stimuli activate brainstem nuclei that are responsible for activating motor pathways to execute movement. This suggests a class of temporally urgent reactions that utilizes a separate neurological network to increase speed of processing.

The second way our CNS can influence reaction time is to modulate the response through synapses along an existing pathway. Such facilitation may occur as a result of a more rapid time to reach threshold at synapses (due to increased excitation), following the LATER model (Reddi & Carpenter, 2000) and/or associated with possible influence of facilitation linked to parallel pathways associated with autonomic activity (Sibley et al., 2008; 2009; 2014; Lakhani et al., 2013; 2013). Possible factors include anticipation (pre-cueing) (Nachev et al. 2008; Mochizuki et al., 2009), arousal (Llewellyn et al., 1990), attention (Posner et al., 1980) and stimulus intensity (Woodworth, 1935; Carlsen et al., 2007; Miller et al., 1999; Lakhani et al, 2012). The current study is focused on the use of stimulus intensity as a modulator of reaction time. As revealed in study 1 the modulation of auditory stimulus intensity had a profound effect on reaction time; as stimulus intensity increased so did reaction time. The argument that modulators influence reaction time via synaptic facilitation is not directly revealed by changes in reaction time. Instead measures of underlying electrophysiology changes could be a more direct measure. Electrophysiological data shows an increase in cortical potentials prior to motor cortex activity with an increase in somatosensory stimulus intensity (Lakhani et al., 2012). Results showed an

increase in EEG amplitude approximately 130 ms prior to the onset of movement. The amplitude was larger in trials where participants responded to the high intensity stimulation. The author suggests that these results reveal a link between reduction in reaction time and task specific augmentation of motor preparation (Lakhani et al., 2012). Therefore, as stimulus intensity increases, it was proposed that there was a facilitation of the pathways that led to more rapid reactions times. The current study focuses on exploring whether such changes in electrophysiology are associated with behaviour changes in reaction time that were evoked by changes in stimulus intensity.

The current study focused on electrophysiological events linked to auditory stimulus and motor reactions. The late latency waveform of auditory evoked potentials are a primary focus because they are cortical in origin and are much larger than early or middle latency potentials (Kraus & Nicol 2009). The late latency (>80 ms) waveform is characterized by 4 distinct waves; P1, N1, P2, N2 (Kraus & Nicol 2009), however the timing and amplitude are largely dependent on the type of stimulus (eg. intensity, frequency etc.). Stimulus intensity appears to have a profound effect on auditory evoked potentials (Picton et al., 1973). A decrease in intensity results in smaller amplitudes and longer latencies. This previous work focused on decibel levels that were 10-80 dB. The current work extends this focus of study to higher amplitude intensities that we know influence reaction times (Carlsen et al., 2004; 2007).

The overarching purpose of this study is to determine if the characteristics of cortically evoked potentials to auditory stimulus are associated with stimulus intensity and associated changes in reaction time (study 1). The primary hypothesis is the N1 auditory evoked potential will increase in amplitude and decrease in latency with increasing stimulus auditory intensity. In addition, consistent with the observation by Lakhani et al. (2012), it is anticipated there will be

an increase in pre-motor cortically evoked potentials in response to greater stimulus amplitudes (and short reaction time) reflecting increased cortical excitability. This would potentially support the perspective that increased auditory stimulation leads to pathway facilitation associated with both sensory and motor processing events. Consistent with the approach in study 1, the current study also examined the autonomic responses to differences in auditory stimulus intensity.

Overall the current study explores the electrophysiological responses to differences in auditory stimulus intensity in an attempt to determine if the underlying cortical activity, potentially revealing pathway facilitation, may account for the more rapid reaction times.

3.2 Methods

3.2.1 Participants

Twelve healthy adults (age 25 ± 3 ; 6 males; 6 females) participated in this study. None of the participants had any neurological, musculoskeletal or hearing impairment that may have affected their ability to complete all reaction time tasks. All participants provide informed consent and the study was approved by a research ethics committee at the University of Waterloo.

3.2.2 Protocol

Stimuli

Participants will be exposed an auditory stimulus consisted of 2 different intensity levels, 80 dB and 120 dB at a frequency of 1000 Hz. A custom LabView program generated the auditory tone and was then amplified using a Bryston ST series amplifier. After the signal was

amplified, presentation occurred through a speaker located behind approximately 30 cm from the participant's ears (posterior). The auditory stimuli intensities were measured using a precision level sound meter (B+K Precision Sound Level Meter).

Task Conditions

Two different task conditions were performed: 1) sensory only (auditory stimulation but no reaction) and 2) auditory reaction time tasks. Each task condition was separated into 2 blocks of 48 trials (24 trials at 80 dB and 24 trials at 120 dB) that were randomized.

During the sensory task the participants were instructed not to react to the auditory stimulus and were exposed to a total of 96 trials, 48 trials at 80 dB and 48 trials at 120 dB.

During the reaction time task the participants responded with dorsiflexion of the right ankle for all trials. Participants were instructed to react as fast as possible to the auditory stimulus and were exposed to a total of 96 trials, 48 trials at 80 dB and 48 trials at 120 dB.

3.2.3 Data Acquisition

Electromyography (EMG) was collected from the right tibialis anterior (rTA) and right sternocleidomastoid (SCM). EMG electrode sites were shaved (if necessary) and cleaned with abrasive cream and alcohol. Silver/silver-chloride electrodes were fixed 2 cm apart over each muscle belly. EMG signals were amplified by a magnitude of 1000 and stored for offline processing.

Galvanic skin response (GSR) was collected using two electrodes placed on the middle phalanges of the third and fourth digits of the participant's left hand. The electrodes were filled with a conducted paste and the sites were cleaned with abrasive gel and alcohol. The signal was pre-amplified and low-pass filtered and stored for offline processing.

Electroencephalographic data were recorded from 34 electrode sites (Fz, FCz, Cz, CPz, Pz, F3, FC3, C3, CP3, P3, F4, FC4, C4, CP4, P4, FP1, FP2, O1, Oz, O2, F7, FT7, T3, TP7, T5, F8, FT8, T4, TP8, T6 and ocular sites), in accordance with the international 10-20 system for electrode placement referenced to the linked mastoids (impedance < 5 k Ω).

A synchronization pulse, at the time of the auditory stimulus presentation was sent to the collection computer as well as the EEG computer and used as the stimulus onset for each trial.

3.2.4 Signal Processing

EEG data were amplified (40000x), filtered (DC-200 Hz), digitized at 1000 Hz and stored on a computer for offline analysis consisting of noise and artifact removal using MATLAB. Average latency and amplitude of the N1 and P2 waves in the sensory task were calculated with respect to the stimulus onset and baseline activity. For sensory trials a 3000 ms epoch was determined with respect to onset of auditory stimulation (time 0: auditory stimulus; -1000 ms to 2000 ms). Average amplitude of the pre-movement negativity (Pre-N) wave, consistent with results from Lakhani et al. (2013), in the motor task will be calculated with respect to the EMG onset and baseline activity. Motor related events data were epoched around the onset of EMG (time 0: EMG onset; -1000 ms to 2000 ms).

EMG signals were digitally filtered from 20-250 Hz, using a 2nd order dual pass Butterworth filter and conditioned by removing and DC offset bias and by full wave rectification of the signal. EMG onset latency was defined as the time with the EMG amplitude exceeded five standard deviations of the mean of a 100ms baseline value taken prior to the stimulus onset (Lakhani et al., 2013). Amplitude of the EMG signal was calculated as the total integrated EMG activity (iEMG) for 100 ms following the EMG onset. EMG duration was determined by

visually placing an EMG offset cursor after the rectified signal returned to baseline and calculating the elapsed time between the EMG onset and offset cursor.

GSR data was filtered offline with a 2nd order low pass filter at 5 Hz. The phasic GSR onset latency was defined as the time when a positive, sustained increase in slope, occurring between 0.5 and 5 seconds following the auditory stimulus. GSR amplitude was calculated as the difference between the onset amplitude and the peak amplitude. GSR time to peak was calculated as the difference between the peak amplitude time occurrence and the GSR onset.

3.2.5 Statistical Analysis

The primary statistical analysis focuses on the effect of stimulus intensity and EEG evoked potentials taken from the Cz electrode site. N1 and P2 waves of auditory evoked potentials have been shown to be cortical in origin and maximally distributed over the Cz electrode site (Kraus & Nicol, 2009; Picton et al., 1974). For the sensory trials, a one-way repeated measures ANOVA was conducted on the mean N1 and P2 latencies and amplitudes across subjects and stimulus intensity. For the motor related tasks, a one-way repeated measures ANOVA was conducted on the amplitude of the Pre-N potential. Significance level was set at 0.05.

Additional analysis focused on the effect of stimulus intensity on GSR amplitude. A one-way repeated measures ANOVA was conducted on the mean GSR amplitudes across subjects and stimulus intensity. Significance level was set at 0.05.

3.3 Results

3.3.1 Sensory Task

The grand average auditory evoked potentials in the sensory task are displayed in **Figure 3-1**. The average latency of the long latency N1 peak was significantly shorter in the high intensity auditory tone trials, decreasing from 106.0 ± 5.5 ms in the 80 dB trials to 94.6 ± 12.1 ms in the 120 dB trials ($F_{[1,11]}=13.88$, $p<0.05$) (**Figure 3-6**). The average amplitude of the long latency N1 peak was significantly larger in the high intensity auditory tone trials, increasing from -19.5 ± 8.9 uV in the 80 dB trials to -29.8 ± 16.4 uV in the 120 dB trials ($F_{[1,11]}=16.43$, $p<0.05$) (**Figure 3-7**). There was a significant difference in the latency of the P2 wave that decreased from 201.6 ± 46.6 ms in the 80 dB trials to 189.6 ± 32.7 ms in the 120 dB trials ($F_{[1,11]}=6.92$, $p<0.05$). Furthermore, there was also a significant difference in the amplitude of the long latency P2 wave increasing from 14.7 ± 7.0 uV in the 80 dB trials to 22.3 ± 14.0 uV in the 120 dB trials ($F_{[1,11]}=7.48$, $p<0.05$).

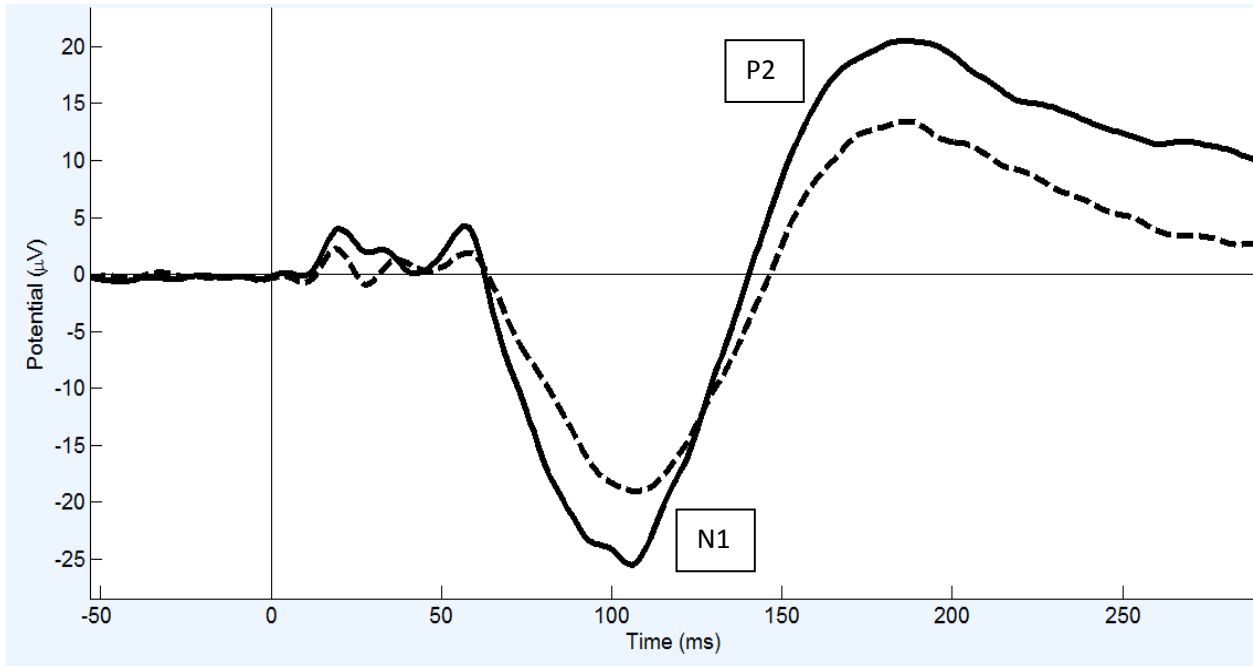


Figure 3-1: Grand average auditory evoked potentials (AEPs). AEPs were recorded from the Cz electrode site. Time 0 represents the auditory stimulus onset. SOLID line indicates 120 dB potentials and the BROKEN line indicates 80 dB potentials. The N1 and P2 waves are labelled.

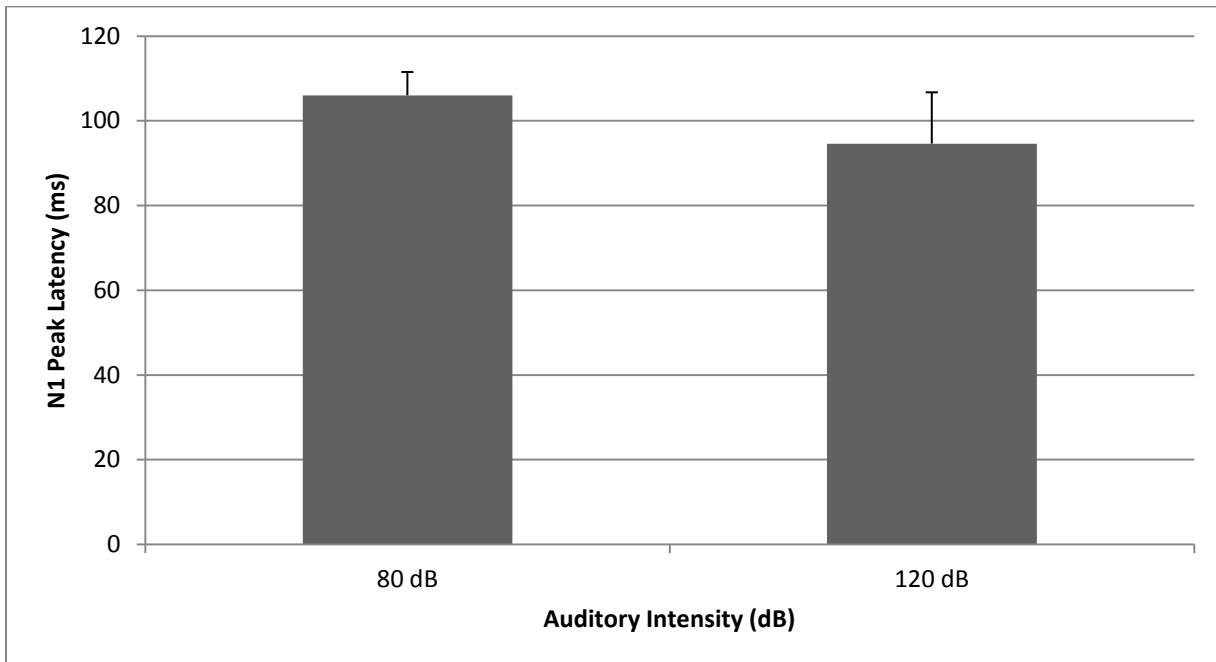


Figure 3-6: Group averages and standard deviations for peak amplitude latency of the N1 potential from the Cz electrode site during the sensory task. The 120 dB peak latencies were significantly shorter than the 80 dB peak latencies ($F_{[1,11]}=13.88, p<0.05$).

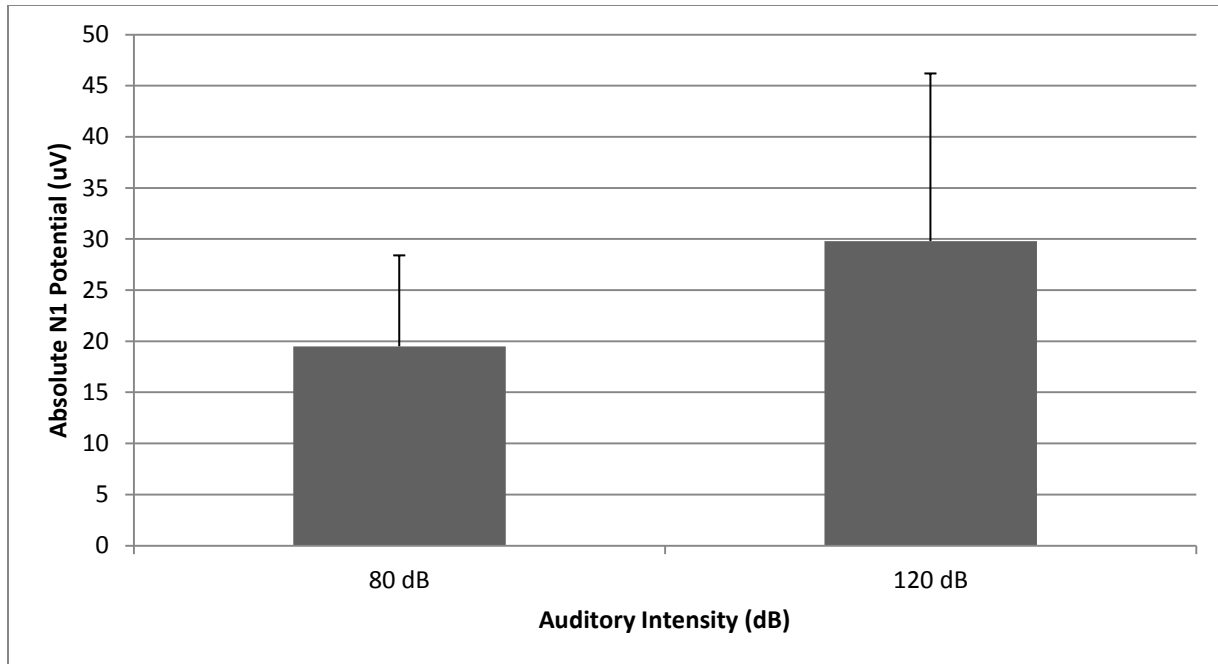


Figure 3-7: Group averages and standard deviations for absolute peak amplitudes of the N1 potential from the Cz electrode site during the sensory task. The 120 dB amplitudes were significantly larger than the 80 dB amplitudes ($F_{[1,11]}=16.43$, $p<0.05$).

3.3.2 Motor Task

The grand average auditory evoked potentials in the motor task are displayed in **Figure 3-8**. The average latency of the long latency N1 peak was significantly shorter in the high intensity auditory tone trials, decreasing from 109.9 ± 10.2 ms in the 80 dB trials to 99.2 ± 15.7 ms in the 120 dB trials ($F_{[1,11]}=8.00$, $p<0.05$) (**Figure 3-9**). The average amplitude of the long latency N1 peak was significantly larger in the high intensity auditory tone trials, increasing from -19.6 ± 13.9 uV in the 80 dB trials to -31.8 ± 17.6 uV in the 120 dB trials ($F_{[1,11]}=18.33$, $p<0.05$) (**Figure 3-10**). There was no significant difference in the latency of the P2 wave, 197.1 ± 60.0 ms in the 80 dB trials and 194.1 ± 60.3 ms in the 120 dB trials ($F_{[1,11]}=1.83$, $p=0.20$).

Furthermore, there was also no significant difference in the amplitude of the long latency P2

wave, 3.5 ± 8.7 uV in the 80 dB trials and 6.0 ± 12.0 uV in the 120 dB trials ($F_{[1,11]}=3.29$, $p=0.097$).

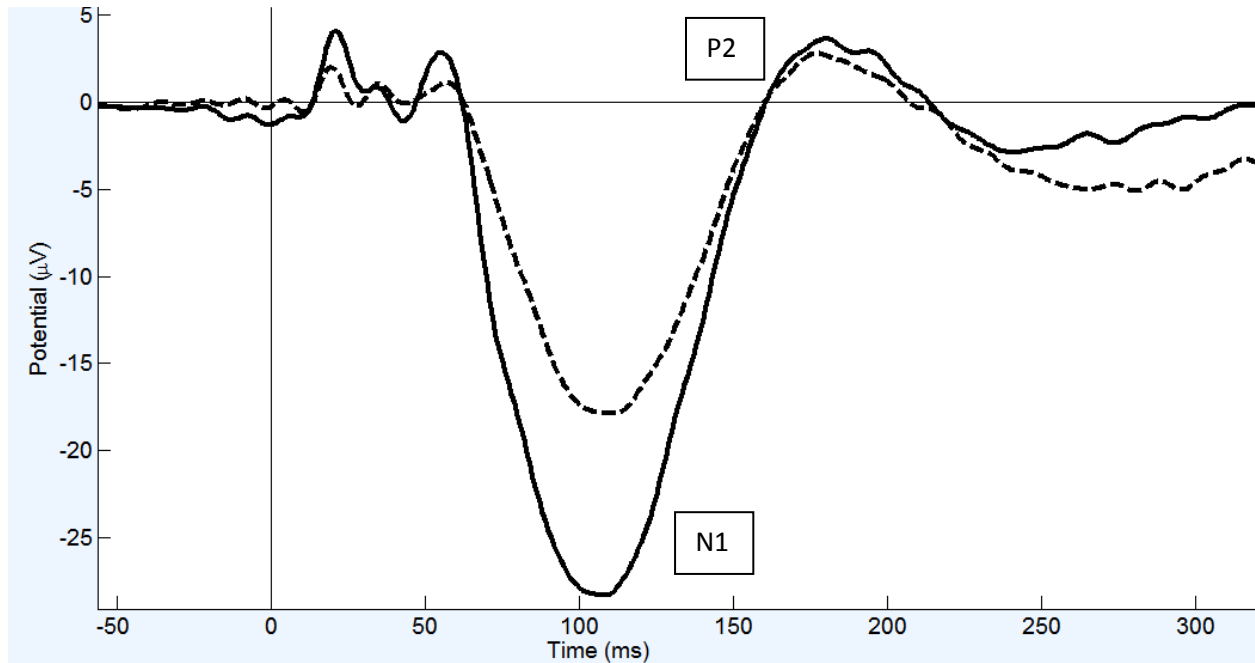


Figure 3-8: Grand average auditory evoked potentials (AEPs). AEPs were recorded from the Cz electrode site. Time 0 represents the auditory stimulus onset. SOLID line indicates 120 dB potentials and the BROKEN line indicates 80 dB potentials. The N1 and P2 waves are labelled.

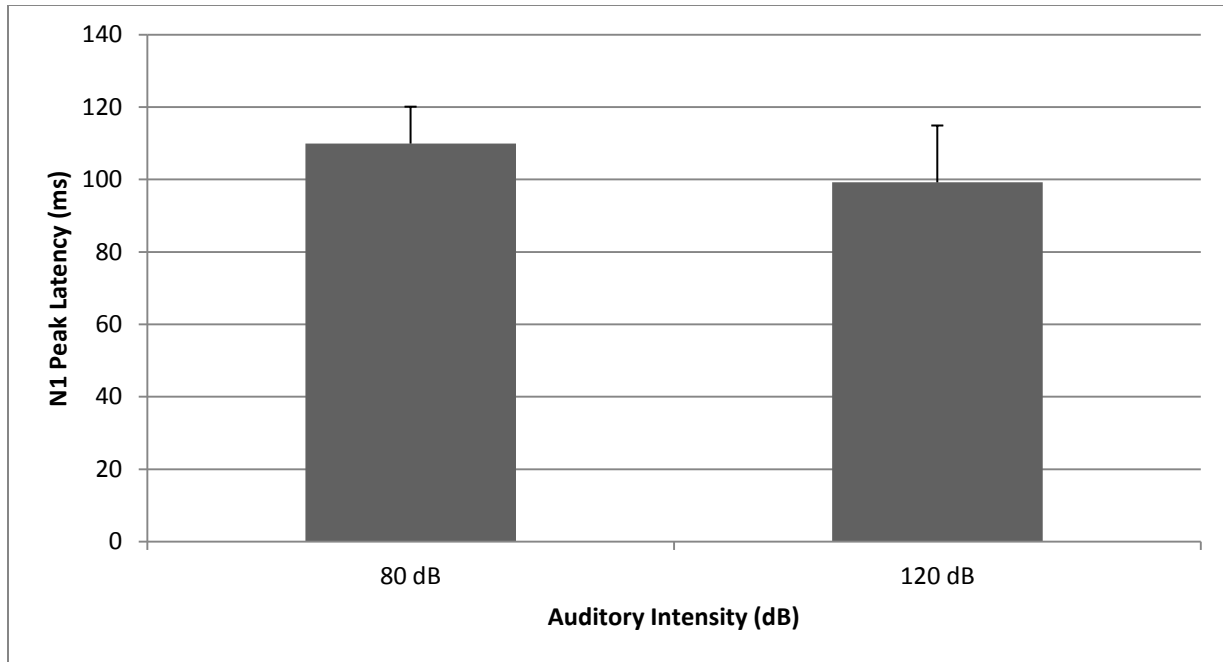


Figure 3-9: Group averages and standard deviations for peak amplitude latency of the N1 potential from the Cz electrode site during the motor task. The 120 dB peak latencies were significantly shorter than the 80 dB peak latencies ($F_{[1,11]}=8.00$, $p<0.05$).

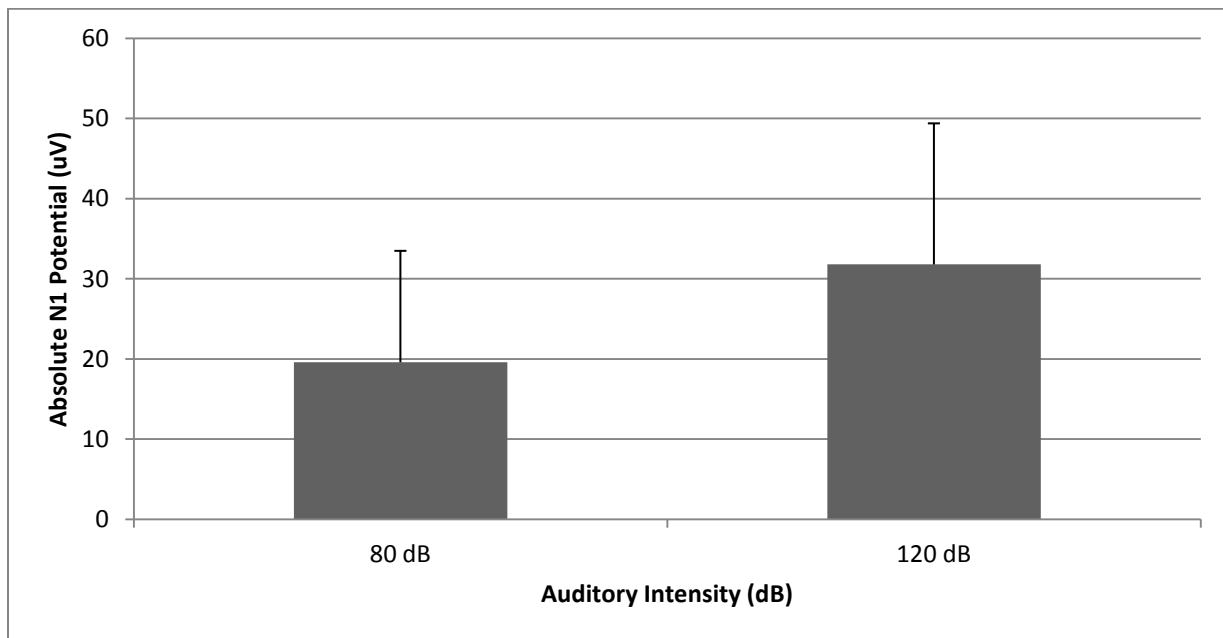


Figure 3-10: Group averages and standard deviations for absolute peak amplitudes of the N1 potential from the Cz electrode site during the motor task. The 120 dB amplitudes were significantly larger than the 80 dB amplitudes ($F_{[1,11]}=18.33$, $p<0.05$).

Overall, there was a consistent large pre-movement negativity (Pre-N) that was maximal at the Cz cortical site (**Figure 3-2**). There was no significant difference in the onset of the Pre-N between high intensity (120 dB = -188.9 ± 30.6 ms) and low intensity (80 dB = -193.2 ± 24.4 ms) task conditions ($F_{[1,11]}=0.84$, $p=0.38$). However, there was a significant difference in the amplitude of the Pre-N potential between the high intensity (120 dB = -23.3 ± 13.8 uV) and low intensity (80 dB = -12.9 ± 10.4 uV) task conditions ($F_{[1,11]}=16.83$, $p<0.05$) (**Figure 3-5**).

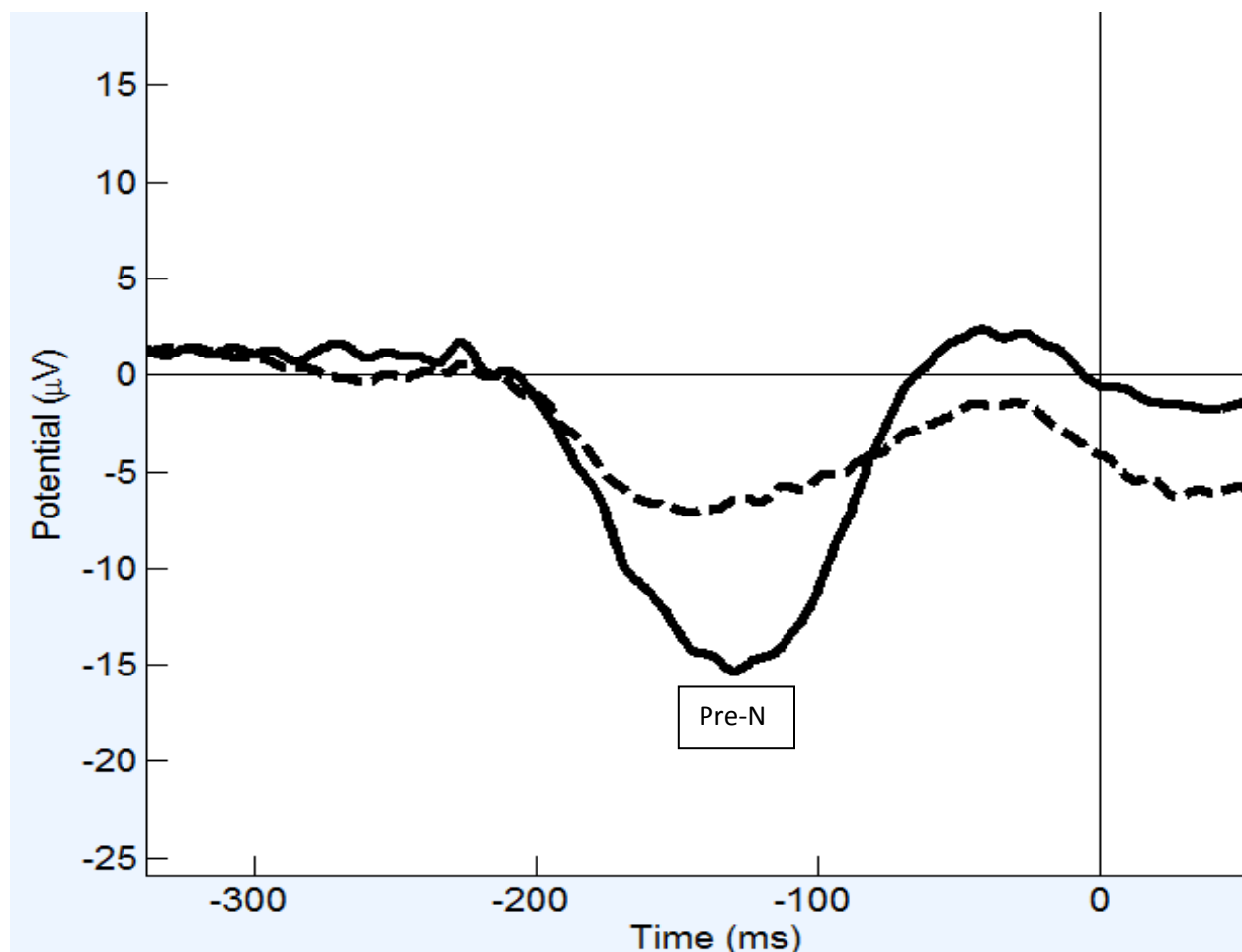


Figure 3-2: Grand average event related potentials (ERPs). ERPs were recorded from the Cz electrode site. Time 0 represents the onset of muscle activity. SOLID line indicates 120 dB potentials and the BROKEN line indicates 80 dB potentials. The Pre-N wave is labelled.

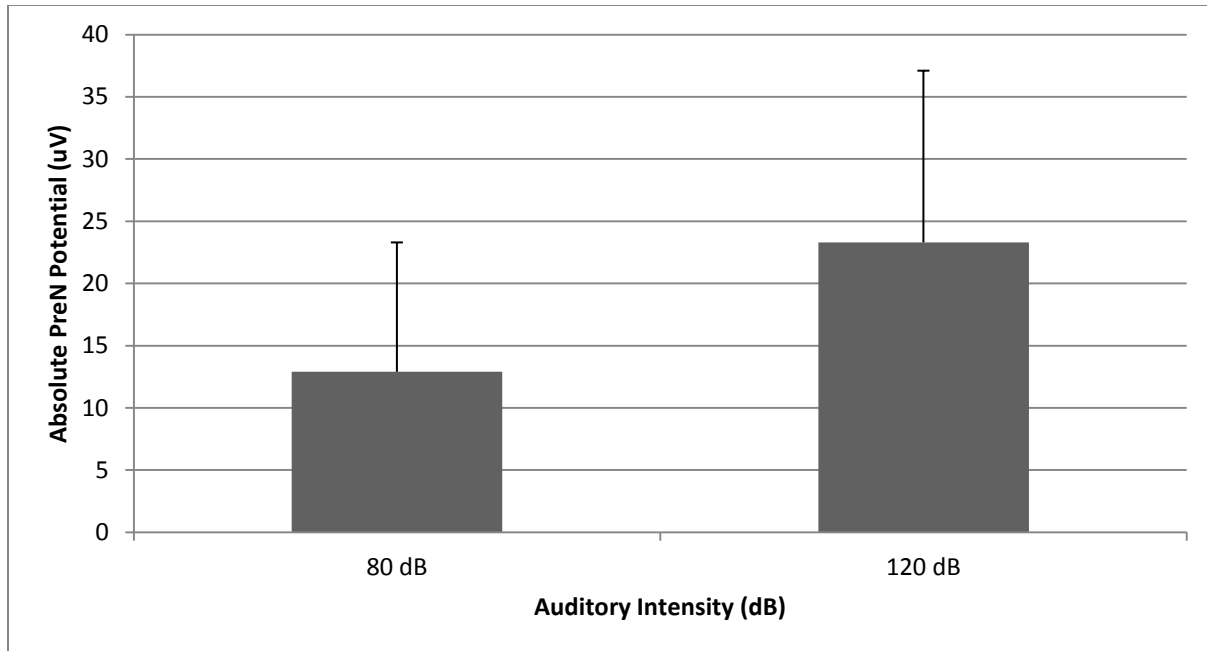


Figure 3-5: Group averages and standard deviations for absolute peak amplitudes of the Pre-N potential from the Cz electrode site. The 120 dB amplitudes were significantly larger than the 80 dB amplitudes ($F_{[1,11]}=16.83$, $p<0.05$).

3.3.3 Reaction Time

The average reaction times for the motor task are shown in **Figure 3-1**. Overall, reaction times measured from tibialis anterior EMG onset were significantly different between stimulus intensities (120 dB = 255.2 ± 56.6 ms; 80 dB = 292.1 ± 37.2 ms; $F_{[1,11]}=24.42$, $p<0.05$). **Figure 3-11** displays all reaction times across all participants. **Figure 3-12** displays an example of reaction times across stimulus intensity for participant 9. Participant 9 is a good representation of the mean showing a gradual decrease in reaction time with increasing stimulus intensity.

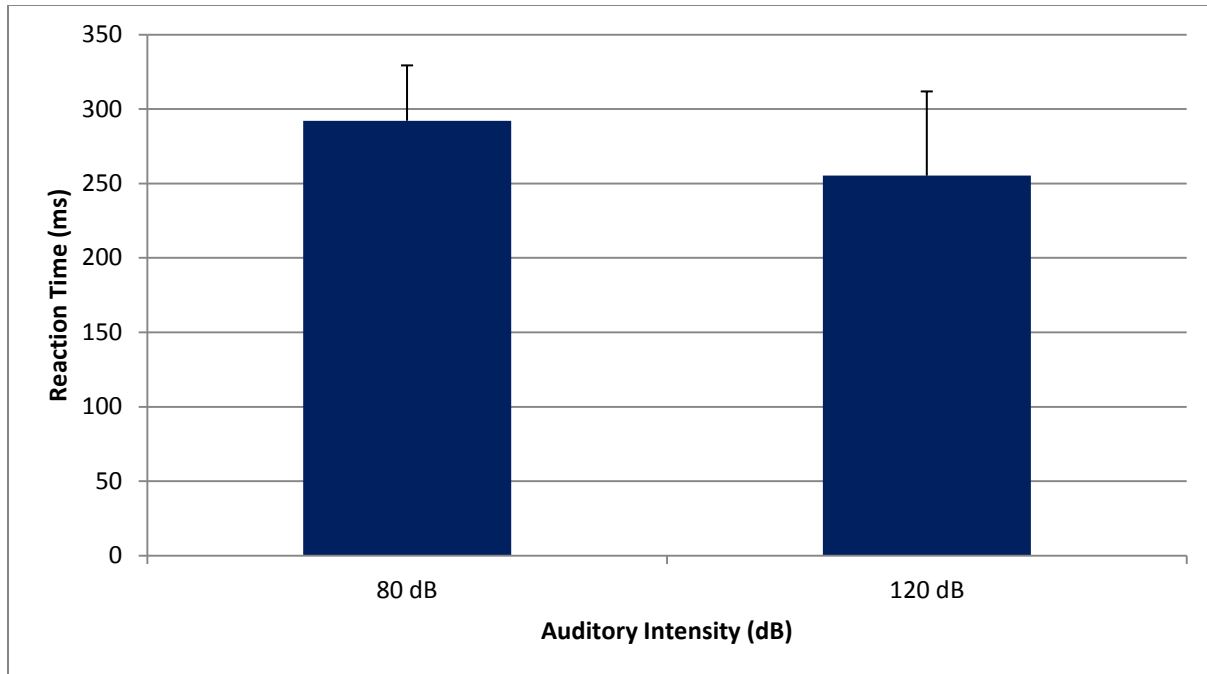


Figure 3-3: Group averages and standard deviation for reaction times by stimulus intensity. There was a significant difference between the 80 dB and 120 dB reaction times ($F_{[1,11]}=24.42$, $p<0.05$).

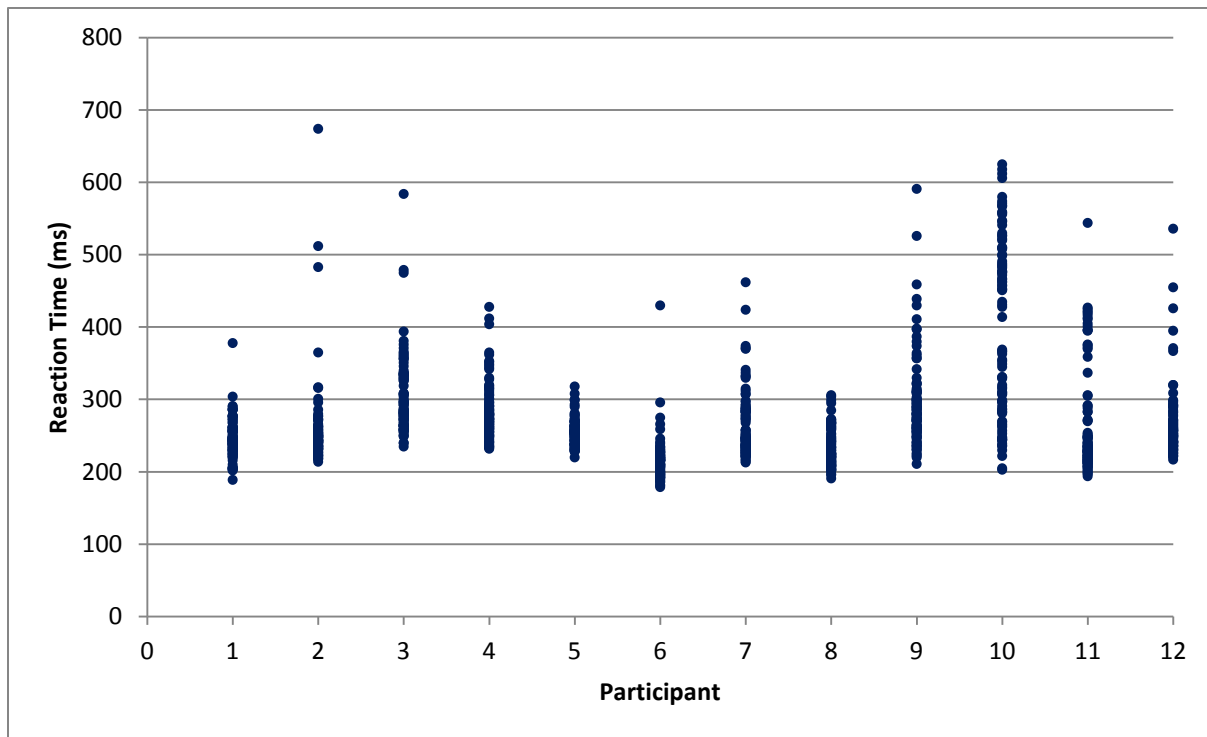


Figure 3-11: Distribution of reaction times for each participant in simple reaction time tasks collapsed across both stimulus intensities (80 and 120 dB).

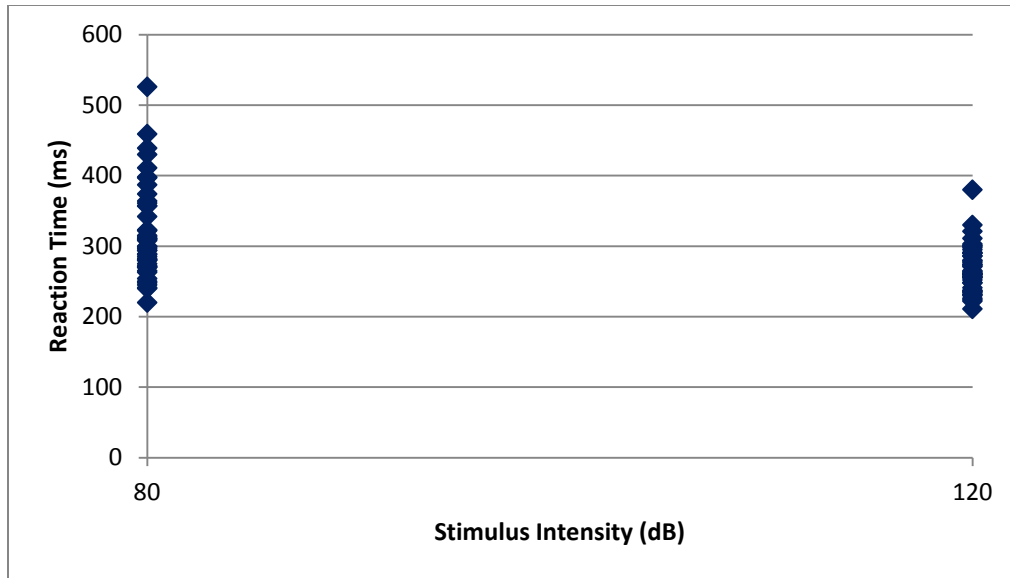


Figure 3-12: Individual reaction times from participant 9 in the motor task across the two stimulus intensities.

3.3.4 Galvanic Skin Response

Galvanic skin response amplitude was greater in response to high intensity auditory stimuli for both motor (120 dB = 6.0 ± 5.3 mS; 80 dB = 2.1 ± 2.0 mS; $F_{[1,11]}=12.82$, $p<0.05$) and sensory (120 dB = 3.7 ± 2.7 mS; 80 dB = 1.4 ± 1.0 mS; $F_{[1,11]}=13.89$, $p<0.05$) task conditions.

The average galvanic skin response amplitudes for motor and sensory task conditions are shown in **Figure 3-4**.

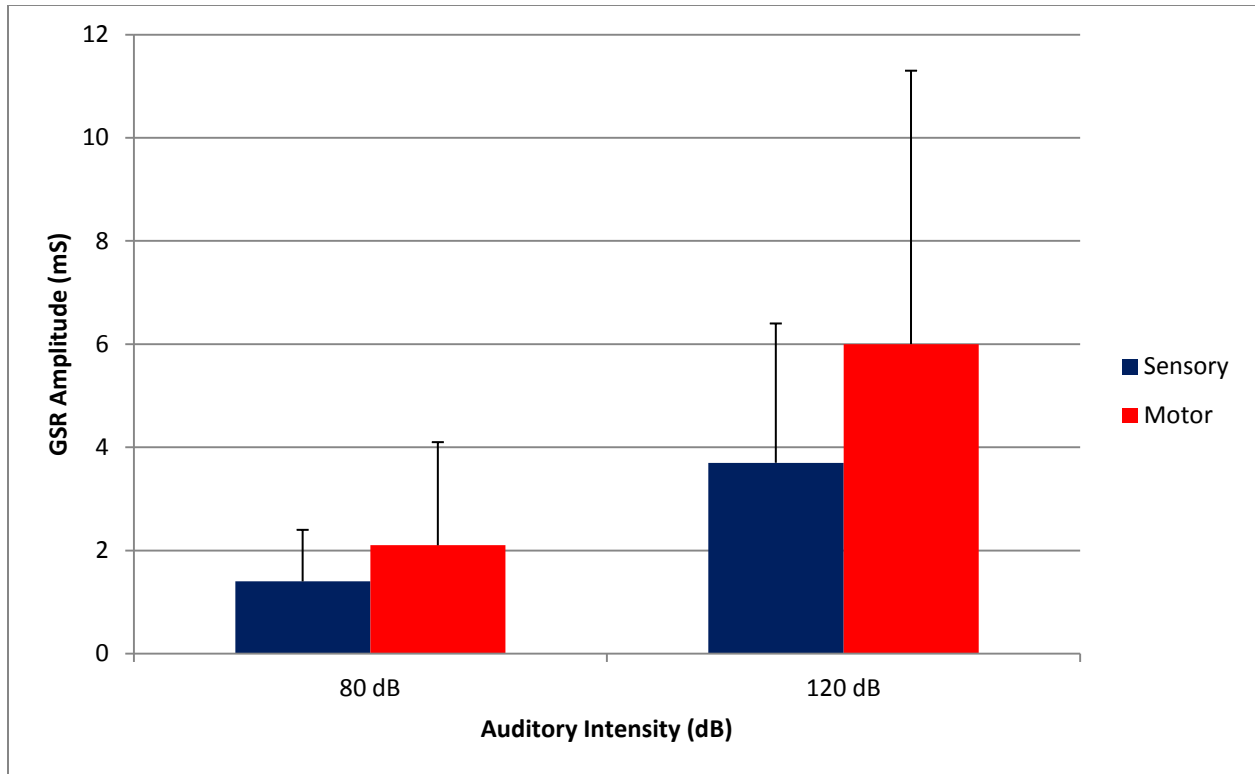


Figure 3-4: Group averages for GSR amplitudes and standard deviations by stimulus intensity and task condition. BLUE bar indicates the sensory task condition and the RED bar indicates the motor task condition. GSR amplitude was greater in response to high intensity auditory stimuli for both motor ($F_{[1,11]}=12.82, p<0.05$) and sensory ($F_{[1,11]}=13.89, p<0.05$) task conditions.

3.4 Discussion

The primary goal of this study was to explore the relationship of auditory stimulus intensity on reaction time, with an emphasis on understanding the electrophysiological correlates associated with auditory stimulus-evoked differences. More specifically the study explored when the application for higher intensity stimulation would lead to increase cortical excitability associated with sensory and movement related potentials. This study demonstrated that high intensity auditory stimuli evoked a more rapid motor responses than low intensity stimuli, consistent with earlier studies (Kohfeld, 1971; Grice, 1958). Furthermore, AEP latencies were significantly different between the 120 dB and 80 dB intensities suggesting that an increase in

sensory processing speed may contribute to faster reaction times. Additionally, ERPs demonstrated a larger cortical negativity in the 120 dB trials approximately 120 to 130 ms prior to motor onset during the reaction time task which may indicate a possible link between a reduction in reaction time and augmentation of motor preparation.

3.4.1 Reaction times are related to stimulus intensity

The current observation of a reduction in reaction time with increasing stimulus intensity confirms the results from study 1. The amplitude of changes observed were comparable (difference of 40.9 ms between 80 and 120 dB in study 1 and difference of 36.9 ms between 80 and 120 in study 2). Reaction time reduction to an increase in stimulus intensity is well established. Many studies, across various domains and modalities, have demonstrated the important role of stimulus intensity on an individual's reaction time (Pins & Bonnet, 1995; Bell et al., 2005; Jaskowski & Sobieralska, 2004; Carreiro et al., 2011). As noted, the potential mechanisms of this change are: 1) increases post-synaptic excitation due to temporal and spatial summation reducing synaptic delays (LATER) and 2) increases engagement of autonomic nervous systems which, via parallel pathways, may augment facilitation. The LATER model proposes that following stimulus presentation the rate of neuronal firing increases the speed required to reach threshold resulting in a reaction (Reddi & Carpenter, 2000). Autonomic contributions via parallel pathways resulting in pathway facilitation will be discussed in the following sections.

Reaction times in the current study were slower compared to others (Carlsen et al., 2007). No pre-cuing was used in the current study which could account for large discrepancies in reaction time. However, reaction times in the present study were approximately 50 ms faster

than reaction times in study 1. One reason for this difference is individual differences among participants where study 1 may have had some abnormally slow individuals. Another possible reason for the discrepancy is practice. Study 2 utilized only the right foot for motor execution with no other movements in between trials, therefore participants may have been able to execute slightly faster reactions simply due to repetition.

3.4.2 Faster reaction time maybe partially due to changes in the latency of auditory processing

The attempt to reveal potential mechanisms underlying faster reaction times using EEG following an auditory stimulus is an important and unique step to better understand the factors that account for significant changes in speed of processing. The present study revealed a significantly reduced latency in the peak of N1 long latency auditory waveform (105.99 ms for low intensity, 94.58 ms for high intensity). The results suggest that the reduction in reaction time to a higher intensity auditory stimulus may begin at the sensory level. Most likely the higher amplitude tone stimulates a larger number of auditory hair cells which begins a cascade of increased neural recruitment (suggested by the increased EEG amplitude), resulting in shorter synaptic delays and faster processing times within the sensory pathway. However, the decrease in N1 latency in the high intensity conditions (105.99 ms to 94.58 ms) is not proportional to the decrease in reaction time (292.12 ms to 255.23 ms). This suggests that the increase in sensory conduction may contribute to the overall decrease in reaction time to higher stimulus intensity but is not the only mechanism responsible.

3.4.3 The amplitude of ERPs is related to the stimulus intensity

There was also a significantly greater Pre-N peak following presentation of the higher stimulus intensity. It is important to note that there was no statistical significance in the timing of the onset of the Pre-N between the high intensity and low intensity auditory stimulus. However, the ERP potentials were epoched around the EMG onset and the higher intensity stimulus resulted in earlier EMG onsets, making it more difficult to interpret the meaning of timing changes. The increased amplitude prior to the motor response suggests a possible mechanism for the faster reaction time in the high intensity trials. It is possible that the Pre-N amplitude influences the processing time of the sensory motor integration. In other words, the greater synchronization of neural activity, recorded from the Cz site, could signify an important component of the transition from somatosensory areas to pre-motor areas and primary motor cortex that acts to encode and plan the appropriate reaction. The increase in neural activity may be related to a greater amount of synaptic facilitation through shorter synaptic delays and resulting in faster speed of processing. However, further research on the Pre-N potential is required to determine any potential link between spatial and temporal properties and reaction time changes.

3.4.4 Increased GSR amplitude is related to faster reaction times

There was significantly greater GSR amplitude after presentation of the high intensity auditory stimulus compared to the low intensity stimulus consistent with study 1. Furthermore GSR amplitude appeared to be greater when a motor response was required compared to the sensory condition. The increase in GSR amplitude suggests a larger amount of ANS activity after the presentation of the high intensity stimulus and during motor execution. This also

suggests that there was a larger amount of ANS activity during the motor task. Such changes in GSR response to sensory stimulation (Sibley et al., 2009; 2010a; 2010b) have been demonstrated previously for rapid balance reactions. In addition, previous studies have also revealed increased GSR when executing challenging motor tasks (Mochizuki et al., 2009). Such findings reveal the complexity in interpreting the autonomic reactivity that appears to consistently occur in response to unpredictable sensory stimuli. That said, it is hypothesized that the increase in ANS activity during the 120 dB motor task may be responsible for the larger Pre-N negativity observed prior to the EMG onset and is the underlying mechanism for the faster reaction times seen in higher intensity stimuli. One possible structure for the increase in ANS activity is the locus coeruleus neurons in the brainstem. These neurons utilize nor-epinephrine as a neurotransmitter and give rise to diffuse innervations of the entire brain that includes the cerebral cortex and the spinal cord (Jones & Yang 1985; Jones & Moore 1977). They are specifically involved in cortical activation as well as sensory-motor activity during waking and are maximally discharged in situations associated with highly aroused conditions (Aston-Jones et al., 1996). The high intensity auditory tones may activate LC neurons which send projections to motor and pre motor cortical areas contributing to the large Pre-N potential influencing the pre planned motor action and decreasing processing time. This hypothesis has not been confirmed and further research is required to determine the potential role of the ANS in the augmentation of rapid reactions.

3.5 Conclusion

The current study set out to investigate the electrophysiological determinants (AEPs and ERPs) of rapid reaction times evoked by differences in auditory stimulus intensity. Increased stimulus intensity has statistically significant effect on the latency and amplitude of cortical

activity, while generating significantly shorter reaction times, however not accounting for the complete reaction time reduction. Additionally, ERPs relative to the reaction time (EMG onset) demonstrated a significantly greater pre-motor negativity following the high intensity stimulus, which may be related to movement planning and execution of more rapid reactions. This work has important implications for understanding the mechanisms by which the CNS processes the various characteristics of stimuli that could be used to assist in rehabilitation methods for individuals who may be at risk of reacting slow, such as individuals who suffer from neurological movement disorders or elderly individuals. Further work is required to explore the potential role of the ANS in reducing reaction time latencies to highly intense stimuli.

CHAPTER 4: GENERAL DISCUSSION

4.1 Overall Summary of Findings

The primary objectives of this thesis were to explore the influence of stimulus intensity as a modulator of speed processing and to identify potential CNS mechanisms of speed of processing augmentation. Previous research in this field has argued that extremely rapid reactions, such as those evoked after an external balance disturbance or in response to a startling auditory stimulus, may be pre-planned motor control programs that are initiated at the subcortical reticular formation (Carlsen et al., 2004; Valls-Solé et al., 1995). This thesis provided evidence that, while subcortical areas may indeed play a role in the facilitation of rapid reactions, processing still takes place along existing cortical pathways of the CNS, which may be modulated by other nervous system structure such as the ANS reactivity.

Simple and choice reaction time both decreased with an increasing in stimulus intensity with the same proportion suggesting the mechanisms accounting for differences were similar between the two tasks. Choice reaction time utilizes a multi-synaptic cortical network pathway to identify the stimulus, decide on the proper reaction, and then execute said reaction (Schmidt & Lee, 1999). Furthermore, GSR amplitude increased as stimulus intensity increased for both simple and choice reaction time tasks. Based on the results of study one it is hypothesized that there are 2 factors by which the CNS increases processing speeds; 1) increase in stimulus intensity leads to a greater recruitment and increased firing rate of cochlear hair cells and 2) activated parallel pathways, possibly mediated by ANS networks, that speed up processing time through synaptic facilitation.

Although results from the first experiment indicated the potential primary influence of the stimulus intensity on reaction time, a further study was undertaken to explore the electrophysiological correlates of the CNS to generate reactions to low and high intensity

auditory stimuli. The study revealed a significantly reduced latency in the peak of N1 long latency auditory waveform for the high intensity auditory stimulus. The results suggest that the reduction in reaction time to a higher intensity auditory stimulus occurs early in the early stages of processing, however, the reduced latency of the N1 could only account for portion of the 40 ms reduction in reaction time latency. ERP analysis, time locked to the onset of EMG activity revealed a large negativity prior to the reaction time consistent with results from Lakhani et al. (2012). Furthermore, GSR activity was significantly greater during the high intensity trials. This increase of cortical activity prior to the motor response and the large GSR output may link cortical facilitation with ANS reactivity to increase speed of processing.

4.2 CNS Influences in Response to High Intensity Stimuli

The primary objective of this thesis was to untangle the factors that may account for the generation of rapid reactions to high stimulus intensities. Experiments within this thesis were designed to explore how reaction time can be modulated to differences in stimulus intensity, using both behavioural and electrophysiology methodologies, along the stimulus-response continuum. Although the specific localization of regions of activation was not within the scope of this work, a number of findings from the two presented experiments can be summarized relative to the general locations within the CNS that reaction time modulations might occur, including increases in sensory nerve recruitment and firing rates and cortical facilitation components.

As mentioned before, the sensory receptors of the inner ear (hair cells) are facilitated or inhibited with movement of the basilar membrane. Greater amplitude sounds will cause a greater movement of the basilar membrane increasing depolarization of the hair cells. The

amplitude of the sound wave (ie loudness) is coded from the firing rate of the hair cell neurons (Kelly, 1991). Electrophysiological results from study two showed that an increase in auditory stimulus intensity results in a faster onset latency of cortical activity. This suggests that faster sensory processing may contribute to the overall reduction in reaction time with an increase in stimulus intensity. However, the reduction in cortical latencies did not account for all of the reduction observed at the behavioural level.

Both studies demonstrated an increase in GSR activity with an increase in stimulus intensity suggesting an increase in autonomic nervous system output. Furthermore, study two results showed a large synchronization of neural activity prior to the muscular onset. One possibility is the increase in ANS activity resulting from an increase in stimulus intensity facilitates faster reactions at the cortical level.

A possible mechanism for the increase in ANS activity is related to activity of the locus coeruleus (LC) neurons in the brainstem. Activation of norepinephrine producing neurons of the LC may contribute to more rapid reaction time seen in high intensity auditory tones and would explain the increase in GSR due to the vast connections of the LC throughout the CNS including motor and pre-motor areas (Bouret & Sara, 2002; Lecas, 2004). It is hypothesized that the high intensity auditory tones activate LC neurons in the brain stem which send projections to motor and pre motor cortical areas influencing the pre planned motor action and decreasing integration time. Further research is required to determine if there is increased LC activity following startle intensity auditory tones and the direct influence on sensorimotor pathways.

4.3 Limitations and Future Directions

Despite identifying stimulus intensity as an important modulator involved in the determination of speed of processing within the CNS, there were a number of limitations that can be addressed by future experimentation. Firstly, although it was beyond the scope of this thesis, discussions regarding the specific CNS mechanisms would be possible via technologies with high spatial resolution in conjunction with the tools that were used within this thesis. In order to reveal the specific networks of activation involved in the reduction of speed of processing, future investigations will benefit from coupling both temporal and spatial lines of inquiry. In addition, the current paradigm evoked reactions in the range of 220-450 ms and did not evoke more rapid reactions. This raises the possibility of different mechanisms if more rapid responses could have been evoked. Finally, the GSR as a measurement tool is limited in its temporal resolution due to the nature of the evoked sweat response, complicating the analysis of the influence of the ANS within the sensory motor transformation. Currently there does not appear to be a measurement tool of ANS activity that offers more precise temporal resolution with adequate spatial (amplitude) information. However, another option for future research designs could possibly utilize participants with autonomic nervous system impairments or exploring the specific effects of drugs that influence ANS reactivity.

4.4 Summary & Conclusions

The primary objectives of this thesis were to recognize stimulus intensity as an important modulator of speed processing in urgent situations and to identify potential CNS mechanisms of speed of processing augmentation. Study one revealed a reduction in reaction time regardless of task with an increase in stimulus intensity as well as increased GSR response amplitude to higher

stimulus intensities. Electrophysiological results from study two showed a reduced latency in sensory cortical activity after being exposed to higher stimulus intensities. Furthermore, there is a large synchronization of cortical activity prior to the EMG onset during the high stimulus intensity trials. The results collected from both studies suggest that an increase in stimulus intensity increased the speed of processing of the CNS in two ways; 1) increased the firing rate of the hair cells within the organ of Corti and 2) activated the ANS to facilitate cortical processing of the motor response.

Outcomes from this work indicate the potential modifiability of reaction time in individuals who suffer from delayed speed of processing due to natural aging processes or neurological movement disorders. Despite potentially damaged areas of injury in these susceptible populations, results from this thesis indicate the potential for increasing reaction time throughout the CNS. This provides a basis for future research to examine novel rehabilitation strategies, which attempt to take advantage of remaining intact features of the CNS in order reduce speed of processing for these individuals to make them less prone to debilitating injuries that accompany delayed speed of processing.

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