USING ACOUSTIC STIMULI TO INHIBIT THE STARTLE RESPONSE TRIGGERED BY WHIPLASH COLLISIONS: IMPLICATIONS FOR INJURY PREVENTION

by

DANIEL MANG

B.Sc, Boston University, 2007

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE STUDIES
(Human Kinetics)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

April 2010

Abstract

Introduction: In British Columbia, whiplash injuries and its associated disorders are serious economical and social burdens to society. Despite affecting less than 1 percent of the population, whiplash injuries costs of over 850 million dollars annually (ICBC 2007). In recent studies, the startle response was shown to form part of the neuromuscular response to whiplash-like perturbations (Blouin et al. 2006a and b). In non-whiplash experiments, a weak or startling pre-stimulus tone presented before a subsequent startling stimulus can inhibit the startle response (Ison and Krauter 1974; Valls-Sole et al. 2005). The **objective** of the present study was to investigate how different pre-stimulus tones (weak and startling) affected the amplitude of muscle responses and the peak magnitude of head kinematics observed in human volunteers during whiplash-like perturbations.

Methods: Twenty healthy subjects experienced five consecutive whiplash-like perturbations presented simultaneously with a loud collision sound (109 decibels (dB)). The three experimental conditions differed with the intensity of pre-stimuli tone presented 250 milliseconds prior to the onset of the perturbation: 1.) no pre-stimulus tone (*Control*), 2.) a weak pre-stimulus tone (85dB) and 3.) a startling pre-stimulus tone (105dB). Electromyography (EMG) of neck and distal limb muscles, and kinematics of the head and trunk were simultaneously collected. Mixed model ANOVAs and *post-hoc* Tukey's honest significant difference test were used to analyze each EMG and kinematic variable (alpha=0.05).

Results: Presenting a startling pre-stimulus tone before the whiplash-like perturbation decreased muscular (sternocleidomastoid: −16%, C4 paraspinal: −26%, biceps brachii: −66%, triceps brachii: −62%, first dorsal interosseous: −68%, and rectus femoris: 78%) and kinematic (peak retraction: −17%, peak horizontal acceleration of the head: −23%, and peak head angular acceleration in extension: −23%) responses from *Control* condition ($p<0.05$). A weak pre-stimulus tone decreased only the muscular responses of triceps brachii (−38%), first dorsal interosseous (−48%) and rectus femoris (−57%) from *Control* condition ($p<0.01$).

Conclusion: A startling tone presented prior to a whiplash-like perturbation alters the head-neck responses in ways that are consistent with reducing neck tissue strains. This study is an initial step in the development of preventive devices to decrease the whiplash injury potential during low-speed, rear-end automotive collisions.

Table of Contents

List of Tables

List of Figures

Acknowledgements

I would like to express my sincerest gratitude to my supervisors, Drs. Jean-Sebastien Blouin and Gunter Siegmund, for their continued support throughout the duration of the Master of Science (MSc) program. Without their vision, guidance, and enthusiasm, this thesis would not have been possible. Throughout the writing period of my thesis, they helped me with my writing technique, provided encouragement, and most of all, were patient with the gradual learning process. To the both of you, thank you for always having your doors open to answer questions, providing the freedom to grow as an independent researcher and making my MSc thesis a memorable experience. I would also like to thank my committee member Dr. Tim Inglis, for his humourous, yet insightful, comments and questions. Thank you once again for all your vast knowledge and assistance at all levels of this thesis project.

Thank you to Mr. Jeff Nickel and Mr. Mircea Oala-Florescu of MEA Forensic Engineers and Scientist for helping me operate, maintain and modify the perturbation sled used in this experiment. I would also like to thank my friends, fellow graduate students and colleagues in the Sensorimotor Physiology Laboratory for their patience, words of encouragement and willingness to be subjects in my experiment.

Lastly, I would like to thank my family for the support they provided me through my entire life. This accomplishment was only possible because of the many opportunities you provided me.

1 Literature Review

1.1 Epidemiology

Whiplash injuries are the most common type of injuries in motor vehicle accidents and rear-end collisions pose the greatest risk of whiplash injury at 48% compared to frontal (20%) and side (14%) collisions (Jakobsson et al. 2000; ICBC 2006; ICBC 2007). Whiplash injuries account for approximately 70% of all injury claims reported by the Insurance Corporation of British Columbia (ICBC) (ICBC 2000). In 2000, ICBC paid out over $500 million—50% of all injury payouts—for whiplash injuries and whiplash-associated disorders (WAD). Half of the money paid for medical treatment and the other half covered the lost wages and diminished earning capacity of drivers and occupants injured (ICBC 2000). In 2006, the estimated cost of whiplash injuries and WAD (excluding litigation costs) increased to approximately $850 million (ICBC 2007).

The annual incidence of WAD in the western world ranges from 28 to 834 per 100,000 inhabitants (Otremski et al. 1989; Cassidy et al. 2000; Holm et al. 2008). Women are 1.2 to 3 times more likely to suffer from whiplash injuries after a rear-end car collision as compared to men (Harder et al. 1998; Versteegen et al. 2000; Mordaka and Gentle 2003). Females between the ages 20 to 24 present the highest incidence rate of reported WAD with 965 cases per 100,000 people annually (Quinlan et al. 2004). The greater susceptibility of younger females is hypothesized to be related to the gender differences in anatomical, physiological, behavioural and sociological parameters

(Mordaka and Gentle 2003) as well as the influence of seat properties on neck biomechanics and occupant dynamics (Viano 2003b).

The whiplash injury, WADs and recovery times following whiplash collisions are greatly variable and depend on factors such as impact severity, seat position and stiffness, and subject initial posture (Suissa et al. 2001; Viano 2003a). The most common symptoms following whiplash injuries are neck pain (88-100% of patients) and headaches (54-66% of patients) (Todman 2007). Other symptoms of whiplash injuries include dizziness, auditory symptoms (tinnitus – perceived ringing noise in the ears), paresthesias in the upper extremities, and back pain (Evans 1992; Spitzer et al. 1995; Mordaka and Gentle 2003; Sterner and Gerdle 2004). The recovery time from whiplash injuries depends on the initial whiplash injury severity, but 26% of subjects recover within the first week and the median recovery time is approximately 32 days (Suissa et al. 2001). However, 12% of patients do not fully recover within six months (Suissa et al. 2001) and 5 to 8% of patients do not return to work within a year following the accident (Evans et al. 2001; Buitenhuis et al. 2009). Between 14 and 42% of individuals develop chronic neck pain and approximately 10% are left with permanent severe pain and disability (Barnsley et al. 1994). Due to the high cost per claim in British Columbia (less than 1 percent of the population valuing over 850 million dollars) and the persistence of chronic symptoms of whiplash injuries and its associated disorders, these injuries are a serious economical and social burden to society. Therefore, it is important to reduce the risk and number of whiplash injury per year.

1.2 Whiplash Injury Mechanism to the Zygapophysial Joint

Although the exact aetiology of whiplash remains unclear, the cervical zygapophysial joints have been identified as a possible source for pain (Barnsley et al. 1995). In a double-blind clinical study, the cervical zygapophysial joint was the most common source of neck pain in approximately 40-68% of patients with whiplash injuries (Barnsley et al. 1995). The cervical zygapophysial joints (or cervical facet joints) are located between each pair of cervical vertebrae from C2 – C7. This joint is classified as a synovial joint because it is enclosed by a thin capsular ligament, or facet joint capsule, which is lined by a synovial membrane as illustrated in **Figure 1.1**. Fibro-adipose meniscoids or synovial folds, are found between the articular facets and function to

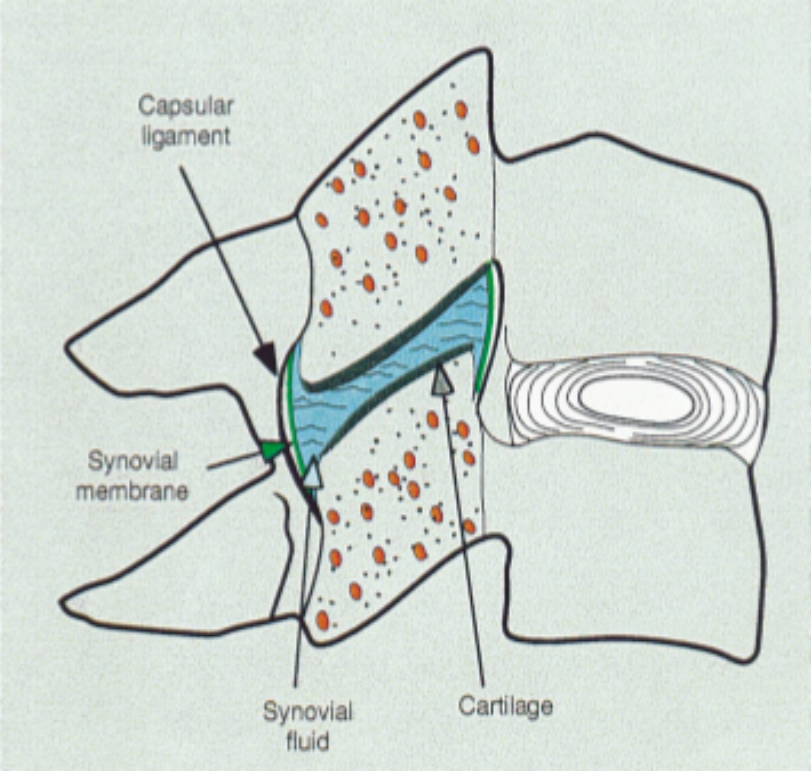


Figure 1.1 Illustration of the zygapophysial joint. Reprinted with permission from (Yoganandan et al. 2001)

protect the articular cartilages during normal movement of the zygapophysial joint (Mercer and Bogduk 1993). The capsular ligament is innervated by both mechanoreceptors and nociceptors providing neural inputs responsible for proprioception and pain sensations, respectively (Wyke 1972; Wyke 1979; McLain 1994; Inami et al. 2000; Inami et al. 2001; Azar et al. 2009). The facet joints and capsular ligaments provide axial rotational, segmental shear strength and lateral bending stability, but contribute little to flexion-extension stability of the cervical spine (Raynor et al. 1985; Onan et al. 1998).

Kinematics of the facets joints and capsular ligaments during simulated whiplash-like perturbations have been observed in human cadaver experiments (Yoganandan et al. 1998; Winkelstein and Myers 2000; Pearson et al. 2004; Stemper et al. 2005) and volunteer studies (Kaneoka et al. 1999). As a result, two mechanisms of injury to the cervical zygapophysial joint have been proposed: pinching of the synovial fold and excessive strain to the facet capsule. The sudden flexion and extension of the neck following a rear-end impact causes abnormal motions of the cervical spine and zygapophysial joints (Kaneoka et al. 1999; Luan et al. 2000). Kaneoka et al. (1999) observed that whiplash motion may shift the instantaneous axis of rotation (IAR) of the cervical vertebra bodies superior causing the posterior facet surfaces to compress together and pinch of the synovial fold (Kaneoka et al. 1999). Consequently, nociceptive fibers found in the synovial fold may be inflamed and could be a possible source of cervical zygapophysial joint pain.

The second possible injury mechanism to the zygapophysial joint is excessive strain to the capsular joint ligament during whiplash motion. Failure testing of the joint capsules has determined mean maximum capsular strain at sub-catastrophic and catastrophic failure threshold to be between 35–65% and 94–104%, respectively (Winkelstein et al. 2000; Siegmund et al. 2001). Pearson et al. (2004) observed capsular ligament strains in the sub-catastrophic range at whiplash-like perturbation accelerations of 6.5 g measure at the thoracic vertebrae T1 and were largest in the lower cervical spine (C6-C7: 39.9%). Peak capsular ligament strains were determined to occur between 200 to 225 ms after the onset of thoracic vertebrae T1 acceleration (Pearson et al. 2004). During whiplash motions, activation of the cervical multifidi spinae muscle coincided with the timing of peak capsular ligament strain and, in about half the subjects (55.6%), the muscle activity was greater than their recorded maximum voluntary contraction (MVC) level (Siegmund et al. 2008a). The cervical multifidi muscles, part of the transversospinal muscle group, insert directly on the cervical capsular ligaments and can be divided into two layers based on their attachment locations: superficial and deep fascicles as shown in **Figure 1.2.** (Anderson et al. 2005). Both the superficial and deep fascicles span two to five vertebral levels in length but differ in their sites of origin and insertion (Malanga and Nadler 2002; Anderson et al. 2005). Most fascicles of the superficial cervical layer originate directly from the lateral to posterolateral aspect of the cervical facet capsules of C4-C7 to insert on the spinous process of the superior vertebrae. Whereas, most of the deep cervical fascicles originate from the cervical facet capsule, more posterior and medial than the superficial layers to insert on the laminae of superior vertebrae. The forces generated by the multifidi during whiplash collisions will

cause the muscle to pull directly on the cervical facet capsular ligament. Increased muscle activity may occur at a moment when the ligament is vulnerable and exacerbate peak strain on the capsular ligament (Winkelstein et al. 2000; Siegmund et al. 2001; Siegmund et al. 2008a). In some subjects, the peak capsular ligament strain may be increased into the sub-catastrophic failure range and result in whiplash injury.

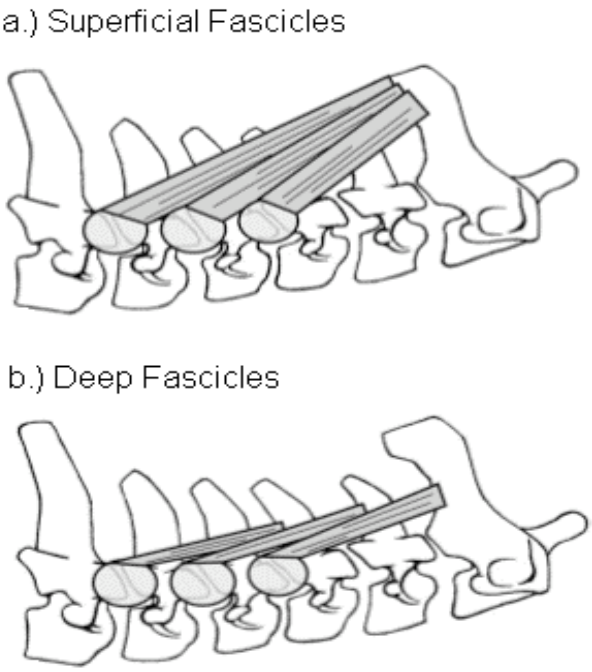


Figure 1.2 Schematic drawings illustrating attachment sites of three fascicular subgroups for a.) superficial cervical multifidus and b.) deep cervical multifidus. Reprinted with permission from (Anderson et al. 2005).

1.3 Low-Velocity Human Volunteer Whiplash Experiments

1.3.1 Biomechanics and Kinematics of Whiplash-Like Perturbations

The biomechanics of human subjects during a low-speed rear-end collision are quite variable and depend on the magnitude and shape of the acceleration pulse, seat back properties (stiffness and angle) and subject's initial posture. The biomechanical movements of the torso, head and neck can be divided into two phases to help understand whiplash injuries: retraction and rebound phases (Brault et al. 2000; Pearson et al. 2004; Vasavada et al. 2007). The retraction phase is defined from onset of head movement to peak head retraction; whereas, the rebound phase is defined from peak head retraction to peak forward head extension relative to the torso. During the retraction phase, the torso is accelerated faster than the head in the horizontal direction and causes the head to lag behind the torso (McConnell et al. 1995; Luan et al. 2000). The forward acceleration causes the torso to ramp up against the seat back compressing the cervical spine. As a consequence of the shear and compressive forces, the cervical spine forms a non-physiological "S"-shaped curve, in which the lower cervical vertebrae are in extension and the upper cervical vertebrae are in flexion. Neck extension begins at the lower cervical vertebrae and progresses upwards generating a net extension moment of the neck. Shear forces are generated as the inferior facet of a vertebra slides posteriorly along the superior facet of lower adjacent vertebra and the resulting shear motion between facet joints stretches the capsular ligament (Luan et al. 2000; Pearson et al. 2004).

After peak head retraction, the head is accelerated forward relative to the torso due to the internally generated forces of the neck (McConnell et al. 1995) and rebound from the head restraint. As the torso pulls on the lower cervical vertebrae, the head is accelerated forward faster than the torso and the neck changes from extension to flexion. Since the head rebounded forward at a greater velocity than the torso, the neck actively decelerates and stops the head at maximum forward excursion with respect to the torso. After the head reaches maximum forward excursion, the subject's head and torso return back to their pre-perturbation position.

1.3.2 Electromyography of Muscle Responses during Whiplash-Like Perturbation

Anterior and posterior neck muscles have the potential to be injured or to cause injury to other cervical structures because they are active during the whiplash-like perturbation (Brault et al. 2000; Hernandez et al. 2006; Vasavada et al. 2007; Siegmund et al. 2008a). The sternocleidomastoid (SCM) muscle is a key landmark of the anterior neck and is a powerful flexor of the neck when contracted bilaterally (Hiatt and Gartner 1987). Computerized simulations modelled from previous whiplash studies determined peak lengthening of the SCM to occur during the retraction phases and peak shortening of the muscle to occur during the rebound phase (Vasavada et al. 2007). Conversely, posterior neck muscles shortened as the head retracted and experienced peak lengthening as the head rebounded. When the recorded muscle activity data (electromyography (EMG)) were superimposed on to the muscle strain curves, both the anterior and posterior muscles were eccentrically contracting – active during muscle lengthening. Eccentric muscle contractions have been shown to damage muscle fibers, resulting in temporary

loss of the ability to generate force (McCully and Faulkner 1985; McCully and Faulkner 1986; Lieber and Friden 1993). In some subjects, the peak lengthening strains for both anterior and posterior muscles (SCM: 15%, splenius capitis (SPL): 37%, and semispinalis capitis (SEMI): 50%) (Vasavada et al. 2007), in combination with the eccentric muscular contractions were observed to exceed the injury threshold between 15–20% and may potentially cause muscle injury (McCully and Faulkner 1985; McCully and Faulkner 1986; Macpherson et al. 1996; Vasavada et al. 2007). Vasavada et al. (2007) modelled from previous whiplash data that lengthening fascicle strains were greater in posterior neck muscles (SPL and SEMI); therefore, these muscles are more likely to be injured than the SCM. However, direct injury to the neck muscles usually persists up to nine days before subsiding and is unlikely to explain the chronic symptoms observed in some patients (Evans et al. 1986; Scott and Sanderson 2002).

In addition to being injured, neck muscles can indirectly cause injury to other anatomical structures of the neck. During whiplash-like perturbations, neck muscle activity may affect the neck kinematics and spinal tissue strains. One example of this interaction is the direct attachment of the cervical multifidus to the capsular ligament (Winkelstein et al. 2001; Anderson et al. 2005). Siegmund et al. (2008a) observed that the early activation of the multifidus muscle following a whiplash-like perturbation may potentially coincide with the peak capsular ligament strain caused by the impact-induced head and neck kinematics. The additional multifidus activity may potentially injure the cervical facet capsular ligament by increasing peak capsular ligament strain beyond the sub-catastrophic threshold.

1.3.3 Factors Affecting the Human Response to Whiplash-Like Perturbations

The muscular and kinematic responses of humans experiencing a whiplash-like perturbation are affected by multiple factors such as state of awareness and gender differences. A subject's state of awareness to an imminent perturbation, or event, can be divided into three components: amplitude, temporal and event awareness (Frank 1986; Siegmund 2001). Amplitude awareness describes whether a subject knows the amplitude of a perturbation, temporal awareness describes whether a subject knows the exact timing of when a perturbation will occur, and event awareness describes whether a subject knows a perturbation will occur. Siegmund (2001) observed that amplitude awareness did not affect the muscular and kinematic responses at low speeds (< 1.26g); however, it still remains unclear whether a subject's response would be affected by knowing the amplitude of more intense whiplash-like perturbations. Likewise, temporal awareness did not affect the muscular and kinematic responses between subjects who received a countdown to the onset of the perturbation and those who did not ($p > 0.05$) (Siegmund et al. 2003a). In the same study, Siegmund et al. (2003a) deceived subjects and surprised them with an unexpected perturbation to investigate the effects of event awareness. The muscular and kinematic responses of subjects who were deceived had larger rearward retraction and peak head angular acceleration in flexion ($p < 0.05$) than subjects who were aware of the imminent perturbation. Despite the significant effects of event awareness, it is impossible to maintain the initial awareness level of subjects deceived to the first perturbation during repeated perturbation studies. Thus, event awareness may

be a potential limitation of repeated whiplash-like perturbation studies and may not accurately represent the responses of unprepared individuals in real rear-end collisions.

Epidemiological data have shown that females are 1.2 to 3 times more at risk to suffer whiplash injuries after a car collision as compared to males (Harder et al. 1998; Versteegen et al. 2000; Mordaka and Gentle 2003). Female necks are not simply scaled versions of male necks but in fact have smaller external neck and vertebral dimensions and lower overall neck strength than males (Vasavada et al. 2008). Gender differences have been observed in the neck muscles responses and the head and neck kinematic responses during whiplash-like perturbations and may possibly be a consequence of the anthropometric and anatomical differences between males and females. Males were observed to have larger normalized muscle response amplitudes of the SCM ($p < 0.0001$) and PARA ($p < 0.01$) muscles than females (Siegmund et al. 2003a). For kinematic responses, females on average exhibited greater (> 10%) peak head forward (horizontal x-direction) acceleration, larger head extension angle (15%) and increased rearward head retraction (~29%) than males (Siegmund et al. 2003a; Linder et al. 2008). These gender differences in muscular and kinematic responses may lead to increased capsular ligament strain in females and may explain the greater potential of whiplash injury previously reported in females.

1.4 Startle Response

Recent work on whiplash simulations in healthy volunteers has shown that a startle response forms part of the neuromuscular response to whiplash injuries and may play a role in the aetiology of whiplash injuries (Blouin et al. 2006a). The startle response is a complex reflex which is elicited by a sudden intense tactile stimulus (e.g. displacement of the skin, hair on skin or muscles), acoustic stimulus (e.g. activation of hair cells in the cochlea), vestibular stimulus (e.g. acceleration of the head) or any combination of these stimuli. This response has been described as a protective mechanism found in virtually all mammalian species (Landis and Hunt 1939; Davis 1984). The startle response elicits a sudden excessive agonist and antagonist muscle contraction throughout the body such as blinking of the eyes, facial expressions, abduction of the upper arms and bending of the knees (Landis and Hunt 1939). In humans, the bilateral muscle activation of the SCM has been described as the most consistent indicator of a startle response (Brown et al. 1991). However, the activation of cervical multifidi has also been observed during the perturbation evoked startle response (Siegmund et al. 2008a). If the startle response elicits excessive muscular responses during the whiplash motion, the increased posterior neck muscle activity may potentially increase strain in the cervical facet capsular ligament. Reducing the startle component of the neuromuscular response to whiplash-like perturbations may decrease neck muscle activity and capsular ligament strain to find an effective way of to prevent or mitigate whiplash injuries.

1.4.1 The Neurophysiology of the Startle Response

Researchers have conducted numerous studies to understand the neurophysiology underlying the startle response and a simple neurophysiological pathway has been proposed (**Figure 1.3**) (Fox 1979; Lee et al. 1996; Koch 1999; Yeomans et al. 2002; Grosse and Brown 2003). Sudden vestibular, acoustic, and tactile stimuli activate fast mechanoreceptors that detect different mechanical stimuli applied to the body. Primary sensory neurons of each modality then activate large secondary neurones in the primary sensory nuclei found in the caudal pons and rostral medulla (Yeomans et al. 2002). Vestibular signals activate large vestibular nucleus neurons that utilize the vestibulospinal tract to evoke muscle responses. On the other hand, auditory afferent inputs activate central cochlear nucleus and nuclei of the lateral lemniscus that relay to the giant neurons of the ventrocaudal pontine reticular formation (PnC). The large axon of a giant neuron branches on to hundreds of motorneurons in the brain stem and spinal cord to evoke rapid muscle responses throughout the body (Mitani et al. 1988; Lingenhohl and Friauf 1994). Signals from tactile mechanoreceptors may use either the reticulospinal tract, vestibulospinal tract or both (Yeomans et al. 2002). Both reticulospinal and lateral vestibulospinal tract terminate on interneurons at all spinal levels (Shamboul 1980). Cross-modal summation of the three stimuli has been shown to be stronger than temporal summation of just one modality and the PnC has been suggested to be the summation point (Lingenhohl and Friauf 1994; Lee et al. 1996; Yeomans et al. 2002).

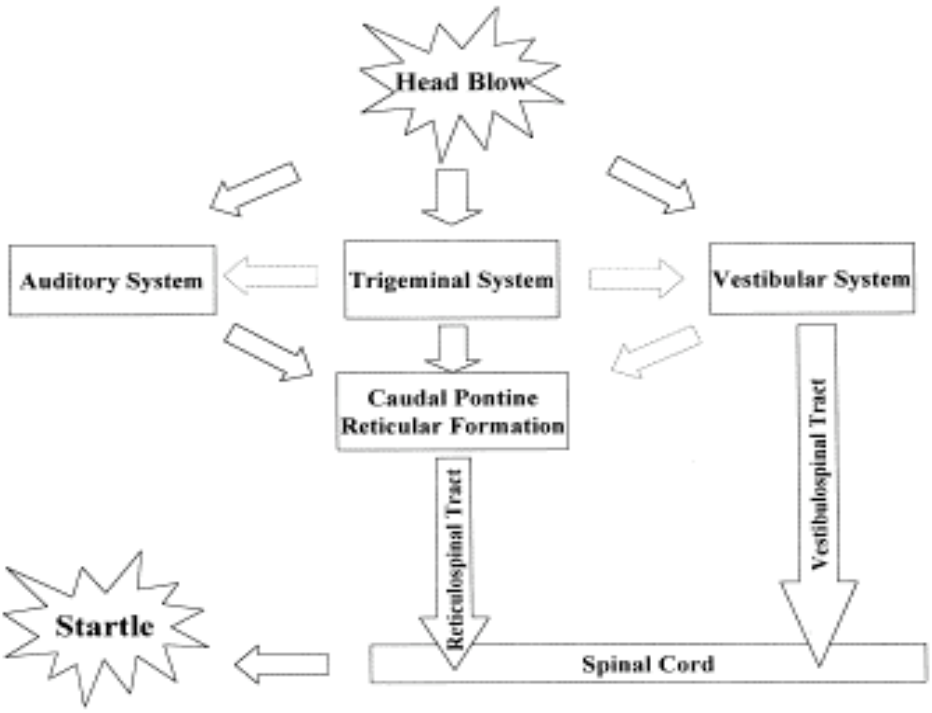


Figure 1.3 Neural circuit for acoustic, vestibular and trigeminal (tactile) startle responses. This model shows convergence of information in the caudal pontine reticular formation (PnC) and spinal cord. Reprinted with permission from (Yeomans et al. 2002).

1.4.2 The Neurophysiology of Whiplash Collisions

A car collision is a complex, multi-sensorial perturbation that stimulates the visual, vestibular, somatosensory, and auditory systems. Little is known about the exact neurophysiological pathways responsible for the triggering and modulation of neck muscle responses during whiplash-like perturbations. However, results from previous perturbation studies have methodologically shifted the importance between each sensory modality. For instance, vision is one of the most important senses to allow people to gain information regarding the orientation of the head throughout the whiplash motion.

However, Siegmund and Blouin (2009) observed that vision (eyes open vs. eyes closed) has little effect on neck muscle responses during whiplash-like perturbations with various levels of acceleration and jerk – the time rate change of acceleration at the leading edge of the collision pulse. Since differences in visual conditions produced the same muscle response, the visual system appears to play a minimal role in the amplitude of the neurophysiology response to whiplash-like perturbations.

The vestibulocollic reflex (VCR) is a compensatory muscle response designed to counteract head movement and keep the head stationary in space. Afferent inputs from the vestibular system (semicircular canals and otolith organs) are activated by movements of the head to evoke responses in the muscles of the neck (Wilson and Schor 1999). Gresty (1989) compared seated normal and avestibular subjects to a transient perturbation and observed similar neck muscle onset latencies. Therefore, the VCR does not contribute to the triggering of the neck muscle responses because subjects with intact and damaged vestibular systems had similar activation times. Additionally, Forssberg and Hirschfeld (1994) compared the postural response of seated subjects to a forward translation and to a legs-up rotation. They observed similar muscle response amplitudes despite the head rotating in two different directions and provided compelling evidence that the VCR does not contribute to the amplitude of neck muscle responses. Based on these two studies, it was suggested that the VCR has a secondary role in the onset and amplitude of the neurophysiology of whiplash response.

During whiplash collisions, somatosensory afferent pathways from the trunk and pelvis are the first detectors of the physical movement of the vehicle as these body parts

are in contact with the car seat. Forssberg and Hirschfeld (1994) proposed that somatosensory afferents derived from the backwards rotation of the pelvis were responsible for the postural responses during sitting (Forssberg and Hirschfeld 1994). Based on nerve conduction velocities and distances between the pelvis and brainstem, it is possible for the somatosensory afferent signals from the trunk to elicit SCM onset latencies of about 70 ms (Siegmund et al. 2008c). Although there is support for trunk/pelvic somatosensory afferents to be responsible for the onset and amplitude of neck muscle responses, there remains questions as to which afferent mechanoreceptor is responsible. In addition to the uncertainty of the afferent mechanoreceptors, little is known about the spinal pathways (i.e. reticulospinal, vestibulospinal, corticospinal, or bulbospinal) involved with transmission of neck muscle responses and further investigation is required.

The acoustic startle reflex (ASR) can be evoked by very loud (over 85 dB) acoustic stimuli comprising of any frequencies within the normal audible range (Yeomans and Frankland 1995). The primary excitatory ASR neural pathway includes the auditory nerve, central cochlear nucleus, nuclei of the lateral lemniscus, PnC, and reticulospinal tract (Davis et al. 1982; Yeomans et al. 2002). However, direct recordings of the reticular structures are inaccessible in awake human subjects. Grosse and Brown (2003) used correlation techniques in the frequency domain (Halliday et al. 1998; Halliday and Rosenberg 2000) on ASR-evoked muscle responses to identify markers of reticulospinal activity. Increased synchronized muscle activity of bilateral homologous upper limb muscles in the 10 – 20 Hz range was observed in response to an auditory startle stimulus (Grosse and Brown 2003). This increase in coherence was not observed following either

a sham startle or a voluntary contraction, suggesting the 10 – 20 Hz bandwidth may represent a surrogate marker of increased reticulospinal activity (Grosse and Brown 2003). Blouin et al. (2006a) compared the muscular and kinematic responses between subjects who were simultaneously exposed to both a whiplash-like perturbation and a loud auditory stimulus (40 ms, 124 dB, 1kHz tone) and subjects who were exposed to only the perturbation. The addition of a loud auditory stimulus increased posterior neck muscle activity and advanced the activation onset times of all muscle (Blouin et al. 2006a). This study revealed strong evidence that suggests the ASR may be a primary pathway of neck muscles responses to whiplash-like perturbations.

1.4.3 Attenuation of Neck Muscle Activity: Habituation of a Startle Response?

In human volunteers, the kinematic and muscular responses during the whiplash motion are greatest during the first exposure to a startling stimulus (Blouin et al. 2003; Siegmund et al. 2003b). In response to a novel startling whiplash-like perturbations, subjects initially co-contract the neck muscles (SCM and PARA) in what has been described as a "strap down" strategy (Nashner 1976). This co-activation appears to be a protective startle response causing the head/neck complex to stiffen with the torso. After repeated exposures to the same whiplash-like perturbation, attenuation, or habituation, of the reflexive muscle responses causes the amplitudes of neck muscles to decrease and, consequently, causes the stiffness of the head/neck complex to decrease. A reduction of muscle response and neck stiffness after habituation are observed to change the kinematic properties of the head by increasing peak angular accelerations of the head in extension (α_1), retraction (r_x) and peak head extension angle (θ) as well as decreasing peak linear

acceleration of the head (a_x) (Siegmund et al. 2003b). Previous studies have shown that habituation changes a subject's response and may be a major confounder during repeated whiplash-like perturbation experiments utilizing human volunteers (Blouin et al. 2003; Siegmund et al. 2003b; Blouin et al. 2006b; Blouin et al. 2006a; Siegmund et al. 2008b). The use of habituated response compromises the external validity of a study if the objective was to test human responses during unexpected rear-end collisions. However, the exaggerated neck muscle responses observed in the first trial suggest that a startle response may form part of the neuromuscular response to whiplash injuries.

To further investigate the presence of the startle response during whiplash-like perturbations, Blouin et al. (2006b) utilized Grosse and Brown's (2003) coherence analysis on EMG data from human repeated rear-end perturbation experiments (**Figure 1.4**) (Brault et al. 2000; Siegmund et al. 2003a; Blouin et al. 2006a). Three experimental datasets were analyzed: 1.) the initial perturbation (EMG_{first}, no auditory stimulus), 2.) the attenuated, or habituated, startle response after multiple repeated- perturbation trials (EMG_{hab}, no auditory stimulus), and 3.) the attenuated startle response presented simultaneously with a startling auditory stimulus ($EMG_{startle}$). Blouin et al (2006b) observed a peak in coherent synchronous EMG activity between 10 – 20 Hz following the initial perturbation (EMG_{first}), but not in the attenuated trials (EMG_{hab}). This suggests that the first trial contains a startle response that significantly decreased during the attenuated trials (Blouin et al. 2006b). When the attenuated trials were presented simultaneously with a startling stimulus ($EMG_{startle}$), the local peak in synchronize EMG activity between 10 and 20 Hz reappeared, similar to EMG_{first}. Thus, the startle response was shown to form part of the neuromuscular response to low-speed whiplash-like

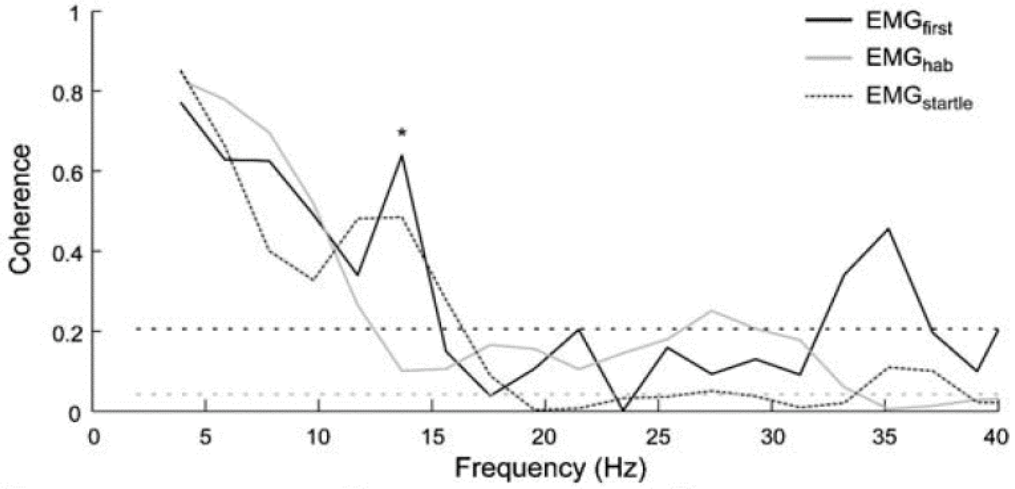


Figure 1.4 Estimated averaged coherence between left and right SCM muscles recorded during exposure to 1.8 km/h forward perturbation. The first perturbation (EMG_{first}), attenuated perturbations (EMG_{hab}), and attenuated perturbations simultaneously with a acoustic startle ($EMG_{startle}$). The horizontal dotted lines represent the 95% confidence limit for the coherence estimates (black = EMG_{first} & grey = EMG_{hab} and $EMG_{startle}$). Reprinted with permission from (Blouin et al. 2006b)

perturbations and may play a role in the aetiology of whiplash injuries (Blouin et al. 2006b; Blouin et al. 2006a). The whiplash-like perturbation and startling stimulus increased the amplitude of posterior muscle responses (Blouin et al. 2006a) and extended to the deep multifidus muscles (Siegmund et al. 2007; Siegmund et al. 2008a). By reducing the startle response during the whiplash-like perturbation, the amplitude of the posterior muscles will be decreased. Consequently, this may reduce the potential of posterior neck muscles to affect other cervical structures such as the capsular ligament and ligament strains during whiplash-like perturbations.

One method to minimize the effects of habituation during whiplash experiments is to increase the inter-perturbation time interval (IPI) between subsequent trials. Brault et al. (1998) used an IPI of at least seven days between their two whiplash-like perturbation conditions (impact speed: 4 km/h and 8 km/h). However, this duration is not practical and too long for experiments with more than two experimental conditions. During a pilot experiment conducted for the proposed study (n = 10), whiplash-like perturbations (peak acceleration: 2.060 ± 0.005g) presented simultaneously with loud collision stimuli (109dB) at IPIs between 15-20 minutes did not show any significant effects of habituation on the muscle and kinematic responses ($p > 0.05$) (Mang et al. 2009). As a result, we suggest that for future repeated whiplash-like perturbation studies, an IPI of 15-20 can effectively minimized the effects of habituation and increase the external validity of the experiment.

1.4.4 Prepulse and Paired-Pulse Inhibition of the Startle Response

Apart from being habituated by a series of repeated stimuli, the startle response is strongly suppressed by preceding the startling stimulus with a weak or startling prepulse stimulus (visual, acoustic or tactile) (Hoffman and Searle 1968; Ison and Krauter 1974; Fendt et al. 2001; Valls-Sole et al. 2005). The suppression by a weak prepulse stimulus is known as "Prepulse Inhibition (PPI)" and is a salient, well-studied feature of the startle response in rats (Yeomans et al. 2006) and in humans (Filion et al. 1998; Fendt et al. 2001; Valls-Sole et al. 2005; Bitsios et al. 2006). PPI exhibits the following characteristics on the startle response: increases in inhibition with increased prepulse intensity (Hoffman and Searle 1968), increases in inhibition with an increased prepulse

duration (Blumenthal 1995), and decreases in inhibition with increased background noise (Hoffman and Searle 1968). In addition, the inter-stimulus time interval (ISI) between the prepulse and the startle stimuli has been shown to influence the effectiveness of PPI (Plappert et al. 1999). Prepulse Facilitation (PPF), facilitation of the startle response produced by a prepulse stimulus, was observed at ISIs below 37.5 ms; whereas, PPI occurred for ISIs greater than 37.5 ms but inhibition decreased as the ISI increased to values greater than 400 ms (Plappert et al. 2004). The most important characteristic of PPI is that the prepulse stimulus must be weak enough to not evoke a muscle response distinguishable from resting muscle activity, yet strong enough to modify the response to a subsequent suprathreshold stimulus (Valls-Sole et al. 2008). The strongest inhibition of startle is observed to occur with a prepulse duration of 10 – 20 ms (Reijmers et al. 1995), prepulse intensity up to, but not exceeding, the startle threshold (Hoffman and Searle 1968; Li et al. 1998), and an ISI between 60 and 120 ms (Braff et al. 1978; Ison and Pinckney 1983).

In contrast to prepulse inhibition, paired-pulse inhibition uses a startling prepulse stimulus (visual, acoustic or tactile) to inhibit a subsequent startling stimulus (Ison and Krauter 1974). Paired-pulse inhibition exhibits the same characteristics as PPI such as increasing the inhibition of the startle response with increased paired-pulse intensity (Hoffman and Searle 1968) and decreasing inhibition with longer ISI (Wilson and Groves 1973). Ison and Krauter (1974) compared the effects of paired-pulse inhibition from an intense and weak startling stimulus in rats **(Figure 1.5)**. A 95 dB, 20ms 10 kHz tone was used as the weak paired-pulse tone (s1) and a 125 dB, 20 ms 10 kHz tone was used as both the intense paired-pulse tone (S1) and startling stimulus (S2). Larger inhibition of

the startle response was observed from paired-pulse inhibition (S1S2) than PPI (s1S2) for ISIs of 0.5, 1, 2, and 4 seconds (**Figure 1.5**). In addition, prepulse and paired-pulse appear to have greater inhibition effects for small ISI (~0.5 seconds) (Ison and Krauter 1974). The early prepulse and paired-pulse inhibition studies were primarily based on rat studies and have repeatedly been generalized to humans. Therefore, due to the inter-species differences in the patterns of neural circuit connectivity and nerve conduction velocities (Koch 1999), further research is required to determine the optimal parameters and effects of PPI and paired-pulse inhibition in humans.

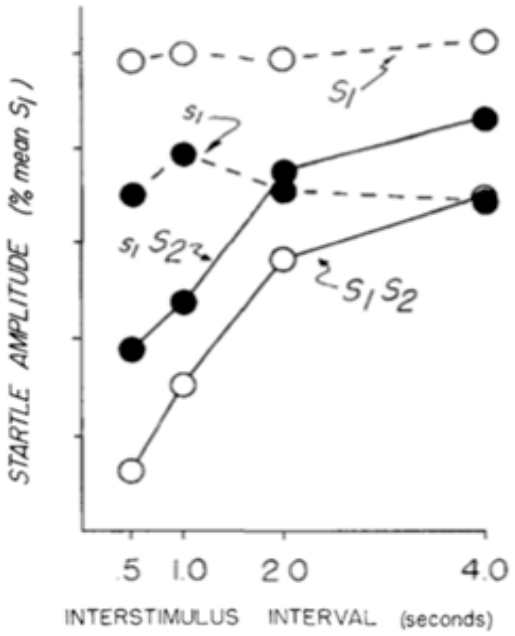


Figure 1.5 Comparison of paired-pulse inhibition on the startle response in rats at various inter-stimulus intervals: 0.5, 1, 2, and 4 seconds. Startle reflexes in response: to an intense acoustic stimulus (S1), to a weak acoustic stimulus (s1), to an intense stimulus when preceded by an equally intense stimulus (S1-S2), and to an intense stimulus when preceded by a weak stimulus. Reprinted with permission from (Ison and Krauter 1974)

1.4.5 Prepulse and Paired-Pulse Inhibition in Human Volunteers

In an experimental pilot study, we conducted a two part experiment to determine the effects of paired-pulse and prepulse inhibition of the ASR in human volunteers (Mang et al. *Unpublished Observations*). For clarification purposes, the term *"Pre-Stimulus"* will be operationally defined as any auditory tone (prepulse or paired-pulse) presented prior to a startle-eliciting sound. Thus, *pre-stimulus inhibition* refers to the inhibitory effects of the pre-stimulus on the subsequent startle tone. In the first study, the objective was to determine the effects of pre-stimulus on the ASR in humans for different ISIs – the time between the pre-stimulus and startling stimuli – while keeping the sound pressure level of the stimuli constant. After determining an optimal ISI for pre-stimulus inhibition, the next study characterized the influence of varying the pre-stimulus sound pressure level at the optimal ISI.

In the first experiment (n = 14), the pre-stimulus and startle stimuli were paired startle tones (124 dB, 40 ms 1 kHz sine waves). We selected ISIs of 100, 250, 500 and 1000 ms to determine the effects of ISI on the ASR and the ISI with the greatest level of inhibition. EMG was recorded from the left and right SCM (L and R SCM), right cervical paraspinals at the level of C4 (RPARA) and right orbicularis oculi (ROOc). ROOc was not further analysed in the study due the large inter-subject variability. Pre-stimulus tones presented at all ISI conditions inhibited the startle responses in all muscles ($p < 0.05$). However, no statistically significant differences were observed in the level percent inhibition between the various ISIs conditions ($F(3,52) = 1.512$, $p = 0.222$). For

some subjects, muscle activity elicited by the pre-stimulus response lasted greater than 100 ms and contaminated the startle-evoked response for the 100 ms ISI condition making it difficult to differentiate the two responses. Thus, we propose that an ISI of 250 ms is optimal for future research because this ISI elicits two distinct responses for analysis, yet still cause significant inhibition of the startle response.

In the second experiment, we kept the ISI constant at 250 ms and varied the intensity of the pre-stimulus tone to characterize the influences of sound pressure level (i.e. comparing prepulse to paired-pulse). The startle tone (40 ms 1 kHz sine waves) had an intensity of 124 dB, whereas, the sound pressure levels of the pre-stimulus tones (40 ms, 1 kHz sine waves) were set at 80, 85, 95, 105 and 124 dB. All intensities of pre-stimulus tones significantly inhibited the startle responses in bilateral SCM ($p > 0.05$), but only pre-stimulus tone intensities of 95 dB or greater produced inhibition in the RPARA. *Post-hoc* Tukey's Honest Significant Difference (HSD) test revealed a significant difference between pre-stimulus tone conditions 80 dB and 105 dB in the RPARA muscle($F(4,65) = 3.180$, $p < 0.05$). To classify the sound pressure level of pre-stimulus tones, we utilized the same characteristic guidelines as prepulse and paired-pulse tones. A weak pre-stimulus tone had a sound pressure level that did not evoke muscle responses distinguishable from resting muscle activity (prepulse); whereas, a startling pre-stimulus tone evoked an independent startle response (paired-pulse). A paired t-test confirmed that the 105 dB pre-stimulus generated a startle response significantly different from background noise levels (ambient room sound pressure level: ~59 dB) ($p < 0.0001$); whereas, the response to the 80 dB pre-stimulus did not differ from background noise ($p = 0.3001$). Similar to the 80 dB pre-stimulus the 85 dB pre-stimulus tone did not vary

from background noise (RSCM: $p = 0.1432$, LSCM: $p = 0.4598$, and ROOc: $p = 0.2214$; with the exception of RPARA: $p = 0.0172$). Thus, we propose that pre-stimulus tone intensities of 85 dB and 105 dB presented 250 ms prior to a startling stimulus are effective intensities to inhibit the startle response representing a weak pre-stimulus tone (*WK-PREP*) and a startling pre-stimulus tone (*ST-PREP*), respectively.

2 Objective and Hypotheses

2.1 Rationale

Whiplash injuries are the most common injury associated with low-speed rear end collisions and are serious economical and social burdens to society. Blouin et al. (2006b) suggested that a startle response may form part of the neurophysiological response to a whiplash-like perturbation and may be an important factor in the genesis of whiplash injuries. One characteristic of the startle response is the ability to be strongly inhibited when a stimulus is presented prior to the startling stimulus (Hoffman and Searle 1968; Ison and Krauter 1974; Fendt et al. 2001; Valls-Sole et al. 2005). Preliminary research has shown that in humans the practical parameters for a pre-stimulus to inhibit the ASR in seated subjects are an 85 dB prepulse tone or a 105 dB paired-pulse tone presented with an ISI of 250 ms (Mang et al. *Unpublished Observations*). If we can inhibit the startle response during low-speed rear-end collisions, we may be able to decouple the startle response from the postural response during the whiplash motion. Reducing the startle component of the neuromuscular response to the whiplash motion should decrease neck muscle activity, decrease head angular and linear accelerations and increase peak head retraction. Increasing peak head retraction may increase the physical strain applied to the capsular ligament, whereas decreasing neck muscle activity and forces acting on the capsular ligament may reduce the capsular ligament strain. Overall, pre-stimulus inhibition could prove to be an effective way to mitigate or prevent whiplash injuries in the future.

The **objectives** of the present research are to investigate the influences of two different pre-stimulus tones (weak and startling) on the 3-D head kinematic and muscle responses observed in human volunteers during the whiplash-like perturbations.

2.2 Hypotheses

We hypothesize that presenting a pre-stimulus auditory tone prior to the startle stimulus will reduce the amplitude of neck muscle activity, which will directly influence the kinematics of the head and neck. More specifically, we hypothesize that reducing neck muscle responses will decrease peak linear forward and angular acceleration in flexion, and increase peak angular acceleration in extension, extension angle and head rearward retraction. We also hypothesize that a startling pre-stimulus tone would have greater effect on the kinematic and muscular responses than a weak pre-stimulus tone. In particular, the startling pre-stimulus tone will generate a larger reduction of muscle amplitudes during whiplash-like perturbations than the weak pre-stimulus tone.

3 Methods

3.1 Subjects

Twenty subjects (10 males/10 females; Age: 26 ± 6 years; Height: 169.2 ± 11.1 cm; Weight: 63.3 ± 11.2 kg) with no history of whiplash injury were recruited. All subjects provided written informed consent and were paid a nominal fee for their participation. The research protocol was approved by the UBC Clinical Ethics Review Board (H07-01281) and conformed to the Declaration of Helsinki.

3.2 Instrumentation

3.2.1 Electromyography

For each subject, surface electromyography (EMG) electrodes (Ambu Blue Sensors: M and N type, Ballerup, Denmark) were placed bilaterally on the sternocleidomastoid (SCM: L and R) and cervical paraspinal muscles at the level of C4 (PARA: L and R) as well as biceps brachii (BIC), triceps brachii (TRI), first dorsal interosseous (FDI) and rectus femoris (RF) on the left side of the body. In addition, two reference electrodes were positioned bilaterally on the acromia (due to equipment requirements). The term cervical paraspinal muscles was used to describe all posterior muscles at the level of C4 due to the difficulty of distinguishing individual muscles in the neck with surface EMG. EMG recording sites were shaved with a disposable razor to remove hair and dead skin cells, cleansed with alcohol and lightly abraded with an abrasive skin prepping gel (NuPrep, D.O. Weaver and Co., Aurora, CO, USA) prior to the placement of surface recording electrodes. All EMG signals were amplified using an

eight-channel Neurolog EMG system (Digitimer: NL 900D with NL844 pre-amp, England, UK) and bandpass filtered from 10 Hz to 1000 Hz.

3.2.2 Kinematics

Head accelerations were measured using a nine accelerometer array (8 Kistler 8302B20S1; ± 20 g, Amherst, NY, USA. and 1 Silicon Design Inc 2220-010; ± 10 g. Issaquah, WA, USA) arranged in a 3-2-2-2 configuration (Padgaonkar et al. 1975). The nine accelerometers were rigidly mounted on an aluminum pyramidal frame and securely fastened to the subject's head by an adjustable headgear device. Torso accelerations and angular velocities were measured respectively with a tri-axial linear accelerometer (summit 34103A; ±7.5 g, Akron, OH) and tri-axial angular rate sensor (DynaCube; ±100 rad/s. ATA-Sensors, Albuquerque, NM). These sensors were fixed to an aluminum plate and strapped tightly to the chest directly below the sternal notch. Sled acceleration was measured with a uni-axial accelerometer (Silicon Design Inc 2220-100; ± 100 g. Issaquah, WA, USA) mounted horizontally to the sled along the axis of motion. A motion capture system (Optotrak Certus System; Northern Digital, Waterloo, ON, Canada) was used to measure head, torso and sled displacements. A total of 12 Optotrak infrared (IRED) markers (four markers per structure) were affixed to the head accelerometer array, trunk chest plate, and car seat/sled platform. All EMG, accelerometer, and angular rate sensor data were simultaneously sampled at 2000 Hz using a National Instrument Data Acquisition (DAQ) system and Labview program, (National Instruments Corporation, Austin, Texas, USA). Optotrak data were acquired at 200 Hz per marker using the same computer.

3.3 Test Procedure

Subjects were instrumented with EMG electrodes and accelerometer arrays before sitting on a custom-fabricated moving platform system, or sled, equipped with a 2005 Honda Accord front driver automobile seat (**Figure 3.1**). The sled was powered by feedback-controlled linear induction motors (Kollmorgen IC55-100A7, Kommack, NY) that allowed for repeatable perturbations to stimulate whiplash motions. This moving platform system generated no audible or mechanical pre-perturbation signals that could have helped subjects predict the onset of a perturbation. The head restraint was removed from the top of the seat back to prevent any head-to-head-restraint interaction that may affect the kinematics of the head and neck or generate additional sensory inputs. To

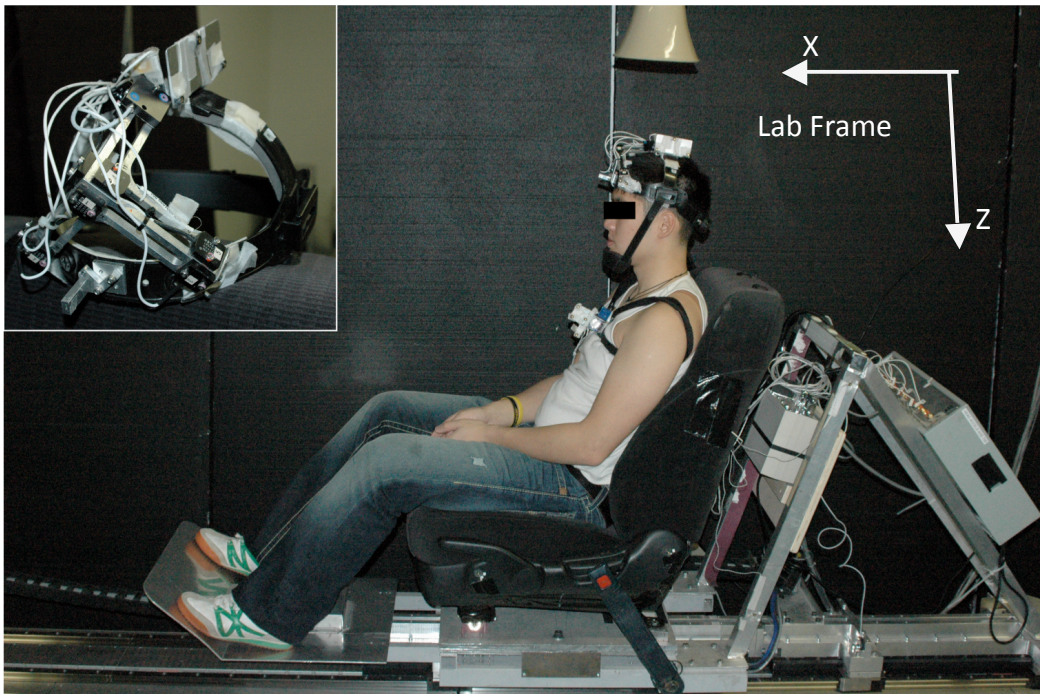


Figure 3.1 Photographs of experimental set up of the car seat on the moving platform. Location of head and torso accelerometer arrays, horn speaker and laboratory reference frame (X, Z) are also included. Inset: Close-up view of the nine accelerometer array on the headgear device. (Electromyography (EMG) electrodes are not shown)

eliminate possible habituation effects, subjects were provided neither practice nor demonstration trials (Blouin et al. 2003; Siegmund et al. 2003b), and an inter-perturbation time interval between 15 and 20 minutes was used (Mang et al. 2009). Subjects were aware of the number of trials presented, but were not told the magnitude or the timing of the perturbation. Once on the sled, subjects were instructed to sit facing forward, adopt a comfortable seated posture, rest their forearms on their lap and relax their head and neck muscles.

The experiment consisted of three different experimental conditions as subjects underwent five forward whiplash-like perturbation trials (**Figure 3.2**) that replicated the initial acceleration profile of an 8 km/h vehicle-to-vehicle collision. For each condition, a collision sound was presented time-locked with the whiplash-like perturbations to simulate a realistic rear-end collision. Based on our previous studies in the lab (over 150 subjects tested), the acceleration pulse (**Figure 3.2**) was sufficient to evoke a startle response in the neck muscles and was reported to be neither painful nor noxious by participants. To further replicate a real rear-end collision, we used a collision sound (109 dB, time-to-peak 34.2 ± 0.2ms) recorded from an 8 km/h frontal crash of a 1987 Ford Mustang into a barrier. The sound was recorded with a microphone and a dB sound meter placed at the driver's ear level with the windows up.

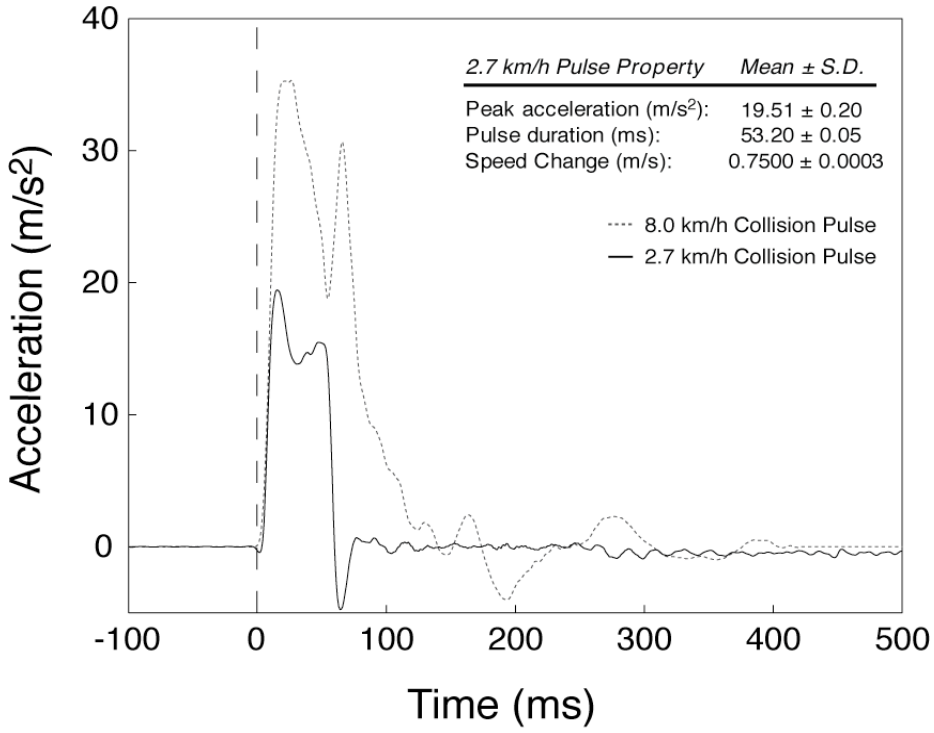


Figure 3.2 A sample of the acceleration profile and pulse properties used to simulate a 2.7 km/h rear-end whiplash-like perturbations. The dashed line shows an 8 km/h vehicle-to-vehicle collision pulse recorded during previous experiments (Siegmund et al. 1997).

The three experimental conditions differed with the type of pre-stimuli tone occurring 250 ms prior to the onset of perturbation and collision sound: 1.) no pre-stimulus tone (*Control*), 2.) a weak pre-stimulus tone (*WK-PREP*) and 3.) a startling pre-stimulus tone (*ST-PREP*) (**Figure 4.1**). *WK-PREP* was a weak auditory tone (85 dB, 1 kHz sine wave, 40 ms duration) delivered 250 ms before the onset of the perturbation. This weak pre-stimulus tone was audible above the background noise (~63.7 dB) from the sled and room, but not loud enough to evoke an independent startle response (see preliminary results). The startling pre-stimulus tone (*ST-PREP*) (105 dB, 1 kHz sine wave, 40 ms duration) was also sent 250 ms before the onset of the perturbation and this tone was capable of eliciting an auditory startle response (see preliminary results). The

WK-PREP and *ST-PREP* tones were delivered through a horn speaker (MG Horn Speaker HS17T, Hauppauge, NY, USA) located directly above the subject's head. In addition to the horn speaker, the collision sound was played through a stereo speaker (Yamaha NS-66, Shizuoka, Japan) and an automotive subwoofer (JL Audio 10" subwoofer, Miramar, FL, USA) surrounding the subject.

Before each perturbation trial, the location of the head and torso accelerometers, and IRED markers relative to anatomical landmarks were digitized using the three-dimensional (3D) digitizer function of Optotrak and a digitization probe tool. The digitized anatomic landmarks (upper incisors, bilateral lower rims of the orbit, external acoustic meati, glabella, vertex, opisthocranion, occiput, manubrium and spinous process of C7) determined the Frankfort plane and allowed resolution of head kinematics to anatomically relevant locations (i.e. atlanto-occipital joint and head centre of mass).

Subjects were seated on the sled for between 15 – 20 minutes before the first perturbation to allow sufficient time for both the subject to adopt a comfortable posture and the digitization process. Subjects were informed to expect the imminent perturbation within the next five minutes after the digitization process – subjects became aware of the event, but remained unaware of the exact timing of when the perturbation would occur. After each perturbation, subjects remained seated on the sled in their initial position until the next trial. The head accelerometer array was loosened and retightened between trials to reduce the compression of the head caused by the tight headgear. Consequently after retightening the headgear, the subject's anatomical landmarks were redigitized prior to the subsequent perturbation to establish proper position and orientation of the head

accelerometers with respect to the Frankfort plane. Once again, after each digitization process, subjects were informed to expect a perturbation within 5 minutes to account for potential effects of different awareness levels. Subjects had no auditory, tactile or visual cues that could have aided in predicting the onset of the perturbation. To reduce the effects of habituation on the kinematic and muscle responses, a IPI between 15 – 20 minutes was used and muted episodes of BBC television series 'The Blue Planet" was shown to distract subjects during the experiment. Of the five trials performed, the first, middle and last trials (*Control 1*, *Control 3*, and *Control 5*) in the series were Control trials to control and determine the potential effects of habituation during the experiment and to provide a comparative scale for the inhibition caused by the pre-stimulus tone. The two pre-stimulus conditions (*WK-PREP* and *ST-PREP*) were randomly distributed into the two remaining test trials (*Trial 2* and *Trial 4*) to investigate the effects of pre-stimuli on th9e startle response evoked by whiplash-like perturbations.

3.4 Reference Frames

Data from the head acceleration array were transformed into the head reference frames with the origin at the atlanto-occipital joint (AOJ), which was estimated to be 24 mm posterior and 37 mm inferior to the head's center of mass (Siegmund et al. 2007). The head's center of mass was estimated to lie in the mid-sagittal plane, rostral to the interaural axis by 17% of the distance between the vertex and the interaural axis (NASA 1978). The Frankfort plane was defined as the plane passing through the external acoustic meatus and lower rim of the orbit (Pozzo et al. 1990). All kinematic responses were transformed into, and subsequently reported in, the global reference frame with the x-axis

horizontal and positive in the forward direction of the sled, the y-axis horizontal and positive to the right of the subject, and the z-axis vertical and positive downwards in the direction of gravity (**Figure 3.1**). All head, trunk, and sled accelerometers were corrected for the effects of earth's gravitational field prior to data analysis (Blouin et al. 2006b).

3.5 Data Analysis

A subject's initial head position and orientation were determined from the average of position/orientation estimated over a 50 ms period preceding the onset of sled perturbation. Initial head angle in the sagittal plane was reported as the relative angle between the Frankfort plane and the positive global X-axis (+θ: Extension, -θ: Flexion). The onset of vertical and horizontal head movements, peak head accelerations (linear and angular), and the time of peak head accelerations were determined directly from the transformed accelerometer data. Onsets of head movement in the vertical and horizontal directions were defined as the first point at which the linear Z- and X-axes accelerometer data reached 10 times the peak background noise amplitude. Peak linear head acceleration (x: first positive peak) was determined from the linear head forward (X-axis) acceleration data. Peak angular head accelerations were defined by two peaks: peak angular acceleration in extension (α_1: first positive peak) and peak angular acceleration in flexion (α_2: first negative peak). Peak retraction was estimated by the maximum relative horizontal displacement in the lab reference frame between the AOJ and the midpoint between the superior margin of the manubrium and the palpable aspect of the C7 spinous process (Queisser et al. 1994)

All EMG muscle data were high-pass filtered (30 Hz) to remove any possible motion artefacts before calculating onsets of muscle activity and muscle response amplitudes. Onsets of muscle activity were determined to be when the root-mean-square (RMS) EMG amplitude (20 ms sliding window) reached 10 percent of the maximum value and was confirmed visually (Siegmund 2001; Siegmund et al. 2003a; Siegmund et al. 2003b). The RMS amplitude of each muscle response to the perturbation (*perturbation response*) was calculated over the entire interval between muscle activation and peak head extension angle. The RMS muscle responses evoked by the pre-stimuli (*pre-stimulus response*) were calculated over the same time interval as the *perturbation response*, but the time interval was shifted to the onset of the pre-stimulus tone ($\Delta t = -250$ ms) (i.e. from onset of muscle activity minus 250ms to peak head extension angle minus 250 ms). Visual inspections were performed to ensure that the *pre-stimulus response* did not contaminate the *perturbation response*. Pre-perturbation background RMS EMG offsets were quantified over the 50 ms time interval preceding the pre-stimulus tone and were subtracted from the *perturbation responses*. Only *perturbation response* RMS EMG data were normalized to the first control trial (*Control 1*) to represent each trial as a percentage of the initial startle trial. Normalizing all the trials to *Control 1* helped to determine: 1.) whether habituation confounded the EMG responses during the experiment and 2.) whether the addition of a pre-stimulus tone affected the EMG response when compared to Control EMG responses.

3.6 Statistical Analysis

For the EMG variables, normalized RMS EMG data from the left and right sides of SCM and PARA were averaged for subsequent analysis (Blouin et al. 2006b; Siegmund et al. 2003b). The amplitudes of the EMG and kinematic responses were first assessed with a one-way, repeated-measures analysis of variance (ANOVA) for all Control trials (*Control 1* vs. *Control 3* vs. *Control 5*) to determine if the responses were significantly affected by habituation. After confirming that there were no statistically significant muscular and kinematic response differences between the three Control trials, the three trials were averaged to calculate a mean *Control* variable. To determine whether *WK-PREP* or *ST-PREP* generated an independent startle response, we used a Paired T-Test to compare the *pre-stimulus response* to the pre-perturbation background noise level. For each EMG and kinematic variable, differences between gender (males vs. females) and pre-stimulus conditions (*Control* vs. *WK-PREP* vs. *ST-PREP*) were tested using a mixed model (2 Group × 3 Condition) ANOVAs with repeated measures on the Condition factor. *Post-hoc* comparisons for the ANOVAs were performed using a Tukey's honest significant difference (HSD) test. All statistical analyses were performed using the [R] statistic program (version 2.10.1) and the significance level was set at $\propto = 0.05$.

4 Results

In response to a whiplash-like perturbation, all subjects exhibited stereotypical muscular and kinematic responses (**Figure 4.1; Table 4.1 and 4.2**). The unexpected forward perturbation evoked generalized muscle activity throughout the body from head to lower limbs (SCM, PARA, BIC, TRI, FDI and RF). All onsets of muscles activity occurred before the time-to-peak of any kinematic variables (**Table 4.1**). We observed the onsets of head movement appear first in the vertical direction before the horizontal direction. The subject's heads experienced peak angular and linear acceleration before peak head retraction and head extension angle. Habituation of the muscular and kinematic responses was not observed over the duration of the experiment ($p > 0.05$).

The addition of a pre-stimulus tone (*WK-PREP* and *ST-PREP*) before a subsequent, startling whiplash-like perturbation decreased the evoked normalized RMS EMG amplitudes in all muscles relative to the *Control* condition (**Figure 4.1 and 4.2; Table 4.1**). The ANOVAs determined that when a weak pre-stimulus tone (85 dB: WK-PREP) was presented, we observed decreases only in TRI (−38%), FDI (−48%) and RF (−57%) from *Control* conditions ($p < 0.01$). However, by increasing the pre-stimulus intensity to a startling pre-stimulus tone (105 dB: *ST-PREP*), we observed significant decreases ($p < 0.01$) in all EMG amplitudes (SCM: −16%, PARA: −26%, BIC: −66%, TRI: −62%, FDI: −68%, and RF: −78%). *Post-hoc* analysis revealed that *ST-PREP* decreased the muscle responses of PARA, BIC, and TRI greater than *WK-PREP* ($p < 0.05$). Thus, greater intensity of pre-stimulus tones produced greater inhibition of the muscle response evoked during whiplash-like perturbations.

The addition of pre-stimulus tones affected the peak kinematic variables of the head during whiplash-like perturbations (**Figure 4.1 and 4.3; Table 4.2**). The addition of the *ST-PREP* tone significantly decreased ($p < 0.05$) peak retraction (r_x) by 5.7 mm (–16.8%), peak horizontal acceleration of the head (a_x) by 4.4 m/s^2 (–22.8%), and peak head angular acceleration in extension (α_1) by 37.0 rad/s^2 (–23.0%). However, no significant effects were observed during the *WK-PREP* condition ($p > 0.05$).

ANOVAs revealed that there were gender-related differences in the initial head angle and peak head extension angles. On average, the initial head angles of female subjects were 4.7° less in extension than male subjects ($p = 0.0045$); whereas, the peak head extension angles of female subjects were 3.7° greater than male subjects ($p = 0.0099$). Therefore, female subjects had a greater angular range of motion of the cervical spine in extension than male subjects. ANOVAs determined that the RMS EMG amplitudes were unaffected by differences in gender.

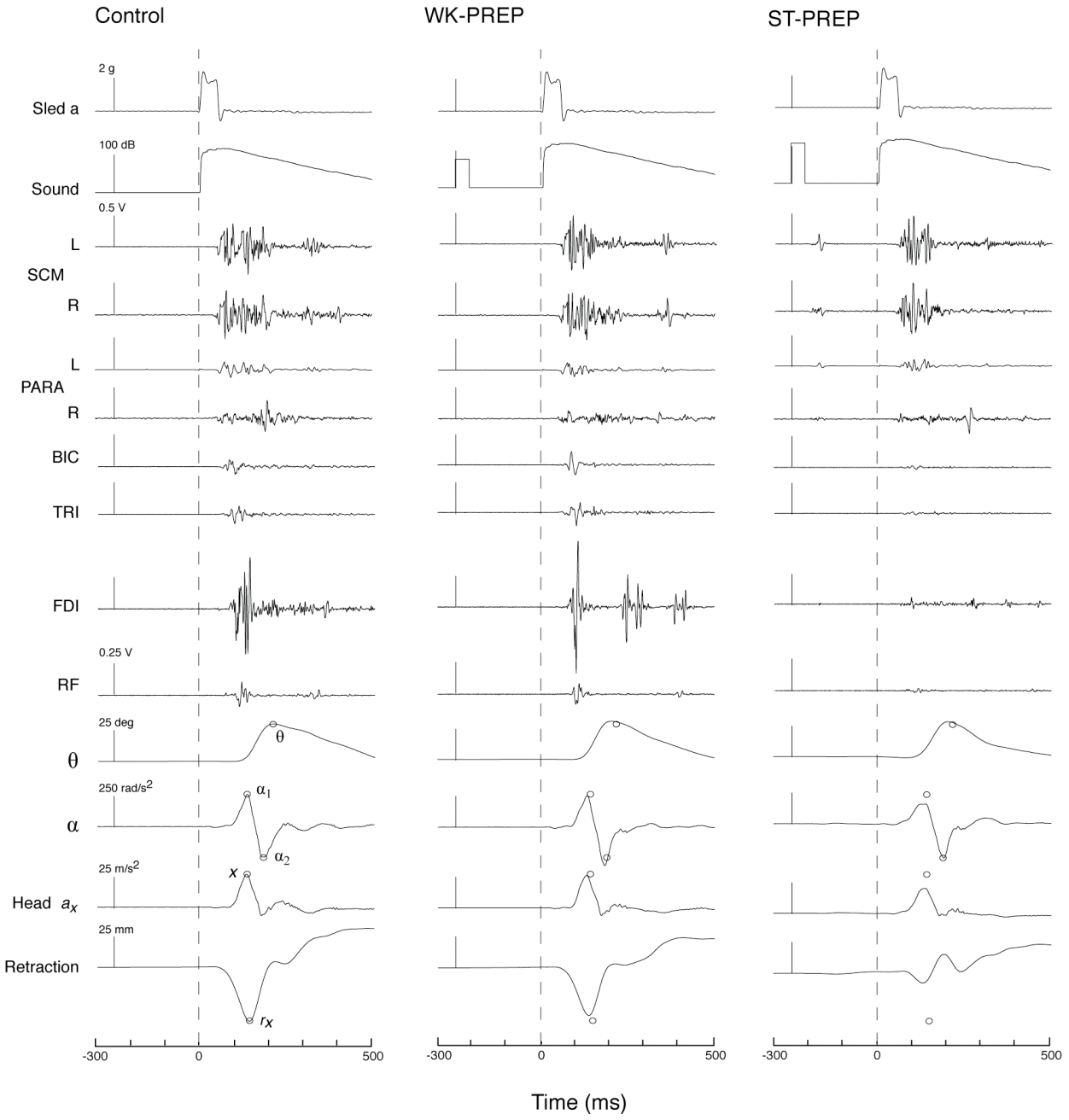


Figure 4.1 A sample of muscular and kinematic responses from a single subject during *Control*, *WK-PREP*, and *ST-PREP* conditions. Labelled hollow circles in the *Control* panel represent kinematic peaks used for analysis and are replicated on *WK-PREP* and *ST-PREP* panels to highlight the changes due to pre-stimulus tones. The vertical scale bars are aligned with the onset of pre-stimulus tones (-250 ms) and are consistent between conditions. The vertical dotted line represents the onset of sled perturbation. Electromyographic data: left (L), right (R), sternocleidomastoid (SCM), cervical paraspinal (PARA), biceps brachii (BIC), triceps brachii (TRI), first dorsal interosseous (FDI), and rectus femoris (RF) muscles. Kinematic data: subscript x refers to the x-direction, linear acceleration (a), head angular acceleration (α), and head angle (θ).

Table 4.1 Mean (SD) of normalized RMS amplitudes and onsets of EMG for *Control*, *WK-PREP* and *ST-PREP* conditions (n = 20). Data also grouped as a function of gender (Female and Male). F-statistics and post-hoc Tukey's HSD summarized at right for mixed-model two-way ANOVAs using gender (G) and condition (C) as independent variables as well as *Control* (Control), *WK-PREP* (WK), and *ST-PREP* (ST) as the three conditions. Electromyographic data: sternocleidomastoid (SCM), cervical paraspinal (PARA), biceps brachii (BIC), triceps brachii (TRI), first dorsal interosseous (FDI), and rectus femoris (RF) muscles.

	Control		*WK-PREP*		*ST-PREP*		ANOVA Results (F; P)			*Post-Hoc* Tukey's HSD		
Variable	Female	Male	Female	Male	Female	Males	Gender	Condition	G x C	Control-WK	Control-ST	WK-ST
EMG RMS Amplitude												
SCM	1.01 (0.07)	1.01 (0.14)	0.97 (0.12)	0.85 (0.22)	0.90 (0.16)	0.78 (0.27)		4.827; p = 0.0118			ST<Control; p < 0.0085	
PARA	1.02 (0.17)	1.11 (0.30)	0.97 (0.28)	0.94 (0.31)	0.80 (0.30)	0.71 (0.23)		7.324; p = 0.0015			ST<Control; p < 0.0012	ST<WK; p = 0.0453
BIC	0.99 (0.38)	1.07 (0.38)	0.63 (0.47)	0.88 (0.88)	0.30 (0.23)	0.39 (0.42)		9.558; p = 0.0003			ST<Control; p = 0.0002	ST<WK; P = 0.0309
TRI	1.02 (0.26)	0.95 (0.17)	0.65 (0.38)	0.57 (0.28)	0.30 (0.11)	0.43 (0.38)		25.72; p < 0.0000		WK<Control; p = 0.0002	ST<Control; p < 0.0000	ST<WK; p = 0.0220
FDI	0.94 (0.40)	1.01 (0.30)	0.57 (0.75)	0.52 (0.46)	0.17 (0.18)	0.29 (0.26)		14.96; p < 0.0000		WK<Control; p = 0.0079	ST<Control; p < 0.0000	
RF	0.98 (0.12)	1.22 (0.89)	0.65 (0.42)	0.24 (0.15)	0.30 (0.23)	0.16 (0.14)		22.98; p < 0.0000		WK<Control; p < 0.0000	ST<Control; p < 0.0000	
Onset of EMG												
SCM (ms)	54.9 (5)	54.8 (4)	49.8 (7)	48 (5)	53.3 (12)	50.3 (6)		3.503; p = 0.0371		WK<Control; p = 0.0282		
PARA (ms)	59.7 (6)	56.1 (6)	50.0 (10)	50.2 (7)	54.9 (10)	49.6 (8)		4.871; p = 0.0114		WK<Control; p = 0.0105		
BIC (ms)	56.7 (12)	52.0 (13)	54.2 (11)	47.8 (11)	59.8 (23)	50.9 (21)						
TRI (ms)	64.4 (10)	63.4 (11)	59.6 (8)	58.4 (14)	66.1 (15)	60.8 (14)						
FDI (ms)	70.2 (16)	64.4 (24)	67.5 (23)	64.7 (32)	70.9 (33)	54.8 (24)						
RF (ms)	82.0 (9)	81.5 (12)	85.7 (11)	74.6 (18)	88.8 (21)	71.8 (21)	5.456; p = 0.0232					

Table 4.2 Mean (SD) of the initial head angle, onsets of head movement, peak linear and angular kinematics for *Control*, *WK-PREP* and *ST-PREP* conditions (n = 20). Data also grouped as a function of gender (Female and Male). F-statistics and post-hoc Tukey's HSD summarized at right for mixed-model two-way ANOVAs using gender (G) and condition (C) as independent variables as well as *Control* (Control), *WK-PREP* (WK), and *ST-PREP* (ST) as the three conditions. Kinematic peaks are labeled with hollow circles in the left panel of Figure 9.1. Onset of head movement X and Z refer to the x- and z-directions of the lab reference frame.

	Control		*WK-PREP*		*ST-PREP*		ANOVA Results (F; P)			*Post-Hoc* Tukey's HSD		
Variable	Female	Male	Female	Male	Female	Males	Gender	Condition	G x C	Control-WK	Control-ST	WK-ST
Initial Head Angle												
Angle (deg)	10.6 (6.3)	15.9 (6.1)	9.7 (5.4)	14.2 (6.4)	10.7 (6.5)	14.9 (7.0)	8.801; p = 0.0045					
Onset of Head Movement												
X (ms)	56 (12)	60 (8)	53 (15)	54 (19)	57 (17)	53 (15)						
Z (ms)	37 (5)	38 (4)	33 (5)	37 (6)	33 (13)	35 (13)						
Linear Kinematics												
a_x (m/s^2)	18.9 (4.7)	19.7 (6.1)	16.9 (4.6)	19.6 (6.6)	15.0 (4.0)	14.8 (4.0)		3.303; p = 0.0444			ST<Control; p = 0.0218	
a_x (ms)	129 (6)	131 (8)	129 (11)	123 (11)	131 (9)	127 (11)						
retraction (mm)	-35.5 (5.4)	-32.3 (7.3)	-31.7 (4.6)	-29.4 (6.5)	-27.2 (8.5)	-29.2 (7.5)		3.532; p = 0.0363			ST<Control; p = 0.0287	
Angular Kinematics												
α_1(rad/s^2)	169 (38)	153 (64)	147 (51)	168 (63)	130 (28)	118 (40)		3.429; p = 0.0396			ST<Control; p = 0.0526	
α_1(ms)	126 (7)	125 (11)	122 (14)	120 (10)	119 (11)	119 (11)						
α_2(rad/s^2)	-188 (72)	-235 (97)	-187 (65)	-208 (96)	-179 (65)	-173 (56)						
α_2(ms)	176 (9)	174 (10)	178 (5)	168 (12)	185 (8)	176 (16)	7.132; p = 0.0100					
θ (deg)	23.4 (5.4)	18.2 (4.4)	20.9 (8.6)	19.1 (4.0)	21.3 (4.7)	17.1 (4.1)	7.142; p = 0.0099					
θ (ms)	214 (21)	187 (15)	205 (15)	200 (22)	204 (18)	196 (20)	4.4279; p = 0.0400					

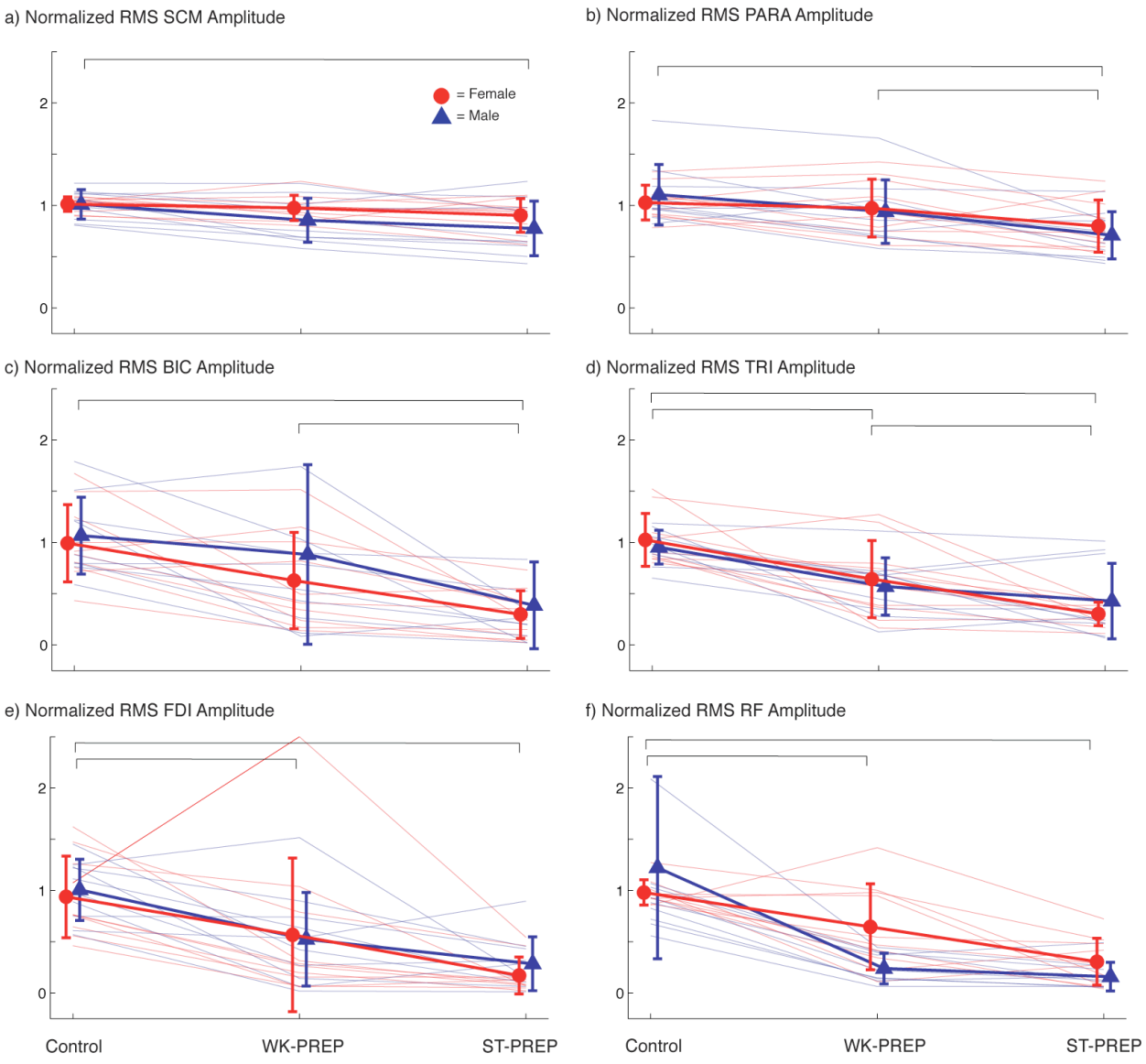


Figure 4.2 Group means and standard deviations of muscular responses for *Control*, *WK-PREP*, and *ST-PREP* conditions. Faded lines in the background depict response of individual subjects for both males (blue lines) and females (red lines). Solid bars above conditions denote that a significant difference was observed between the two indicated conditions ($p < 0.05$).

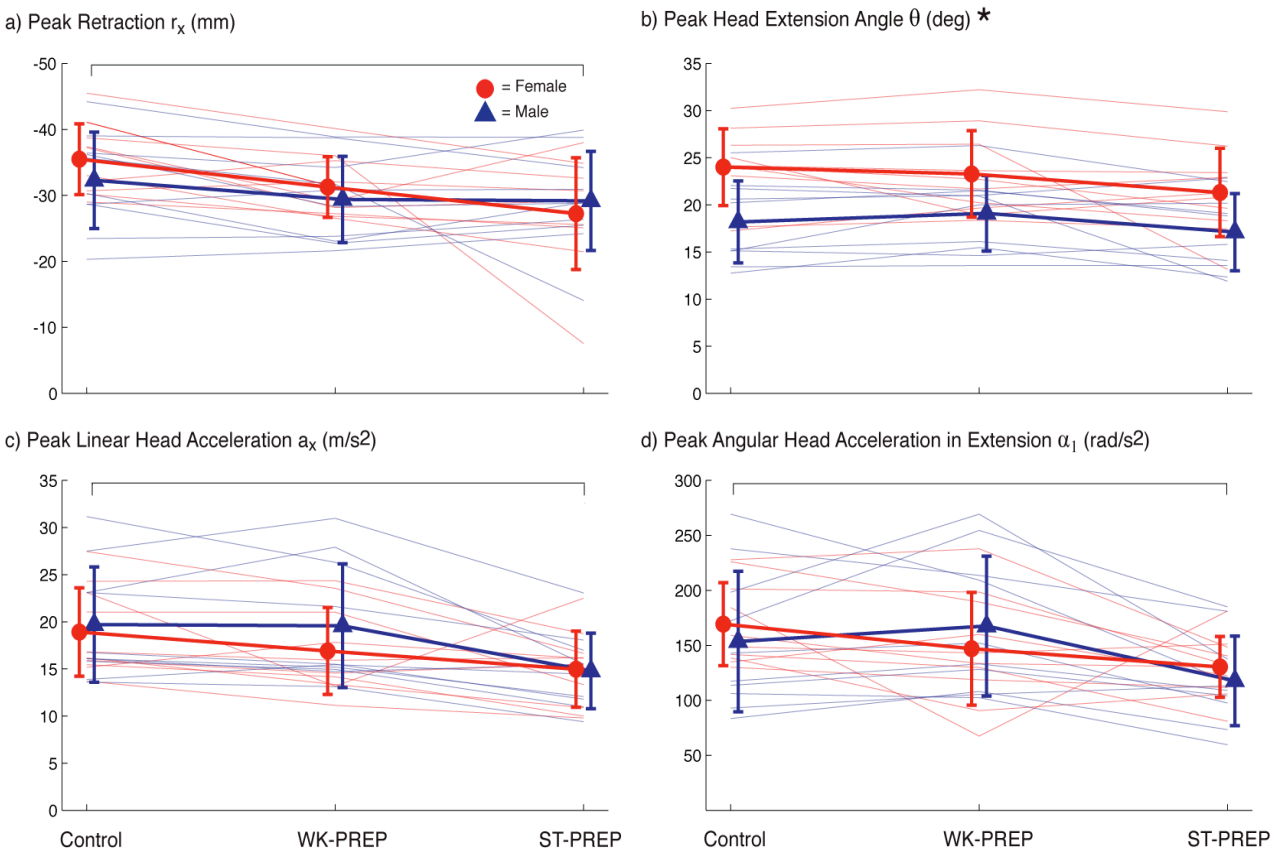


Figure 4.3 Group means and standard deviations of head kinematic responses for *Control*, *WK-PREP*, and *ST-PREP* conditions. Faded lines in the background depict response of individual subjects for both males (blue lines) and females (red lines). Solid bars above conditions denote that a significant difference was observed between the two indicated conditions ($p < 0.05$). * denotes a significant difference between gender ($p < 0.05$).

5 Discussion

The human startle response has been suggested to form part of the neurophysiological response of seated subjects exposed to rear-end, whiplash-like perturbations (Blouin et al. 2006b). The objective of the current study was to investigate if presenting pre-stimulus tones (*WK-PREP*: 85 dB and *ST-PREP*: 105 dB) before a subsequent whiplash-like perturbation could inhibit the perturbation evoked startle response in human volunteers. We initially anticipated our muscular and kinematic responses to mimic the responses of habituated subjects because habituation was shown to decrease neck muscle activity (Siegmund et al. 2003b; Blouin et al. 2006a; Mang et al. *Unpublished Observations*). Thus, we hypothesized that pre-stimulus inhibition would decrease the amplitude of whole-body muscle responses, decrease peak linear forward and angular acceleration in flexion, and increase peak angular acceleration in extension, extension angle and head rearward retraction. We observed the expected decrease in all muscle response amplitudes when we presented a startling pre-stimulus tone prior to a subsequent startling whiplash-like perturbation. Contrary to our hypothesis, pre-stimulus inhibition decreased certain peak kinematic variables (retraction, head linear acceleration and head angular acceleration in extension and flexion) during the retraction phase of the head movement (**Figure 4.1**).

When comparing the current study to previous habituation experiments, our results clearly suggested that pre-stimulus inhibition and habituation are two independent behavioural phenomena **(Table 5.1)** (Siegmund et al. 2003b; Blouin et al. 2006a). Despite a similar decrease in the ratio between the reduction of flexor and extensor muscle responses of the neck, the resulting changes in kinematic responses were considerably different between habituation and pre-stimulus inhibition (**Table 5.1**). In a habituation experiment, Siegmund et al. (2003b) suggested that habituated subjects became more familiar with the acceleration profile of subsequent repeated perturbations and responded more passively. Consequently, a decreased co-activation of the neck muscles caused a reduction in stiffness of the connection between the torso and head. The decrease in neck stiffness may have contributed to decreased linear forward head acceleration and angular head acceleration in flexion, and increased rearward head displacements, extension angle and angular head acceleration in extension (Siegmund et al. 2003b). Interestingly, we observed that pre-stimulus inhibition decreased most peak kinematic variables including linear forward head acceleration, angular head acceleration in extension and rearward head displacement. Some possible explanations for the deceased kinematic responses caused by pre-stimulus inhibition may be due to changes to the active component of neck and torso muscle activity.

Table 5.1 Comparison between habituation and pre-stimulus inhibition experiments during repeated whiplash-like perturbations. All variables represent a percentage change from first perturbation trial variables. Electromyographic data: sternocleidomastoid (SCM), cervical paraspinal (PARA); Kinematic data: peaks are labeled with hollow circles in the left panel of **Figure 9.1**.

Variables	Siegmund et al. (2003b)	Blouin et al. (2006a)	Mang et al. (2010)
Type of Experiment	Habituation	Habituation	Startling Pre-Stimulus
EMG Amplitude			
SCM	↓48%	↓28%	↓16%
PARA	↓56%	↓45%	↓26%
Linear Kinematics (AOJ)			
a_x (m/s^2)	↓9%†	↓21%	↓23%
retraction (mm)	↑11%	↑4%‡	↓17%
Angular Kinematics (AOJ)			
α_1 (rad/s^2)	↑8%	↑15%‡	↓23%
α_2 (rad/s^2)	↓8%	↓11%‡	↓17%‡
θ (deg)	↑17%	↑22%	↓8%‡

Note: †: a_x at the mastoid process; ‡: not significantly difference ($p > 0.05$)

As the whole body responds to the pre-stimulus inhibition, changes to the muscle responses of the neck and torso may explain the decreased neck muscle and peak kinematic responses observed (**Table 5.1**). Changes to the stiffness of the neck may have affected the dynamics of the head because decreasing the stiffness of the neck was previously shown to decrease linear head forward accelerations (Siegmund et al. 2003b; Blouin et al. 2006a). The smaller co-contractions of the neck muscles suggest that neck

stiffness may potentially affect the kinematic responses. Alternatively, if a pre-stimulus tone can decrease the muscle responses and the stiffness of the torso, there may be less force transferred from the upper torso to the base of the neck. Decreasing the forces applied to the base of the neck would cause the neck to respond as if it was perturbed by a lower intensity whiplash-like perturbation (Siegmund et al. 2004). Further analysis of muscular and kinematic responses of the torso would be needed to support this explanation. Although the exact cause of the observed kinematic changes remain uncertain, decreasing the peak kinematics of the head and neck would be beneficial in preventing whiplash injury.

One proposed whiplash injury mechanism is excessive strain to the cervical facet capsular joint ligament during the whiplash-like perturbations (Winkelstein et al. 2000; Siegmund et al. 2001; Winkelstein et al. 2001). Increased neck muscle activity during the whiplash motion may increase the capsular ligament strain at a moment when the ligament is vulnerable. Angular and linear head accelerations have been suggested to be proportional to the internal reaction forces of the neck; whereas, changes to peak head retraction have been suggested to be proportional to neck tissue strains (Blouin et al. 2003; Siegmund et al. 2003b). Reducing the accelerations applied to the head would decrease the internal forces generated by the neck muscles on the facet capsule and may reduce the capsular ligament strain (Winkelstein et al. 2001). On the other hand, limiting head displacement would decrease head rearward retraction and also reduce strains in the cervical facet capsular ligament (Winkelstein et al. 2000; Siegmund et al. 2001). The results from the current study observed a reduction in both the (linear and angular)

accelerations and rearward displacement of the head. Therefore, pre-stimulus inhibition demonstrated multiple mechanisms that can potentially reduce the capsular ligament strain during whiplash-like perturbations and may be applicable in the prevention or reduction of whiplash injuries. Further research is required to determine the exact effects of pre-stimulus inhibition on facet capsular ligament stain; however, direct calculations of capsular ligament strain in human volunteers are currently very difficult and may require the extensive use of mathematical models.

In the current study, the secondary objective was to compare the effectiveness of two pre-stimulus tones with difference auditory intensities on the inhibition of the human startle response. We observed that the muscle responses evoked by a whiplash-like perturbation could be significantly inhibited by a startling pre-stimulus tone (*ST-PREP*: 105 dB) (**Figure 4.1**). *ST-PREP* decreased the amplitude of all muscle responses ($p < 0.01$); whereas, *WK-PREP* decreased the normalized RMS EMG amplitudes from *Control* for only TRI, FDI and RF muscles ($p < 0.01$). When comparing the effects of different pre-stimulus tone intensity on the peak kinematic response variable, only *ST-PREP* significantly ($p < 0.05$) decreased peak head retraction (r_x), peak linear head forward acceleration (a_x) and peak angular head acceleration during extension (α_1). Thus, pre-stimulus tone with greater auditory intensities (105 dB vs. 85 dB) produced greater inhibition of the startle responses evoked during whiplash-like perturbations.

The largest inhibition of muscle amplitudes during the *ST-PREP* condition were observed in the distal and proximal limbs (greater than 60%); whereas, SCM decreased by 16% and PARA decreased by 26%. These results suggest that not only did the startle

response elicit whole-body muscle contractions in seated subjects, but pre-stimulus inhibition affected the whole-body and had greater inhibitory effects on appendicular muscles than neck muscles. Greater inhibition of appendicular muscles may have occurred because these muscles were not as important as the neck muscles in maintaining upright seated posture during the perturbation-induced motion. In contrast, neck muscles could not be inhibited as much as appendicular muscles because the co-activation of the neck muscles was required to increase neck stiffness and maintain upright head position. Vibert et al. (2001) observed that the neck of some subjects responded in a "floppy" manner when the neck muscles were not consistently activated during transient perturbations. Those subjects appeared to rely on the passive biomechanical properties of their head and neck to maintain upright head position. Some "floppy" subjects activated reflex muscular synergies that exaggerate the inertial kinematic response to the perturbation and may potentially cause injury to the neck (Vibert et al. 2001). If pre-stimulus inhibition completely inhibited the startle component of neck muscle responses, the observed amplitudes of neck muscle responses would represent the minimum amplitudes required to maintain upright head position. Alternatively, we propose that at least 16% of SCM and 26% of PARA muscle responses contribute to the startle response evoked during whiplash-like perturbations.

The mammalian neurophysiology of pre-stimulus inhibition from an auditory pulse is mediated by nuclei located in the brainstem and share similar neural pathways as the startle response (Davis et al. 1982; Davis 1984; Koch et al. 1993; Yeomans et al. 1993; Yeomans and Frankland 1995). A commonly accepted pre-stimulus inhibition

circuit includes the following neuroanatomical structures: inferior colliculus (IC), superior colliculus (SC), pedunculopontine tegmental nucleus (PPTg) and ventrocaudal pontine reticular formation (PnC) (Koch and Schnitzler 1997; Koch 1999; Fendt et al. 2001; Leumann et al. 2001). It is believed that maximum pre-stimulus inhibition occurs when the inhibitory circuit produces maximum inhibition of the PnC (the summation site for the startle response and pre-stimulus inhibition) at the moment that the excitatory startle response arrives (Hoffman and Ison 1980). The level of inhibition has been shown to increase with increased intensity of the pre-stimulus tone (Blumenthal 1996) and to decrease with increased pre-stimulus ISI (pre-stimulus facilitation occurred at 30 ms or less (Valls-Sole et al. 1999) and pre-stimulus inhibition was still effective after 1000 ms (Mang et al. *Unpublished Observations*)). Thus, this model may explain the different intensities of pre-stimulus inhibition observed between *WK-PREP* and *ST-PREP* in the current study. The only difference between *WK-PREP* and *ST-PREP* was the different sound pressure level of the pre-stimulus tone because the ISI was held at a constant 250 ms. Thus, the non-significant decreases of muscular and kinematic responses observed in *WK-PREP*, suggested that the intensity of *WK-PREP* tone did not surpass a threshold to elicit a significant inhibition effect on the subsequent startle response.

In the current study, we observed gender-related differences more predominantly in the kinematic responses than in the muscular responses (**Table 4.1 and 4.2**). Female subjects started with a more flexed initial head angle and reached greater peak head extension angle than male subjects. This increased range of angular motion may be a result of females having significantly smaller geometry of the vertebrae in the anterior-

posterior dimension (Vasavada et al. 2008). Overall, females have a lower head mass and smaller neck geometry than males, but female necks and heads are not equally proportionally smaller than males (Vasavada et al. 2008). In previous studies, female subjects were found to activate their neck muscles 3 to 8 ms earlier than male subjects (Brault et al. 2000; Siegmund et al. 2003a); however, Blouin et al. (2006a) and our results did not observe this difference. The effect of pre-stimulus inhibition and fewer subjects used in the current study may potentially hide the gender–related difference between the onsets of muscle activity. Regardless, the absence of significant interaction between gender and condition observed in the current study suggested that pre-stimulus inhibition affected males and females equally.

The rapid habituation of muscle and kinematic responses had been quantified for sequential whiplash-like perturbations with short inter-perturbation time intervals (IPI) (< 10 minutes) and, potentially, confounded the results of many previous whiplash studies. The current protocol utilized a longer IPI (15-20 minutes) that was previously shown to minimize the habituation of muscle and kinematic response during the series of five sequential whiplash-like perturbations (Mang et al. 2009). To ensure correct positioning and orientation of all accelerometers and angular rate sensors throughout the experiment, we re-digitized all anatomical landmarks and IRED markers immediately prior to the perturbation. Statistical analysis of the three *Control* trials positioned in the first, middle and last trials found no significant differences ($p > 0.05$) between the muscular and kinematic responses of the three *Control* trials. The present observations for the two pre-stimulus conditions were unlikely to be limited by habituation between trials, but a direct

result of pre-stimulus inhibition on the startle response during whiplash-like perturbations.

Another limitation of the current study was the amplitude of the whiplash-like perturbation (speed change: 2.7 km/h, peak acceleration: 2.060 ± 0.005g; Δt: 53.2 ± 0.05ms; Δv: 0.7500 ± 0.0003m/s) used in the current study as compared to many actual whiplash inducing collisions. Other studies have implemented greater speed changes between 4 to 16 km/h resulting in peak accelerations up to 6.0 g (Matsushita et al. 1994; Szabo et al. 1994; McConnell et al. 1995; Brault et al. 1998; Brault et al. 2000), but the muscular and kinematic response have been shown to exhibit a graded response proportional to perturbation intensity (Siegmund et al. 2004). Despite subjects having larger muscle responses to more intense perturbations, we would expect pre-stimulus tones to evoke inhibition of the muscular and kinematic responses similar to the observed results of this study.

Our goal for future research would be to implement pre-stimulus inhibition techniques in experiments exposing subjects to more intense perturbation amplitudes (> 2.7 km/h). These studies would allow us to better understand how pre-stimulus inhibition would influence the muscular and kinematic responses and, hopefully, reduce the risk of whiplash injuries during real-life low-speed rear-end collisions. The results from the proposed studies would help to lay the foundation for developing new preventive devices used in cars to mitigate whiplash injuries. These preventive devices would be easily implemented into vehicles because existing car audio systems are capable of reaching a startling sound pressure level of 105 dB (Mang et al., *Unpublished Observations*). These

new devices would rely on pre-collision warning systems already installed in many new vehicles to trigger a startling pre-stimulus tone to cause the inhibition of the startle response elicited by the imminent automotive collision.

6 Conclusion

The results of this experiment showed that presenting a pre-stimulus tone (85 dB weak: *WK-PREP* or 105 dB startling: *ST-PREP*) before a startling whiplash-like perturbation could inhibit the muscular responses and decrease peak kinematic response variables evoked by the perturbation. The use of a startling pre-stimulus tone was shown to be more effective than a weak pre-stimulus tone and, consequently, should be used in future pre-stimulus research. A startling pre-stimulus tone significantly reduced the amplitudes of all muscle responses and decreased peak kinematic variables such as peak head accelerations and rearward head retraction. The results suggested a startling pre-stimulus tone could reduce cervical facet joint capsular ligament strains and the potential of whiplash injuries resulting from low-speed rear-end collisions.

References

Anderson, J. S., Hsu, A. W. and Vasavada, A. N. (2005). Morphology, architecture, and biomechanics of human cervical multifidus. *Spine* **30(4)**: E86-91.

Anderson, R. W. G. and Baldock, M. R. J. (2008). Vehicle improvements to reduce the number and severity of rear end crashes. CASR REPORT SERIES. South Australia, Australia, Centre for Automotive Safety Research, The University of Adelaide.

Azar, N. R., Kallakuri, S., Chen, C., Lu, Y. and Cavanaugh, J. M. (2009). Strain and load thresholds for cervical muscle recruitment in response to quasi-static tensile stretch of the caprine C5-C6 facet joint capsule. *J Electromyogr Kinesiol*.

Barnsley, L., Lord, S. and Bogduk, N. (1994). Whiplash injury. *Pain* **58(3)**: 283-307.

Barnsley, L., Lord, S. M., Wallis, B. J. and Bogduk, N. (1995). The prevalence of chronic cervical zygapophysial joint pain after whiplash. *Spine (Phila Pa 1976)* **20(1)**: 20-5; discussion 26.

Bitsios, P., Giakoumaki, S. G., Theou, K. and Frangou, S. (2006). Increased prepulse inhibition of the acoustic startle response is associated with better strategy formation and execution times in healthy males. *Neuropsychologia* **44(12)**: 2494-9.

Blouin, J. S., Descarreaux, M., Belanger-Gravel, A., Simoneau, M. and Teasdale, N. (2003). Attenuation of human neck muscle activity following repeated imposed trunk-forward linear acceleration. *Exp Brain Res* **150(4)**: 458-64.

Blouin, J. S., Inglis, J. T. and Siegmund, G. P. (2006a). Auditory startle alters the response of human subjects exposed to a single whiplash-like perturbation. *Spine* **31(2)**: 146-54.

Blouin, J. S., Inglis, J. T. and Siegmund, G. P. (2006b). Startle responses elicited by whiplash perturbations. *J Physiol* **573(Pt 3)**: 857-67.

Blumenthal, T. D. (1995). Prepulse inhibition of the startle eyeblink as an indicator of temporal summation. Percept Psychophys. **57:** 487-494.

Blumenthal, T. D. (1996). Inhibition of the human startle response is affected by both prepulse intensity and eliciting stimulus intensity. *Biol Psychol* **44(2)**: 85-104.

Braff, D., Stone, C., Callaway, E., Geyer, M., Glick, I. and Bali, L. (1978). Prestimulus effects on human startle reflex in normals and schizophrenics. *Psychophysiology* **15(4)**: 339-43.

Brault, J. R., Siegmund, G. P. and Wheeler, J. B. (2000). Cervical muscle response during whiplash: evidence of a lengthening muscle contraction. *Clin Biomech (Bristol, Avon)* **15(6)**: 426-35.

Brault, J. R., Wheeler, J. B., Siegmund, G. P. and Brault, E. J. (1998). Clinical response of human subjects to rear-end automobile collisions. *Arch Phys Med Rehabil* **79(1)**: 72-80.

Brown, P., Rothwell, J. C., Thompson, P. D., Britton, T. C., Day, B. L. and Marsden, C. D. (1991). New observations on the normal auditory startle reflex in man. *Brain* **114 (Pt 4)**: 1891-902.

Buitenhuis, J., de Jong, P. J., Jaspers, J. P. and Groothoff, J. W. (2009). Work disability after whiplash: a prospective cohort study. *Spine (Phila Pa 1976)* **34(3)**: 262-7.

Cassidy, J. D., Carroll, L. J., Cote, P., Lemstra, M., Berglund, A. and Nygren, A. (2000). Effect of eliminating compensation for pain and suffering on the outcome of insurance claims for whiplash injury. *N Engl J Med* **342(16)**: 1179-86.

Davis, M. (1984). The mammalian startle response. Neural Mechanisms of Startle Behavior. R. C. Eaton. New York, Plenum Press**:** 287-351.

Davis, M., Gendelman, D. S., Tischler, M. D. and Gendelman, P. M. (1982). A primary acoustic startle circuit: lesion and stimulation studies. *J Neurosci* **2(6)**: 791-805.

Evans, R. W. (1992). Some observations on whiplash injuries. *Neurol Clin* **10(4)**: 975-97.

Evans, T. H., Mayer, T. G. and Gatchel, R. J. (2001). Recurrent disabling work-related spinal disorders after prior injury claims in a chronic low back pain population. *Spine J* **1(3)**: 183-9.

Fendt, M., Li, L. and Yeomans, J. S. (2001). Brain stem circuits mediating prepulse inhibition of the startle reflex. *Psychopharmacology (Berl)* **156(2-3)**: 216-24.

Filion, D. L., Dawson, M. E. and Schell, A. M. (1998). The psychological significance of human startle eyeblink modification: a review. *Biol Psychol* **47(1)**: 1-43.

Forssberg, H. and Hirschfeld, H. (1994). Postural adjustments in sitting humans following external perturbations: muscle activity and kinematics. *Exp Brain Res* **97(3)**: 515-27.

Fox, J. E. (1979). Habituation and prestimulus inhibition of the auditory startle reflex in decerebrate rats. *Physiol Behav* **23(2)**: 291-7.

Frank, J. S. (1986). Spinal motor preparation in humans. *Electroencephalogr Clin Neurophysiol* **63(4)**: 361-70.

Gresty, M. (1989). Stability of the head in pitch (neck flexion-extension): studies in normal subjects and patients with axial rigidity. *Mov Disord* **4(3)**: 233-48.

Grosse, P. and Brown, P. (2003). Acoustic startle evokes bilaterally synchronous oscillatory EMG activity in the healthy human. *J Neurophysiol* **90(3)**: 1654-61.

Halliday, D. M., Conway, B. A., Farmer, S. F. and Rosenberg, J. R. (1998). Using electroencephalography to study functional coupling between cortical activity and electromyograms during voluntary contractions in humans. *Neurosci Lett* **241(1)**: 5-8.

Halliday, D. M. and Rosenberg, J. R. (2000). On the application, estimation and interpretation of coherence and pooled coherence. *J Neurosci Methods* **100(1-2)**: 173-4.

Harder, S., Veilleux, M. and Suissa, S. (1998). The effect of socio-demographic and crash-related factors on the prognosis of whiplash. *J Clin Epidemiol* **51(5)**: 377-84.

Hernandez, I. A., Fyfe, K. R., Heo, G. and Major, P. W. (2006). The role of sternocleidomastoid muscle in simulated low velocity rear-end impacts. *Eur Spine J* **15(6)**: 876-85.

Hiatt, J. L. and Gartner, L. P. (1987). Textbook of Head and Neck Anatomy. Baltimore. MD, USA, Williams & Wilkins.

Hoffman, H. S. and Ison, J. R. (1980). Reflex modification in the domain of startle: I. Some empirical findings and their implications for how the nervous system processes sensory input. *Psychol Rev* **87(2)**: 175-89.

Hoffman, H. S. and Searle, J. L. (1968). Acoustic and temporal factors in the evocation of startle. *J Acoust Soc Am* **43(2)**: 269-82.

Holm, L. W., Carroll, L. J., Cassidy, J. D., Hogg-Johnson, S., Cote, P., Guzman, J., Peloso, P., Nordin, M., Hurwitz, E., van der Velde, G., Carragee, E. and Haldeman, S. (2008). The burden and determinants of neck pain in whiplash-associated disorders after traffic collisions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* **33(4 Suppl)**: S52-9.

ICBC (2000). Annual Report. British Columbia, Insurance Company of British Columbia.

ICBC (2006). Annual Report. British Columbia, Insurance Company of British Columbia.

ICBC (2007). Traffic Collision Statistics: Police-attended Injury and Fatal Collisions. British Columbia, Insurance Company of British Columbia.

Inami, S., Kaneoka, K., Hayashi, K. and Ochiai, N. (2000). Types of synovial fold in the cervical facet joint. *J Orthop Sci* **5(5)**: 475-80.

Inami, S., Shiga, T., Tsujino, A., Yabuki, T., Okado, N. and Ochiai, N. (2001). Immunohistochemical demonstration of nerve fibers in the synovial fold of the human cervical facet joint. *J Orthop Res* **19(4)**: 593-6.

Ison, J. R. and Krauter, E. E. (1974). Reflex-inhibiting stimuli and the refractory period of the acoustic startle reflex in the rat. *J Comp Physiol Psychol* **86(3)**: 420-5.

Ison, J. R. and Pinckney, L. A. (1983). Reflex inhibition in humans: sensitivity to brief silent periods in white noise. *Percept Psychophys* **34(1)**: 84-8.

Jakobsson, L., Lundell, B., Norin, H. and Isaksson-Hellman, I. (2000). WHIPS--Volvo's Whiplash Protection Study. *Accid Anal Prev* **32(2)**: 307-19.

Kaneoka, K., Ono, K., Inami, S. and Hayashi, K. (1999). Motion analysis of cervical vertebrae during whiplash loading. *Spine* **24(8)**: 763-9; discussion 770.

Koch, M. (1999). The neurobiology of startle. *Prog Neurobiol* **59(2)**: 107-28.

Koch, M., Kungel, M. and Herbert, H. (1993). Cholinergic neurons in the pedunculopontine tegmental nucleus are involved in the mediation of prepulse inhibition of the acoustic startle response in the rat. *Exp Brain Res* **97(1)**: 71-82.

Koch, M. and Schnitzler, H. U. (1997). The acoustic startle response in rats--circuits mediating evocation, inhibition and potentiation. *Behav Brain Res* **89(1-2)**: 35-49.

Krafft, M. (2002). When do AIS 1 neck injuries result in long-term consequences? Vehicle and human factors. *Traffic Inj Prev* **3**: 89-97.

Landis, C. and Hunt, W. A. (1939). The Startle Pattern. New York, Farrar and Rinehart.

Lee, Y., Lopez, D. E., Meloni, E. G. and Davis, M. (1996). A primary acoustic startle pathway: obligatory role of cochlear root neurons and the nucleus reticularis pontis caudalis. *J Neurosci* **16(11)**: 3775-89.

Leumann, L., Sterchi, D., Vollenweider, F., Ludewig, K. and Fruh, H. (2001). A neural network approach to the acoustic startle reflex and prepulse inhibition. *Brain Res Bull* **56(2)**: 101-10.

Li, L., Priebe, R. P. and Yeomans, J. S. (1998). Prepulse inhibition of acoustic or trigeminal startle of rats by unilateral electrical stimulation of the inferior colliculus. *Behav Neurosci* **112(5)**: 1187-98.

Lieber, R. L. and Friden, J. (1993). Muscle damage is not a function of muscle force but active muscle strain. *J Appl Physiol* **74(2)**: 520-6.

Linder, A., Carlsson, A., Svensson, M. Y. and Siegmund, G. P. (2008). Dynamic responses of female and male volunteers in rear impacts. *Traffic Inj Prev* **9(6)**: 592-9.

Lingenhohl, K. and Friauf, E. (1994). Giant neurons in the rat reticular formation: a sensorimotor interface in the elementary acoustic startle circuit? *J Neurosci* **14(3 Pt 1)**: 1176-94.

Luan, F., Yang, K. H., Deng, B., Begeman, P. C., Tashman, S. and King, A. I. (2000). Qualitative analysis of neck kinematics during low-speed rear-end impact. *Clin Biomech (Bristol, Avon)* **15(9)**: 649-57.

Macpherson, P. C., Schork, M. A. and Faulkner, J. A. (1996). Contraction-induced injury to single fiber segments from fast and slow muscles of rats by single stretches. *Am J Physiol* **271(5 Pt 1)**: C1438-46.

Malanga, G. A. and Nadler, S. (2002). Whiplash. Philadelphia, Hanley & Belfus.

Mang, D. W. H., Siegmund, G. P., Inglis, J. T. and Blouin, J. S. (2009). Whole body Physiological and Muscle Responses to Startle Evolked by Whiplash Perturbations. 19th Annual Conference, The Society for the Neural Control of Movement, Waikoloa Beach, "Big Island", Hawaii, USA.

Matsushita, T., Sato, T. B., Hirabayashi, K., Fujimara, A., Asazuma, T. and Takatori, T. (1994). X-ray study of the human neck due to head inertia loading (942208). Proceedings of the 38th Stapp Car Crash Conference, Society of Automotive Engineers, Warrendale, PA.

McConnell, W. E., Howard, R. P., van Poppel, J., Krause, R., Guzman, H. M., Bomar, J. B., Raddin, J. H., Benedict, J. V. and Hatsell, C. P. (1995). Human head and neck kinematic after low velocity rear-end impacts - Understanding "whiplash". Proceedings of the 39th Stapp Car Crash Conference, Coronado, CA, USA.

McCully, K. K. and Faulkner, J. A. (1985). Injury to skeletal muscle fibers of mice following lengthening contractions. *J Appl Physiol* **59(1)**: 119-26.

McCully, K. K. and Faulkner, J. A. (1986). Characteristics of lengthening contractions associated with injury to skeletal muscle fibers. *J Appl Physiol* **61(1)**: 293-9.

McLain, R. F. (1994). Mechanoreceptor endings in human cervical facet joints. *Spine (Phila Pa 1976)* **19(5)**: 495-501.

Mercer, S. and Bogduk, N. (1993). Intra-articular inclusions of the cervical synovial joints. *Br J Rheumatol* **32(8)**: 705-10.

Mitani, A., Ito, K., Mitani, Y. and McCarley, R. W. (1988). Morphological and electrophysiological identification of gigantocellular tegmental field neurons with descending projections in the cat: I. Pons. *J Comp Neurol* **268(4)**: 527-45.

Mordaka, J. and Gentle, C. R. (2003). Biomechanical analysis of whiplash injuries: Women are not scaled down men., *4th European LS-DYNA Users Conference.*

NASA (1978). Anthropometric Source Book, NASA Reference Publication 1024. Hanover, MD, USA, National Aeronautics and Space Adminstration, Scienticic and Technical Information Office.

Nashner, L. M. (1976). Adapting reflexes controlling the human posture. *Exp Brain Res* **26(1)**: 59-72.

Onan, O. A., Heggeness, M. H. and Hipp, J. A. (1998). A motion analysis of the cervical facet joint. *Spine* **23(4)**: 430-9.

Otremski, I., Marsh, J. L., Wilde, B. R., McLardy Smith, P. D. and Newman, R. J. (1989). Soft tissue cervical spinal injuries in motor vehicle accidents. *Injury* **20(6)**: 349-51.

Padgaonkar, A. J., Krieger, K. W. and King, A. I. (1975). Measurement of angular acceleration of a rigid boody using linear accelerometers. Applied Mechanics Summer Conference, Symposium on Biomechanics, Rensselaer Polytechnic Institue, Troy, N.Y., USA, *The American Society of Mechanical Engineers.*

Padmanaban, J., burnett, R. and Levitt, A. E. (2009). Relationship between Seatback Stiffness/Strength and Risk of Serious/FatalInjury in Rear-Impact Crashes. *SAE International Journal of Passenger Cars - Mechanical Systems* **2(1)**: 8.

Pearson, A. M., Ivancic, P. C., Ito, S. and Panjabi, M. M. (2004). Facet joint kinematics and injury mechanisms during simulated whiplash. *Spine* **29(4)**: 390-7.

Plappert, C. F., Pilz, P. K. and Schnitzler, H. U. (1999). Interaction between acoustic and electric sensitization of the acoustic startle response in rats. *Behav Brain Res* **103(2)**: 195-201.

Plappert, C. F., Pilz, P. K. and Schnitzler, H. U. (2004). Factors governing prepulse inhibition and prepulse facilitation of the acoustic startle response in mice. *Behav Brain Res* **152(2)**: 403-12.

Pozzo, T., Berthoz, A. and Lefort, L. (1990). Head stabilization during various locomotor tasks in humans. I. Normal subjects. *Exp Brain Res* **82(1)**: 97-106.

Queisser, F., Bluthner, R. and Seidel Dozent, H. (1994). Control of positioning the cervical spine and its application to measuring extensor strength. *Clin Biomech* **9(3)**: 157-161.

Quinlan, K. P., Annest, J. L., Myers, B., Ryan, G. and Hill, H. (2004). Neck strains and sprains among motor vehicle occupants-United States, 2000. *Accid Anal Prev* **36(1)**: 21-7.

Raynor, R. B., Pugh, J. and Shapiro, I. (1985). Cervical facetectomy and its effect on spine strength. *J Neurosurg* **63(2)**: 278-82.

Reijmers, L. G., Vanderheyden, P. M. and Peeters, B. W. (1995). Changes in prepulse inhibition after local administration of NMDA receptor ligands in the core region of the rat nucleus accumbens. *Eur J Pharmacol* **272(2-3)**: 131-8.

Shamboul, K. M. (1980). Lumbosacral predominance of vestibulospinal fibre projection in the rat. *J Comp Neurol* **192(3)**: 519-30.

Siegmund, G. P. (2001). The Reflex Response of Human Neck Muscles to Whiplash-like Perturbations. School of Human Kinetics. Vancouver, BC, University of British Columbia. **Doctroal Thesis**.

Siegmund, G. P., Blouin, J. S., Brault, J. R., Hedenstierna, S. and Inglis, J. T. (2007). Electromyography of superficial and deep neck muscles during isometric, voluntary, and reflex contractions. *J Biomech Eng* **129(1)**: 66-77.

Siegmund, G. P., Blouin, J. S., Carpenter, M. G., Brault, J. R. and Inglis, J. T. (2008a). Are cervical multifidus muscles active during whiplash and startle? An initial experimental study. *BMC Musculoskeletal Disorders* **9(80)**.

Siegmund, G. P., Blouin, J. S. and Inglis, J. T. (2008b). Does startle explain the exaggerated first response to a transient perturbation? *Exerc. Sport Sci. Rev.* **36(2)**: 76-82.

Siegmund, G. P., King, D. J., Lawrence, J. M., Wheeler, J. B., Brault, J. R. and Smith, T. A. (1997). Head/neck kinematic response of human subjects in low-speed rear-end collisions., *41st Stapp Car Crash Conference*.

Siegmund, G. P., Mang, D. W. H. and Blouin, J. S. (2008c). Sensory pathways mediating the neck muscle response in rear-end impacts. Proceedings of the Thirty-Sixth International Workshop, *Injury Biomechanics Research*.

Siegmund, G. P., Myers, B. S., Davis, M. B., Bohnet, H. F. and Winkelstein, B. A. (2001). Mechanical evidence of cervical facet capsule injury during whiplash: a

cadaveric study using combined shear, compression, and extension loading. *Spine* **26(19)**: 2095-101.

Siegmund, G. P., Sanderson, D. J. and Inglis, J. T. (2004). Gradation of Neck Muscle Responses and Head/Neck Kinematics to Acceleration and Speed Change in Rear-end Collisions. *Stapp Car Crash J* **48**: 419-30.

Siegmund, G. P., Sanderson, D. J., Myers, B. S. and Inglis, J. T. (2003a). Awareness affects the response of human subjects exposed to a single whiplash-like perturbation. *Spine* **28(7)**: 671-9.

Siegmund, G. P., Sanderson, D. J., Myers, B. S. and Inglis, J. T. (2003b). Rapid neck muscle adaptation alters the head kinematics of aware and unaware subjects undergoing multiple whiplash-like perturbations. *J Biomech* **36(4)**: 473-82.

Spitzer, W. O., Skovron, M. L., Salmi, L. R., Cassidy, J. D., Duranceau, J., Suissa, S. and Zeiss, E. (1995). Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. *Spine* **20(8 Suppl)**: 1S-73S.

Stemper, B. D., Yoganandan, N., Gennarelli, T. A. and Pintar, F. A. (2005). Localized cervical facet joint kinematics under physiological and whiplash loading. *J Neurosurg Spine* **3(6)**: 471-6.

Sterner, Y. and Gerdle, B. (2004). Acute and chronic whiplash disorders--a review. *J Rehabil Med* **36(5)**: 193-209; quiz 210.

Suissa, S., Harder, S. and Veilleux, M. (2001). The relation between initial symptoms and signs and the prognosis of whiplash. *Eur Spine J* **10(1)**: 44-9.

Szabo, T. J., Welcher, J. B., Anderson, R. D., Rice, M. M., Ward, J. A., Paulo, L. R. and Carpenter, N. J. (1994). Human occupant kinematic response to low speed rear-end impacts (940532). International Congress & Exposition. Detroit, MI.

Todman, D. H. (2007). Whiplash injuries: A historical review. *The Internet Journal of Neurology* **8(2)**.

Valls-Sole, J., Kofler, M., Kumru, H., Castellote, J. M. and Sanegre, M. T. (2005). Startle-induced reaction time shortening is not modified by prepulse inhibition. *Exp Brain Res* **165(4)**: 541-8.

Valls-Sole, J., Kumru, H. and Kofler, M. (2008). Interaction between startle and voluntary reactions in humans. *Exp Brain Res* **187(4)**: 497-507.

Valls-Sole, J., Valldeoriola, F., Molinuevo, J. L., Cossu, G. and Nobbe, F. (1999). Prepulse modulation of the startle reaction and the blink reflex in normal human subjects. *Exp Brain Res* **129(1)**: 49-56.

Vasavada, A. N., Brault, J. R. and Siegmund, G. P. (2007). Musculotendon and fascicle strains in anterior and posterior neck muscles during whiplash injury. *Spine* **32(7)**: 756-65.

Vasavada, A. N., Danaraj, J. and Siegmund, G. P. (2008). Head and neck anthropometry, vertebral geometry and neck strength in height-matched men and women. *J Biomech* **41(1)**: 114-21.

Versteegen, G. J., Kingma, J., Meijler, W. J. and ten Duis, H. J. (2000). Neck sprain after motor vehicle accidents in drivers and passengers. *Eur Spine J* **9(6)**: 547-52.

Viano, D. C. (2003a). Influence of seat properties on occupant dynamics in severe rear crashes. *Traffic Inj Prev* **4(4)**: 324-36.

Viano, D. C. (2003b). Seat influences on female neck responses in rear crashes: a reason why women have higher whiplash rates. *Traffic Inj Prev* **4(3)**: 228-39.

Vibert, N., MacDougall, H. G., de Waele, C., Gilchrist, D. P., Burgess, A. M., Sidis, A., Migliaccio, A., Curthoys, I. S. and Vidal, P. P. (2001). Variability in the control of head movements in seated humans: a link with whiplash injuries? *J Physiol* **532(Pt 3)**: 851-68.

Wilson, C. J. and Groves, P. M. (1973). Refractory period and habituation of acoustic startle response in rats. *J Comp Physiol Psychol* **83(3)**: 492-8.

Wilson, V. J. and Schor, R. H. (1999). The neural substrate of the vestibulocollic reflex. What needs to be learned. *Exp Brain Res* **129(4)**: 483-93.

Winkelstein, B. A., McLendon, R. E., Barbir, A. and Myers, B. S. (2001). An anatomical investigation of the human cervical facet capsule, quantifying muscle insertion area. *J Anat* **198(Pt 4)**: 455-61.

Winkelstein, B. A. and Myers, B. S. (2000). Experimental and computational characterization of three-dimensional cervical spine flexibility. *Stapp Car Crash J* **44**: 139-58.

Winkelstein, B. A., Nightingale, R. W., Richardson, W. J. and Myers, B. S. (2000). The cervical facet capsule and its role in whiplash injury: a biomechanical investigation. *Spine* **25(10)**: 1238-46.

Wyke, B. (1972). Articular neurology--a review. *Physiotherapy* **58(3)**: 94-9.

Wyke, B. (1979). Neurology of the cervical spinal joints. *Physiotherapy* **65(3)**: 72-6.

Yeomans, J. S. and Frankland, P. W. (1995). The acoustic startle reflex: neurons and connections. *Brain Res Brain Res Rev* **21(3)**: 301-14.

Yeomans, J. S., Hempel, C. M. and Chapman, C. A. (1993). Axons and synapses mediating startle-like responses evoked by electrical stimulation of the reticular formation in rats: symmetric and asymmetric collision effects. *Brain Res* **617(2)**: 309-19.

Yeomans, J. S., Lee, J., Yeomans, M. H., Steidl, S. and Li, L. (2006). Midbrain pathways for prepulse inhibition and startle activation in rat. *Neuroscience* **142(4)**: 921-9.

Yeomans, J. S., Li, L., Scott, B. W. and Frankland, P. W. (2002). Tactile, acoustic and vestibular systems sum to elicit the startle reflex. *Neurosci Biobehav Rev* **26(1)**: 1-11.

Yoganandan, N., Kumaresan, S. and Pintar, F. A. (2001). Biomechanics of the cervical spine Part 2. Cervical spine soft tissue responses and biomechanical modeling. *Clin Biomech (Bristol, Avon)* **16(1)**: 1-27.

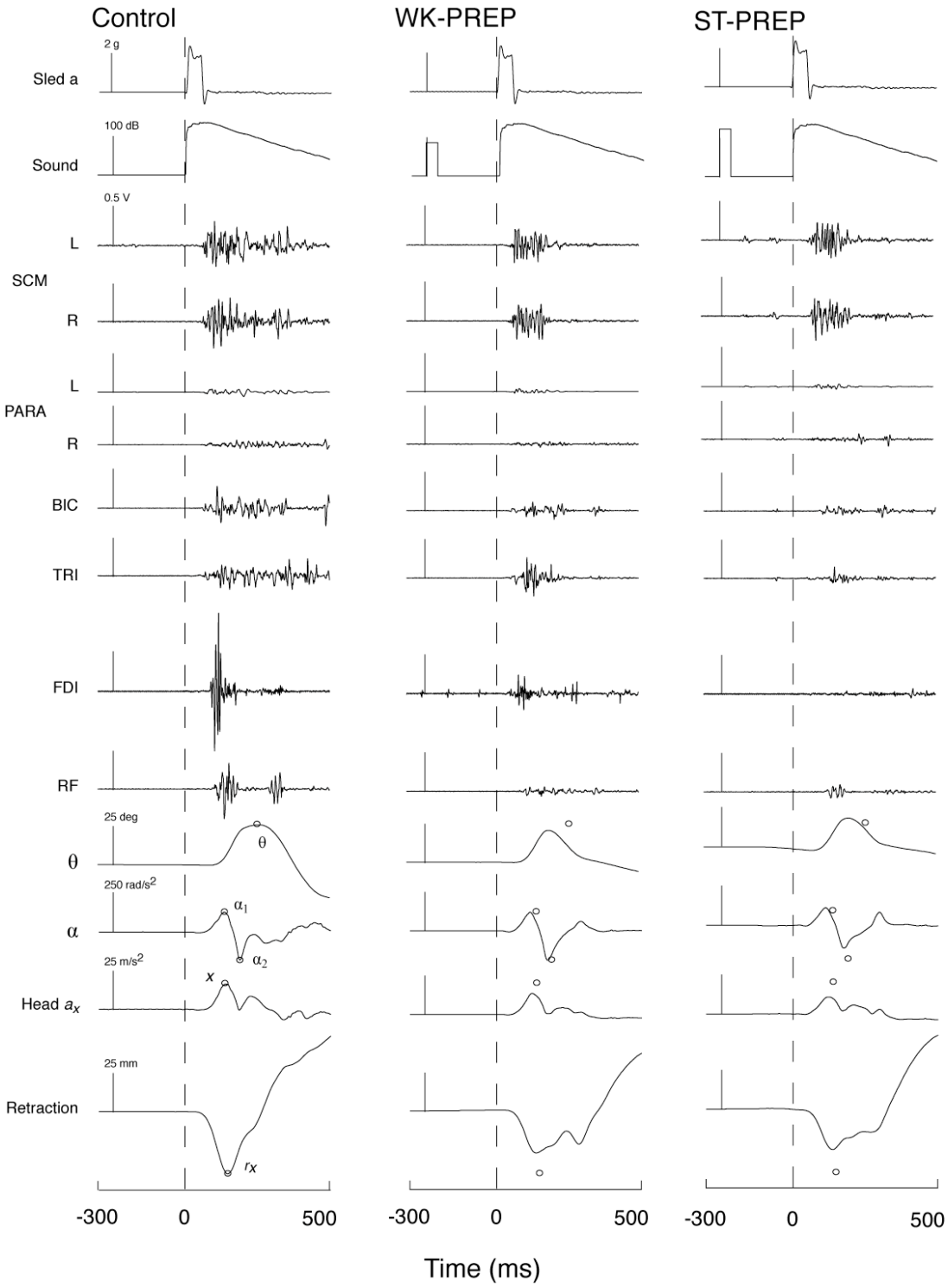
Yoganandan, N., Pintar, F. A. and Klienberger, M. (1998). Cervical spine vertebral and facet joint kinematics under whiplash. *J Biomech Eng* **120(2)**: 305-7.

Appendices

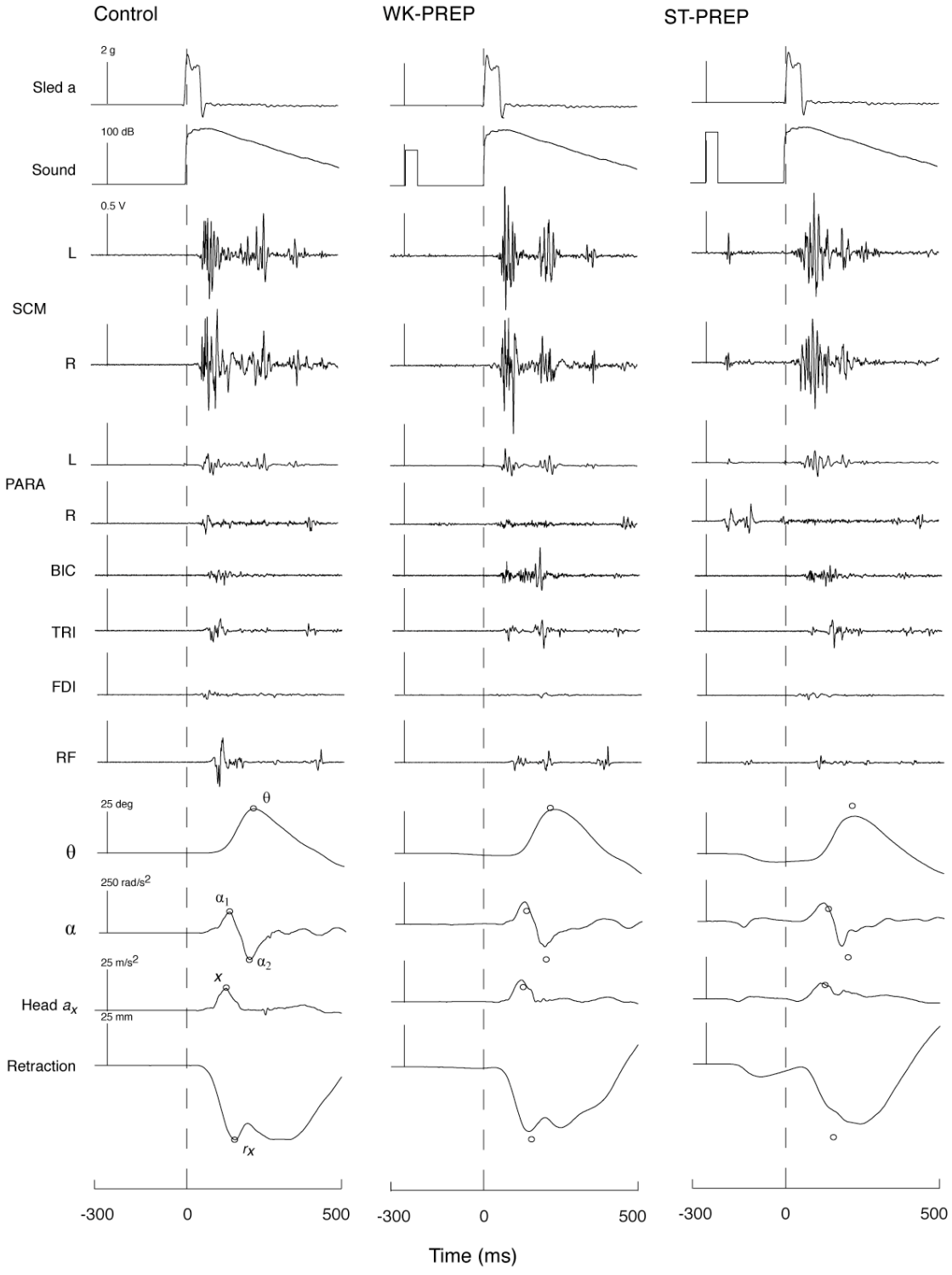
Appendix A: Graphical Figures of Individual Subject Data

The following figures illustrate the muscular and kinematic responses for each subject during *Control*, *WK-PREP*, and *ST-PREP* conditions, similar to **Figure 4.1**. Labelled hollow circles in the *Control* panel represent kinematic peaks used for analysis and are replicated on *WK-PREP* and *ST-PREP* panels to highlight the changes due to pre-stimuli tones. The vertical scale bars are aligned with the onset of pre-stimulus tone (−250 ms) and are consistent between conditions. The vertical dotted line represents the onset of sled perturbation. Kinematic data: subscript x refers to the x-direction, linear acceleration (x), head angular acceleration (α), and head angle (θ). Electromyographic (EMG) data: left (L), right (R), sternocleidomastoid (SCM), cervical paraspinal (PARA), biceps brachii (BIC), triceps brachii (TRI), first dorsal interosseous (FDI), and rectus femoris (RF) muscles. Please note that the EMG data are limited to ±1 volt and may appear clipped in the figures. During the data analysis process, all EMG data were visually confirmed to ensure no actual data was lost due to clipping.

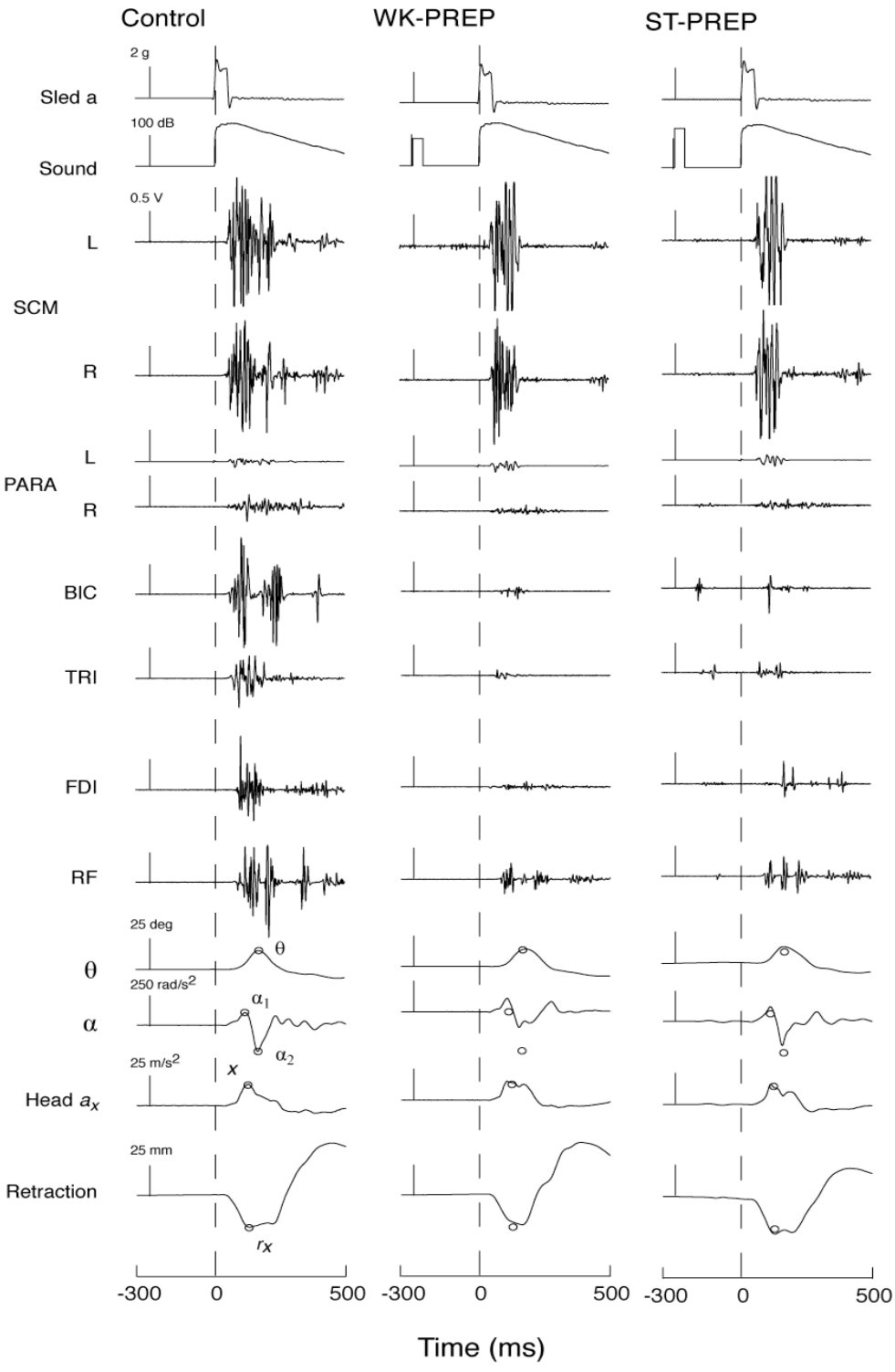
Subject 01


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

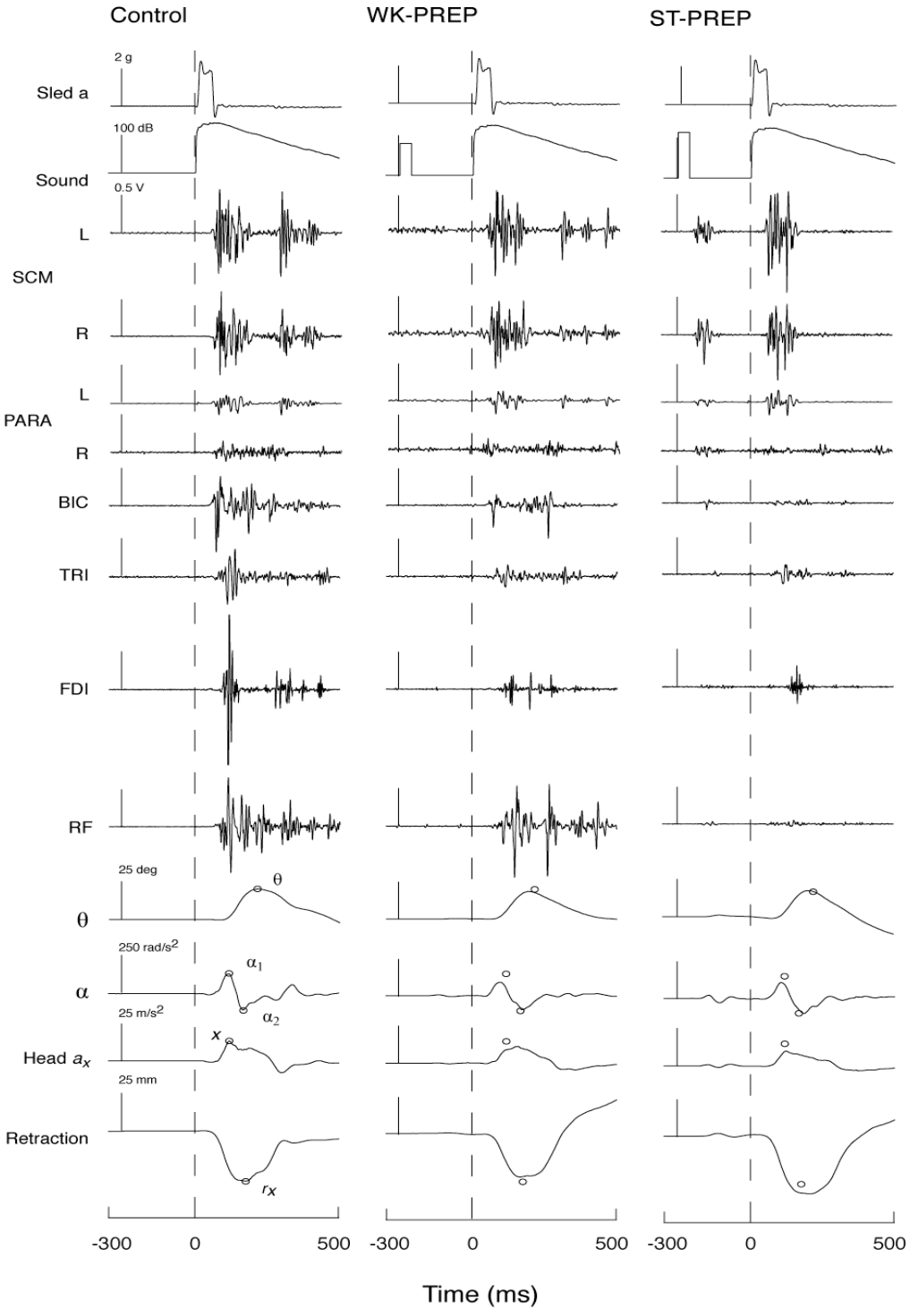
Subject 02


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
Head ax
x
25 mm
Retraction
rx
-300
0
500
Time (ms)

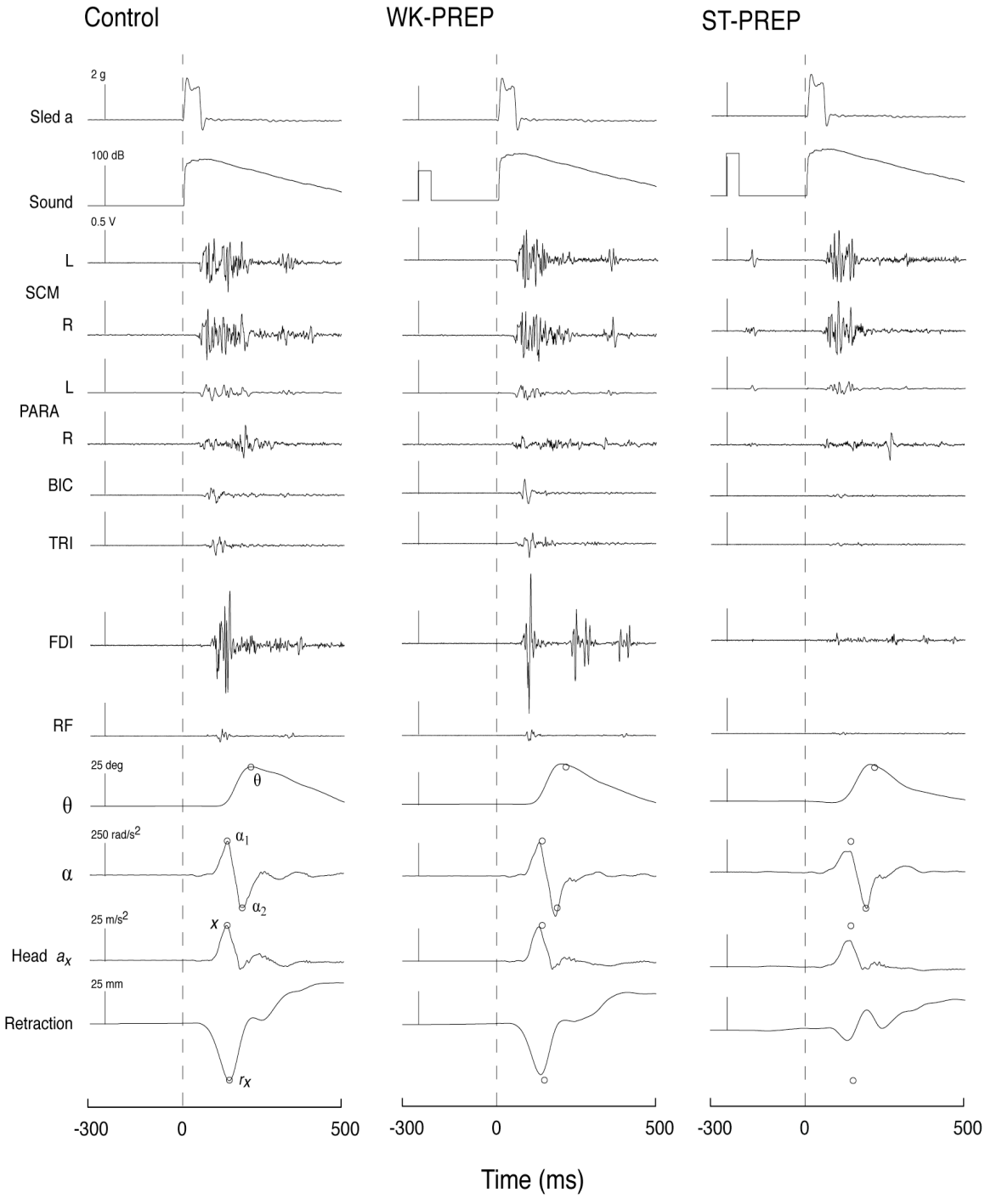
Subject 03


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

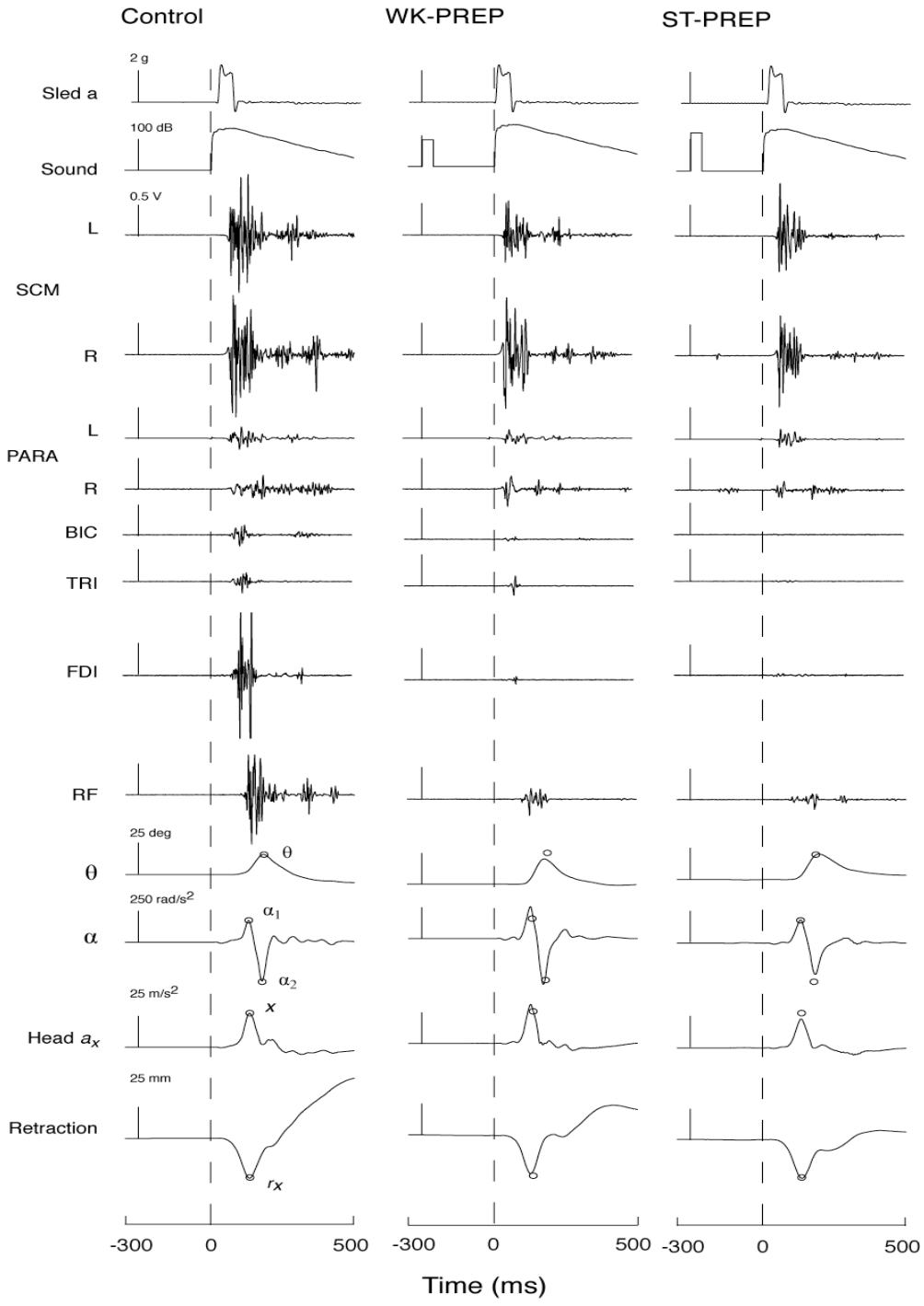
Subject 04


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
-300
0
500
-300
0
500
Time (ms)

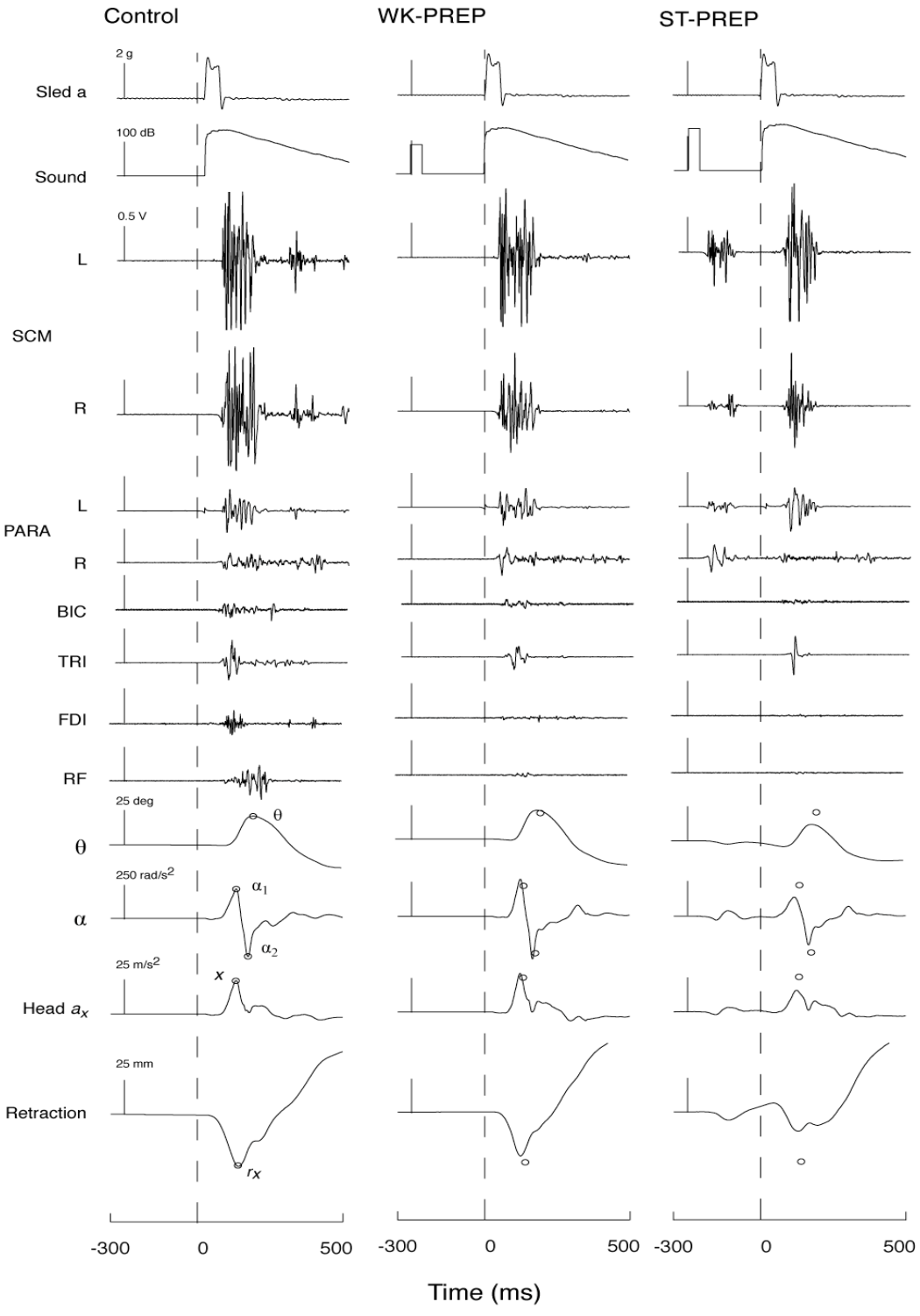
Subject 05


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

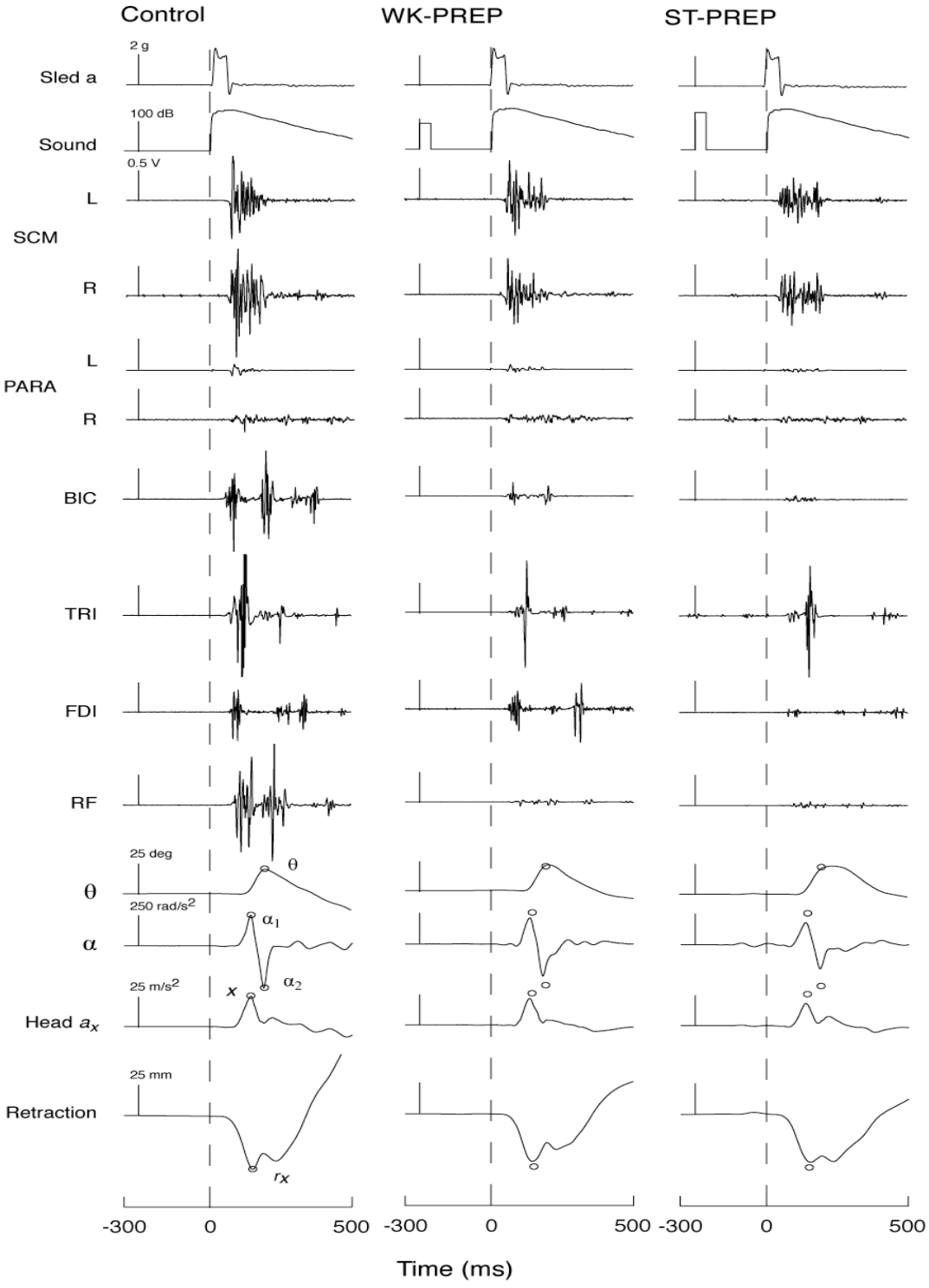
Subject 06


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

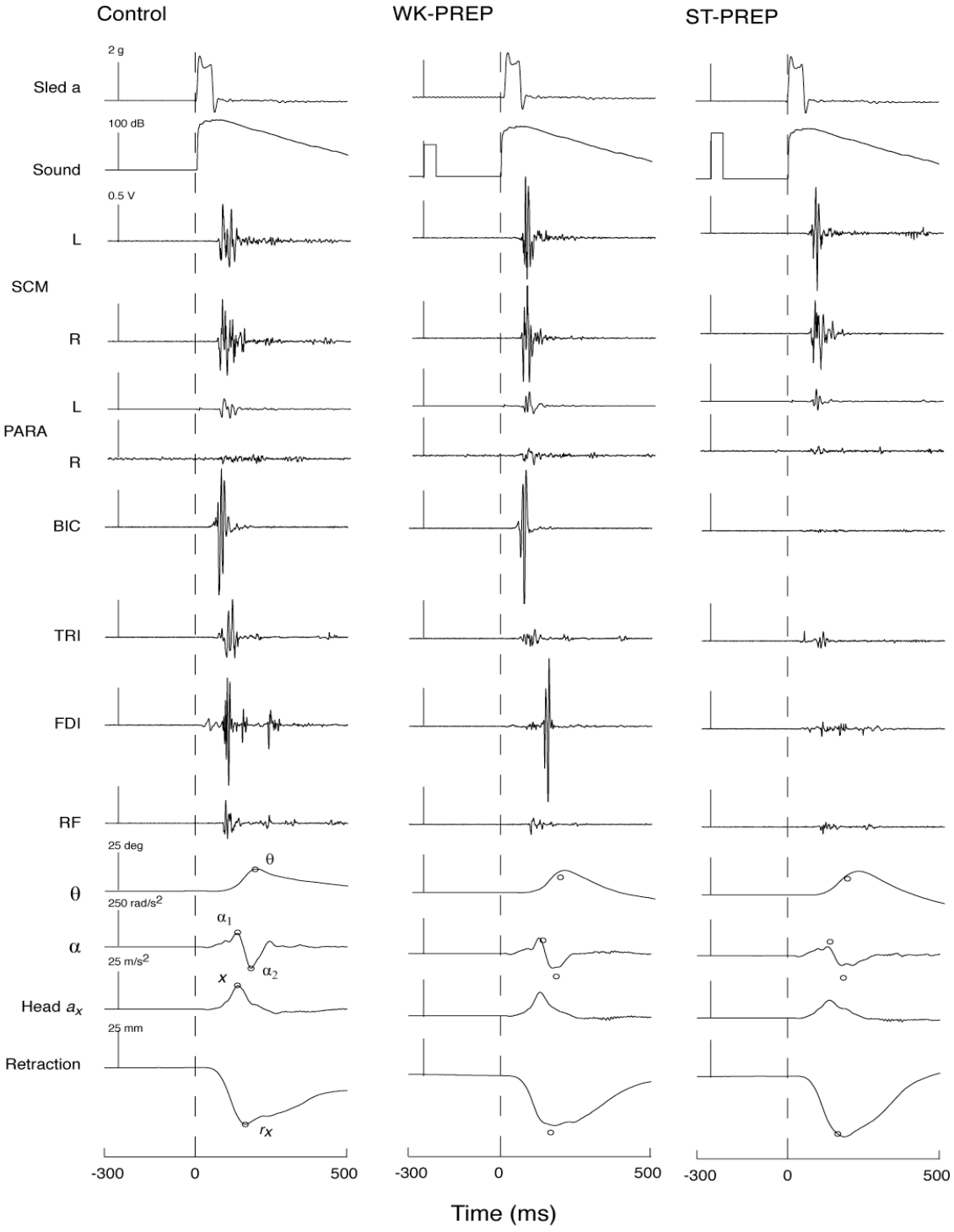
Subject 07


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

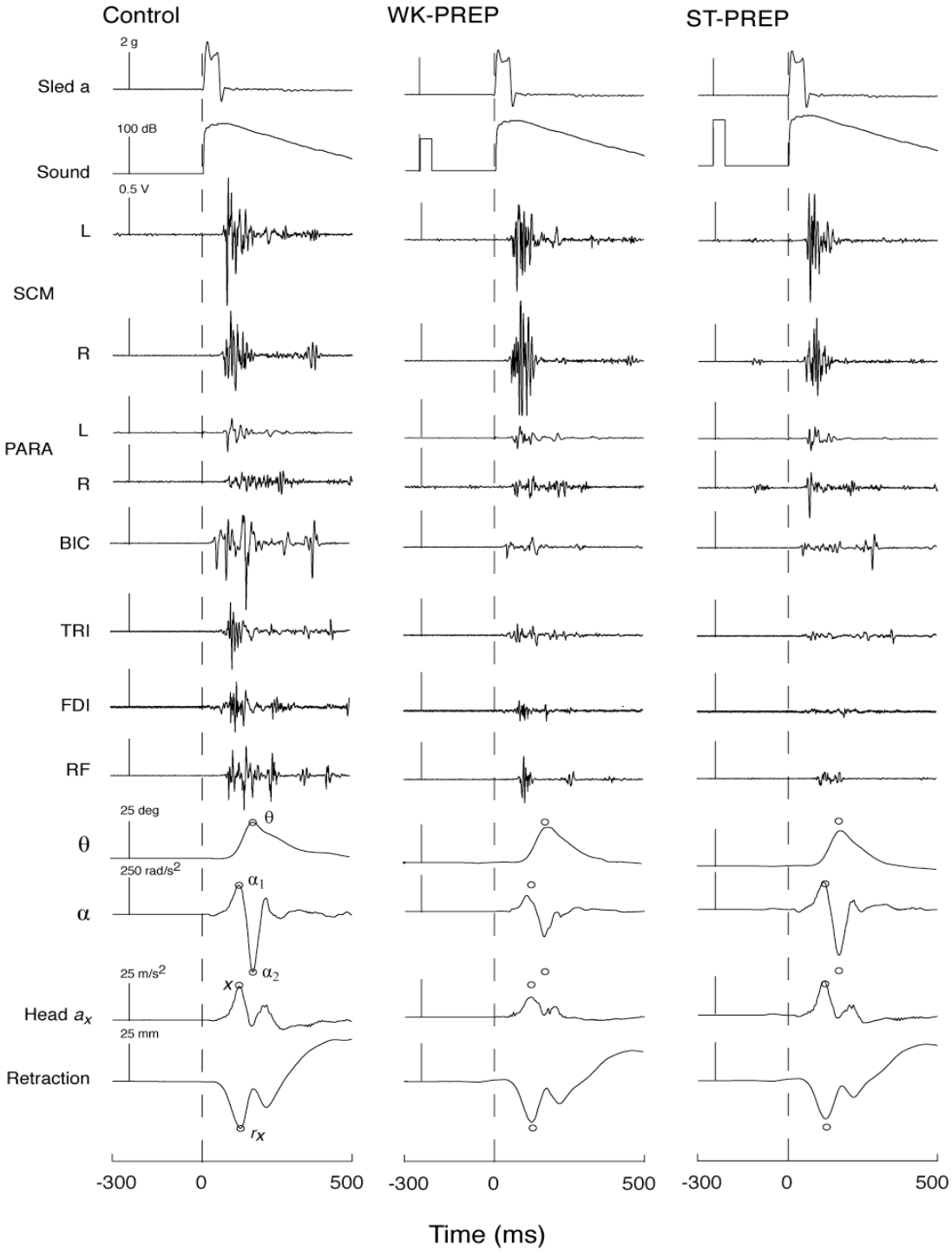
Subject 08


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

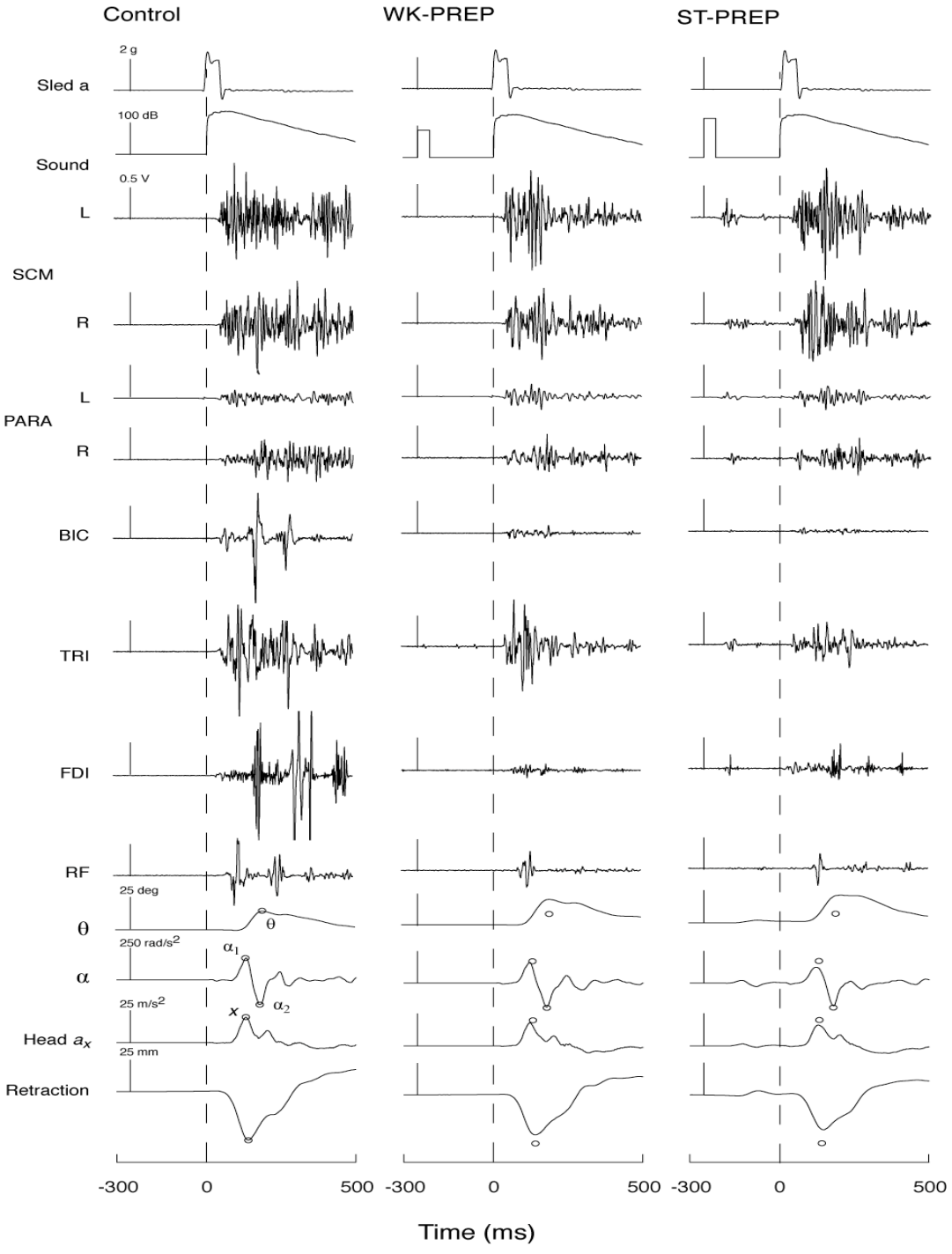
Subject 09


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
25 m/s2
Head ax
25 mm
Retraction
θ
α1
α2
x
rx
-300
0
500
Time (ms)

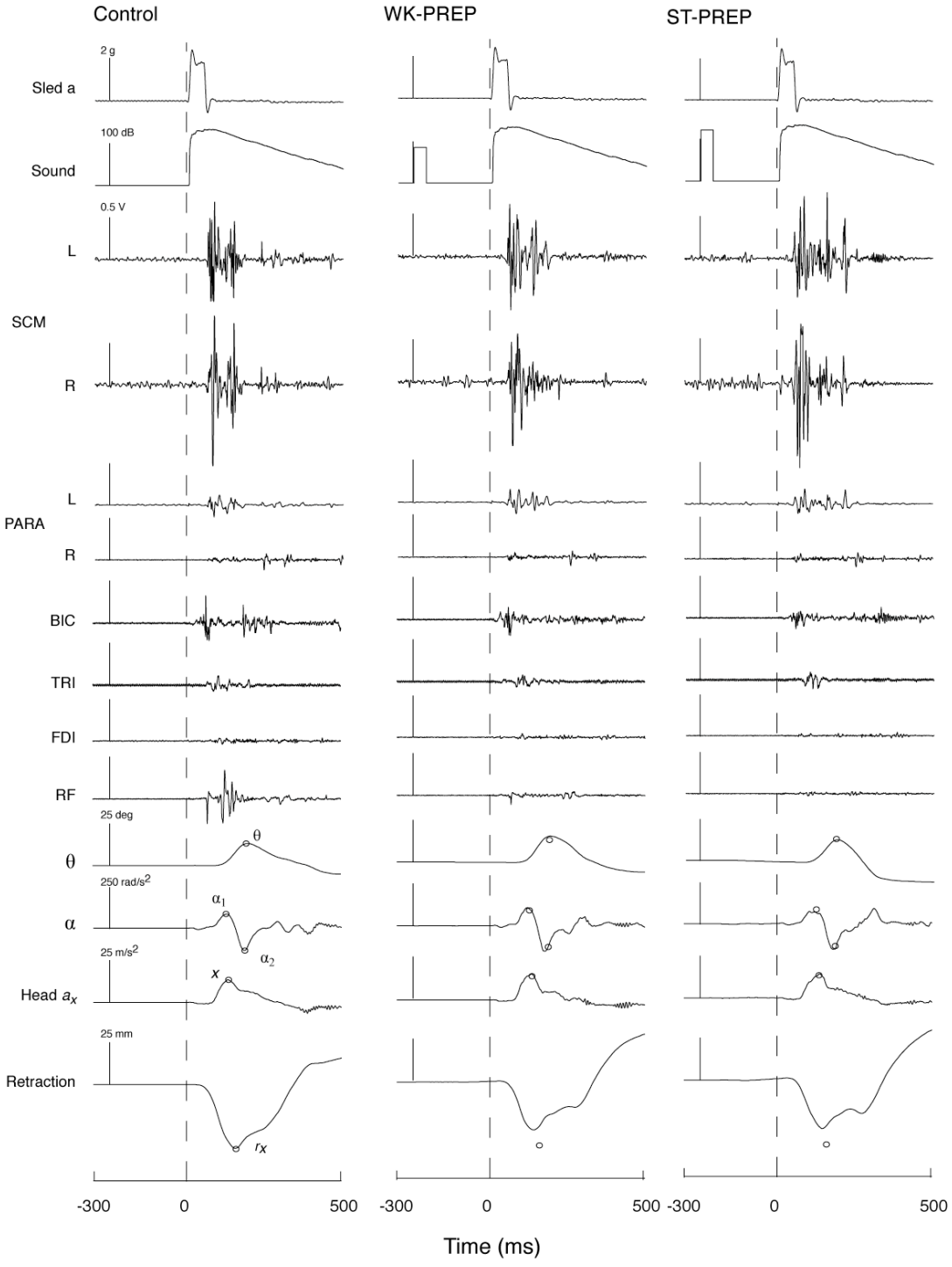
Subject 10


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

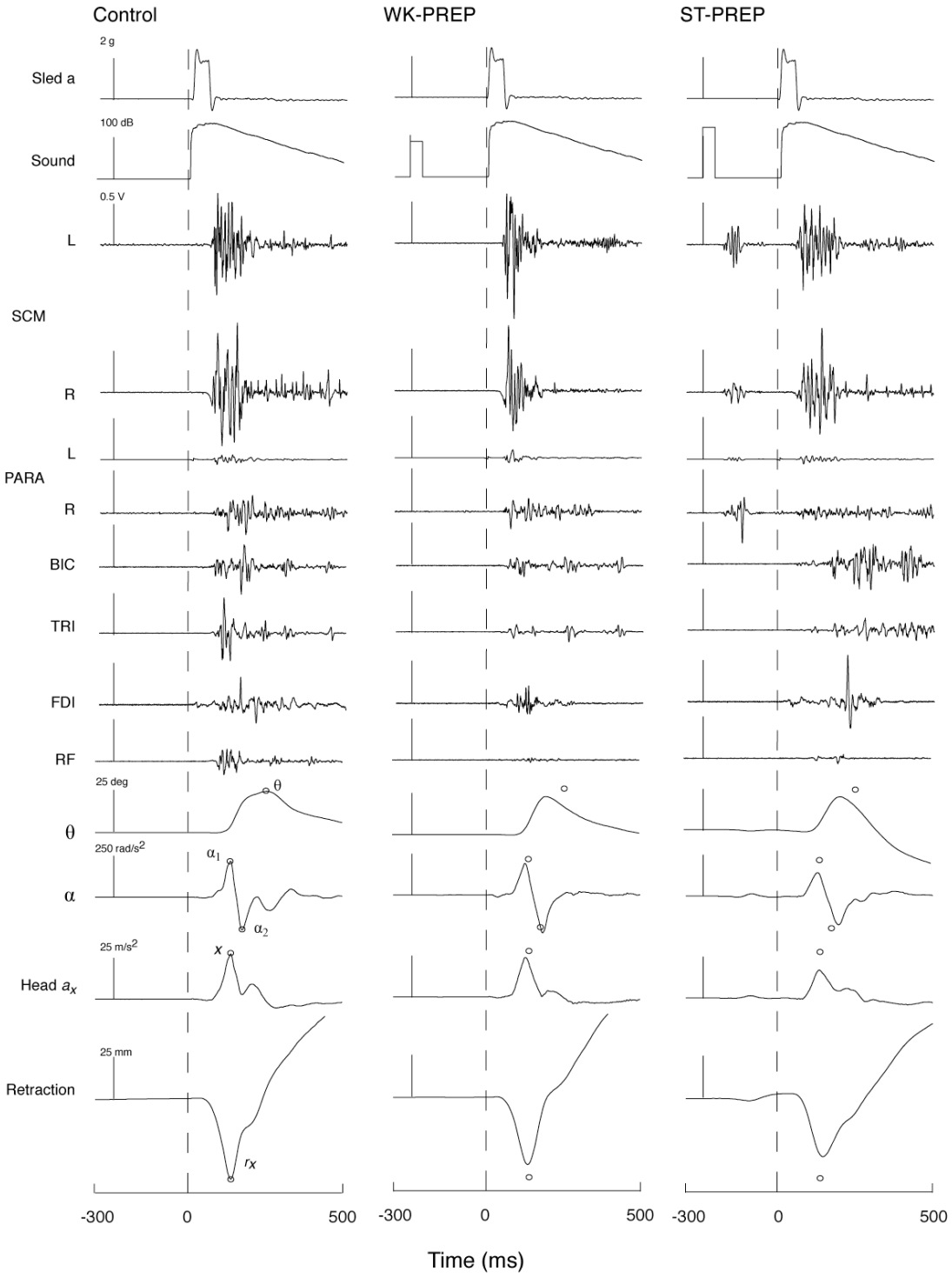
Subject 11


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
25 m/s2
x
α2
Head ax
25 mm
Retraction
-300
0
500
-300
0
500
-300
0
500
Time (ms)

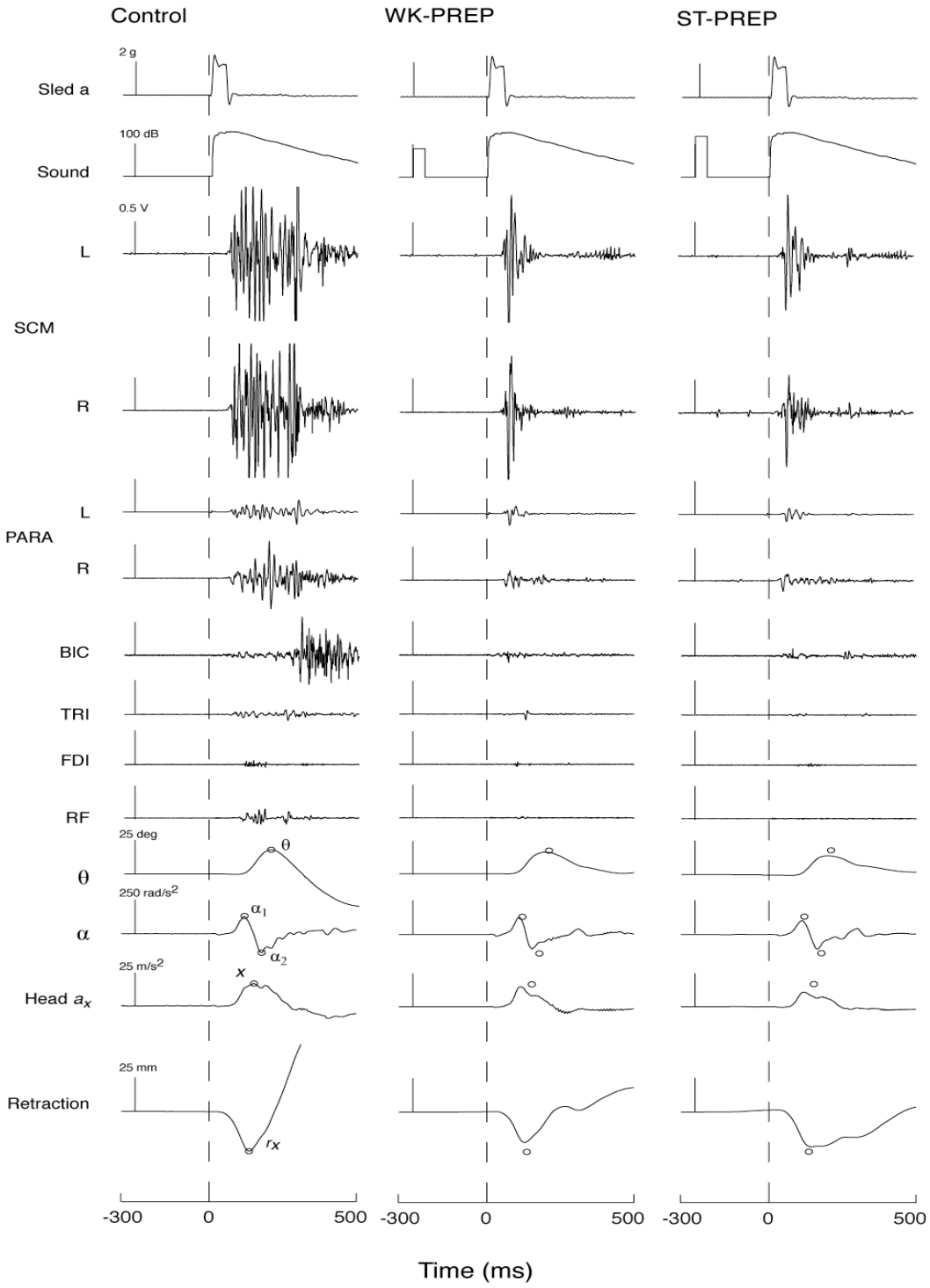
Subject 12


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

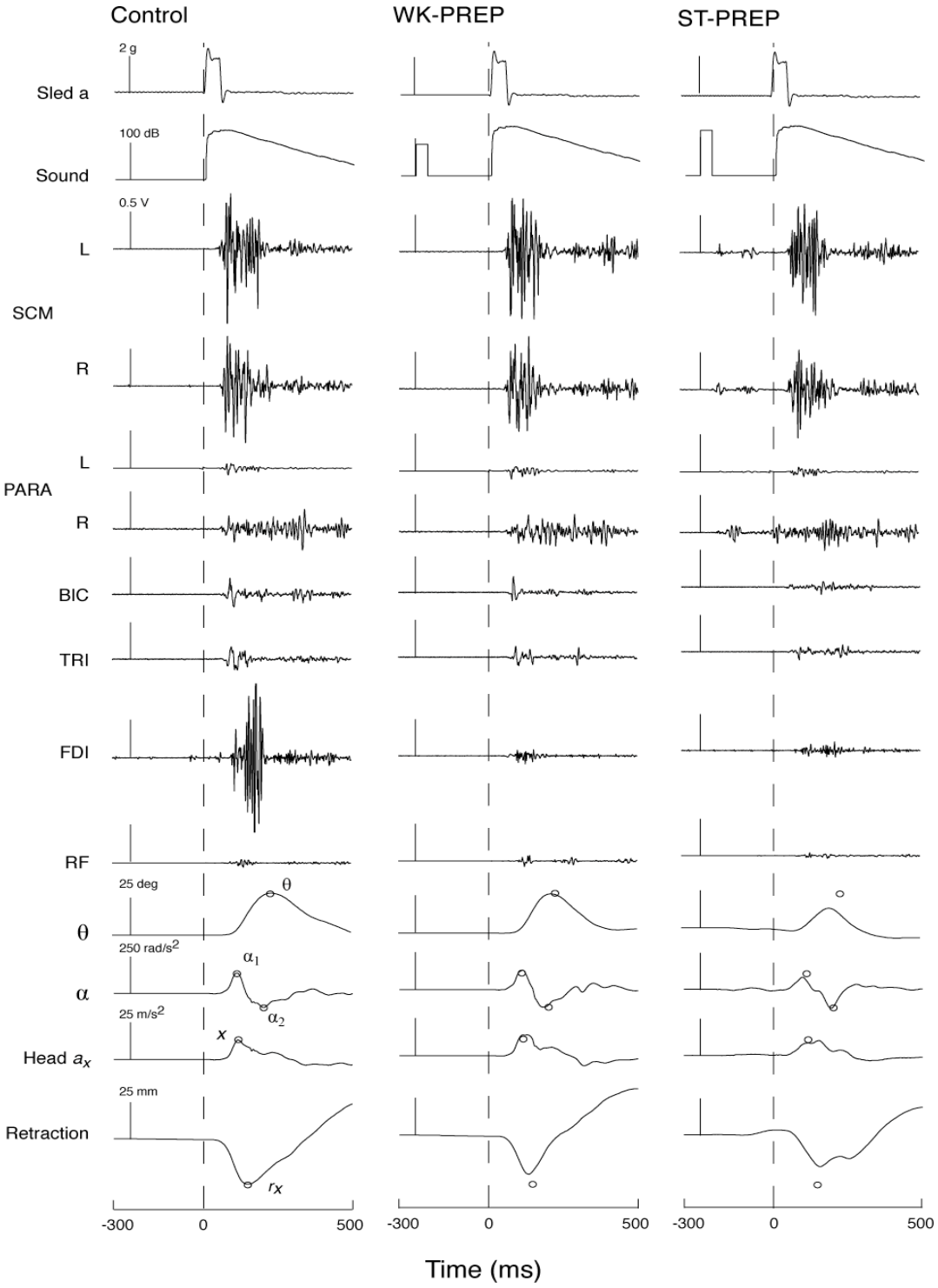
Subject 13


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
Head ax
x
25 mm
Retraction
rx
-300
0
500
Time (ms)

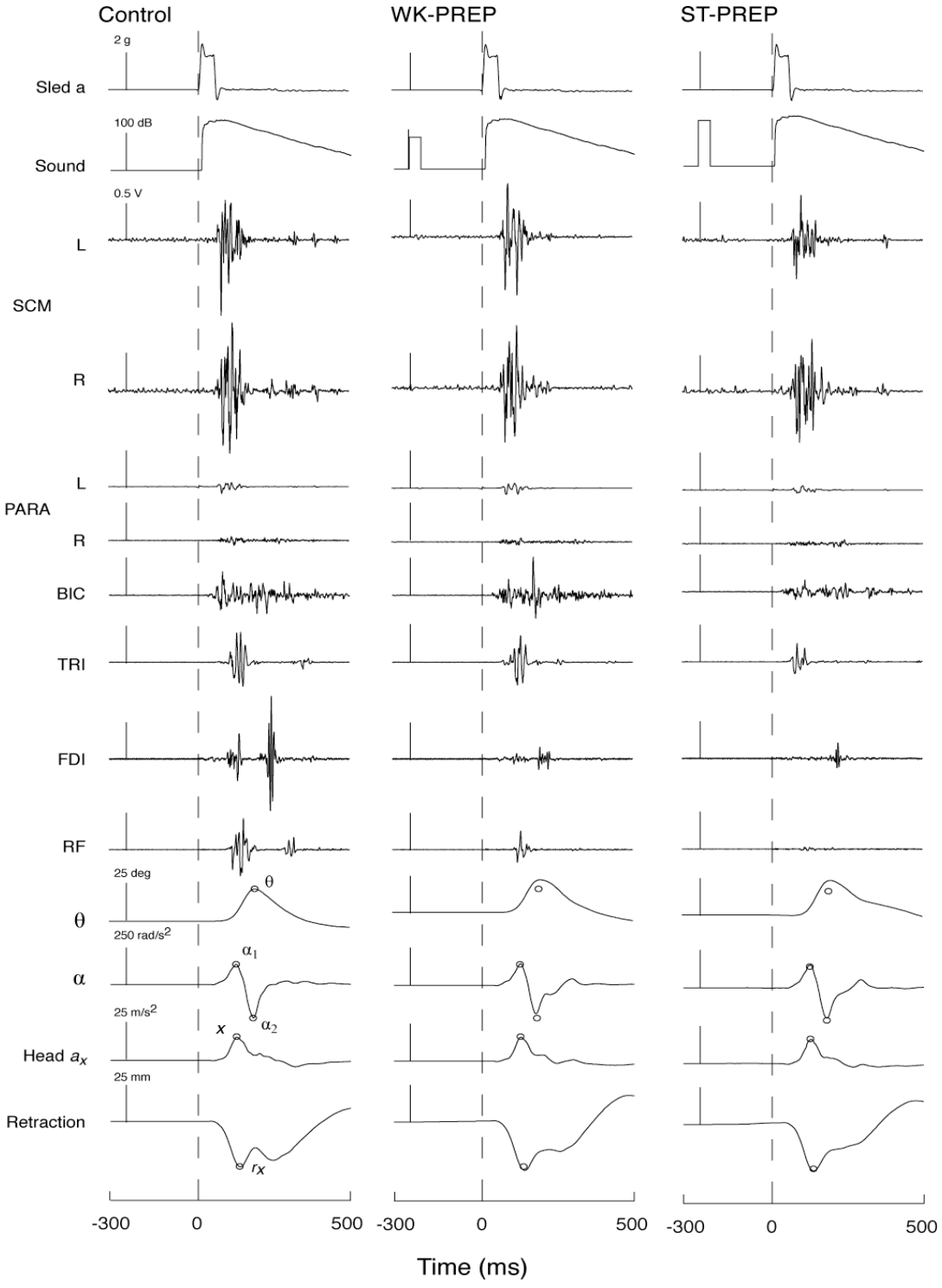
Subject 14


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

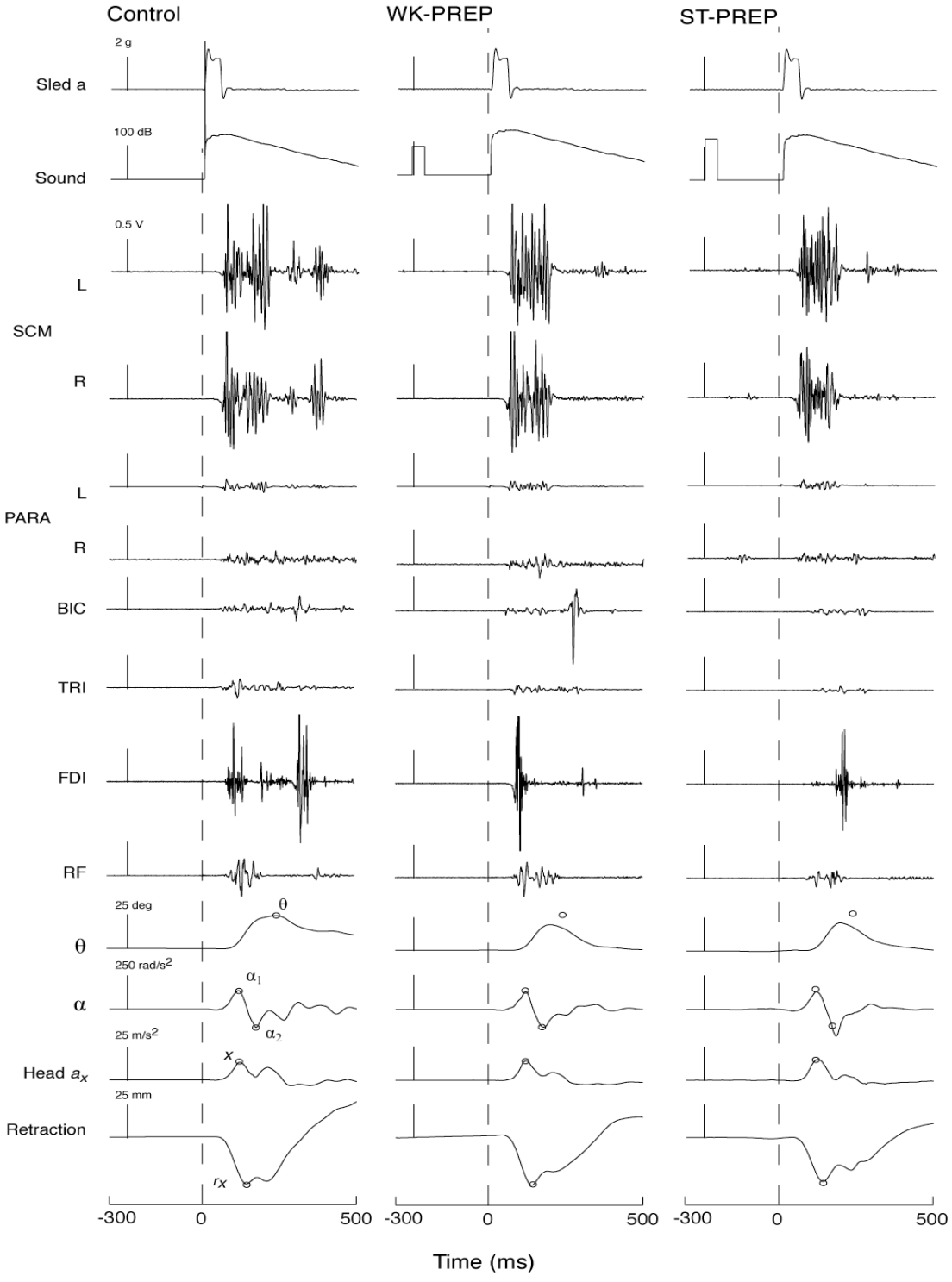
Subject 15


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

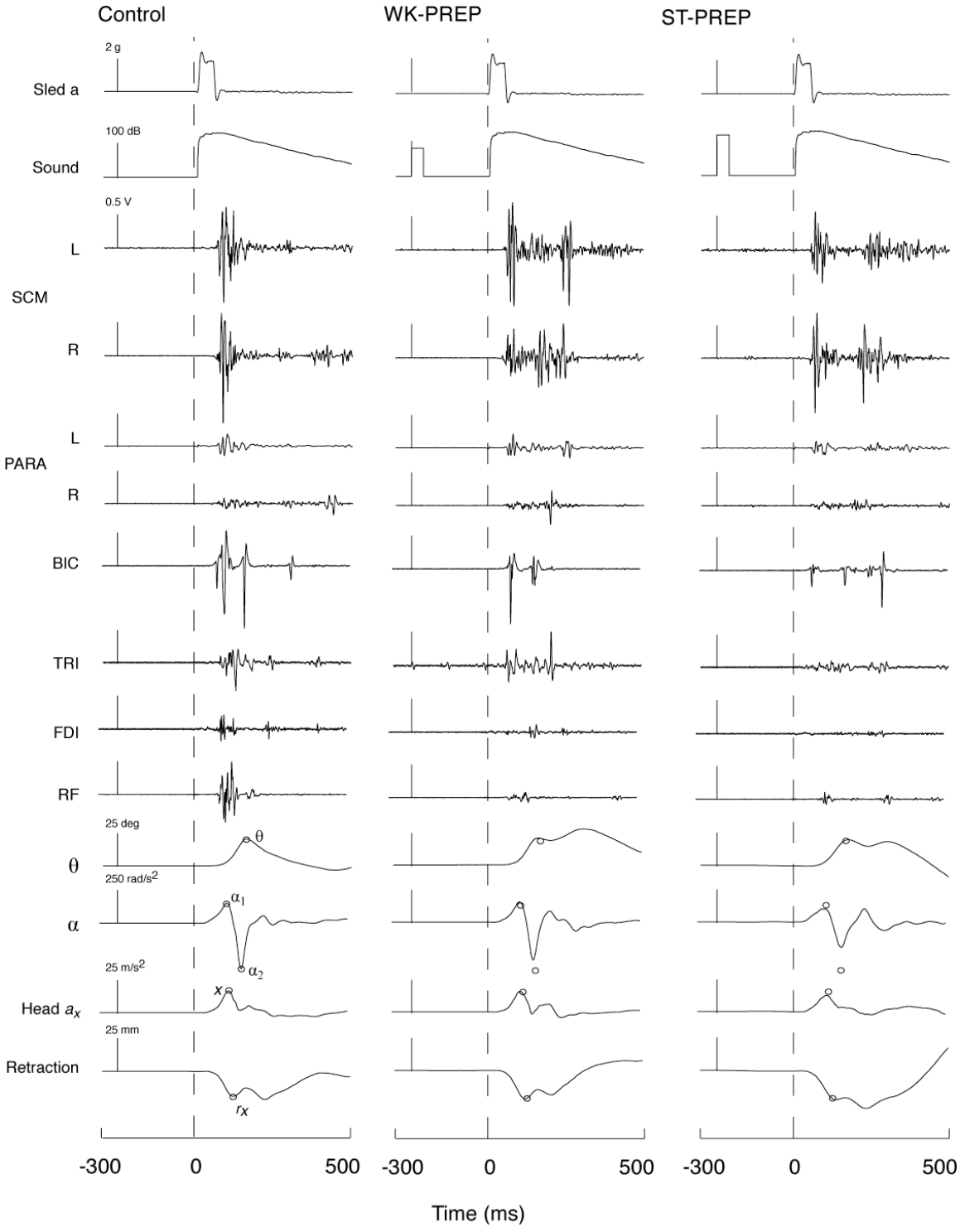
Subject 16


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
25 m/s2
Head ax
25 mm
Retraction
α1
α2
x
rx
-300
0
500
Time (ms)

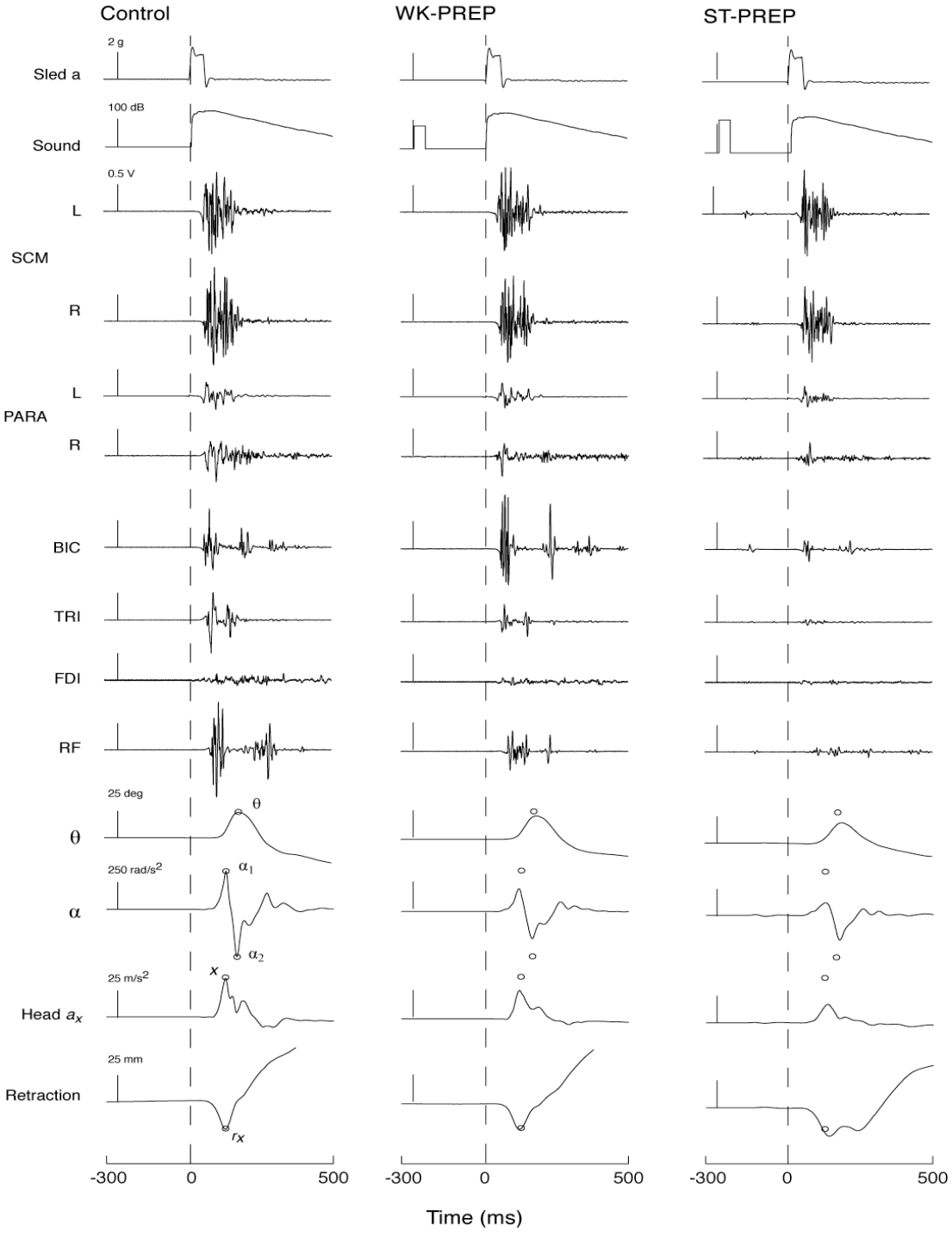
Subject 17


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

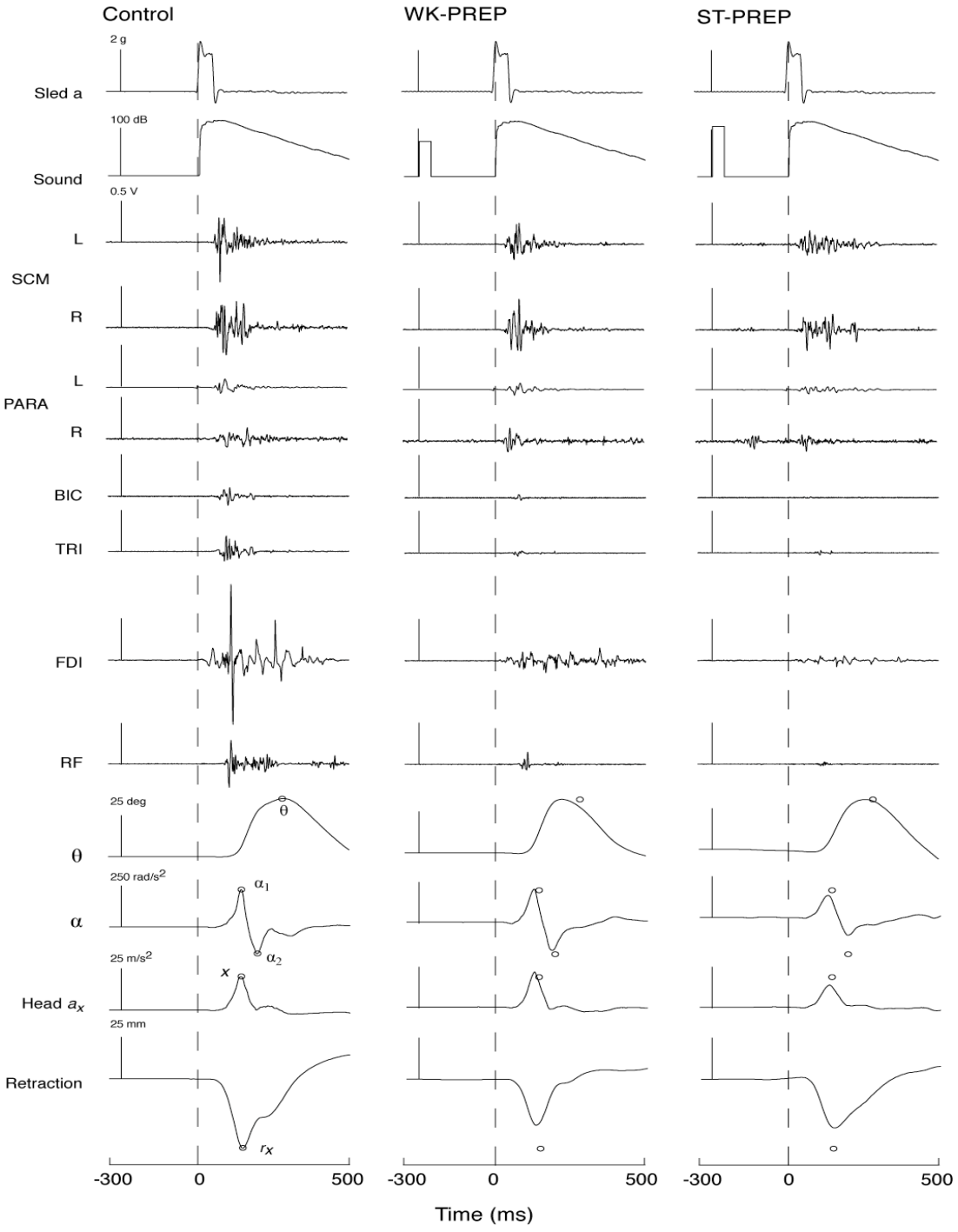
Subject 18


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
250 rad/s2
α
α1
α2
25 m/s2
Head ax
x
25 mm
Retraction
rx
-300
0
500
Time (ms)

Subject 19


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

Subject 20


Control
WK-PREP
ST-PREP
2 g
Sled a
100 dB
Sound
0.5 V
L
SCM
R
L
PARA
R
BIC
TRI
FDI
RF
25 deg
θ
θ
250 rad/s2
α1
α
α2
25 m/s2
x
Head ax
25 mm
Retraction
rx
-300
0
500
Time (ms)

Appendix B: Research Ethics Board Certification of Approval

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF FULL BOARD APPROVAL

PRINCIPAL INVESTIGATOR:	INSTITUTION / DEPARTMENT:	UBC CREB NUMBER:
Jean-Sébastien Blouin	UBC/Education/Human Kinetics	H07-01281

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
N/A	N/A

Other locations where the research will be conducted:
MEA Forensic Engineers and Scientists, Richmond B.C.

CO-INVESTIGATOR(S):
Gunter P. Siegmund
Donald C. McKenzie
J.Timothy Inglis
Daniel Mang

SPONSORING AGENCIES:
Canadian Institutes of Health Research (CIHR)

PROJECT TITLE:
Startle reflexes and whiplash injuries: New perspectives on injury prevention and clinical assessment

THE CURRENT UBC CREB APPROVAL FOR THIS STUDY EXPIRES: June 26, 2008

The full UBC Clinical Research Ethics Board has reviewed the above described research project, including associated documentation noted below, and finds the research project acceptable on ethical grounds for research involving human subjects and hereby grants approval.

REB FULL BOARD MEETING REVIEW DATE: June 26, 2007	

DOCUMENTS INCLUDED IN THIS APPROVAL:			DATE DOCUMENTS APPROVED:
Document Name	Version	Date	
Protocol:			
Research protocol	Version 2	September 17, 2007	
Consent Forms:			
Consent form	Version 2	September 17, 2007	**September 26, 2007**
Advertisements:			
Advert_StWL	Version 2	September 17, 2007	

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL WITH AMENDMENTS TO THE STUDY

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC CREB NUMBER:
Jean-Sébastien Blouin	UBC/Education/Human Kinetics	H07-01281

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
N/A	N/A

Other locations where the research will be conducted:
MEA Forensic Engineers and Scientists, Richmond B.C.

CO-INVESTIGATOR(S):
Gunter P. Siegmund
Donald C. McKenzie
J.Timothy Inglis
Daniel Mang

SPONSORING AGENCIES:
- Canadian Institutes of Health Research (CIHR) - "Salary: Startle reflexes and whiplash injuries: new perspectives on injury prevention and clinical assessment"
- Michael Smith Foundation for Health Research - "Role of the startle reflex and cervical multifudus in whiplash injury"

PROJECT TITLE:
Role of the startle reflex and cervical multifidus in whiplash injury

The current UBC CREB approval for this study expires: June 16, 2009

AMENDMENT(S):			AMENDMENT APPROVAL DATE:
Document Name	Version	Date	June 16, 2008
Consent Forms:			
Consent form	Version 3	June 4, 2008	
Advertisements:			
Advertisement	Version 3	June 4, 2008	

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC CREB NUMBER:
Jean-Sébastien Blouin	UBC/Education/Human Kinetics	H07-01281

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
N/A	N/A

Other locations where the research will be conducted:
MEA Forensic Engineers and Scientists, Richmond B.C.

CO-INVESTIGATOR(S):
Gunter P. Siegmund
Donald C. McKenzie
J.Timothy Inglis
Daniel Mang

SPONSORING AGENCIES:
- Canadian Institutes of Health Research (CIHR) - "Salary: Startle reflexes and whiplash injuries: new perspectives on injury prevention and clinical assessment"
- Michael Smith Foundation for Health Research - "Role of the startle reflex and cervical multifidus in whiplash injury"

PROJECT TITLE:
Role of the startle reflex and cervical multifidus in whiplash injury

EXPIRY DATE OF THIS APPROVAL: June 15, 2010

APPROVAL DATE: June 15, 2009

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

Approval of the Clinical Research Ethics Board by one of:

Dr. Peter Loewen, Chair
Dr. James McCormack, Associate Chair
Dr. John Russell, Associate Chair
Dr. Caron Strahlendorf, Associate Chair