

EFFECTS OF CYCLING EXERCISE ON SELF-REPORTED ANXIETY
AND THE HOFFMANN REFLEX

by

ROBERT WAYNE MOTL

(Under the direction of Rod K. Dishman)

ABSTRACT

Acute exercise consistently has reduced symptoms of anxiety. Yet, there are several limitations of previous research into effects of acute exercise on anxiety. One limitation has been that study participants were characterized by low pre-exercise state anxiety scores. Another limitation has been that researchers have ignored the concurrent effects of acute exercise on symptoms of anxiety and neuromuscular variables that might be correlates of anxiety. Two studies were conducted to examine the H-reflex as a neuromuscular substrate of anxiety that is altered by acute exercise using individuals with high trait anxiety or caffeine ingestion to increase pre-exercise anxiety scores.

In the first study, the effects of low and high intensity cycling exercise on state anxiety and the H-reflex were examined among males having low or high trait anxiety. The results indicated that (1) exercise and quiet rest resulted in similar reductions of state anxiety, and the magnitude of the reductions was larger for males having high trait anxiety than low trait anxiety; (2) exercise, but not quiet rest, resulted in a reduction of the H-reflex; the magnitude of the reduction did not differ between males having low or high trait anxiety; and (3) reductions of self-reported state anxiety were unrelated to reductions of the H-reflex.

Next, the effects of moderate intensity cycling exercise on state anxiety and the H-reflex were examined in individuals whose anxiety was experimentally manipulated by a large dose of caffeine. The results indicated that (1) caffeine consumption increased state anxiety, but it did not influence the amplitude of the soleus H-reflex; (2) acute exercise reduced state anxiety only after consumption of caffeine, but it reduced the soleus H-reflex after consumption of either caffeine or placebo; (3) there was no evidence of a relationship between changes in state anxiety and soleus H-reflex; and (4) neither caffeine nor acute exercise influenced the flexor carpi radialis H-reflex.

Contrary to prevailing opinion, the post-exercise reduction in the H-reflex appears to be unrelated to self-reported anxiety after exercise. Researchers should examine the influence of processes within the spinal cord (e.g., presynaptic inhibition of Ia afferent fibers) and brain (e.g., inhibition of interneurons and neurons within the motor cortex) on the post-exercise reduction of the soleus H-reflex.

INDEX WORDS: H-reflex, Anxiety, Acute Exercise, Caffeine

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DEDICATION

This dissertation is dedicated to Jane R. VandenBerge and my parents, Ron and Ginny Motl. You have provided steadfast and unwavering patience, support, and love throughout this long and sometimes arduous process. Thank you!

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If we knew what it was we were doing, it would not be called research, would it?

Albert Einstein

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CHAPTER 1

INTRODUCTION

Anxiety disorders are a problem throughout the world (World Health Organization, 2000) including the United States (Kessler et al., 1994). The twelve-month and lifetime prevalence of anxiety disorders in the United States approximates 17% and 25% of the population, respectively (Kessler et al., 1994). The annual financial impact of anxiety disorders was estimated to be 42.3 billion dollars in 1990 (Greenberg et al., 1999).

The symptoms associated with anxiety disorders can influence the quality of an individual's life and be psychologically and physically debilitating. Common symptoms of anxiety disorders include excessive feelings of apprehension, nervousness, and worry. Additional symptoms of anxiety disorders include restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, and disturbed sleep (American Psychiatric Association, 2000). Related to muscle tension, there may be symptoms of trembling, twitching, feeling shaky, and muscle aches and soreness (American Psychiatric Association, 2000).

Pharmacological and psychological therapies are effective for treating symptoms of anxiety disorders. Yet, only 20-30% of U.S. adults who report symptoms of anxiety seek help from a mental health professional (Kessler et al., 1994; Shapiro et al., 1984). This likely is related to the financial burden and negative stigma associated with seeking treatment from a mental health professional. Moreover, the prescription drugs used to treat anxiety disorders

have undesirable side effects (e.g., Mavissakalian, Perel, & Guo, 2002). There is a need to identify non-pharmacological treatments such as exercise that produce short- and long-term reductions of symptoms of anxiety and enhance mental hygiene (Dishman, 1998).

Exercise is an effective method for reducing self-reported anxiety (e.g., Dishman, 1998; O'Connor, Raglin, & Martinsen, 2000) and putative physiological correlates of anxiety. The mean effect of acute exercise on symptoms of anxiety has approximated $\frac{1}{4}$ to $\frac{1}{2}$ standard deviation (SD; Landers & Petruzzello, 1994; Petruzzello, Landers, Hatfield, Kubitz, & Salizar, 1991). The mean effect of acute exercise on physiological correlates has approximated $\frac{1}{2}$ SD (Petruzzello et al., 1991). Most studies examining the concomitant effect of exercise on symptoms and physiological correlates of anxiety have focused on blood pressure and brain electrocortical activity (e.g., Raglin & Morgan, 1987; Youngstedt, Dishman, Cureton, & Peacock, 1993), but generally have ignored neuromuscular correlates.

The Hoffmann reflex (i.e., H-reflex) has been viewed as a neuromuscular correlate of anxiety that is altered by acute exercise (Bulbulian & Darabos, 1986; deVries, Wiswell, Bulbulian, & Moritani, 1981; Petruzzello et al., 1991). The H-reflex commonly is evoked through stimulation of the tibial nerve and recorded in the soleus muscle (Hugon, 1973; Magladery & McDougal, 1950). Researchers have interpreted the H-reflex to reflect either the efficacy of synaptic transmission between Ia afferent fibers and alpha motoneurons (Capaday, 1997) or alpha motoneuron excitability (Angel & Hofmann, 1963). The H-reflex is directly and indirectly influenced by brain and brain stem regions involved in motor and affective processes (Holstege & Kuypers, 1987; Rotto-Perceland, Wheeler, Osorio, Platt, & Loewy, 1992;

Táboriková, 1973). Experimental conditions that impact affective and motor processes have influenced the H-reflex (Bonnet, Decety, Jeannerod, Requin, 1997; Eke-Okoro, 1982; Inghilleri, Berardelli, Marchetti, & Manfredi, 1996; Moulder, Bradley, Requin, & Lang, 1995; Ørsnes, Crone, Krarup, Petersen, & Nielsen, 2000; Palmeri et al., 1999; Sandrini et al., 1999; Timmann, Plummer, Schwarz, & Diener, 1995; Willer & Albe-Fessard, 1980).

We are aware of seven published studies that have examined the effect of acute exercise on the H-reflex (Avela, Kyröläinen, Komi, & Rama, 1999; Bulbulian, 2002; Bulbulian & Bowles, 1992; Bulbulian & Darabos, 1986; deVries et al., 1981, deVries, Simard, Wiswell, Heckathorne, & Carabetta, 1982; Mimasa, Matsumoto, & Moritani, 1990). Those studies reported that acute bouts of cycling and jogging reduced the magnitude of the H-reflex recorded in the soleus muscle. Five of the studies interpreted the reduced H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian, 2002; Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990), but none of the studies included a concurrent measure of state anxiety when recording the H-reflex. Hence, exercise-induced anxiolysis has not been identified as a concomitant of the post-exercise reduction of the H-reflex.

One major limitation of previous research into the effects of acute exercise on anxiety has been that study participants were characterized by low pre-exercise state anxiety scores. This “floor effect” has resulted in small effects of acute exercise on anxiety (O’Connor et al., 2001; Tieman, Peacock, Cureton, & Dishman, 2001). One strategy for minimizing potential floor effects is to recruit volunteers characterized by high or low trait anxiety. Groups of this type likely will differ in state anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983)

and allow for the relationships among exercise, anxiety, and the H-reflex to be examined across an adequate range of anxiety scores. Another strategy for minimizing potential floor effects involves the consumption of a high dose of caffeine (Youngstedt, O'Connor, Crabbe, & Dishman, 1998). The consumption of a high dose of caffeine has been associated with increases in self-reported anxiety (e.g., Charney, Galloway, & Heninger, 1984) and has influenced neuromuscular variables such as resting EMG and physiological tremor (Hasenfratz & Bättig, 1992; James, 1990; Miller, Lombardo, & Fowler, 1998).

Statement of the Problem

The objective of the two experiments presented here was to examine whether exercise-induced anxiolysis correlated with the post-exercise reduction of the H-reflex. The first study examined the effects of low and high intensity cycling exercise on self-reported state anxiety and the soleus H-reflex in males having low or high trait anxiety. Low and high intensity cycling exercise were hypothesized to reduce self-reported anxiety and the H-reflex, and the reduction of self-reported anxiety was expected to correlate with post-exercise reductions of the H-reflex. The effects of cycling exercise on state anxiety and the H-reflex were expected to be larger in males having high trait anxiety relative to those having low trait anxiety.

The second study further examined the effects of cycling exercise on changes in self-reported anxiety and the soleus H-reflex in males using caffeine model of anxiogenesis (Nickell & Uhde, 1994; Youngstedt, O'Connor, Crabbe, & Dishman, 1998) to experimentally manipulate anxiety. Experimentally increasing and decreasing anxiety and measuring the effect of exercise on the H-reflex provided a stronger test of the relationships among exercise,

anxiety, and the H-reflex. Consumption of a large dose of caffeine was expected to increase both self-reported anxiety and the H-reflex, and cycling exercise was expected to reduce self-reported anxiety and the H-reflex. Hence, anxiety was evaluated as a cause of changes in the magnitude of the H-reflex.

An additional purpose of the second study involved comparing the effect of cycling exercise on the H-reflex recorded in the soleus and flexor carpi radialis muscles. The H-reflex was recorded in the soleus and flexor carpi radialis muscles to examine the possible influence of repetitive and cyclical leg muscle activation during cycling on post-exercise changes in the H-reflex. If the post-exercise reduction of the soleus H-reflex is a result of the cyclical and repetitive activation of the leg musculature rather than exercise-induced anxiolysis, then cycling exercise would be expected to result in a reduction of the H-reflex recorded in the soleus muscle, but not in the flexor carpi radialis muscle.

CHAPTER 2

LITERATURE REVIEW

Previous literature reviews (Dishman, 1998; O'Connor, Raglin, & Martinsen, 2000) and meta-analyses (Landers & Petruzzello, 1994; Petruzzello et al., 1991) have thoroughly summarized the effect of acute exercise on self-reported and putative physiological measures of anxiety. Self-ratings of anxiety have been reduced by $\frac{1}{4}$ to $\frac{1}{2}$ of a standard deviation after exercise; physiological variables have been reduced by $\frac{1}{2}$ of a standard deviation. Most research, however, has been conducted with individuals characterized by low pre-exercise anxiety scores (O'Connor et al., 2000). This "floor effect" likely has resulted in small changes in anxiety after exercise and can be minimized by selecting subjects who are more prone to anxiety or experimentally manipulating anxiety. Previous researchers also have ignored the concurrent effects of acute exercise on changes in self-reported anxiety and neuromuscular variables. This is surprising because muscle tension, trembling, twitching, feeling shaky, and muscle aches and soreness are common features of anxiety disorders (American Psychiatric Association, 2000).

Researchers have speculated that the post-exercise reduction of the H-reflex recorded in the soleus muscle reflects a tranquilizing, muscle relaxing, or anxiolytic effect of acute exercise (e.g., Bulbulian & Darabos, 1986; de Vries et al., 1981; Petruzzello, Landers, Hatfield, Kubitz, & Salizar, 1991). Yet, those researchers have not (1) measured concomitant changes in self-

reported anxiety along with measurements of the H-reflex, (2) provided a rationale linking anxiety and the H-reflex, or (3) discussed alternative explanations for the post-exercise reduction of the H-reflex such as a prolonged presynaptic Ia inhibition or altered brain cortical modulation. Moreover, there have been no published reviews that discuss the effect of acute exercise on the H-reflex; one literature review has focused on the effect of chronic exercise training on the H-reflex (Zehr, 2002).

This literature review provides a detailed discussion of the H-reflex, with particular foci on its history, neurophysiology, measurement, and meaning. This review of the literature describes possible neuroanatomical influences of the H-reflex originating in the spinal cord, brain stem, and brain. Drugs that influence the H-reflex, with a particular focus on caffeine, will be reviewed to provide a neurobiological basis for the modulation of the H-reflex. This literature review then discusses the findings and limitations of published studies that have examined the effect of acute exercise on the H-reflex. Finally, this review of the literature discusses studies manipulating CNS state-dependent processes to provide a basis for exercise-induced anxiolysis as an explanation for the post-exercise reduction of the H-reflex.

History of the H-reflex

This section provides a brief history of the H-reflex. Piper (1912) initially demonstrated that electrical stimulation of the posterior tibial nerve in the popliteal fossa evoked a contraction of the calf muscles. This process was more clearly described by Hoffmann (1918, 1922). Hoffmann (1918) initially reported that sub-maximal electrical stimulation of the posterior tibial nerve produced a delayed response in the calf muscles that was recorded with

electromyography (EMG). Hoffmann (1918) believed that this delayed response was the result of a mono-synaptic reflex similar to the myotatic or muscle stretch reflex. Hoffmann (1922) later reported that further increases in the intensity of the stimulation applied to the posterior tibial nerve resulted in a reduction of the delayed response in the calf muscles. In fact, the delayed response was completely abolished by maximal intensity stimulation, which resulted in a short-latency, immediate response in the calf muscles. Hoffmann (1922) postulated that this diminution was attributable to anterior horn cells (i.e., alpha motoneurons) being depolarized by antidromic impulses carried by the axons of motor nerves.

Magladery and McDougal (1950) reported that electrical stimulation of the posterior tibial nerve produced an immediate and a delayed response recorded in the soleus muscle using EMG. Sub-maximal electrical stimulation of the posterior tibial nerve resulted in a delayed response in the calf muscle named the H-wave. The H-wave was maximal with only moderate intensity electrical stimulation. With yet stronger electrical stimulation, the H-wave was abolished and a second, more immediate response was recorded in the calf muscles; it was named the M-wave. The M-wave reached a plateau with maximal intensity electrical stimulation. Hence, Magladery and McDougal (1950) confirmed the earlier reports by Hoffmann (1918, 1922) and designated the delayed wave that resulted from sub-maximal stimulation of the tibial nerve as the “H-wave” or H-reflex. Magladery and McDougal (1950) designated the immediate wave the “M-wave.”

Magladery, Porter, Park, and Teasdall (1951a) further examined the nature of the H-reflex as a two-neuron reflex by correlating action potentials recorded in the muscle, spinal

roots, and spinal cord following stimulation of afferent fibers in the popliteal fossa. The subjects were normal young adults and volunteers from older age groups without neurological disease affecting the spinal cord or lower limbs. Nerve stimulation of liminal, sub-maximal intensity, which just evoked an H-reflex, produced a detectable anterior root action potential that increased in amplitude and then declined similarly to the H-reflex; this anterior root action potential reflected the reflex outflow through anterior roots. Nerve stimulation of greater intensity than that initiating the first H-reflex produced dorsal root action potentials that increased similarly with the amplitude of the H-reflex; this represented a synchronous volley of afferent impulses in dorsal roots. The dorsal and anterior action potentials were separated by only 1.5 ms, thereby allowing for the inference that the H-reflex tapped a monosynaptic reflex arc. With nerve stimulation of greater intensity there was a small spike potential that increased similarly with the amplitude of the M wave. The small spike potential was indicative of antidromic impulses in motor axons. Hence, Magladery et al. (1951a) provided evidence for the H-reflex as a two-neuron reflex arc and that the diminution of the H-reflex was attributable to anterior horn cells (i.e., alpha motoneurons) being depolarized by antidromic impulses carried by axons of motor nerves. This confirmed the earlier reports by Hoffmann (1918, 1922).

Within the same period of time, Magladery, Porter, Park, and Teasdall (1951b) provided evidence that a conditioning electrical impulse delivered to the tibial nerve immediately before a subsequent test impulse influenced the amplitude of the soleus H-reflex. Teasdall, Park, Porter, and Magladery (1951) provided evidence that electrical stimulation of the

peroneal nerve reduced the amplitude of the soleus H-reflex. Park, Teasdall, and Magladery (1951) provided evidence that a brief stretch of the calf muscle both increased and decreased the soleus H-reflex. Hence, those studies outlined a number of spinal influences on the H-reflex that were confirmed in subsequent research.

Paillard (1955 as cited in Schieppati, 1987, 1959) conducted a systematic analysis of the H-reflex and confirmed many of the earlier findings of Hoffmann (1918, 1922). Of importance, Paillard (1955, 1959) undertook a meticulous investigation of factors influencing the measurement of the H-reflex, resulting in a detailed description of stimulating and recording electrode placements; duration and rate of the stimulus parameters; and optimal body and limb placements. Many of the methodological considerations discussed by Paillard (1955, 1959) were further described, confirmed, and refined by Hugon (1973).

The H-reflex was commonly evoked only in the soleus muscles until the late 50's and early 60's. Johns, Grob, and Harvey (1957) recorded the H-reflex in the hypothenar muscles of the hand. Pinelli and Valle (1960) later measured the H-reflex in the flexor digitorum brevis muscles of the foot. Hence, those studies, and others (e.g., Thomas & Lambert, 1960), demonstrated that the H-reflex could be recorded in muscles other than the soleus muscles.

The late 50's and early 60's were characterized by studies of the effects of sleep on the amplitude of the H-reflex (Hodes & Dement, 1964; Hodes & Gribetz, 1962a, 1962b; Paillard, 1959; Shimizu, Yamada, Yamamoto, Fujiki, & Kaneko, 1966). Those researchers demonstrated that the H-reflex amplitude decreased in the early stages of sleep, and was completely abolished during REM sleep. Yet, the decrease in the H-reflex amplitude during

REM sleep was prevented by a lesion of the descending pathways along the anterior funiculi, and by a brain stem lesion extending into the central portion of the medulla (Shimizu et al., 1966). Hence, the H-reflex was modulated during sleep through mechanisms originating in the central nervous system.

As reported by Angel and Hofmann (1963, p. 591),

“Under appropriate conditions, a single shock to the human tibial nerve will evoke two discrete action potentials in the calf muscles. The first potential, the M wave, results from direct stimulation of motor nerve fibers. The second potential, the H wave, is the expression of a monosynaptic reflex, which runs in afferents from the muscle and back again through efferents of the same muscle. Since no internuncial neurons are involved, the size of the second action potential will provide a measure of motoneuron excitability under a variety of experimental and pathological conditions.”

Angel and Hofmann (1963) further reported that the H/M ratio provides an indication of the number of motoneurons that can be excited monosynaptically, and that this can be estimated as a fraction of the motoneuron pool. Hence, the idea that the amplitude of the largest obtainable H wave, divided by the largest M wave, provides a measure of motoneuron excitability has been credited to Angel and Hofmann (1963). Yet, other researchers previously reported that the H-reflex was a measure of alpha motoneuron excitability (e.g., Magladery & McDougal, 1950; Magladery et al, 1951a).

Hugon (1973) provided an often cited publication on the methodology of the soleus H-reflex. This publication provided a confirmation (e.g., Paillard, 1955, 1959) and an

improvement on previous reports of the H-reflex by better defining the parameters of the soleus H-reflex and the methods employed for its study. The methodology for eliciting and recording the soleus H-reflex will be described in detail in a forthcoming section titled Measurement of the H-reflex.

Braddom and Johnson (1974b) provided a standardized and convenient method of recording the H-reflex; this methodology was not reviewed because it is inferior to method reported by Hugon (1973). Importantly, Braddom and Johnson (1974b) examined relationships between the H-reflex and other variables to provide “normal” data for interpretation of the H-reflex and demonstrated the clinical usefulness of the H-reflex for diagnosing S1 radiculopathy. Braddom and Johnson (1974b) recorded the age, leg length, H-wave latency, and H-wave amplitude of 100 subjects; the relationships among those measures were examined using Pearson product-moment correlations and multiple linear regression. Braddom and Johnson (1974b) also recorded the H-wave bilaterally in 25 patients suspected of having S1 radiculopathy. The H-wave latency was correlated with leg length ($r = .561$), age ($r = .441$), tibial nerve conduction velocity ($r = -.530$), and H-wave amplitude ($r = -.378$). H-wave amplitude was related to age ($r = -.578$) and tibial nerve conduction velocity ($r = .311$). Among the 25 patients suspected of having S1 radiculopathy, the H-wave latency was either prolonged in latency or absent on the affected side. Sixteen of the 25 patients exhibited a reduced H-wave amplitude. Hence, Braddom and Johnson (1974b) demonstrated that the H-reflex is influenced by both subject characteristics and S1 radiculopathy.

Braddom and Johnson (1974a) reviewed the physiology of the H-reflex and then proposed a number of clinical uses for the H-reflex. Braddom and Johnson (1974a) first described the muscle stretch reflex in four steps.

1. Initially, the muscle is stretched by a hammer striking its tendon.
2. The muscle has a fusimotor system that maintains its length through a follow-up-length servo system. Muscle stretch causes impulses from the annulospiral endings of the nuclear bag fibers to be transmitted by way of large Ia afferent fibers to the alpha motoneurons innervating that muscle.
3. The Ia afferent fibers are facilitatory to the alpha motoneuron and cause them to discharge.
4. This causes the muscle to contract, and restores the original muscle length.

The H-reflex involves part of the muscle stretch reflex pathway; it by-passes the muscle spindle by direct activation of the Ia afferent fibers via electrical stimulation. Interestingly, some individuals with an absent stretch reflex exhibit an H-reflex, and vice versa. Hence, the H-reflex and stretch reflex are not synonymous. Braddom and Johnson (1974a) further suggested that the H-reflex can be used clinically to diagnose (1) a central nervous system lesion from below the mid-brainstem; (2) proximal neuropathy; (3) first sacral root compromise; and (4) central nervous system immaturity.

In an attempt to correlate the H-reflex with changes in the central nervous system, Van Boxtel (1976) examined the relationship between alpha brain electrocortical activity and the H-reflex. Van Boxtel (1976) hypothesized that (1) no change in the H-reflex would be observed

with stable alpha brain electrocortical activity, but that (2) an increase in alpha brain electrocortical activity, indicating a decrease in brain cortical activity, would be correlated with a reduction in the H-reflex. Van Boxtel (1976) reported that the H-reflex amplitude was related to the percentage of alpha activity in the ongoing EEG. Under conditions of fairly stable alpha brain electrocortical activity, the H-reflex amplitude did not change significantly; but as alpha brain electrocortical activity increased and reflected a decrease in brain cortical activity, there was a concomitant reduction in the H-reflex amplitude. Hence, Van Boxtel (1976) provided some evidence that the H-reflex is modified by influences from the central nervous system.

There was an increased interest in the H-reflex in the forearm muscles in the 1980's. This was largely attributable to a publication by Jabre (1981). Jabre (1981) provided a detailed, yet simple description of the methodology for recording the H-reflex in the flexor carpi radialis (i.e., forearm flexors). This publication provided an improvement on previous reports of the H-reflex by better defining the parameters of the flexor carpi radialis H-reflex and the methods employed for its study. The methodology is described in detail in a forthcoming section that will be titled Measurement of the H-reflex.

In the early and mid 80's and early 90's, there was an interest in the effects of acute exercise on the H-reflex (Bulbulian & Darabos, 1986; deVries, Simard, Wiswell, Heckathorne, & Carabetta, 1982; deVries, Wiswell, Bulbulian, & Moritani, 1981; Mimasa, Matsumoto, & Moritani, 1990). Those studies all reported a reduction in the soleus H-reflex after exercise. This reduction was interpreted as supporting a “tranquilizing” or relaxing like effect of acute exercise.

Four extensive reviews of literature on the Hoffmann reflex have been provided by Schieppati (1987), Capaday (1997), Pierrot-Deseilligny and Mazevet (2000), and Zehr (2002). Schieppati (1987) discussed the historical and methodological aspects of the H-reflex, and then discussed the measurement of the H-reflex in muscles other than the soleus. This was followed by a discussion of the meaning of the H-reflex based on a comparison of the H-reflex as reflecting either motoneuron excitability or reflex arc excitability. Schieppati (1987) also discussed state-dependent influences on the H-reflex including mental alertness, attention, and sleep, and influences on the H-reflex from cutaneous afferents and vestibular inputs. The paper concluded with a discussion of modulation of the H-reflex through reciprocal inhibition and recurrent inhibition, and modulation as a function of joint position during muscle contraction (i.e., motor control).

In a review of neurophysiological methods for studies of the motor system, Capaday (1997) provided detailed descriptions of the H-reflex meaning, methodology, and influences. Initially, Capaday (1997) specifically addressed previous reports that the H-reflex measures the excitability of alpha motoneurons, and pointed-out that this view is both gravely flawed and perhaps myopic. He also provided an overview of the basic experimental arrangement for recording the H-wave and M-wave. The paper then discussed the affects of reciprocal inhibition of the alpha motoneuron by antagonist muscles, reciprocal inhibition of the Ia-afferent by antagonist muscles, and stimulation of the motor cortex on the amplitude of the H-reflex.

Pierrot-Deseilligny and Mazevet (2000) discussed the H-reflex as a tool for exploring the excitability of alpha motoneurons and understanding motor control in humans. Issues

specific to neuroanatomy of the mono-synaptic reflex arc, the principal of the mono-synaptic test, and orderly recruitment of alpha motoneurons in the mono-synaptic reflex were initially discussed by Pierrot-Deseilligny and Mazevet (2000). They then described the recording, stimulation, measurement of H-waves and M-waves, and the formation of a recruitment curve for the H-reflex. Importantly, Pierrot-Deseilligny and Mazevet (2000) reviewed the contribution of oligosynaptic pathways to the H-reflex, including disynaptic pathways (i.e., Ib inhibitory inter-neurons that are co-activated by Ia afferents & Renshaw cells activated by alpha motoneuron discharge), presynaptic inhibition of Ia terminals (i.e., activation of antagonist muscles that produces primary afferent depolarization), and reciprocal Ia inhibition of alpha motoneurons (i.e., activation of antagonist muscles that produces inhibition of alpha motoneurons).

The review by Zehr (2002) focused specifically on considerations for using the H-reflex in exercise training studies. The review initially discussed the origin of the H-reflex, and then presented an overview of the procedure for recording the H-reflex. The paper then described the measurement of the H-reflex in human limb muscles, with particular foci on the soleus and flexor carpi radialis muscles. Importantly, Zehr (2002) challenged the interpretation of the H-reflex as a measure of alpha motor excitability based on the erroneous assumption by Angel and Hofmann (1963) that the H-reflex only involves the Ia-afferent and alpha motoneuron; Zehr (2002) recognized that the connection between the Ia-afferent and alpha motoneuron was modified by other synaptic inputs, particularly by presynaptic Ia inhibition. Hence, this paper provided an important discussion of presynaptic Ia inhibition, and basic procedures for

manipulating the influence of presynaptic Ia inhibition on the magnitude of the H-reflex. Zehr (2002) then described other factors that influence the amplitude of the H-reflex, and the use of the H-reflex to measure adaptive plasticity in human movement based on chronic exercise training.

Summary

The H-reflex was originally discovered by Piper (1912) and Hoffmann (1918, 1922) and better defined by Magladery and McDougal (1950). The H-reflex is a relatively simple muscle reflex to elicit and record. The H-reflex commonly is evoked through electrical stimulation of the posterior tibial nerve and recorded in the calf or soleus muscles using electromyography (Hugon, 1973); it also can be recorded elsewhere, most notably in the flexor muscles of the forearm (e.g., flexor carpi radialis; Jabre, 1981). One primary misconception about the H-reflex is its meaning. Although the H-reflex has been considered to be a measure of alpha motoneuron excitability (Angel & Hofmann, 1963), this interpretation is flawed as pointed-out indirectly by Schieppati (1987) and more directly by Capaday (1997) and Zehr (2002). The methodology of recording the H-reflex in the soleus and FCR muscles, as proposed by Hugon (1973) and Jabre (1981), is quite simple and straight-forward, and provides a background for studying the multi-faceted influences on the efficacy of synaptic transmission between the Ia afferent fibers and alpha motoneurons within the spinal cord (e.g., sleep, S1 radiculopathy, or acute exercise). The next section discusses the basic neurophysiology underlying the H-reflex.

Basic Neurophysiology Underlying the H-reflex

The H-wave and M-wave are the result of electrical stimulation of mixed nerve bundles containing Ia afferent fibers from muscle spindles and efferent fibers or axons from alpha motoneurons. Initially, sub-maximal electrical stimulation activates primarily the large Ia afferent fibers; the Ia afferents have a lower threshold for activation than the axons from alpha motoneurons. The Ia afferent fibers project through the dorsal horn of the spinal cord to synapse on the alpha motoneurons primarily within the ventral horn (i.e., laminae IX) of the spinal cord (Hendry, Hsiao, & Bushnell, 1999; Parent, 1996); there also are projections to laminae VI and VII (Hendry et al., 1999). The Ia afferent fibers release glutamate as an excitatory neurotransmitter (Parent, 1996), and the glutamate binds to AMPA and NMDA receptors on the dendrites of alpha motoneuron cell bodies. This results in an excitatory postsynaptic potential (EPSP). If threshold is met by temporal and spatial summation of EPSPs, an action potential is initiated that propagates along the axon or efferent fiber of the alpha motoneuron until it reaches the plasma membrane surrounding the muscle. The terminal boutons of the alpha motoneuron release acetylcholine from the presynaptic membrane onto the plasma membrane (i.e., neuromuscular junction). The acetylcholine binds to postsynaptic cholinergic receptors and results in the depolarization of the sarcolemma or plasma membrane and then the propagation of an action potential along the plasma membrane. The action potential traveling along the plasma membrane leads to a muscle contraction through a series of reactions involving the T-tubules, sarcoplasmic reticulum, calcium, ATP, and myofilaments. The action potential

that propagates along the plasma membrane is recorded through surface electrodes and EMG, and it is measured in mV. This is the H-wave or H-reflex.

Maximal electrical stimulation activates both the Ia afferent fibers and the efferent or alpha motoneuron fibers; the alpha motoneurons have a higher threshold for activation than the Ia afferent fibers. The Ia afferent fibers project through the dorsal horn of the spinal cord to synapse on the alpha motoneuron within laminae IX of the ventral horn of the spinal cord. The depolarized alpha motoneuron fibers propagate an action potential both orthodromically toward the plasma membrane surrounding the muscle and antidromically back toward the alpha motoneuron cell bodies in Laminae IX of the ventral horn of the spinal cord. The antidromic propagation of an action potential collides with the orthodromic action potential associated with the firing of the alpha-motor neuron by activation from the Ia afferent fibers. Hence, only the action potential propagating directly to the muscle results in an action potential along the plasma membrane. This action potential along the plasma membrane is recorded by surface electrodes and EMG, and it is measured in mV. This is the M-wave. The next section discusses the procedures for elicitation and measurement of the H-reflex in muscles in the calf and forearm.

Measurement of the H-reflex

The H-reflex can be measured throughout the human body (Jušić, Baraba, & Bogunovic, 1995; Zehr, 2002). This section focuses on the measurement of the H-reflex in the soleus (Hugon, 1973) and flexor carpi radialis (Jabre, 1981) muscles; those muscles are being examined in the present investigations, have been most commonly employed in H-reflex studies

(Capaday, 1997; Pierrot-Deseilligny & Mazevet, 2000), and are associated with an H-reflex that is most easily and reliably evoked and measured (Jušić et al., 1995; Zehr, 2002).

Electrode Position for Recording the H-reflex

Hugon (1973) provided a standard methodology for eliciting and recording the H-reflex from the soleus muscle. The soleus H-reflex was elicited by stimulating the tibial nerve with one electrode placed in the popliteal fossa and the other electrode placed above or superior to the patella; the tibial nerve can be easily located by eliciting an eversion of the foot based on stimulation of the common peroneal nerve, and then moving the stimulating electrode ~2-3 cm medially toward the center of the leg. The stimulus duration should be 1 ms and the frequency should be 1 pulse every 5 or more s. The recording electrodes are placed ~3 cm apart on the abraded and de-greased skin overlying the soleus muscles. The electrodes are placed along the mid-dorsal line of the leg, ~4 cm above the point where the 2 heads of the gastrocnemius muscles join the Achilles tendon; this can be approximated as 2 cm below the 2 heads of the gastrocnemius muscles. The active electrode is placed proximal, and a third, ground or indifferent electrode is placed above the lateral malleolus. Hugon (1973) reported that the maximal H-wave is approximately 52% of the maximal M-wave for a sample of 12 normal adults. Hence, the H/M ratio or H-reflex is approximately .50. The mean latency of the H-wave has been reported to be ~30 ms (Braddom & Johnson, 1974; Hugon, 1973; Zhu, Starr, Halderman, Chu, & Sugerman, 1998). The latency of the M-wave is ~8 ms (Zhu et al., 1998).

Jabre (1981) provided a brief communication outlining the measurement of the H-reflex in the flexor carpi radialis (FCR) muscle, and then provided data on the amplitude and latency

of the H-wave and M-wave using a sample of male and female subjects ranging in age from 15 to 56 years. The FCR H-reflex was elicited by stimulating the median nerve near the elbow and proximal to the cubital fossa using bipolar surface electrodes with the subject supine and the elbow slightly flexed; the median nerve can be easily located by palpitation for the brachial artery and biceps tendon. The stimulus was a rectangular pulse of .5 to 1.0 ms duration delivered at a frequency not exceeding 1 pulse per 2 s. The FCR H-reflex was recorded by placing an active electrode over the FCR, the reference electrode over the brachioradialis, and the ground between the stimulating and recording electrodes; the FCR belly was located $\sim a$ of the distance between the medial epicondyle and the radial styloid. The mean H-wave and M-wave amplitude were 1.6 (SD = .4) and 7.6 (SD = 2.5) mV, respectively. Hence, the H/M ratio or H-reflex was $\sim .21$. The mean latency for the H-wave and M-wave were 15.9 (SD = 1.5) and 3 (SD = .5) ms, respectively.

Recently, researchers have begun to record the H-reflex in the FCR muscle with a different arrangement for the recording electrodes (e.g. Baldissera, Bellani, Cavalleri, & Lalli, 2000; Paik, Han, & Im, 2001; Rossi, Decchi, Zalaffi, & Mazzocchio, 1995). Two electrodes are placed $\sim a$ of the distance between the medial epicondyle and the radial styloid. The ground or indifferent electrode is placed above the ulnar styloid. The EMG signal appears to be significantly improved with the bipolar placement of the recording electrodes.

Stimulus Duration for Eliciting the H-reflex

There appears to be an optimal stimulus duration for optimally measuring the H-reflex. Panizza, Nilsson, and Hallett (1989) examined the optimal stimulus duration for the H-reflex in the soleus and flexor carpi radialis muscles. The H-wave and M-wave were recorded in the soleus and FCR muscles from ten subjects aged 29 to 45 years, and elicited with the stimulus durations of 0.1, 0.3, 0.5, 0.8, 1, 2, and 3 ms. The amplitude of the H-reflex in the soleus muscle was largest with stimulus durations between 0.3 and 1 ms; the maximal amplitude of the soleus H-reflex, before eliciting a M-wave, was largest with stimulus durations between 0.5 and 1 ms. The maximal amplitude of the H-reflex in the FCR muscle was largest with stimulus durations between 0.5 and 0.8 ms, and the maximal amplitude of the H-reflex in the FCR muscle before eliciting a M-wave was largest with stimulus durations between 0.5 and 1 ms. Importantly, some of the subjects complained about pain or discomfort when stimulus durations were longer than 1 ms. This has been confirmed in reports by other researchers (Capaday, 1997), and, more importantly, the pain associated with recording the H-reflex in the soleus muscle recently has been quantified by Motl, O'Connor, Boyd, and Dishman (in press).

Number of Trials to Reliably Measure the H-reflex

Researchers have examined the optimal number of trials necessary to reliably measure the H-reflex. Williams, Sullivan, Seaborne, and Morelli (1992) examined the intra-session reliability of the soleus H-reflex in two samples of healthy subjects. The first sample consisted of 20 subjects who completed 4 control conditions with 10 trials or recordings of H-reflex per condition. The second sample consisted of 18 subjects who completed 5 control conditions and

20 trials or recordings of H-reflex per condition. The intra-session reliability for the 10 trials ranged between .964 and .980 for the 4 control conditions in the 1st sample. The intra-session reliability for the 20 trials ranged between .995 and .998 for the 5 control conditions in the 2nd sample. The reliability for only 4 trials ranged between .864 and .965 across the 4 control conditions in the 1st sample; the reliability for 4 trials ranged between .918 and .984 for the 5 control conditions in the 2nd sample. Hence, a reliable measure of the H-reflex can be obtained with only 4 trials; 10 trials yield a very reliable measure of the H-reflex that is nearly as reliable as 20 trials.

Hopkins, Ingersoll, Cordova, and Edwards (2000) examined the intra-session and inter-session reliability of the soleus H-reflex in 13 healthy volunteers. The sample underwent 12 trials of maximal H-reflex recording on 5 consecutive days. The intra-session reliability of the maximal H-reflex was .932 for the 12 trials; it was .932 for 12 trials minus the high and low score, .935 for 7 trials minus the high and low score, and .932 for 5 trials. The inter-session reliability was .938. Hence, the H-reflex can be measured reliably between trials and across days using between 5 and 10 recordings.

To date, no studies have examined the reliability of the H-reflex in the flexor carpi radialis muscles. Studies evaluating the H-reflex in the flexor carpi radialis muscle commonly have measured the maximal H-reflex across 10 recording trials (e.g., Baldissera et al., 2000; Paik et al., 2001). Moreover, there is no strong reason to believe that the reliability of the H-reflex in the flexor carpi radialis would differ from the reliability of the H-reflex recorded in the

soleus muscle. Hence, 5 to 10 trials should be adequate to reliably record the maximal H-reflex in both the soleus and the flexor carpi radialis muscles.

Position of the Subject

The body position, leg position, and background muscle activity might all be important methodological influences to control when recording the H-reflex in the soleus and flexor carpi radialis muscles. Hugon (1973) suggested that the H-reflex in the soleus muscle should be recorded with the subject in a semi-reclined, supine position with the head and arms supported to avoid the influences of changes in head position and contractions of the shoulder and neck muscles on the soleus H-reflex. Supporting Hugon's (1973) recommendation for a semi-reclined, supine position, there were no significant differences in the amplitude of the maximal M-wave and H-wave or the latency of the H-wave when measured in a prone lying position and a semi-reclined sitting position in 12 healthy males and females (Al-Jawayed, Sabbahi, Etnyre, & Hasson, 1999). Other researchers have reported that movement of the head and/or body induces contralateral and ipsilateral increases and decreases in the amplitude of the H-reflex, respectively (Anson & Kasai, 1995; Traccis et al., 1987); this supports Hugon's (1973) recommendation for stable head and body positions when recording the H-reflex.

Hugon (1973) suggested that the foot should be maintained on a foot-plate and flexed dorsally to place the soleus under adequate stretch; this was recommended, however, only to enable access to the Achilles tendon reflex. Hence, others have suggested both maintaining the ankle joint at a neutral angle of $\sim 90^\circ$ (Kawakami, Sale, MacDougall, & Moroz, 1998; Trimble, Du, Brunt, & Thompson, 2000) and placing a small load against the soleus muscle to

standardize the level of alpha motoneuron pool activity (Capaday, 1997). The H-reflex was demonstrated to be potentiated with a tonic, isometric load placed against the soleus muscles when the subject was in a seated, reclined position and the knee and ankle were flexed at 60E and 90E, respectively (Trimble et al., 2000). Yet, there was no effect of the isometric load placed against the soleus muscles on the H-reflex when the subject was in a prone position and the knee was fully extended and the ankle was maintained at 90E (Trimble et al., 2000). There has been a similar potentiated effect of a tonic, isometric load on the amplitude of the soleus H-reflex in other studies (e.g., Bonnet, Decety, Jeannerod, & Requin, 1997). Hence, the H-reflex in the soleus muscle should be measured with the ankle positioned at ~90E and a standard load placed against the soleus muscle to control the background muscle activity.

Hugon (1973) suggested that the knee should be flexed to about 120E. This position stretches the soleus muscle for optimal activation of the mono-synaptic reflexes; the gastrocnemius is relaxed by knee flexion thereby reducing the potential depressive influence of afferents from the gastrocnemius on the soleus H-reflex. Yet, Kawakami et al. (1998) reported no effect of knee joint angle on the soleus H-reflex. Trimble et al. (2000) reported that the H-reflex was larger with the knee fully extended than flexed to ~60E during a resting condition with no load placed against the soleus muscle. Thus, there appears to be no clear effect of knee angle on the H-reflex. The best option appears to be a nearly extended knee angle of perhaps 160E.

To date, there is no evidence that the hip angle influences the soleus H-reflex. Knikou and Rymer (2002) examined the effect of changes in hip angle on the soleus H-reflex in 21

healthy adults. The H-reflex was measured across 20 trials with the hip in four different positions: 10E, 30E, and 40E hip flexion and 10E hip extension. There were no significant differences in the soleus H-reflex across the four different hip angle positions. This is not surprising as there were no differences in the soleus H-reflex amplitude or latency when it was recorded in prone, lying and semi-reclined, sitting positions (Al-Jawayed et al., 1999).

The soleus H-reflex is differentially modulated by eyes open versus eyes closed. Hoffman and Koceja (1995) examined the influence of visual input and surface stability on the soleus H-reflex in 17 subjects. Visual input consisted of eyes open versus eyes closed; surface stability consisted of standing on the floor versus standing on a mini-trampoline. Independent of surface stability, there was a main effect of visual input on the H-reflex. The H-reflex was larger with the eyes open versus the eyes closed. There was a similar effect among young subjects in a study by Earles, Koceja, and Shiverly (2000). Hence, the H-reflex should be measured with the eyes open or closed, but not both.

Baldissera et al. (2000) examined the effect of forearm position on the H-reflex in the flexor carpi radialis muscle. The recruitment profiles of the H-waves and M-waves were compared in 9 adult volunteers with the forearm in prone versus supine position. The H-reflex in the flexor carpi radialis, normalized to the M-wave, was lower when the arm was in a supine position relative to a prone position. The average size of the reduction was ~50% across the recruitment curve. The changes in the H-reflex were not related to displacements of the stimulating or recording electrodes. Hence, the FCR H-reflex should be measured with the forearm in a prone position.

Summary

In general, there appears to be a large body of information for standardizing the measurement of the soleus H-reflex; there is little information for standardizing the measurement of the FCR H-reflex. Hugon (1973), and Jabre (1981) with some modifications, have provided sound criteria for electrode placement for evoking and recording the soleus and FCR H-reflex. Hugon's (1973) recommendations for the body and joint positions generally have been supported by subsequent research. The soleus H-reflex should be measured in a semi-reclined, supine position with supports for the head and arms, and the hip, knee, and ankle joint angles of 120E, 160E, and 90E, respectively. There should be a load placed against the soleus muscles and the eyes should be open. There only is research pertaining to prone forearm position for the FCR H-reflex.

What Does the H-reflex Measure?

There have been two primary interpretations of the H-reflex. One interpretation has been alpha motoneuron excitability (Angel & Hofmann, 1963; Schieppati, 1987). The other has been the efficacy of synaptic transmission between Ia afferent fibers and alpha motoneurons (Capaday, 1997; Zehr, 2002).

Alpha Motoneuron Excitability

Angel and Hofmann (1963) commonly have been cited for interpreting the H-reflex or H/M ratio as a measure of alpha motoneuron excitability. This interpretation was based on the observation of a lack of differences in the threshold and amplitude of the H-wave across normal, spastic, and rigid subjects. Moreover, Angel and Hofmann (1963) noted that the size of

the H-wave was affected by irrelevant factors such as electrode placement and skin thickness, and that the relative size of the H-wave and M-wave per any given stimulus is problematic because the ratio changes as a function of shock intensity. Hence, Angel and Hofmann (1963) argued that the best approach is to measure the H-wave and M-wave across an entire stimulus response curve, and then form the H/M ratio or H-reflex as a ratio of the maximal values for the H-wave and M-wave. This ratio estimates the number of motoneurons that can be elicited monosynaptically and thus provides an estimate of the fraction of the alpha motoneuron pool excited by stimulation of the Ia afferent fibers because there are no interneurons involved in the presumed monosynaptic reflex pathway. The H/M ratio exhibits striking contrasts between spastic and normal limbs. Moreover, the H/M ratio was altered by a number of experimental maneuvers including passive stretch and shortening of the muscle and plantar stimulation. Thus, Angel and Hofmann (1963) provide a rationale and some, but not comprehensive, evidence for interpreting the H/M ratio as a measure of motoneuron excitability.

Schieppati (1987, p. 347) reported that the “H-reflex amplitude is a measure of the excitability of the motoneurons, and consequently may change in various conditions as a function of segmental and supraspinal influences playing upon them.” Hence, there is agreement between Schieppati (1987) and Angel and Hofmann (1963). Yet, Schieppati (1987) later reported that the amplitude of the H-reflex may not be determined only by the excitability of the alpha motoneurons, but also by activation of oligo-synaptic spinal interneuron systems, presynaptic Ia inhibition, and brain stem, cerebellar, and cerebral brain regions. Therefore,

Schieppati (1987) provides evidence that refutes the original interpretation of the H-reflex as a measure of alpha motoneuron excitability.

Efficacy of Synaptic Transmission

Capaday (1997, p. 202) has reported that interpreting the H-reflex as a measure of alpha-motoneuron excitability is “gravely flawed.” The excitability of motoneurons is an intrinsic property that depends on the total membrane conductance, the membrane potential relative to threshold, and the presence of neuromodulators such as serotonin and norepinephrine (Capaday, 1997). Moreover, the intrinsic excitability of motoneurons is not the only factor involved in the net output of the motoneuron pool. Based on neural modeling studies and animal experiments, Capaday and Stein (1987, 1989) have illustrated that for a fixed level of alpha motoneuron pool activity and stimulus intensity, the H-reflex output depends primarily on the level of presynaptic inhibition of Ia afferent terminals in the spinal cord. Hence, the H-reflex is a measure of the efficacy of synaptic transmission between Ia afferent fibers and alpha motoneurons, when measurements are made across matched levels of motor activity (Capaday, 1997, p.202).

Zehr (2002) suggested that the direct synaptic connection between Ia afferent fibers and alpha motoneurons has provided a tempting background for interpreting the H-reflex as a measure of alpha motoneuron excitability. Yet, Zehr (2002) correctly pointed-out that the connection between the Ia afferent fibers and alpha motoneurons is subject to modulation, for example, by presynaptic inhibition of Ia afferents and the subsequent influence on neurotransmitter release between the Ia afferent fiber and alpha motoneuron. Although there

might be possible conditions that enable an interpretation of the H-reflex as a measure of alpha motoneuron excitability (Zehr, 2002), this interpretation is likely flawed and should be avoided. As reported by Capaday (1997), the best available interpretation of the H-reflex is – a measure of the efficacy of synaptic transmission between the Ia afferent and alpha-motoneuron.

Neuroanatomical Influences on the H-reflex

The H-reflex presumably is represented by a simple monosynaptic network of Ia afferent fibers and alpha motoneurons. Yet, many spinal pathways influence the amplitude of the H-reflex by converging on Ia afferent fibers and alpha motoneurons (Aymard et al., 2000). Moreover, there might be brain and brain stem structures that influence the magnitude of the H-reflex. The next section discuss the neuroanatomical influences of the H-reflex.

Influences Originating in the Spinal Cord

There are many pathways within the spinal cord that likely influence the amplitude of the H-reflex. Some of the primary influences within the spinal cord include presynaptic Ia inhibition; homosynaptic depression; reciprocal inhibition; recurrent inhibition; and Ib interneuron inhibition.

Presynaptic Ia inhibition. By definition, presynaptic Ia inhibition involves a GABA mediated depolarization of Ia afferent terminals resulting in a reduced release of the excitatory neurotransmitter glutamate (Pierrot-Deseilligny & Mazevet, 2000; Pierrot-Deseilligny & Meunier, 1998). Very simply, presynaptic Ia inhibition involves the modification of the connection between two neurons (i.e., Ia afferent fiber and alpha motoneuron) by a third neuron, labeled a presynaptic inhibitor (Stein, 1995).

Presynaptic Ia inhibition primarily is the result of “primary afferent depolarization” or PAD (Rudomin, 1999; Rudomin & Schmidt, 1999). PAD presumably is caused by activation of GABA_A receptors through axo-axonal synapses made by GABAergic interneurons with the primary afferent terminals (Pierrot-Deseilligny, 1997; Rudomin, 1999; Rudomin & Schmidt, 1999). Though activation of GABA_A receptors typically results in Cl⁻ influx and hyperpolarization, with PAD there is an outward efflux of Cl⁻ ions resulting in depolarization. In the primary afferent terminal, the steady-state intracellular Cl⁻ concentration is higher than predicted from passive distribution, and this likely is the result of an active transport system maintaining the outward directed Cl⁻-electrical gradient. The active transport system involves the inward transportation of Cl⁻ coupled with the inward transportation of Na⁺ and K⁺ (i.e., a secondary active transport system rather than a Cl⁻ pump driven by energy derived from ATP splitting); the Na⁺ is immediately extruded via the Na⁺-K⁺-pump and the K⁺ passively moves via K⁺ channels, thereby keeping the intracellular Na⁺ and K⁺ constant. Thus, activation of GABA_A receptors in primary afferent terminals increases the outward efflux of Cl⁻ ions, depolarizes the cell, and inhibits the release of glutamate by either (1) blocking action potential invasion into Ia afferent terminals or (2) reducing the amplitude of the propagating action potential, thereby blocking or reducing Ca²⁺ influx (Rudomin, 1999; Rudomin & Schmidt, 1999).

Presynaptic Ia inhibition of the H-reflex in the soleus muscle can be tested using either electrical stimulation of the common peroneal nerve or vibration of the tendon for the tibialis anterior (e.g., Morin, Pierrot-Deseilligny, & Hultborn, 1984; Pierrot-Deseilligny & Mazevet,

2000). With electrical stimulation, a conditioning stimulus is applied to the common peroneal nerve ~20 ms before the application of a test stimulus to the tibial nerve. The conditioning stimulus is generally a train of 3, 1 ms stimuli, $1.20 \times$ motor threshold. The application of the conditioning stimulus results in a marked reduction of the H-reflex measured by the test stimulus.

Brief vibration of the heteronymous tendon is another method for estimating presynaptic Ia inhibition (Pierrot-Deseilligny & Meunier, 1999). As an example, a brief vibration (10 ms, 3 shocks at 200 Hz) is applied to the tendon of the heteronymous muscle, specifically the tibialis anterior for measuring presynaptic Ia inhibition in the soleus muscle. The conditioning vibration evokes a clear inhibition of the soleus H-reflex.

Homosynaptic depression. By definition, homosynaptic or post-activation depression involves a reduced probability of the release of the excitatory neurotransmitter glutamate from the Ia afferent terminals (Hultborn & Nielsen, 1998; Kohn, Floeter, & Hallett, 1997; Pierrot-Deseilligny & Mazevet, 2000); glutamate is the excitatory neurotransmitter promoting an EPSP in the alpha motoneuron cell body. This reduced probability of neurotransmitter release is the result of previous activation of the pathway between the Ia afferent fibers and alpha motoneurons. Essentially, the amplitude of the H-reflex is reduced by repetitive stimuli presented within a short interstimulus interval (e.g., 2 s). Thus, homosynaptic depression does not involve input from other spinal pathways, but simply the repetitive activation of the H-reflex pathway.

Homosynaptic depression can be simply tested by varying the interstimulus interval between successive electrical stimuli applied to the tibial nerve (e.g., Crone & Nielsen, 1989). The interstimulus interval is varied between 2 s and 8 s and the intensity of the stimulus is set so that the amplitude of the H-reflex for the 8 s interval is $\frac{1}{2}$ of the maximal H-reflex. The application of the 2 s interstimulus interval results in a marked reduction of the H-reflex compared with the application of the 8 s interstimulus interval. The magnitude of the reduction is indicative of the magnitude of homosynaptic depression. Hultborn and Nielsen (1998) have described another method of testing homosynaptic depression based on passive stretch of the calf muscles, but the effects are nearly identical to those found by varying the inter-stimulus interval.

Reciprocal inhibition. Reciprocal or disynaptic inhibition involves the inhibition of the agonist alpha motoneuron by activation of Ia afferent fibers from the antagonist muscle (Crone & Nielsen, 1994; Schieppati, Gritti, & Romano, 1991). The inhibition is the result of a disynaptic pathway with a single interneuron between Ia afferent fibers of the antagonist muscle and alpha motoneurons of the agonist muscle (Crone & Nielsen, 1994). The single interneuron promotes an IPSP within the alpha motoneuron cell body, presumably through the release of GABA (Crone & Nielsen, 1994). Summation of small or moderately sized IPSPs produced by the Ia inhibitory interneurons hyperpolarize the alpha motoneuron and shunt EPSPs, thereby preventing depolarization of the alpha motoneuron. Hence, reciprocal inhibition differs from presynaptic Ia inhibition based on (1) location of inhibition and (2) number of interneurons between Ia afferent fiber and alpha motoneuron.

Reciprocal inhibition can be simply tested using electrical stimulation of the common peroneal nerve (Crone & Nielsen, 1994, Schieppati et al., 1991). The protocol involves the application of a conditioning stimulus applied to the common peroneal nerve ~0-3 ms before the application of a test stimulus to the tibial nerve. The conditioning stimulus is a 1 ms stimulus $1.0 \times$ motor threshold. The application of the conditioning stimulus results in a marked reduction of the H-reflex measured by the test stimulus.

Recurrent inhibition. Recurrent inhibition was initially described by Renshaw (1941, 1946). Very simply, the axons of alpha motoneurons have direct synaptic connections with target muscles, and have recurrent collaterals that synapse on Renshaw cells. The recurrent collaterals activate the Renshaw cells through acetylcholine, and the Renshaw cells in turn inhibit the recruited alpha motoneurons through the release of the inhibitory neurotransmitter glycine. Hence, the classic circuit involves axon collaterals of motor neurons projecting to Renshaw cells, which inhibit subsequent firing of homonymous motor neurons. As described by Katz and Pierrot-Deseilligny (1998), the connections of the Renshaw cells are far more complex: (1) Renshaw cells are excited by collaterals of many homonymous and synergistic alpha motoneurons; (2) Renshaw cells are activated and/or inhibited by segmental pathways and descending tracts; (3) Renshaw cells project not only to alpha motoneurons, but also gamma motoneurons, Ia inhibitory interneurons, and other Renshaw cells. Hence, recurrent inhibition represents a potent means of modulating the alpha motoneuron and Ia-afferent involved in the H-reflex pathway.

The effect of recurrent inhibition on the H-reflex can be evaluated in humans as described by Katz and Pierrot-Deseilligny (1998). This is accomplished by paired conditioning and test stimulations separated by 10 ms and delivered through the same unipolar electrode configuration employed to measure the H-reflex in the soleus muscle. Initially, a conditioning stimulus (S1) results in the firing of a group of alpha motoneurons; this has been termed the conditioning reflex discharge or H1. This conditioning reflex discharge activates Renshaw cells via recurrent collaterals. The subsequent test stimulus is supramaximal in intensity and intended to measure the resulting recurrent inhibition. Interestingly, supramaximal intensity stimulation alone is not followed by a reflex response because of the collision between the reflex discharge and antidromic motor volley. But, if the supramaximal stimulation is preceded by a S1 conditioning stimulus generating an H1 reflex, an H-reflex labeled H₂ appears in the EMG. This is caused by the collision of the H1 conditioning reflex with the antidromic motor volley caused by the test stimulus. The collision eliminates the antidromic motor volley and enables the H₂ test reflex associated with supramaximal stimulation to pass along the motor axons to the muscle. Recurrent inhibition is expressed as a reduction in the amplitude of the H₂ reflex relative to the H1 reflex as a function of the conditioning stimulus intensity.

Mazzocchio and Rossi (1997) have provided another method of assessing Renshaw cell activity in humans. This method is accomplished through the pharmacological and electrophysiological activation of Renshaw cells. The pharmacological activation of Renshaw cells is accomplished through the cholinergic properties of L-acetylcarnitine. L-acetylcarnitine acts by potentiating the synaptic drive of motoneuron collaterals through nicotinic receptors that

are the main source of activation of Renshaw cells. The experimental procedure involves intravenous infusion of 30 mg·kg⁻¹ body weight of L-acetylcarnitine hydrochloride in 100 ml saline. The effect of recurrent inhibition on the H-reflex is then evaluated using the electrophysiological method described by Katz and Pierrot-Deseilligny (1998).

Ib interneuron inhibition. The Ib inhibitory interneurons exert a powerful influence on alpha motoneurons. Ib inhibitory interneurons are GABAergic and are activated by (1) homonymous Ia and Ib afferent fibers (i.e., Ia and Ib afferents indirectly inhibit the alpha motoneuron through activation of Ib inhibitory interneurons); (2) Ia and Ib afferent fibers from synergist muscles (i.e., Ia and Ib heteronymous or non-reciprocal inhibition from the gastrocnemius); (3) Type III and Type IV nociceptive afferent fibers; (4) cutaneous tactile and thermal afferent fibers (Type II, III, and IV afferents); and (5) segmental and descending inputs originating in the brain. The large number of inputs to the Ib inhibitory interneuron is not surprising as its main function is considered to be coordinating the activity of muscles operating across different joints (Rossi, Decchi, Dami, Della Volpe, & Groccia, 1999a).

Pierrot-Deseilligny and Mazevet (2000) described the coactivation of Ib inhibitory interneurons and alpha motoneurons by homonymous Ia afferents. The Ia afferent from the soleus muscle synapses directly on alpha motoneurons and on Ib inhibitory interneurons; the Ib inhibitory interneurons then synapse on alpha motoneurons. The direct activation of the alpha motoneuron produces an EPSP; the indirect pathway produces an IPSP. The IPSP results ~0.8 ms after the EPSP, and might derecruit the last alpha motoneurons contributing to the H-reflex.

The effect of activating Ib afferent fibers from homonymous muscles on Ib interneuron inhibition has been described by Hayward, Nielsen, Heckman, and Hutton (1986). The Ib afferent fiber from the Achilles tendon synapses on a Ib inhibitory interneuron; the Ib inhibitory interneuron then synapses on the alpha motoneuron. This is tested by a prolonged vibration of the Achilles tendon. The prolonged vibration produces a depression or abolition of the soleus H-reflex that lasts between 10 and 55 min.

Heteronymous Ib interneuron inhibition from the gastrocnemius has been described by Rossi et al (1999a). The Ia and Ib afferent fibers from the gastrocnemius muscle synapse on the Ib inhibitory interneuron. The synapse on the Ib interneuron promotes a subsequent inhibition of the alpha motoneuron involved in the soleus H-reflex. This is tested by applying a 1 ms pulse just below motor threshold through bipolar electrodes to the gastrocnemius nerve ~4-5 ms before measuring the soleus H-reflex.

Rossi and Decchi (1995) illustrated the indirect effect of nociceptive, Type IV afferent fibers on the soleus H-reflex. The Type III and IV afferents have indirect influences on the alpha motoneuron through two interneurons. The Type III and IV afferents synapse on an excitatory interneuron that in-turn synapses on the Ib inhibitory interneuron. Thus, activation of Type III and IV afferents can modulate the magnitude of the soleus H-reflex. Empirical evidence supporting this observation was provided by Rossi and Decchi (1995). Rossi and Decchi (1995) examined the effect of a subcutaneous injection of 25 and 50 mg levo-ascorbic acid (L-AS) into the latero-dorsal aspect of the ipsilateral foot, 3-4 cm proximal to the metatarso-phalangeal joint on heteronymous Ib interneuron inhibition of the soleus muscle. The

soleus H-reflex exhibited a dose-dependent inhibition associated with activation of Type IV afferents; the dose-dependent inhibition was consistent with pain ratings associated with the L-AS injections.

Rossi et al. (1999a) provided further evidence for the role of Type IV afferents on Ib interneuron inhibition of the soleus H-reflex. Subjects received a subcutaneous injection of 30 mg levo-ascorbic acid (L-AS) into the extensor digitorum brevis muscle of the ipsilateral foot. The H-reflex was measured with and without the effect of heteronymous Ib interneuron inhibition of the soleus muscle. The H-reflex in the soleus muscle was reduced after injection of L-AS, and the reduction corresponded with changes in ratings of pain. The soleus H-reflex exhibited an inhibition associated with heteronymous Ib interneuron inhibition of the soleus muscle. Hence, activation of Type IV afferents by L-AS seems to impact the soleus H-reflex.

Ellrich, Steffens, and Schomburg (2000) examined the effect of nociceptive inputs from the foot on the soleus H-reflex. Noxious radiant heat stimulation was applied to the ball of the big toe (45EC) and the medial arch and proximal heel (50EC). The H-reflex was recorded 10 ms before and 70 ms after application of the radiant heat stimulus. The H-reflex was increased with application of radiant heat to ball of the big toe; it was unchanged with application to the medial arch; and it was reduced by application to the proximal heel. This pattern was consistent with expectations based on the withdrawal reflex activated by a noxious stimulus. The application of radiant heat to anterior, medial, and posterior locations of the sole of the foot presumably differentially impacted the H-reflex through the influence of Type IV afferents on Ib inhibitory interneurons.

Other researchers have examined the effect of muscle pain induced in the extensor digitorum brevis (EDB; Rossi, Decchi, & Ginanneschi, 1999b) and soleus muscle (Matre, Sinkjær, Svenson, & Arendt-Nielsen, 1998) on the soleus H-reflex. Pain induced by L-AS injection in the EDB muscle had similar effects to previous studies (Rossi & Decchi, 1995; Rossi et al., 1999a), but the nature of the effect was mediated by presynaptic inhibition of Ia afferent fibers for both the soleus and gastrocnemius muscles. Pain induced by infusion of hypertonic saline into the soleus muscle did not impact the H-reflex (Matre et al., 1998).

Urbscheit and Bishop (1970) examined the effects of cooling the skin overlying the calf on the soleus H-reflex. The H-reflex was measured before and every minute after beginning the cooling of the skin; the skin was cooled by placing a bag filled with crushed ice between the stimulating electrodes in the popliteal fossa and the Achilles tendon. Skin temperature was reduced within 1 min of the application of the ice, and exhibited no further changes across the remaining 9 min. The H-reflex was increased within the 1st min of skin cooling, and remaining significantly elevated for the remaining 9 min. Similar results were obtained in a study by Oksa et al. (2000). Both decreases and increases in the skin temperature of the ankle correlated with increases and decreases in the H-reflex in another study (Krause, Hopkins, Ingersoll, Cordova, & Edwards, 2000). Hence, cooling and warming of the skin impacted the H-reflex presumably by affecting Ib inhibitory interneurons through activation of cutaneous afferents by temperature. The signal was likely carried by Type IV afferent fibers, which convey information about temperature (Parent, 1996).

As an example of cutaneous tactile inputs to Ib inhibitory interneurons and subsequent influences on the H-reflex, Wood, Nicol, and Thulin (1998) demonstrated that the soleus H-reflex was attenuated during brushing of a 2 cm × 10 cm area of skin overlying the triceps surae; the speed, but not duration of brushing further increased the amount of attenuation. The brushing of the skin presumably activated cutaneous receptors and afferent fibers (Type II and III afferent fibers). Those fibers, in turn, presumably exerted an influence on the alpha motoneuron through effects on the Ib interneuron.

Importantly, researchers have reported that segmental pathways originating within the central nervous system can modulate the nociceptive influences on the Ib inhibitory interneuron impacting the soleus H-reflex (Rossi & Decchi, 1995; Rossi et al., 1999b). Even the influences of Type Ia, Ib, II, III, and IV afferents on the Ib interneuron inhibitory pathway can be modulated by the central nervous system (Pierrot-Deseilligny, Bergego, & Katz, 1982; Rossi & Mazzocchio, 1988).

Brain Stem and Brain

Brain stem and brain structures might influence the magnitude of the H-reflex by directly or indirectly converging on Ia afferent fibers and alpha motoneurons (e.g., Aimonetti, Schmied, Vedel, & Pagni, 1999; Capaday, 1997; Mercuri, Wassermann, Ikoma, Samii, & Hallett, 1997; Rotto-Perceley, Wheeler, Osorio, Platt, & Loewy, 1992). The primary influences from the brain stem include serotonergic and noradrenergic nuclei. The primary influences from the brain include motor and somatosensory cortices, cerebellum, and vestibular nuclei. Additional influences from the brain might include limbic structures and the basal ganglia.

Brain stem. Noradrenergic and serotonergic containing nuclei within the brain stem are potent modulators of Ia afferent fibers and alpha motoneurons (Jankowska, Hammar, Chojnicka, & Hedén, 2000) involved in the soleus H-reflex. As described by Capaday (1997), the excitability of alpha motoneurons partly depends on the presence of neuromodulators such as serotonin and norepinephrine. Based on a computer simulation study, Heckman (1994) reported that for a given stimulus intensity and level of motor activity in two different motor tasks, the excitability of alpha motoneurons may be greater in one task because of greater release of serotonin.

Evidence linking noradrenergic and serotonergic containing nuclei in the brain stem with Ia afferent fibers and alpha motoneurons involved in the soleus H-reflex mainly is derived from animal studies; there are few human studies that indirectly support possible noradrenergic influences on alpha motoneurons. Rotto-Perceley et al. (1992) conducted a transneuronal labeling study with pseudorabies virus injections into the rat medial gastrocnemius muscle. The purpose of the study was to identify dorsal root ganglion cells and supraspinal nuclei that project directly or indirectly via interneurons to the alpha motoneurons innervating the calf muscles. As expected, there was extensive labeling in the L5 region of the spinal cord, particularly in laminae IX and in laminae V, VI, VII, and X; there also was labeling in the intermediolateral cell column of the T11 - L2 regions of the spinal cord. In the brain stem, cell body labeling was observed in the caudal raphe nuclei, paramedian reticular formation, rostral ventrolateral medulla, and A5 cell group. There was cell body labeling in the locus coeruleus,

subcoeruleus nucleus, and A7 noradrenergic neurons of the brain stem. There even was labeling in the paraventricular hypothalamic nucleus.

Holstege and Kuypers (1987) summarized the results of multiple transneuronal labeling studies in animals, and described direct inputs from the noradrenergic containing nuclei in the locus coeruleus and subcoeruleus to the alpha motoneurons. Holstege and Kuypers (1987) described direct inputs from the serotonergic containing nuclei in the raphe magnus, pallidus, and obscurus to the alpha motoneurons. Those direct inputs have been discussed by Parent (1996), along with indirect projections to alpha motoneurons through interneurons originating in Lamina X.

One study supports the possible existence of noradrenergic influences from the locus coeruleus on the H-reflex in humans. Palmeri et al. (1999) examined the effect of clonidine on the H-reflex in health males and females. Clonidine is a noradrenergic alpha₂ receptor agonist that presumably acts primarily within the locus coeruleus (Palmeri et al., 1999). Intravenous infusion of clonidine significantly reduced the H-reflex; there was no effect of saline infusion on the H-reflex. There clearly is a need for additional studies examining the influence of noradrenergic and serotonergic containing nuclei in the brain stem on the H-reflex in humans.

Brain. Relatively little is known about the influence of many structures and regions within the brain on the H-reflex. This section reviews the available literature on some of the possible influences originating in the brain. The most prominent influence on the H-reflex is the motor cortex. As described initially by Táboríková (1973) and then later by others (e.g., Baldissera, Hultborn, & Illert, 1981; Schieppati, 1987; Rudomin, 1999), the motor cortex

directly influences alpha motoneurons involved in the H-reflex. More recently researchers have recognized that the motor cortex might even impact the H-reflex through presynaptic inhibition of Ia afferent fibers and reciprocal inhibition (e.g., Pierrot-Deseilligny, 1996).

The motor cortex influences the alpha motoneuron through the corticospinal tract (Parent, 1996). The corticospinal tract originates with pyramidal cells in somatotopically-organized regions of the motor cortex, and then descends through the internal capsule. After the internal capsule, the corticospinal tract continues through the pyramid until it reaches the pyramidal decussation located in the medullary region of the brain stem. The fibers then cross to the contralateral side of the spinal cord and finally synapse on alpha motoneurons and interneurons throughout the ventral segments of the spinal cord.

The influence of the motor cortex on the H-reflex has been demonstrated in several studies using transcranial electrical and magnetic stimulation. Nielsen, Petersen, Deuschl, and Ballegaard (1993) demonstrated that stimulation of the contralateral motor cortex facilitated the soleus H-reflex. Similar effects were observed in the soleus and FCR by other researchers (e.g., Mercuri et al., 1997; Nielsen & Petersen, 1994). This facilitation presumably is the result of activation of large-diameter, fast-conducting pyramidal fibers with monosynaptic projections to spinal motoneurons. Yet, recent research has identified both a direct and an indirect effect of pyramidal fibers on spinal motoneurons through monosynaptic connections with alpha motoneurons and modulation of presynaptic Ia afferent fibers and reciprocal inhibition (Aimonetti et al., 1999; Mercuri et al., 1997; Nielsen & Petersen, 1994; Pierrot-Deseilligny, 1996).

Vestibular nuclei influence the alpha motoneurons associated with the H-reflex (Delwaide & Delbecq, 1973); there is no apparent evidence linking vestibular nuclei with Ia afferent fibers. Briefly, two types of vestibular transducer organs (i.e., semicircular canals and otolithic maculae) located in the labyrinth of the ear are responsive to linear and rotational accelerations of the head (Baker, 1999). Those organs project onto several nuclei within the vestibular nuclear complex; one of nuclei is the descending vestibular nucleus. The descending vestibular nucleus forms a direct connection with alpha motoneurons through the ipsilateral vestibulospinal tract. Hence, there is a neuroanatomical basis linking vestibular function with the H-reflex. This link has been confirmed by studies examining the effect of head acceleration on the H-reflex (e.g., Anson & Kasai, 1995; Delwaide & Delbecq, 1973; Traccis et al., 1987). More recent studies have provided further evidence linking vestibular nuclei with the H-reflex (e.g., Kennedy & Inglis, 2001; Kolev & Milanov, 1995).

As discussed by Táboríková (1973), there are additional brain areas associated with motor control that impact the H-reflex. Those additional areas include the cerebellum, superior colliculus, reticular nuclei, red nucleus, and basal ganglia. Those systems have direct, indirect, and interactive influences on Ia afferent fibers and alpha motoneurons involved in the H-reflex. See Táboríková (1973) and Thach (1999) for a description of the functional nature of those areas in modulating the H-reflex.

Importantly, Holstege and Kuypers (1987) discussed the influences of brain structures classically associated with the limbic system on Ia afferent fibers and alpha motoneurons involved in the H-reflex; the links were established based on animal studies. The limbic system

classically includes the amygdala, hippocampus, anterior nucleus of the thalamus, hypothalamus, cingulate gyrus, and septum (Isaacson, 1982; Papez, 1937). Those brain areas have either direct or indirect influences on Ia afferent fibers and alpha motoneurons involved in the H-reflex; the indirect influences are mediated through the raphe and locus coeruleus brain stem nuclei (Holstege & Kuypers, 1987).

Brain regions involved in pain, particularly those associated with descending modulation of nociceptive inputs, might impact the Ia afferent fibers and alpha motoneurons involved in the H-reflex. This is supported by research illustrating the influence of noxious stimuli on the H-reflex (e.g., Rossi & Decchi, 1995; Rossi et al., 1999b). One of the common segmental pathways originates with the anterior cingulate, amygdala, and hypothalamus (Bonica, 1990b). Those brain regions project to the rostral ventromedial medulla, dorsolateral pontine tegmentum, and locus coeruleus, which in-turn directly and indirectly influence the Ia afferent fibers and alpha motoneurons through opioid containing interneurons within spinal cord (Bonica, 1990b).

Summary. The H-reflex, in its most simple form, involves only a pathway containing Ia afferent fibers and alpha motoneurons. Yet, there are many spinal pathways that influence the H-reflex by converging on Ia afferent fibers and alpha motoneurons (Aymard et al., 2000). Some of the primary influences within the spinal cord include presynaptic Ia inhibition; homosynaptic depression; reciprocal inhibition; recurrent inhibition; and Ib interneuron inhibition. Brain stem and brain structures even influence the H-reflex by directly or indirectly converging on the Ia afferent fibers and alpha motoneurons (e.g., Aimonetti et al., 1999;

Capaday, 1997; Mercuri et al., 1997; Rotto-Percelay et al., 1992). The primary influences from the brain stem and brain include serotonergic and noradrenergic containing nuclei, motor cortex, cerebellum, and vestibular nuclei. Additional influences from the brain might include the basal ganglia, limbic structures, and segmental pathways associated with pain modulation. This clearly indicates that the H-reflex is a complicated circuit with a multitude of inputs; this complexity makes it difficult to identify a single factor responsible for modulating the H-reflex in experimental studies, particularly with a stimulus such as exercise. The next section reviews pharmacological influences on the H-reflex.

Pharmacological Influences on the H-reflex

Researchers have examined the effect of pharmacological substances on the H-reflex in humans. This section will focus on pharmacological substances with implications for neurotransmitter systems possibly linked with anxiety and muscle tension. Particular attention is dedicated to the effect of caffeine on the H-reflex as it exhibits a strong anxiogenic effect in large doses (Nehlig, Daval, & Debry, 1992), and it is being employed in one of the current studies.

GABAergic Substances

The GABA neurotransmitter system may be involved in the modulation of the Ia afferent fibers and alpha motoneurons of the H-reflex. There are receptors for GABA in the ventral and dorsal regions of the spinal cord, particularly on presynaptic Ia terminals and postsynaptic alpha motoneurons (Rudomin, 1999; Rudomin & Schmidt, 1999). There are GABA receptors in brain areas involved in affective (e.g., amygdala, cingulate cortex, & ventral

tegmental area) and motor (e.g., basal ganglia) processes (Feldman, Meyer, & Quenzer, 1997; Singewald & Sharp, 2000); those areas can exert direct and indirect influences on Ia afferent fibers and alpha motoneurons involved in the H-reflex, as discussed in the previous section.

Several researchers have examined the effect of diazepam on the H-reflex. Diazepam is an antianxiety and muscle relaxant drug that acts as an agonist of GABA_A receptors. Diazepam binds to specific benzodiazepine receptor sites and it enhances the binding of GABA to GABA_A receptors. This increases the conductance of Cl⁻ through the GABA ionophore. Diazepam enhances presynaptic inhibition of primary afferent terminals in the spinal cord. Diazepam can reduce anxiety and muscle tension through effects within the central nervous system.

Brunia (1973) examined the effect of diazepam on the soleus H-reflex and the T-reflex in 24 normal subjects. Subjects received an intravenous infusion of 10 mg of diazepam. The H-reflex and T-reflex were recorded in the soleus muscle before and 16 minutes after the diazepam infusion. Diazepam significantly reduced both the H-reflex and the T-reflex. Because of the similar reduction in the H-reflex and T-reflex, Brunia (1973) argued that the effects of diazepam were not likely attributable to the muscle spindle apparatus, but rather an effect within the spinal cord or central nervous system.

Verrier, Ashby, and MacLeod (1977) examined the effect of diazepam on the soleus H-reflex in patients with complete and incomplete lesions of the spinal cord. The sample consisted of 14 patients; 5 patients had a complete spinal lesion, 3 had incomplete lesions, and 6 had multiple sclerosis. Acute, intravenous administration of diazepam reduced the soleus H-

reflex by ~12% in the patients with incomplete spinal cord lesions and multiple sclerosis; there was no effect of diazepam on the H-reflex in the patients with a complete spinal cord lesion. Thus, the effect of diazepam on the H-reflex may be mediated by the central nervous system, perhaps through effects on the substantia nigra (Turski et al., 1990) or other areas involved in motor and affective processes.

Another study examined the effect of PK 8165 (pipequaline), a quinoline derivative, on the H-reflex. PK 8165 is an antianxiety drug with no sedative effects (von Frenckell, Ansseau, & Bonnet, 1986) that acts as a partial agonist of GABA_A receptors. Willer, von Frenckell, Bonnet, and Le Fur (1986) examined the effect of PK 8165 on the H-reflex in response to a stressful situation in normal male subjects. Eight healthy volunteers consumed placebo and 50, 100, and 150 mg of PK 8165. The H-reflex was measured during periods of threat and application of a noxious, stress-inducing electrical stimulus beginning 2 h after administration of PK 8165 or placebo. The threat and application of a noxious stimulus resulted in an increase of the H-reflex in 5 of the 8 subjects. PK 8165 resulted in a dose-dependent diminution of the H-reflex in the 5 subjects exhibiting an elevated H-reflex in response to the threat and application of the noxious stimulus.

Several researchers have examined the effect of baclofen on the H-reflex. Baclofen is an antispastic medication that acts as an agonist of GABA_B receptors. Baclofen increases the level of presynaptic inhibition of primary afferent terminals in the spinal cord. Baclofen might work postsynaptically by directly depressing motoneuron excitability. Those actions are

accomplished by hyperpolarizing the cells in the spinal cord through an increase in potassium conductance.

Inghilleri, Berardelli, Marchetti, and Manfredi (1996) examined the effect of baclofen on the H-reflex in the forearm flexor muscles. Five subjects received an intravenous infusion of baclofen ($0.6\text{mg}\cdot\text{kg}^{-1}$) and the H-reflex was measured in the flexor carpi radialis muscle before and 30 minutes after the infusion. The FCR H/M ratio was significantly reduced 30 minutes after infusion of baclofen.

Ørsnes, Crone, Krarup, Petersen, and Nielsen (2000) examined the effect of baclofen on the H-reflex in the soleus muscle. Using a placebo-controlled, double-blind cross-over study, 13 patients with multiple sclerosis orally consumed either baclofen or placebo for 11 days, and then underwent H-reflex measurement in the soleus muscle. Baclofen reduced the H/M ratio compared to placebo. Using another sample of 7 patients with multiple sclerosis, Ørsnes et al. (2000) examined the effects of intrathecal injections of baclofen into the subarachnoid space of the lumbar spinal cord; the H-reflex was measured before and 1-hour after the injection. Baclofen again reduced the soleus H/M ratio.

Another study examined the effect of gamma-hydroxybutyrate (GHB) on the H-reflex. GHB is an antianxiety and narcoleptic drug that acts as an agonist of GABA_B receptors. Mamelak and Sowden (1983) examined the effect of GHB on the H-reflex and F-reflex in 4 normal and 4 narcoleptic subjects. GHB resulted in a diminution of the H-reflex in all 8 subjects, regardless of whether sleep was induced. There was no effect of GHB on the F-reflex. Hence, GHB may exert an effect presynaptically.

Those studies and other studies (e.g., Azouvi et al., 1993; Delwaide, Schoenen, & Burton, 1983; Kaieda et al., 1981; Willer & Ernst, 1986) provided support for the GABA neurotransmitter system in the modulation of the H-reflex. The pharmacological substances have targeted both GABA_A and GABA_B receptors. The actual site of action, although not yet systematically investigated, might be within the spinal cord or within the central nervous system. Overall, the GABA neurotransmitter system represents a strong candidate for modulating the H-reflex based on the results of studies using the GABAergic substances of diazepam, PK 8165, baclofen, and GHB.

Opioid Influences

The opioid neurotransmitter system may be involved in the modulation of Ia afferent fibers and alpha motoneurons within the H-reflex pathway. There are opioid receptors in the ventral and dorsal regions of the spinal cord (Bonica, 1990a), particularly on Ib inhibitory interneurons that might impact Ia afferent fibers and alpha motoneurons. There are opioid receptors in brain areas involved in affective (e.g., amygdala, cingulate cortex, & ventral tegmental area) and nociceptive (e.g., PAG, LC, & Raphe) processes (Bonica, 1990b); those areas can exert direct and indirect influences on Ia afferent fibers and alpha motoneurons involved in the H-reflex, as previously noted.

Researchers primarily have examined the effect of naloxone on the H-reflex. Naloxone is an opioid receptor antagonist with the highest affinity for μ receptors. Hence, naloxone can be used to examine the role of opioids in regulating the H-reflex. The site of action of naloxone is unclear; it may work either directly in the spinal cord or indirectly through segmental pathways

involving brain stem nuclei and brain regions such as anterior cingulate cortex, amygdala, or hypothalamus.

Two older published studies have described the influence of naloxone on the H-reflex and R-III reflex in healthy human subjects (Boureau, Willer, & Dauthier, 1978) and chronic paraplegic subjects (Willer & Bussel, 1980). In 10 healthy human subjects, a low dose of naloxone (0.8 mg in 3 cm³ saline) produced a moderate facilitation of the H-reflex, but did not influence the R-III reflex; placebo (3 cm³ saline vehicle) did not influence either the H-reflex or R-III reflex (Boureau et al., 1978). In another study, there were no effects of a low dose of naloxone on the H-reflex and R-III reflex among chronic paraplegic patients (Willer & Bussel, 1980). Those early studies suggested that the opioid system exerted an influence on the H-reflex. Moreover, the influence of the opioid system was mediated by segmental pathways originating in the brain stem and brain because there were no effects of naloxone on the H-reflex in paraplegic subjects.

Willer and Ernst (1985) examined the effect of naloxone on diazepam induced modulations in the H-reflex in response to the application of a noxious, stress-inducing stimulus. Using a cross-over, double-blind design, 8 volunteers received diazepam (3, 2-mg tablets per day) or placebo across a 4-day period, and then intravenous infusions of either naloxone (0.08 mg·kg⁻¹ body weight in 10 ml saline) or saline vehicle 45 minutes after beginning a 90-min period involving the threat and application of a painful, noxious stimulus. The consumption of diazepam attenuated the stress-induced modification of the H-reflex, when compared with the change observed in the placebo condition. Naloxone potentiated the H-reflex independent of

the stress-induced modification of the H-reflex, and the magnitude of the increase in the H-reflex was attenuated by diazepam. Hence, the opioid and GABA neurotransmitter systems might interactively influence the H-reflex.

Recently, Sandrini et al. (1999) examined the effect of a high dose of naloxone on the H-reflex and R-III reflex in normal subjects and chronic paraplegic patients. Subjects were 5 normal healthy subjects and 3 patients with chronic paraplegia (lesion between D5 and D12). The pharmacological procedure was as follows: 15 min intravenous infusion of saline followed by 60 min infusion of $1.66 \text{ mg}\cdot\text{kg}^{-1}$ body weight of naloxone in 100 cm^3 saline. The H-reflex and R-III reflex were recorded before and after 15 min saline infusion, and then every 15 min for the next 120 min. Naloxone did not influence the R-III reflex in normal or paraplegic subjects, but there was a dose-dependent facilitation of the H-reflex in the normal subjects; naloxone did not impact the H-reflex in the paraplegic subjects. Thus, the opioid system appears to exert an influence on the H-reflex, and the influence appears to be mediated by segmental pathways originating in the brain stem and brain, as mentioned previously.

Those studies and others (e.g., Willer & Albe Fessard, 1980, Willer, Dehen, & Cambier, 1981) have supported the role of the opioid neurotransmitter system in modulating the H-reflex. Yet, the site of action is still unclear; it might be within the spinal cord, brain stem, or brain. The effect of opioids on the H-reflex also might interact with the GABA neurotransmitter system (Willer & Ernst, 1985). Strong evidence supports the opioid neurotransmitter system as a candidate for an independent, or perhaps interactive, role in modulating the H-reflex.

Noradrenergic Influences

The noradrenergic neurotransmitter system may be involved in the modulation of the Ia afferent fiber and alpha motoneuron (Jankowska et al., 2000) of the H-reflex. There are noradrenergic receptors in the ventral and dorsal regions of the spinal cord, particularly on interneurons that might impact Ia afferent fibers and alpha motoneurons (Jankowska et al., 2000; Simmons & Jones, 1988). There are noradrenergic receptors throughout the brain, including areas involved in affective (e.g., hypothalamus, LC) and motoric (e.g., striatum, motor cortex) processes (Singewald & Sharp, 2000); those areas can exert direct and indirect influences on Ia afferent fibers and alpha motoneurons involved in the H-reflex (Holstege & Kuypers, 1987; Rotto-Percelay et al., 1992). For example, the locus coeruleus has receptors for alpha₂ receptor agonists such as clonidine and tizanidine, and it has a direct and indirect influence on alpha motoneurons involved in the H-reflex. Importantly, the exact site of action of noradrenergic agonists and antagonists is unclear; the possible effect may be either in the spinal cord (e.g., interneurons) or through brain stem nuclei (e.g., locus coeruleus) and forebrain structures (e.g., hypothalamus, amygdala, striatum, cortex).

Two studies have examined the effect of clonidine on the H-reflex. Clonidine is a noradrenergic alpha₂ receptor agonist. Palmeri et al. (1999) examined the effect of clonidine on the H-reflex in healthy males and females. Fifteen healthy volunteers received intravenous infusion of 0.5 $\mu\text{g}\cdot\text{kg}^{-1}$ clonidine in 5 ml saline; 5 control subjects received an equal intravenous infusion of saline. The H-reflex and blood pressure were recorded every 10 min during a 20-min baseline period before infusion, and then again every 10 min for 100 min after infusion of

clonidine. Overall, clonidine significantly reduced the soleus H/M ratio from before to after the intravenous infusion of clonidine; there was no effect of only saline infusion on the H-reflex. Clonidine exerted an effect on the H-reflex within 10 min after infusion, with a peak effect ~30 min after infusion; the effect was still present 100 min post-infusion. The reduction in the H-reflex was independent of an effect of clonidine on diastolic or systolic blood pressure; clonidine did not alter blood pressure. The effect of clonidine on the H-reflex was largely attributed to the locus coeruleus (Palmeri et al., 1999), but the possibility of local effects within the spinal cord and effects within other regions of the brain stem and brain should not be overlooked.

Rémy-Néris, Barbeau, Daniel, Boiteau, and Bussel (1999) examined the effect of intrathecal clonidine injection on the H-reflex in incomplete paraplegic subjects. Seven subjects with incomplete paraplegia received intrathecal injections of 60 µg and 90 µg clonidine in the L2 and L3 region of the spinal cord; 4 subjects received 30 µg injections. The H-reflex was measured before and 1 h after the injections. There was no effect of the intrathecal clonidine injections on the H-reflex. Because clonidine only was injected in the lumbar spine and there was no effect on the H-reflex, clonidine might work through brain stem nuclei such as locus coeruleus or brain regions such as hypothalamus and amygdala based on the strong effects observed by Palmeri et al. (1999); clonidine also may need to be injected directly within the sacral spinal cord to observe an effect on the H-reflex.

One study has examined the effect of tizanidine on the H-reflex. Tizanidine is a noradrenergic α_2 receptor agonist. Hence, it should exhibit effects similar to clonidine. Delwaide and Pennisi (1994) examined the effect of tizanidine on the H-reflex using data from 5

studies involving between 3 and 14 patients with spasticity. The dose of tizanidine differed across the studies as did the mode of administration (i.e., oral ingestion vs. intramuscular injection). The H-reflex was measured before and then every 30 min for 120 min after administration of tizanidine. Results from all 5 studies indicated that tizanidine did not influence the H-reflex independent of dose or mode of administration.

Two studies have examined the effect of thymoxamine on the H-reflex. Thymoxamine primarily is a noradrenergic α_1 receptor antagonist. Phillips, Richand, and Shand (1973) reported that alpha-adrenergic blockade by thymoxamine did not influence the H-reflex in normal, healthy male subjects. Mai (1978) examined the effect of thymoxamine on the H-reflex in a sample of 19 patients with spasticity. The H-reflex was measured immediately before and after intravenous infusion of thymoxamine. Thymoxamine reduced the amplitude of the H-reflex by ~26%; the effect was not influenced by stasis induced by a sphygmomanometer cuff above the knee and pressure raised above systolic blood pressure.

Two studies examined the effect of propranolol on the H-reflex. Propranolol primarily is a noradrenergic β_1 and β_2 receptor antagonist. Mai and Pedersen (1976) examined the effect of propranolol on the H-reflex in 13 spastic patients. The H-reflex was measured before and 10 min after intravenous injection of $0.15 \text{ mg}\cdot\text{kg}^{-1}$ body weight of propranolol. Propranolol had no effect on the H-reflex. Similar results were reported by Phillips et al. (1973).

Those studies provide mixed support for the influence of alpha noradrenergic receptor agonists and antagonists on the H-reflex. Moreover, the potential site of action for alpha noradrenergic agonists and antagonists remains unclear. Beta noradrenergic receptor

antagonists do not appear to influence the H-reflex. Only null effects were found for beta noradrenergic drugs. To date, the research does not provide strong support for noradrenergic influences on the H-reflex.

Other Neurotransmitter Systems

Three studies have reported that N-methyl-D-aspartate (NMDA) receptor antagonist do not influence the magnitude of the H-reflex in normal, healthy subjects (Andersen et al., 1996; Schepelmann, Schugens, Loschmann, Klockgether, & Dichgans, 1998; Timman, Plummer, Schwarz, & Diener, 1995). Yet, two other studies using the anesthetics isoflurane (Zhou, Mehta, & Leis, 1997) and propofol (Kerz, 2001), which are antagonists for NMDA, AMPA, and kainate receptors, have reported large reductions in the H-reflex. Two studies have reported that cholinergic agonists (Nicotine & L-acetylcarnitine) do not directly influence the H-reflex, but indirectly influence the H-reflex through recurrent inhibition of alpha motoneurons (Mazzocchio & Rossi, 1997; Shefner, Berman, & Young, 1993). Finally, one study reported that haloperidol reduced the H-reflex, but the effect was reversed by thyrotropin-releasing hormone (TRH) tartrate in 15 healthy volunteers (Raffaele et al., 1992); this study implicates the role of TRH in modulating the H-reflex. To my knowledge, no studies have examined the effect of pharmacological agents that impact serotonergic or dopaminergic neurotransmitter systems on the H-reflex.

Adenosine

The adenosine neuromodulatory system may be involved in the modulation of the H-reflex via direct and indirect influences on Ia afferent fibers and alpha motoneurons. Adenosine

is considered to be a neuromodulator rather than a neurotransmitter (Dunwiddie & Masino, 2001). Adenosine does not appear to be released in a classical Ca^{2+} -dependent fashion; it is not stored in vesicles; and there are no synapses where adenosine is the primary transmitter (Fredholm, 1995). Moreover, adenosine is linked to the inhibition of release of virtually every classical neurotransmitter (e.g., glutamate, GABA, acetylcholine, norepinephrine, serotonin, & dopamine). The most prominent inhibitory action is exerted on the glutamatergic system. The mechanism of inhibition of neurotransmitter release appears to be G-protein coupled inhibition of Ca^{2+} channels in nerve endings (Dunwiddie & Masino, 2001). Another major role of adenosine is the hyperpolarization of the resting membrane potential. This is mediated through G-protein dependent activation of inward rectifying K^+ channels.

There are 4 types of adenosine receptors: A_1 , $\text{A}_{2\text{A}}$, $\text{A}_{2\text{B}}$, and A_3 . The adenosine A_1 receptor has the highest abundance in the brain and brain stem, particularly in areas involved in affective and motor processes (e.g., frontal, motor, & cingulate cortex; basal ganglia; midbrain nuclei of VTA, raphe, LC, substantia nigra), and is coupled with the G-protein dependent activation of K^+ channels and inhibition of Ca^{2+} channels. There even is an abundance of adenosine A_1 receptors in the dorsal and ventral portions of the spinal cord, particularly the substantial gelatinosa (Choca, Proudfit, & Green, 1987; Glass, Faull, Dragunow, 1996; Greiger, LaBella, & Nagy, 1984). The adenosine A_1 receptors are located on the terminals of primary afferent fibers and postsynaptic neurons. The localization and physiological effect of the other adenosine receptors subtypes are not, as yet, well established.

Caffeine acts primarily as an antagonist of adenosine A₁ receptors; there also is an antagonist effect of caffeine on adenosine A_{2A} receptors. Researchers have ruled-out effects of caffeine on cyclic nucleotide phosphodiesterases and intracellular Ca²⁺ release, presumably through ryanodine receptors, because the effects of caffeine occur only under physiological concentrations that are above toxic levels in humans (Fredholm, 1995; Nehlig et al., 1992). The only known mechanism of action for physiological relevant doses of caffeine in humans is binding to adenosine receptors and antagonism of the actions of agonists for these receptors (Fredholm, 1995).

Caffeine has a number of psychological effects, including the promotion of anxiety (Nehlig et al., 1992). In fact, anxiety can be experimentally increased using a caffeine model of anxiogenesis (Nickell & Uhde, 1994; Youngstedt, O'Connor, Crabbe, & Dishman, 1998). The consumption of a high dose of caffeine has been associated with increases in self-reported anxiety (e.g., Charney, Galloway, & Heninger, 1984; Youngstedt et al., 1998) and muscle tension (e.g., Pritchard, Robinson, deBethizy, Davis, & Stiles, 1995). The consumption of caffeine has produced dose-dependent increases in anxiety (Boulenger, Salem, Marangos, & Udhe, 1987; Kaplan et al., 1997; Nickell & Udhe, 1994; Uhde, Boulenger, Jimerson, & Post, 1984); this effect has not been observed for other anxiety manipulations (Youngstedt et al., 1998). Caffeine consumption has impacted neuromuscular variables such as resting EMG and physiological tremor (Hasenfratz & Bättig, 1992; James, 1990; Miller, Lombardo, & Fowler, 1998). Those effects presumably were the result of antagonism of adenosine A₁ receptors.

Caffeine consumption has demonstrated mixed positive and null influences on the soleus H-reflex (Eke-Okoro, 1982; Kalmar & Cafarelli, 1999). Eke-Okoro (1982) examined the effects of consumption of 1.3 g of instant coffee (~100-150 mg caffeine) on the H-reflex in 5 subjects. The H-reflex was measured immediately before and 1 h after consumption of the caffeine. The H-wave was significantly potentiated by consumption of caffeine. But, the M-wave also was significantly potentiated by consumption of caffeine. The effect of caffeine on the H/M ratio was not examined, but could possibly be deduced to be a null effect based on changes in both the H-wave and M-wave.

Kalmar and Cafarelli (1999) examined the effects of caffeine consumption on the H-reflex in 11 male volunteers. Using a within-subjects design and a double-blind procedure, the H-reflex was measured in the soleus muscle immediately before and 1 h after consumption of gelatine capsules containing caffeine (6 mg·kg⁻¹ body weight caffeine) or placebo (all-purpose flour) and a control condition (no consumption of gelatine capsules). There was no observed effect of caffeine on the H-wave, but the H-wave was not expressed relative to the maximal M-wave and was not evoked with a constant current device; this is important as caffeine exerts an effect on skin conductance and temperature (Quinlan et al., 2000), and therefore might impact input-output parameters when recording the H-reflex. Hence, the H-reflex should be expressed relative to the maximal M-wave.

Those two studies provided mixed support for the role of caffeine in modulation of the H-reflex. Yet, consumption of a large dose of caffeine exerts a strong influence on anxiety. Thus, the caffeine model serves as an ideal pharmacological intervention for testing the

association between anxiety and the H-reflex. To the extent that the H-reflex is associated with anxiety, an anxiogenic dose of caffeine should result in concurrent modifications of the H-reflex.

Summary

Based on a review of drug studies, GABA and opioids are the primary neurotransmitter systems that influence the H-reflex. Yet, there are other neurotransmitter systems that might influence the H-reflex. Some of those include the noradrenergic, cholinergic, and NMDA neurotransmitter systems, and the adenosine neuromodulatory system. To my knowledge, researchers have not examined the effects of the serotonergic and dopaminergic systems on the H-reflex. Hence, there are many possible neurobiological influences of the H-reflex. This complexity makes it difficult to identify a single neurobiological factor responsible for modulating the H-reflex in experimental studies, particularly with a stimulus such as exercise. The next section reviews studies of acute exercise on the H-reflex.

Acute Exercise and the H-reflex

Seven studies have examined the effect of acute exercise on the H-reflex (Avela et al., 1999; Bulbulian, 2002; Bulbulian & Bowles, 1992; Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Those studies reported that acute bouts of cycling and jogging reduced the amplitude of the H-reflex recorded in the soleus muscle by ~1 SD (90% CI = 0.63 - 1.37). Five of the studies interpreted the reduced H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian, 2000; Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990).

deVries et al. (1981) initially examined the effect of acute cycling ergometry on the H-reflex among 10 subjects who were males and females. Two of the 10 participants were older (i.e., 66 and 80 years of age) and had been solicited for the following symptoms: (1) general nervous tension; (2) difficulty getting to sleep; (3) persistent feelings of tension or strain; (4) irritability; (5) unrelenting worry; (6) restlessness; (7) inability to concentrate; or (8) feelings of panic in everyday life situations. The other 8 subjects were young and had been recruited from among Gerontology Center faculty, staff, and students, and had a mean age of 27.3 ($SD = 4.8$) years. Using a within-subjects design, participants underwent measurement of the H-reflex in the soleus muscle before and 10 min after 3 bouts of both exercise and control. Exercise consisted of 20 min of cycling on a stationary ergometer at 40% of heart rate range. Control consisted of an equivalent amount of time spent quietly sitting and reading. deVries et al. (1981) found that exercise significantly reduced the H/M ratio compared to sitting, quiet rest. The reduction in the H/M ratio with cycling was ~18%; control resulted in ~1% increase in the H/M ratio. deVries et al. (1981) concluded that “The findings in the present study of a highly significant reduction in H/M ratio in every subject tested provides strong support for the ‘tranquilizer effect’ of exercise performed at appropriate levels of intensity and duration” (pp. 63-64).

deVries et al. (1982) then examined the effect of acute exercise on the H-reflex and T-reflex. The sample consisted of 3 males and 3 females with a mean age of 25.5 ($SD = 8.8$) years; 4 other volunteers were excluded based on unstable T-reflex. Using a within-subjects design, participants underwent T-reflex and then H-reflex testing before and 5 min after 2 bouts

of both exercise and control; the measurement of the T-reflex and H-reflex lasted ~1 h. The H-reflex and T-reflex were measured in the soleus muscle. Exercise consisted of 20 min of cycling on a stationary ergometer at 40% of heart rate range. Control consisted of an equivalent amount of time spent quietly sitting and reading. deVries et al. (1982) found that after exercise the H-reflex was significantly reduced by ~16%; the control condition resulted in ~8% increase in the H-reflex. The T-reflex was reduced after exercise by a mean of ~15%. The T-reflex was reduced after exercise by ~16, 13, 12, 14, 14, and 24% for hammer drop heights of 220, 180, 140, 100, 60, and 20 mm, respectively; the control condition resulted in an increase of the T-reflex by between ~6-16% across 5 of 6 conditions. Because exercise resulted in similar reductions of the H-reflex and T-reflex, deVries et al. (1982) concluded that “the data reported here provide no support for the involvement of the fusimotor system in the ‘tranquilizer effect’ of exercise” (p.121).

Bulbulian and Darabos (1986) examined the effect of low and high intensity exercise on the H-reflex. The sample consisted of 10 subjects who were college students and faculty members; 5 were male and 5 were female. The mean age of the sample was 28.7 (SD = 8.2) years. Using a within-subjects design, participants underwent measurement of the H-reflex in the soleus muscle before and 10 min after 2 bouts of exercise and a single control session. The 2 bouts of exercise consisted of 20 min of cycling ergometry performed at 40 and 75% of $\dot{V}O_{2max}$. The control session consisted of 20 min of sitting quietly and reading. Bulbulian and Darabos (1986) found that the M-wave did not significantly differ across time and conditions. The H-wave decreased significantly after cycling at 40% $\dot{V}O_{2max}$ and even more after cycling at

75% $\dot{V}O_{2max}$; there was a similar change in the H/M ratio. The reduction in the H/M ratio after cycling at 40% $\dot{V}O_{2max}$ was ~13%; it was ~22% after cycling at 75% $\dot{V}O_{2max}$; the H/M ratio was increased by ~2% after control. Bulbulian and Darabos (1986) concluded that “the finding of highly significant reductions in the H_{max}/M_{max} ratio provides additional support for the ‘tranquilizer effect’ of exercise under conditions of high and low intensity” (p.700).

Mimasa et al. (1990) studied the effect of acute aerobic exercise on the H-reflex and brain electrocortical activity. The subjects were 7 college students. Using a within-subjects design, the students underwent measurement of the H-reflex in the soleus muscle and resting brain electrocortical activity before and after 2 sessions of both exercise and control. The exercise consisted of 20 min of cycling on an ergometer with the resistance adjusted to elicit 60% $HR_{reserve}$. The control condition consisted of 20 min of quiet sitting. Results indicated that the H/M ratio did not change after quiet rest (0.27%), but there was a significant reduction in the H/M ratio after exercise of ~16%. There also were significant increases in delta (23.8%) and alpha (18.1%) electrocortical activity after exercise. Mimasa et al. (1990) concluded that “These results confirm earlier resting EMG results and further suggest that tranquilizer effect of exercise may reside not only in the peripheral muscle motoneuron excitability, but also in the higher central nervous system” (p. 261).

Bulbulian and Bowles (1992) compared the effects of running on level and downhill treadmill surfaces on the H-reflex. Six males with a mean age of 27 (SD = 3.9) completed 3, 20-min conditions: treadmill running on a level surface (0% grade); treadmill running on a downhill surface (-10% grade); and quiet rest. The intensity of the treadmill running was 50%

$\dot{V}O_{2max}$. The H-reflex was measured in the soleus muscle immediately before and after the conditions, and 24 h after the conditions. There were no statistically significant differences in absolute H-wave, M-wave, or H/M ratio values across treatment conditions and time. Yet, when expressed as a percent change, the H/M ratio was increased from immediately before to after the control condition by ~13%. The H/M ratio was decreased from immediately before to after running on a level surface and downhill surface by ~9% and ~25%, respectively. The effect of running on the downhill surface on the H/M ratio was larger than running on the level surface. The H/M ratio did not differ from immediately before to 24 hours after exercise or control. The presumed cause of the greater inhibition with downhill treadmill running was the inhibition of the slower conducting Type I fibers by Type II fibers; Type II fibers are more readily activated with downhill running because of the eccentric nature of the exercise mode.

Avela et al. (1999) examined the effect of running a marathon on the H-reflex. Subjects included 6 male and 1 female who were experienced triathletes and reported a mean age of 28.7 years (range = 25 - 39 years). The H-reflex was measured in the right and left soleus muscle 1-hour before the marathon, and then immediately after, 2 h after, and 2, 4, and 6 d after the marathon. During the immediate after marathon measurement, a cuff was placed on the right leg to induce ischemia. There were no significant differences between measurements of the H-reflex in the right and left soleus muscle. Immediately after the marathon, the H/M ratio was decreased by ~71% and ~68% in the right and left legs, respectively. This reduction was related to a ~75% reduction in the maximal H-wave after the marathon; the maximal M-wave was reduced minimally. The H/M ratio remained reduced for 2 h after the marathon. The H/M

ratio on days 2, 4, and 6 was not different from values recorded before the marathon. The acute reduction in reflex sensitivity was concluded to be of reflex origin and attributable to two mechanisms: dis-facilitation of the gamma-loop and presynaptic inhibition of Ia terminals. The presynaptic inhibition was likely associated with mechanical and metabolic activation of type III and IV afferent fibers. The disfacilitation was presumably the result of a progressive withdrawal of spindle-mediated fusimotor support to the alpha motoneuron pool.

Most recently, Bulbulian (2002) examined the role of endogenous opioid release on the exercise-induced modulation of the soleus H-reflex. Subjects were 3 males and 3 females who were tested 6 times over a 4-week period. The 6 trials included high-intensity treadmill exercise at 75% $\dot{V}O_{2max}$ with placebo or naloxone, low-intensity exercise at 40% $\dot{V}O_{2max}$ (placebo or naloxone) and no exercise control (placebo or naloxone). The H-reflex in the soleus muscle was measured before and after exercise. Naloxone (10 mg) or isovolumic saline solution was administered double-blind (1 ml bolus) after recovery from exercise and before H-reflex measurement. There was a significant reduction in the H/M ratio for both exercise conditions, but naloxone did not influence the exercise-induced changes in the H/M ratio. Endogenous opioids do not appear to modulate the effect of exercise on the soleus H-reflex under the experimental conditions employed by Bulbulian (2002). There are several alternative explanations including low power associated with the small sample, an inadequate dose of naloxone (Thorén, Floras, Hoffmann, & Seals, 1990), and the timing of naloxone administration. Moreover, Bulbulian (2002) did not even demonstrate an effect of naloxone on the H-reflex in the control condition.

Limitations of Research on Acute Exercise and H-reflex

Perhaps the most important limitation of previous studies interpreting the post-exercise reduction of the soleus H-reflex as a tranquilizing effect of acute exercise has been a lack of concurrent self-report measurements of anxiety, muscle tension, or somatic symptoms related to anxiety. The H-reflex may indeed represent a neuromuscular substrate of anxiety. But, until researchers provide theoretical and experimental evidence linking changes in the H-reflex and self-reported symptoms of anxiety, those interpretations are speculative. The relationship between exercise, anxiety, and the H-reflex could be tested with an experimental manipulation of anxiety, perhaps using a pharmacological manipulation such as consumption of caffeine or intravenous injections of yohimbine (Uhde et al., 1984), followed by acute exercise. Such an experiment would clarify the nature of the relationships among exercise, anxiety, and the H-reflex.

The sample sizes of previous studies have been small and the samples are somewhat homogeneous. This makes inferential testing based on statistical analyses very difficult and limits generalizability of the results. Future studies should employ larger samples, perhaps even samples differing in anxiety proneness or other psychological and somatic conditions. This would clarify the magnitude of the effect of exercise on the H-reflex and whether the effect exists across diverse samples, particularly those with anxiety or somatic disorders.

Previous studies only have examined the H-reflex in the soleus muscle of the lower leg after cycling or jogging. To my knowledge, researchers have not examined the effect of arm ergometry on the soleus H-reflex, or examined leg ergometry on the H-reflex in the arm,

perhaps the FCR muscle. This line of research would clarify the specificity of the change in the H-reflex. Is the change in the H-reflex specific to the muscle-groups exercised? Or, does the effect of exercise on the H-reflex represent a more generalized response across muscle groups? This might have implications for local or central modulation of the H-reflex after exercise.

Only one study has examined the mechanism underlying exercise-induced modifications of the H-reflex (i.e., Bulbulian, 2002). This is a needed area of research. One approach, as previously mentioned, involves examining possible relationships between exercise-induced changes in the H-reflex and anxiety. Other approaches involve examining the influence of spinal processes such as presynaptic Ia inhibition, homosynaptic depression, recurrent inhibition, reciprocal inhibition, and Ib interneuron inhibition on the post-exercise reduction of the H-reflex. The effect of Type III and IV afferent fibers on the H-reflex is important as those fibers are likely activated during acute exercise (O'Connor & Cook, 1999), and can directly and indirectly impact Ia afferent fibers and alpha motoneurons through opioid mediated processes (Thorén et al., 1990). There also is a need to examine the role of the GABA and opioid neurotransmitter systems in the post-exercise reduction of the H-reflex; other neurotransmitter systems such as the serotonergic system warrant examination in exercise studies and in general. Those lines of research could clarify the underlying neurobiological nature of the post-exercise reduction of the H-reflex.

Exercise and the H-reflex: A Case for Modulation by Anxiety

To my knowledge, no experiment has been conducted examining the relationship between changes in the H-reflex and anxiety after acute exercise. Hence, a provisional basis

will be formulated for a link between changes in anxiety and the H-reflex. The provisional basis for this relationship will be generated based on the general literature examining influences on the H-reflex that might pertain to CNS states linked with anxiety, affective, and motor processes. The basis of the relationship between anxiety and the H-reflex already has been provided based on neuroanatomical substrates of anxiety (e.g., limbic system and noradrenergic and serotonergic brain stem nuclei) and pharmacological manipulations that presumably impact anxiety (e.g. GABA agonists).

Several studies have examined the effect of combined threat and application of a noxious painful stimulus (i.e., stress-induced analgesia) on the soleus H-reflex (Willer, 1980; Willer & Albe-Fessard, 1980; Willer & Ernst, 1985). Those studies used a stress procedure consisting of an auditory warning followed by random tactile or noxious foot-shocks (70-80 mA; 7-8 times pain threshold) . The stress procedure potentiated the amplitude of the H-reflex. For example, Willer (1980) reported that the H-reflex was increased by ~49% in response to the threat and application of a noxious painful stimulus across a 45-min period. Willer and Ernst (1985) reported that the H-reflex was increased by ~52%. The increase in the H-reflex was observed concurrently with changes in indices of autonomic activity (i.e., heart rate and respiration). If the threat and application of a noxious painful stimulus was perceived as threatening and thus increased anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), then those studies provided some support for the relationship between the H-reflex and anxiety. Yet, none of the studies measured changes in self-report symptoms of anxiety.

One study has examined the effect of viewing pictures differing in emotional valence and arousal on the H-reflex (Moulder, Bradley, Requin, & Lang, 1995). Twenty-seven subjects viewed 54 pictures from the International Affective Picture System, which consisted of 18 pleasant, 18 neutral, and 18 unpleasant pictures, as determined by normative valence ratings. Pictures were presented for 6 s and were separated by a variable time interval. The H-reflex was measured every 12 s, and was measured 500, 2000, or 4000 ms after picture onset and during the variable time interval between pictures. The amplitude of the H-reflex varied as a function of picture valence, but not arousal; this was opposite to the pattern of changes in the T-reflex (Bonnet, Bradley, Lang, & Requin, 1995). Unpleasant pictures were associated with a potentiated response relative to neutral pictures; pleasant pictures were associated with an attenuated response relative to neutral pictures. Hence, the amplitude of the H-reflex varied as a function of slide valence. This provides some evidence for affective modulation of the H-reflex.

Van Boxtel (1976) examined the relationship between alpha brain electrocortical activity and the H-reflex, and hypothesized that (1) no change in the H-reflex would be observed with stable alpha brain electrocortical activity, but that (2) a change in alpha brain electrocortical activity, indicating a decrease in brain cortical activity, would be correlated with a reduction in the H-reflex. This is important because elevated alpha brain electrocortical activity presumably represents a state of relaxed wakefulness (Brown, 1970; Nowlis & Kimaya, 1970). Van Boxtel (1976) reported that the H-reflex amplitude was related to the percentage of alpha activity in the ongoing EEG. Hence, Van Boxtel (1976) provided some

evidence that the H-reflex is modified by influences from the central nervous system, and that it correlates with presumed changes in states of relaxed wakefulness.

The H-reflex has been influenced by changes in other state-dependent mental processes (Schieppati, 1987). For example, the H-reflex has been increased during mental alertness (Bathien & Hugelin, 1969) and attention (Bathien & Morin, 1972). Mental effort associated with task demands has influenced the amplitude of the H-reflex (Brunia, 1973; Grillon & Zarifian, 1985). Some researchers have demonstrated that the H-reflex amplitude decreased in the early stages of sleep, and was completely abolished during REM sleep (Hodes & Dement, 1964; Hodes & Gribetz, 1962a, 1962b; Paillard, 1959; Shimizu et al., 1966). The H-reflex has been reported to change in response to mental simulation of an action (e.g., Bonnet, Decety, Jeannerod, & Requin, 1997; Oishi, Kimura, Yasukawa, Yoneda, & Maeshima, 1994).

To my knowledge, one study has included a measure of mood while measuring the H-reflex. Raglin, Koceja, Stager, and Harms (1996) examined the effect of seasonal changes in training load on mood, the H-reflex, and physical power in 12 collegiate swimmers. As swimming distance increased during intensive training, there was an increase in mood disturbance while there was a decrease in the H-reflex. With reductions in swimming distance during taper, there was a decrease in mood disturbance while there was an increase in the H-reflex. But, those changes were not significantly correlated. The lack of a significant correlation may be indicative of low statistical power associated with a sample of 12 subjects, or an actual lack of a relationship between changes in mood and the H-reflex.

Summary

Previous meta-analyses (Landers & Petruzzello, 1994; Petruzzello et al., 1991) have indicated that self-ratings of anxiety are reduced by $\frac{1}{4}$ to $\frac{1}{2}$ of a standard deviation after exercise; physiological variables have been reduced by $\frac{1}{2}$ standard deviation. Most research has been conducted with individuals characterized by low pre-exercise anxiety scores (O'Connor et al., 2000). This likely has resulted in small changes in anxiety after exercise and can be minimized by using subjects who are more prone to anxiety or experimentally manipulating anxiety scores, perhaps with caffeine ingestion. Previous researchers generally have ignored the concurrent effects of acute exercise on symptoms of anxiety and neuromuscular variables. This is surprising because muscle tension, trembling, twitching, feeling shaky, and muscle aches and soreness are common features of anxiety disorders (American Psychiatric Association, 2000).

Researchers have speculated that the post-exercise reduction of the H-reflex recorded in the soleus muscle reflects a tranquilizing, muscle relaxing, or anxiolytic effect of acute exercise (e.g., Bulbulian & Darabos, 1986; de Vries et al., 1981; Petruzzello et al., 1991). Yet, previous research did not include measures self-reported anxiety or provide an argument based on neuroanatomical or neurobiological evidence and experimental studies for interpreting the reduced H-reflex as a measure of anxiety or muscle tension. Hence, this review of the literature focused on the H-reflex.

The H-reflex is an electrically evoked spinal reflex with a long history. After its initial discovery by Hoffmann (1918, 1922) and refinement by Magladery and McDougal (1951),

researchers increasingly examined its many neuroanatomical and neurobiological influences. Some of the primary neuroanatomical influences are located within the spinal cord (e.g., presynaptic Ia afferent inhibition); additional influences originate in regions of the brain stem and brain associated with motor and affective processes (e.g., motor cortex). The primary neurobiological influences are GABA and opioids, but the research on neurobiological influences is not comprehensive; there may indeed be other neurobiological influences including serotonin and norepinephrine (Jankowska et al., 2000), as based on neuroanatomical findings.

The H-reflex has been examined under many experimental conditions. Of central interest, researchers have examined the effect of acute exercise on the amplitude of the H-reflex in the soleus muscle. Those studies have found that the soleus H-reflex is reduced after an acute bout of running or jogging; some of the studies have interpreted the reduction as a tranquilizing effect of acute exercise. Yet, none of the studies included a concurrent measure of anxiety or somatic symptoms, or provided a compelling argument for affective influences on the H-reflex.

There is some evidence possibly linking the H-reflex with affective and other mental states. The H-reflex covaried with conditions of threat and application of a noxious stimulus, the viewing of pictures differing in positive and negative valence, and relaxed wakefulness. There even are influences on the H-reflex associated with mental alertness, attention, and effort; stages of sleep; and mental simulation of an action.

Two studies were conducted to examine the relationship between changes in anxiety and the H-reflex after acute exercise. The 1st study examined the effect of exercise on state anxiety and the soleus H-reflex using individuals with low or high trait anxiety. The 2nd study

examined the effect of exercise on state anxiety and the soleus and FCR H-reflex in individuals whose anxiety was increased with a large dose of caffeine. Those studies clarified the nature of the relationships among exercise, anxiety, and the H-reflex.

CHAPTER 3

EFFECTS OF CYCLING EXERCISE ON STATE ANXIETY AND THE SOLEUS H- REFLEX AMONG MALES WITH LOW OR HIGH TRAIT ANXIETY ¹

¹Motl, R.W., O'Connor, P.J., & Dishman, R.K. Submitted to Psychophysiology

Abstract

The present study examined the effects of low and high intensity cycling exercise on state anxiety and the H-reflex among males having low ($n = 20$) or high ($n = 20$) trait anxiety. Participants completed measures of state anxiety and underwent elicitation and recording of the H-reflex in the soleus muscle before and 10 minutes after three 20-minute conditions: (1) quiet rest; (2) cycling at 40% $\dot{V}O_{2peak}$; and (3) cycling at 70% $\dot{V}O_{2peak}$. We found that (1) exercise and quiet rest resulted in similar reductions of state anxiety, and the magnitude of the reductions was larger for males having high trait anxiety than low trait anxiety; (2) exercise, but not quiet rest, resulted in a reduction of the H-reflex; the magnitude of the reduction did not differ between males having low or high trait anxiety; and (3) reductions of self-reported state anxiety were unrelated to reductions of the H-reflex across all three conditions. Contrary to prevailing opinion, the post-exercise reduction in the H-reflex reported by previous researchers and in the present study appears to be unrelated to self-reported anxiety after exercise.

Keywords: Hoffmann reflex, trait anxiety, state anxiety, acute exercise

Introduction

Exercise is an effective method of reducing symptoms of anxiety (Dishman, 1998; O'Connor, Raglin, & Martinsen, 2000; Thayer, Newman, McClain, 1994) and several physiological variables that are potential correlates of anxiety. The mean effect of acute exercise on symptoms of anxiety has approximated $\frac{1}{4}$ to $\frac{1}{2}$ standard deviation (SD; Landers & Petruzzello, 1994; Petruzzello, Landers, Hatfield, Kubitz, & Salizar, 1991). The mean effect of acute exercise on putative physiological correlates of anxiety has approximated $\frac{1}{2}$ SD (Petruzzello et al., 1991). Most studies that have examined the concomitant effects of acute exercise on symptoms of anxiety and physiological correlates have measured either blood pressure or brain electrocortical activity (e.g., Raglin & Morgan, 1987; Youngstedt, Dishman, Cureton, & Peacock, 1993). We are aware of no previous reports that have examined the concomitant effects of acute exercise on symptoms of anxiety and measures of neuromuscular activity, which is a prominent feature of anxiety disorders.

The Hoffmann reflex (i.e., H-reflex) has been viewed as a neuromuscular substrate of anxiety that is influenced by acute exercise (Bulbulian & Darabos, 1986; deVries et al., 1981; Petruzzello et al., 1991). The H-reflex is a muscle reflex commonly evoked through percutaneous electrical stimulation of the tibial nerve and recorded in the soleus muscle using electromyography (EMG; Hugon, 1973; Magladery & McDougal, 1950). It measures either the efficacy of synaptic transmission between the Ia afferent and the alpha motoneuron (Capaday, 1997) or alpha motoneuron excitability (Angel & Hofmann, 1963). Supra-spinal factors involved in motor and affective processes can affect the H-reflex through direct and indirect influences on Ia afferents and/or alpha motoneurons within the sacral spinal cord

(Holstege & Kuypers, 1987; Rotto-Perceland, Wheeler, Osorio, Platt, & Loewy, 1992; Táboríková, 1973). The H-reflex has been reported to be affected by the anticipation and application of electrical shock (Willer, 1980; Willer & Albe-Fessard, 1980; Willer & Ernst, 1986), the viewing of pictures differing in emotional content (Moulder, Bradley, Requin, & Lang, 1995), mental imagery (Bonnet, Decety, Jeannerod, Requin, 1997), and drugs that influence anxiety and motor tension (Eke-Okoro, 1982; Inghilleri, Berardelli, Marchetti, & Manfredi, 1996; Ørsnes, Crone, Krarup, Petersen, & Nielsen, 2000; Palmeri et al., 1999; Sandrini et al., 1999; Timmann, Plummer, Schwarz, & Diener, 1995).

We are aware of seven studies that have examined the effect of acute exercise on the H-reflex (Avela et al., 1999; Bulbulian, 2002; Bulbulian & Bowles, 1992; Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Those studies reported that acute bouts of cycling and jogging reduced the magnitude of the H-reflex recorded in the soleus muscle by about 1 SD (90% CI = 0.63 - 1.37). Five of the studies interpreted the reduced H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian, 2002; Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990), but none of the studies included a concurrent measure of state anxiety when recording the H-reflex. Hence, it is unclear whether exercise-induced anxiolysis is a concomitant of the post-exercise reduction of the H-reflex.

One major limitation of previous research into the effects of acute exercise on anxiety has been that study participants were characterized by low pre-exercise state anxiety scores. This “floor effect” has resulted in small effects of acute exercise on anxiety (O’Connor et al., 2001; Tieman, Peacock, Cureton, & Dishman, 2001). One strategy for minimizing potential floor effects is to recruit volunteers characterized by high or low trait anxiety. Groups of this

type likely will differ in state anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) and allow for the relationships among exercise, anxiety, and the H-reflex to be examined across an adequate range of anxiety scores.

The present study examined the effects of low and high intensity cycling exercise on self-reported state anxiety and the soleus H-reflex in males characterized by low or high trait anxiety scores. We hypothesized that low and high intensity cycling exercise would reduce state anxiety and the H-reflex, and that the reduction of state anxiety would be correlated with post-exercise reductions of the H-reflex. We also expected that the effects of cycling exercise on state anxiety and the H-reflex would be larger in males who reported high trait anxiety scores relative those reporting low trait anxiety scores.

Methods

Participants

Male students ($N = 297$) in psychology and exercise science classes at the University of Georgia completed a measure of trait anxiety (Spielberger et al. 1983) during an initial screening phase of the study. We sought a sample with trait anxiety scores that exceeded ± 1 SD of the male college-aged normative value (38 ± 9 ; Spielberger et al. 1983).

Of the 297 students who participated in the screening, 107 met the inclusion criteria and were eligible to participate in the present study. Fifty of the 107 individuals volunteered to participate in the study, and complete data were obtained from 40 of the 50 volunteers. Ten of the 50 volunteers either did not exhibit a measurable H-reflex ($n = 4$) or reported smoking ($n = 2$), using anti-depressant medication ($n = 2$), or the presence of disease contraindicated for the completion of maximal exercise ($n = 2$) and were excluded from the study. Of the 40 volunteers

who completed the study, those who reported trait anxiety scores ≤ 29 were categorized as low anxious ($n = 20$) and those who reported trait anxiety scores ≥ 47 were categorized as high anxious ($n = 20$).

Selected subject characteristics are provided in Table 3.1. Independent samples t-tests indicated that the low and high trait anxiety groups differed in trait anxiety scores and age. Neither group was highly trained and there were no statistically significant differences between groups in physical activity and fitness.

Measures

State-Trait Anxiety Inventory. The State-Trait Anxiety Inventory (STAI) is a self-report measure of state (STAI Form Y1) and trait (STAI Form Y2) anxiety (Spielberger et al., 1983). The STAI contained 40 items; 20 items measure state anxiety and 20 items measure trait anxiety. The items were rated on a 4-point scale anchored by Not at all (1) and Very much so (4). The STAI has acceptable internal consistency and test-retest reliability (Spielberger et al., 1983). There is an abundance of correlational and experimental evidence supporting the validity of the inference that scores on the STAI reflect anxiety (Spielberger et al., 1983).

Seven-day physical activity recall. Estimates of weekly energy expenditure were calculated using a seven-day physical activity recall interview (7-d PAR) (Blair, 1984). Evidence supports the reliability and validity of scores from the seven-day physical activity recall interview for college students (Dishman & Steinhardt, 1988).

Perceived exertion scale. Perceptions of exertion were measured using Borg's (1998) 15-point, 6-20 category rating scale. The scale is anchored by Very, very light (7) and Very, very hard (19), and it has well established reliability and validity (Borg, 1998).

Peak oxygen consumption ($\dot{V}O_{2peak}$). To measure $\dot{V}O_{2peak}$, participants performed an incremental exercise test on an electronically-braked, computer-driven cycle ergometer (Minjhardt, model KEM-3) using standard procedures (Breus & O'Connor, 1998). Initially, participants were fitted to the cycle ergometer, and provided with instructions for the perceived exertion scale (Borg, 1998). After inserting a mouthpiece for collecting expired gases, the participants undertook a 5-min warm-up at 25 W. The initial workrate for the exercise test was 50 W, and the workrate continuously increased at a rate of 24 W·min⁻¹. Using an open-circuit spirometry system (SensorMedics Metabolic Cart, model 2900), ventilation (\dot{V}_E), oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), respiratory exchange ratio (RER), and workrate were measured every 20 s. Heart rate was continuously displayed using a UNIQ heart rate monitor (Polar Electro Oy, Kempele, Finland). Heart rate and perceptions of exertion were recorded every minute. $\dot{V}O_{2peak}$ was defined by three criteria: (1) heart rate within 10 beats·min⁻¹ of age-predicted maximum; (2) respiratory exchange ratio ≥ 1.10 ; or (3) perceived exertion > 18 . Ventilatory threshold (\dot{V}_T) was estimated based on plots of $\dot{V}_E / \dot{V}O_2$ and $\dot{V}_E / \dot{V}CO_2$ as a function of time (Davis, Frank, Whipp, & Wasserman, 1979).

H-reflex. The H-reflex was elicited and recorded using a standardized protocol (Hugon 1973). Participants were prepared for surface EMG measurements of soleus muscle activity and percutaneous electrical stimulation of the tibial nerve in the right leg. The skin surface was shaved, and abraded and cleaned using fine grain sand-paper and alcohol swabs. Two 1-cm Ag-AgCl surface electrodes (MED associates, Georgia, VT) with Grass EC2 cream (Astro-Med, Inc., West Warwick, RI) were attached 3-cm apart aligned along the midline of the right soleus 2-3 cm below the gastrocnemius muscles (i.e., bipolar configuration). Another 1-cm Ag-

AgCl surface electrode (MED associates, Georgia, VT) with Grass EC2 cream (Astro-Med, Inc., West Warwick, RI) was attached superior to the lateral malleolus. The electrodes were outlined with semi-permanent marker, secured with 3M Micropore tape, and connected to a GRASS P511 amplifier (Astro-Med, Inc., West Warwick, RI). The amplifier was connected to an oscilloscope (Kenwood CS-8010; Kenwood TMI, Corp., Yokohama, Japan) and a data acquisition system (GRASS PolyVIEW; Astro-Med, Inc., West Warwick, RI).

Round (2.50 cm) and rectangular (3.75×4.50 cm) carbon rubber stimulating electrodes (Medtronic, Inc., Minneapolis, MN) with Tac gel (Pharmaceutical Innovations, Inc., Newark, NJ) were placed above the tibial nerve in the popliteal fossa and superior to the patella (i.e., unipolar configuration). The electrodes were outlined with semi-permanent marker, secured with 3M Micropore tape and 3M Coban, and connected to a constant current unit (GRASS CCU1A; Astro-Med, Inc., West Warwick, RI) in-line with a stimulus isolation unit (GRASS SIU8TB; Astro-Med, Inc., West Warwick, RI) and a somatosensory stimulation unit (GRASS S10DSCM). There was a Velcro® circumferential ground electrode between the stimulating and recording electrodes (GRASS F-E10SG1; Astro-Med, Inc., West Warwick, RI).

Impedance of the stimulating and recording electrodes was measured using an electrode impedance meter (GRASS EZM 4; Astro-Med, Inc., West Warwick, RI) and maintained below 5 k Ω . The average impedance of the recording electrodes across time, conditions, and groups was 0.62 ± 0.19 k Ω . The average impedance of the stimulating electrodes was 2.12 ± 1.02 k Ω .

The H-reflex procedure was performed in a thermoneutral ($23 \pm 1^{\circ}\text{C}$, $\sim 40\%$ relative humidity), sound dampened (100 db less than ambient), electrically shielded, earth-grounded chamber. Participants sat on a chair that controlled head, body, and joint positions. The hip and knee joint angles were 120° and 160° , respectively. The chair also had a rotating platform for the right foot. The rotating platform was connected to a pneumatic actuator (RLF06A-SAP-AA00 Round Line Actuator, Norgren, Littleton, CO) with an air pressure regulator (R21 Dial AirTM Regulator; Wilkerson, Englewood, CO) set at 15 psi to control the activity of the soleus muscle and to a potentiometer (WPM 18-09, Servo Pot; Omega, Stamford, CT) with a digital display (DP25-E Process Panel Meter; Omega, Stamford, CT) to monitor the ankle joint angle. Participants maintained the angle of the ankle joint between $88-92^{\circ}$ prior to each stimulus. Hence, the chair provided a standardized preparation for eliciting and recording the H-reflex within and between the three conditions.

Rectangular 1-ms impulses were delivered to the tibial nerve every 8 s, and the resulting soleus muscle activity was recorded via EMG. The EMG signal was sampled at a rate of 1 kHz, bandwidth filtered from 3 Hz to 1 kHz, and amplified by 1,000. The strength of the impulse was progressively increased to form a stimulus response curve for the H-reflex and M-wave. Five electrical impulses were provided for each stimulus increment; this number has yielded a reliable measure of the H-reflex (Hopkins, Ingersoll, Cordova, & Edwards, 2000). The five electrical impulses also yielded reliable measures of the H-reflex (range of Intraclass Correlation Coefficients [ICCs] = .95 - .97; \underline{M} = .96) and M-wave (range of ICCs = .95 - .97; \underline{M} = .96) across time, conditions, and groups in the present study.

The maximal H-reflex and M-wave were retrieved from an analysis of the stimulus response curve, and averages were computed from the five consecutive responses associated with the same electrical stimulus increment. The maximal H-reflex and M-wave were employed to compute the H/M ratio. The H/M ratio represents the magnitude of the reflex (i.e., H-reflex) relative to the recruitment of all motor axons (i.e., M-wave). Hence, the H/M ratio represents an estimate of the proportion of the motoneuron pool recruited by the muscle reflex (Pierrot-Deseilligny & Mazevet, 2000).

The current applied during stimulation of the nerve was measured using a current probe amplifier (Tektronix AM 503A; Tektronix, Inc., Beaverton, OR) connected to an oscilloscope (Kenwood CS-8010; Kenwood TMI, Corp., Yokohama, Japan). The average and peak current across time, conditions, and groups were 47.26 ± 12.22 mA and 87.27 ± 19.41 mA, respectively. The number of stimuli applied to the nerve was 48.28 ± 12.32 . The time it took to complete the H-reflex testing was 6.50 ± 1.50 min.

Procedures

The procedures were approved by the University of Georgia Institutional Review Board. Participants completed one day of baseline testing and three days of experimental testing. The three days of experimental testing were separated by 24 to 72 h and completed in a counter-balanced order. The time of day in which experimental testing was conducted was standardized within (± 1 h), but not between, subjects. Participants were asked to abstain from exercising, eating, drinking alcohol or caffeinated beverages, and using tobacco for at least 2 h before experimental testing.

Baseline day. Participants read and signed an informed consent document and completed a pre-exercise medical history questionnaire. The researcher then performed a 7-d PAR interview. Next, participants performed the incremental exercise test.

After the exercise test, participants were prepared for recording soleus muscle activity and electrical stimulation of the tibial nerve, moved to a chamber and placed in a seated position, and underwent measurements of the H-reflex. Participants completed the measure of state anxiety immediately before and after eliciting the H-reflex. The baseline day data were not analyzed. The testing was undertaken to familiarize subjects with the testing protocol and ensure that subjects exhibited a measurable H-reflex.

Experimental test days. Participants were prepared for recording soleus muscle activity and electrical stimulation of the tibial nerve, moved to the environmental chamber and placed in a seated position, and underwent measurements of the H-reflex. Participants completed the measure of state anxiety immediately before and after eliciting the H-reflex.

Participants then walked 10 m to an adjacent exercise room, sat on a cycle ergometer, and completed one of the three 20-minute conditions: (1) quiet rest (i.e., seated on the cycle ergometer in the same room that exercise was performed); (2) cycling at 40% $\dot{V}O_{2peak}$; and (3) cycling at 70% $\dot{V}O_{2peak}$. Heart rate and perceptions of exertion were recorded every 5 minutes. Expired gases were analyzed using open-circuit spirometry after 5 and 15 minutes to verify the exercise intensity. Minor adjustments to the workrate were undertaken to maintain the appropriate exercise intensity. The physiological and perceptual responses to the three conditions for males in the low and high trait anxious groups are provided in Table 3.2.

After quiet rest or exercise, participants returned to the environmental chamber, were placed in a seated position, and underwent measurements of the H-reflex; the procedure was initiated 10 minutes after completion of the condition. Participants completed the measure of state anxiety immediately before and after eliciting the H-reflex.

Data Analysis

The primary dependent variables were state anxiety and the maximal H-reflex, maximal M-wave, and H/M ratio. State anxiety data were analyzed with a 2 (Time: pre-post condition) \times 2 (Stimulation: pre-post H-reflex) \times 3 (Condition: quiet rest, 40% $\dot{V}O_{2peak}$, & 70% $\dot{V}O_{2peak}$) \times 2 (Groups: low & high trait anxiety) mixed model ANOVA based on the multi-variate F-statistic (Pillai-Bartlett). Measurements of the H-reflex, M-wave, and H/M ratio were analyzed with similar 2 (Time) \times 3 (Condition) \times 2 (Groups) mixed model ANOVAs based on the multi-variate F-statistic (Pillai-Bartlett) (Keselman, 1998). Effect sizes associated with F-statistics were expressed as eta-squared (η^2). Effect sizes based on mean differences were expressed as Cohen's d (Cohen, 1988). The Greenhouse-Geisser epsilon (ϵ) was reported when the sphericity assumption was violated (i.e., if Mauchly's test of sphericity was statistically significant at $p < .05$). The family-wise error rate was controlled using the Bonferroni adjustment when tests of simple effects were conducted (Keselman, 1998).

The relationship between changes in state anxiety and the H/M ratio was examined using a Group \times Condition mixed model ANCOVA on pre-post condition change scores for the H/M ratio with pre-post condition change scores for state anxiety as a time varying covariate (Winer, Brown, & Michels, 1991). The result of this analysis was compared with a Group \times Condition mixed model ANOVA on only pre-post condition change scores for the

H/M ratio. Changes in the univariate F-statistic and η^2 were indicative of a difference between models, and hence an effect of state anxiety on the H-reflex; the univariate F-statistic was compared across models (Winer et al., 1991) as the multi-variate F-statistic was unavailable with the mixed model ANCOVA that included the time varying covariate. We also examined the relationship between self-reported anxiety and the H/M ratio using partial correlation coefficients on post-condition anxiety and the H/M ratio controlling for the associated pre-condition values.

Results

State Anxiety: Exercise vs. Quiet Rest

Results of a $2 \times 2 \times 3 \times 2$ mixed model ANOVA on state anxiety scores indicated a significant Group \times Time interaction, $F(1, 38) = 9.50, p < .005, \eta^2 = .20$. The other interactions were not statistically significant ($p > .05$). As illustrated in Figure 3.1, state anxiety scores decreased more from before to after all three conditions combined for males having high trait anxiety ($d = -0.31$) than males having low trait anxiety ($d = -0.14$).

H-reflex, M-Wave, and H/M Ratio: Exercise vs. Quiet Rest

The results of a $2 \times 3 \times 2$ mixed model ANOVA on maximal H-reflex values indicated that there was a significant Condition \times Time interaction, $F(2, 37) = 17.29, p < .0001, \eta^2 = .48$. The other interactions were not statistically significant ($p > .05$). As illustrated in Figure 3.2a, the H-reflex did not change from before to after the quiet rest condition ($d = 0.01$), but it decreased from before to after the 40% $\dot{V}O_{2peak}$ ($d = -0.35$) and 70% $\dot{V}O_{2peak}$ ($d = -0.42$) conditions.

In contrast to the H-reflex, the results of a $2 \times 3 \times 2$ mixed model ANOVA on maximal M-wave values indicated that there was not a significant Condition \times Time interaction, $F(2, 37) = 1.70$, $p = .20$, $\eta^2 = .08$. The other interactions also were not statistically significant ($p > .05$). As illustrated in Figure 3.2b, the M-wave did not change significantly from before to after the quiet rest ($d = -0.05$) or the 40% $\dot{V}O_{2peak}$ ($d = -0.01$) and 70% $\dot{V}O_{2peak}$ ($d = 0.07$) conditions.

The results of a $2 \times 3 \times 2$ mixed model ANOVA on H/M ratio values indicated a significant Condition \times Time interaction, $F(2, 37) = 19.89$, $p < .0001$, $\eta^2 = .52$, $\epsilon = .87$. The other interactions were not statistically significant ($p > .05$). As illustrated in Figure 3.2c, H/M ratio values increased slightly from before to after quiet rest ($d = 0.11$). The H/M ratio decreased from before to after the 40% $\dot{V}O_{2peak}$ ($d = -0.47$) and 70% $\dot{V}O_{2peak}$ ($d = -0.58$) conditions. The histograms of pre-post condition change scores for the H/M ratio in Figure 3.3 further illustrates the differential changes across conditions.

Relationship Between Changes in Anxiety and the H-reflex

The results of the 2×3 mixed model ANCOVA on pre-post condition change scores for the H/M ratio with pre-post condition state anxiety change scores as a time varying covariate indicated a significant Condition main effect, $F(2, 75) = 26.56$, $p < .0001$, $\eta^2 = .42$. The 2×3 mixed model ANOVA on only pre-post condition change scores for the H/M ratio also indicated a significant Condition main effect, $F(2, 76) = 28.25$, $p < .0001$, $\eta^2 = .43$. Because the magnitude of the univariate F-statistic and η^2 for the Condition main effects did not differ between analytic models (Winer et al., 1991), changes in self-reported anxiety were unrelated to changes in the H/M ratio across the conditions.

We also performed partial correlation analyses on the post-condition measures of state anxiety and the H/M ratio controlling for pre-condition values across the three conditions. The partial correlations between post-condition state anxiety scores and H/M ratio were not statistically significant: quiet rest ($r = .05$, $p = .76$), 40% $\dot{V}O_{2peak}$ ($r = .26$, $p = .12$), and 70% $\dot{V}O_{2peak}$ ($r = .24$, $p = .14$). The scatter-plot of change scores for state anxiety and the H/M ratio with lines-of-best-fit per condition is presented in Figure 3.4. The scatter-plot supports the lack of an association between changes in anxiety and the H/M ratio. Hence, the change in self-reported anxiety was unrelated to the change in the H/M ratio across the three conditions.

Discussion

Low and high intensity exercise and quiet rest resulted in similar reductions of state anxiety, and the reductions of state anxiety were larger for high trait anxious males than low trait anxious males. In contrast, only low and high intensity exercise, but not quiet rest, resulted in reductions of the H-reflex and the H/M ratio; the magnitude of the reductions did not differ between males having low or high trait anxiety. The reduction of state anxiety was unrelated to the reduction of the H/M ratio across all three conditions. Contrary to prevailing opinion (Petruzzello et al., 1991), the post-exercise reduction in the H-reflex reported by previous researchers (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990) and observed in the present study appears to be unrelated to changes in self-reported state anxiety after exercise.

Exercise and Anxiety

Twenty minutes of low and high intensity cycling exercise and quiet rest resulted in similar reductions of state anxiety. The magnitude of the reduction was small ($d = -0.26$), but consistent with the mean effect ($\sim 1/4$ SD) reported in a meta-analysis by Petruzzello et al. (1991).

The effect of low and high intensity cycling exercise and quiet rest on state anxiety was moderated by trait anxiety. High trait anxious males reported a larger reduction in state anxiety ($d = -0.31$) than the low trait anxious males ($d = -0.14$). The likely explanation for the difference involved the pre-condition anxiety scores (Breus & O'Connor, 1998; O'Connor et al., 2001; Tieman et al., 2001). The mean pre-condition state anxiety score for the high trait anxious males was 35.71; it was 23.57 for the low trait anxious males. Hence, the high trait anxious males had room to improve in state anxiety scores, but the low trait anxious males had relatively little room to improve; the lowest possible score was 20 (Spielberger et al., 1983).

Quiet rest was as effective for reducing anxiety as low and high intensity cycling exercise. This was not surprising. Other studies have reported similar effects of acute exercise and quiet rest on anxiety (Bahrke & Morgan, 1978; Raglin & Morgan, 1987; Smith, O'Connor, Crabbe, & Dishman, in press). The most likely explanation for the similar changes in anxiety with exercise and quiet rest is the "time-out" hypothesis (Bahrke & Morgan, 1978). This hypothesis suggests that time taken out from one's daily routine promotes a break from whatever is causing an individual's problems or worries (Bahrke & Morgan, 1978; Breus & O'Connor, 1998).

Exercise and H-reflex

The H/M ratio was reduced after low ($d = -0.47$) and high ($d = -0.58$) intensity exercise; quiet rest resulted in a slight increase in the H/M ratio ($d = 0.11$). Our findings of a reduced H-reflex were comparable with previous research interpreting the post-exercise reduction of the H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Those researchers reported that 20 minutes of low to high intensity cycling or jogging exercise resulted in approximately 13-22% reductions of the H/M ratio. We found that 20 minutes of low and high intensity cycling exercise resulted in 20 and 27% reductions of the H/M ratio, respectively.

Exercise, Anxiety, and H-reflex

Previous researchers have interpreted the post-exercise reduction of the H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Our results do not support this interpretation. We observed that the reduction of self-reported anxiety was unrelated to the reduction of the H/M ratio across three conditions of low and high intensity exercise and quiet rest. The lack of an association was supported in two sets of analyses and by the scatterplot of change scores for self-reported anxiety and the H/M ratio (Figure 3.4). Moreover, trait anxiety was unrelated to the magnitude of the H-reflex or H/M ratio in the present study. The post-exercise reduction in the H-reflex reported by previous researchers (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990) and in the present study appears to be unrelated to changes in self-reported anxiety after exercise. Anxiety still might be an explanation for the post-exercise reduction in the H-reflex because the relationship was examined across a truncated range of

state anxiety change scores. By recruiting individuals differing in trait anxiety we were able to examine the relationship between the H-reflex and anxiety across a broad range of anxiety change scores, but there still was a truncated distribution of state anxiety change scores (See Figure 3.4). Hence, experimentally increasing and decreasing anxiety and measuring the effect of exercise on the H-reflex would provide a stronger test of the relationships among exercise, anxiety, and the H-reflex.

There are several possible alternative explanations for the post-exercise reduction in the H-reflex. One possibility is that the cyclical and repetitive activation of the leg musculature during cycling or jogging exercise results in a post-exercise inhibition of the Ia afferents and/or alpha motoneurons involved in the soleus H-reflex. Four spinal pathways that are involved in the inhibition of Ia afferents and/or alpha motoneurons are good candidates for such an effect (Capaday, 1997; Pierrot-Deseilligny & Mazevet, 2000). These pathways include (1) Ib inhibitory interneurons which are co-activated by Ia afferents from the soleus muscle; (2) Renshaw cells activated by discharge of alpha motoneurons projecting to the soleus muscle (i.e., recurrent inhibition); (3) reciprocal Ia inhibition of alpha motoneurons through activation of the tibialis anterior (i.e., antagonist muscle); and (4) presynaptic inhibition of Ia terminals through activation of the tibialis anterior muscle.

Another possibility is that cycling or jogging exercise activates Type III and IV afferent nerve endings and fibers originating in the soleus and other leg muscles. Type III and IV myelinated and unmyelinated afferent fibers originate from nociceptive and non-nociceptive nerve endings located primarily in the walls of arterioles and the surrounding connective tissue of skeletal muscles. Type III nerve endings are primarily responsive to mechanical pressure;

Type IV nerve endings are polymodal and responsive to temperature, mechanical pressure, and biochemical by-products of muscle metabolism. Cycling exercise near ventilatory threshold likely activates Type III and IV nerve endings (Mitchell & Schmidt, 1996), and the associated afferent fibers have powerful inputs to terminals of Ia afferents and to Ib inhibitory interneurons within the spinal cord (Rossi, Decchi, Ginanneschi, 1999; Rossi, Decchi, Dami, Della Volpe, & Groccia, 1999). Hence, activation of type III and IV nerve endings and fibers during exercise might lead to presynaptic inhibition of the Ia afferent terminals or activation of Ib inhibitory interneurons involved in the soleus H-reflex that lasts into the post-exercise period.

We are unaware of research that has examined the effects of cycling or jogging exercise on inhibition of the Ia afferent and/or alpha motoneuron pathways to explain the post-exercise reduction of the H-reflex. Recent research has indicated that simultaneous and repeated electrical stimulation and/or mechanical stretching of the calf muscle for 1 h reduces the soleus H-reflex (Avela, Kyröläinen, & Komi, 1999, 2001), and this research has implicated the aforementioned possibilities in explaining the post-condition reduction of the H-reflex.

Other possibilities include effects of cycling or jogging exercise on (1) interneurons and neurons within the motor cortex that project to soleus alpha motoneurons and (2) core body and spinal cord temperature. Cycling or jogging exercise might lead to an inhibition of interneurons and neurons within the motor cortex that provide excitatory inputs to soleus alpha motoneurons (Mercuri, Wassermann, Ikoma, Samii, & Hallett, 1997). The post-exercise reduction of the H-reflex also might be related to an increase in core body temperature during exercise. This likely is not a viable explanation as there is a linear and proportional increase in core temperature as a function of the exercise intensities we employed (Saltin & Hermansen,

1966). We did not observe a similar linear and proportional change in the H-reflex from quiet rest to 40% $\dot{V}O_{2peak}$ and 40% $\dot{V}O_{2peak}$ to 70% $\dot{V}O_{2peak}$. Hence, core body temperature does not appear to explain the post-exercise reduction of the H-reflex.

Conclusions

We found that (1) exercise and quiet rest resulted in a similar reduction of state anxiety, and the magnitude of the reduction was larger for males having high trait anxiety compared to those having low trait anxiety; (2) exercise, but not quiet rest, resulted in a reduction of the H-reflex, but the magnitude of the reduction did not differ according to trait anxiety; and (3) reductions of state anxiety were unrelated to reductions of the H-reflex across all three conditions. Future studies should experimentally increase and decrease anxiety symptoms and measure the effect of exercise on the H-reflex. This would provide a stronger test of the relationships among exercise, anxiety symptoms, and the H-reflex. Researchers also should examine the effects of cycling or jogging exercise on inhibition of the Ia afferent and/or alpha motoneuron pathways to explain the post-exercise reduction of the H-reflex. This could be accomplished by testing the effects of cycling exercise on presynaptic Ia inhibition or reciprocal Ia inhibition between antagonist muscles (e.g., conditioning-testing paradigms; Capaday, 1997) or by examining the effects of cycling exercise on the H-reflex recorded in the soleus muscle and the flexor carpi radialis muscle.

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Table 3.1

Characteristics of the males in the low (n = 20) and high (n = 20) trait anxious groups.

Characteristic	Low Trait Anxious	High Trait Anxious	P-value
STAI Form Y-2	26.40 ± 1.79	51.20 ± 4.06	0.0001
Age (y)	22.25 ± 3.80	20.35 ± 1.66	0.047
Height (cm)	179.81 ± 5.12	178.24 ± 7.32	0.437
Mass (kg)	73.88 ± 8.84	76.87 ± 12.46	0.387
7-d PAR (kJ·kg ⁻¹ ·wk ⁻¹)	138.40 ± 49.12	134.27 ± 50.46	0.794
$\dot{V}O_{2peak}$ (ml·kg ⁻¹ ·min ⁻¹)	48.91 ± 8.22	44.30 ± 8.88	0.097
$\dot{V}O_{2peak}$ (l·min ⁻¹)	3.59 ± 0.57	3.35 ± 0.59	0.215
HR _{peak} (beats·min ⁻¹)	184.05 ± 12.32	183.90 ± 11.06	0.968
RER _{peak}	1.18 ± 0.07	1.20 ± 0.08	0.451
RPE _{peak}	19.05 ± 0.83	18.70 ± 0.86	0.198
\dot{V}_T (% $\dot{V}O_{2peak}$)	68.13 ± 6.54	65.84 ± 5.37	0.235

Note. Tabled values are mean ± standard deviation. Two-tailed p-values are from independent samples t-tests. STAI Form Y-2 = State-Trait Anxiety Inventory Form Y-2 (Trait portion). 7-d PAR = Seven-day Physical Activity Recall. $\dot{V}O_{2peak}$ = Peak oxygen consumption. HR_{peak} = Peak heart rate. RER_{peak} = Peak respiratory exchange ratio. RPE_{peak} = Peak rate of perceived exertion. \dot{V}_T = Ventilatory threshold.

Table 3.2

Physiological and perceptual responses to quiet rest and low and high intensity exercise for the males in the low trait anxious (n = 20) and high trait anxious (n = 20) groups.

Group	Condition	% $\dot{V}O_{2peak}$	Heart Rate	RPE
Low Trait Anxious	Quiet rest	9.09 ± 3.47	72.98 ± 8.58	6.00 ± 0.00
	40% $\dot{V}O_{2peak}$	40.08 ± 4.11	110.40 ± 13.27	10.20 ± 1.54
	70% $\dot{V}O_{2peak}$	69.83 ± 4.69	151.92 ± 14.41	14.36 ± 1.34
High Trait Anxious	Quiet rest	10.52 ± 3.30	74.46 ± 12.07	6.00 ± 0.00
	40% $\dot{V}O_{2peak}$	43.50 ± 5.26	115.70 ± 13.04	9.65 ± 1.37
	70% $\dot{V}O_{2peak}$	71.64 ± 7.68	151.23 ± 14.37	14.13 ± 1.24

Note. Tabled values are mean ± standard deviation. $\dot{V}O_{2peak}$ = Peak oxygen consumption. RPE = Rate of perceived exertion.

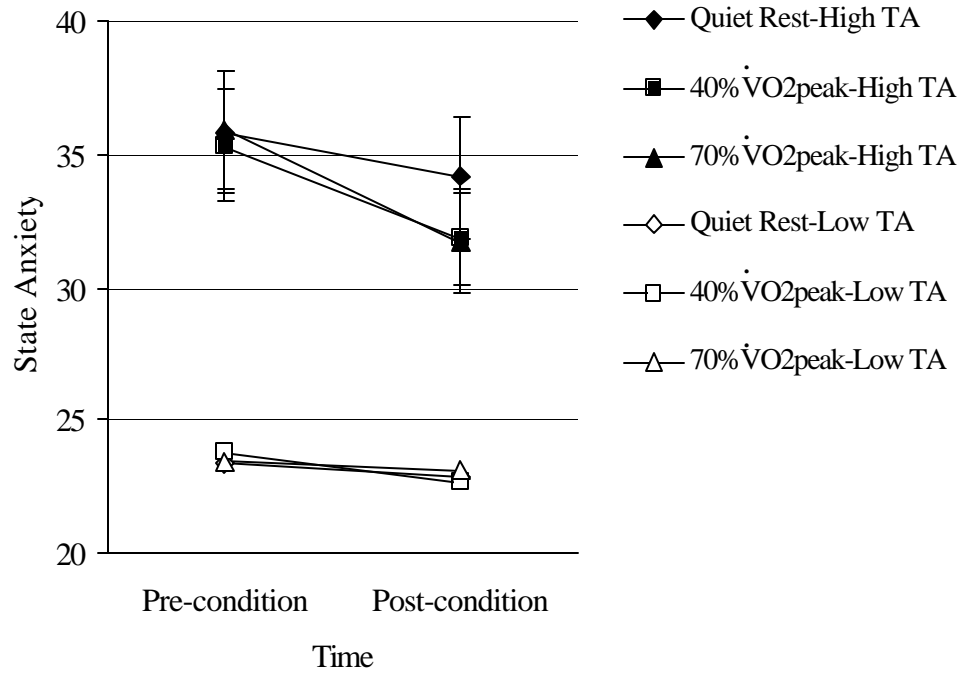


Figure 3.1. State anxiety scores for subjects in the low trait anxious (n = 20) and high trait anxious (n = 20) groups before and after quiet rest and low and high intensity exercise. TA = Trait Anxiety. Values in the figure are mean \pm standard error.

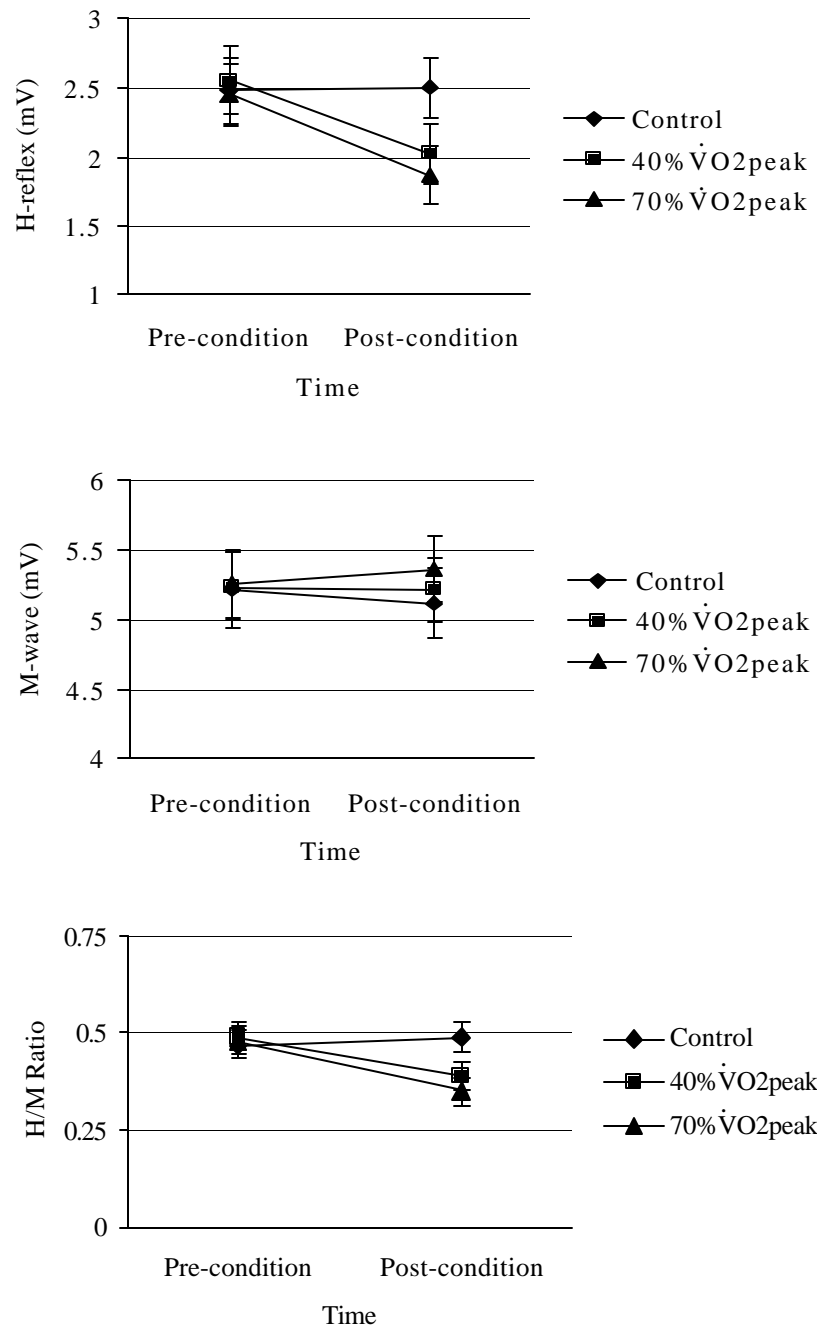


Figure 3.2. H-reflex, M-wave, and H/M ratio recorded before and after quiet rest and low and high intensity exercise. Values in the figure are mean \pm standard error.

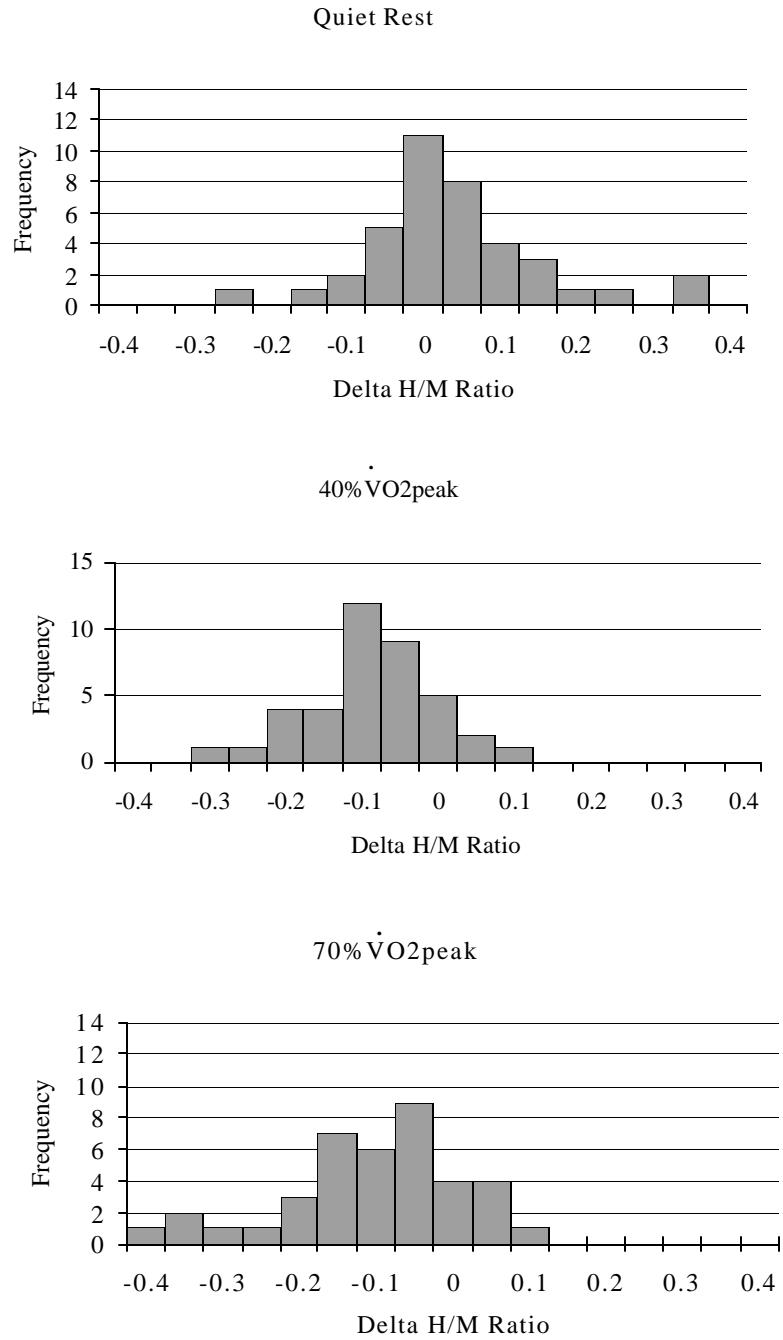


Figure 3.3. Histograms of pre- to post-condition change scores for the H/M ratio across the quiet rest and low and high intensity exercise conditions.

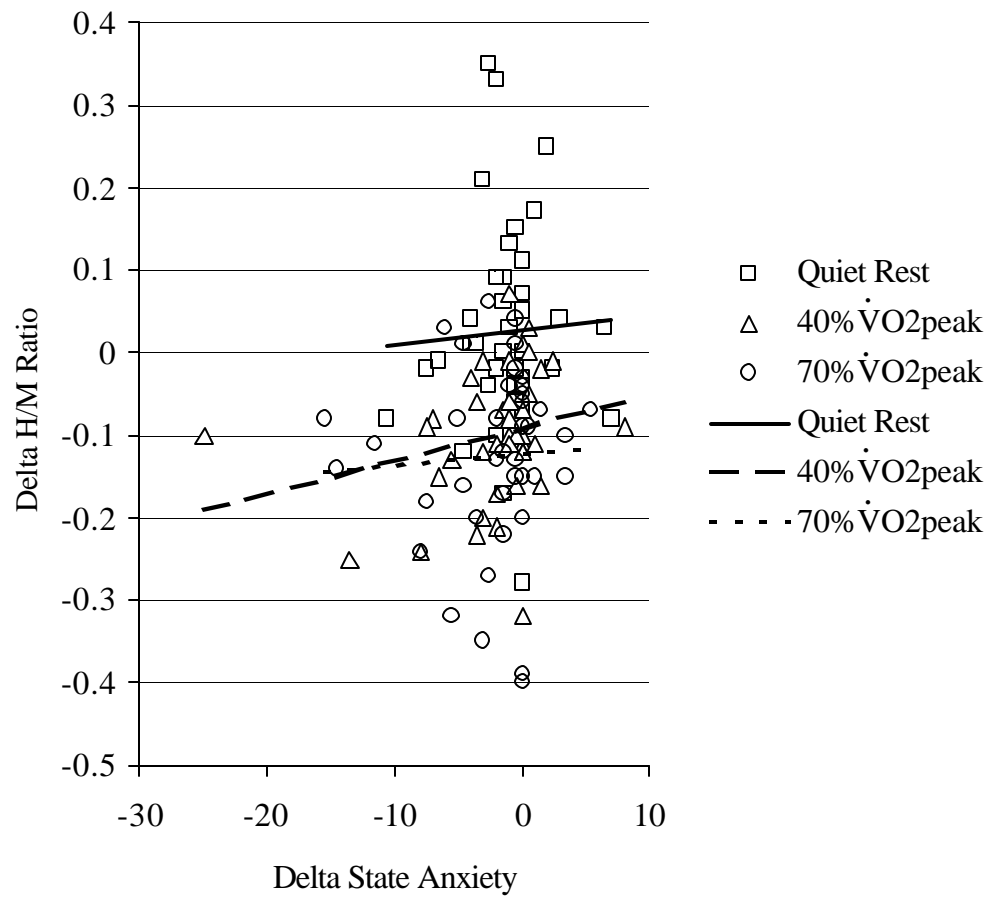


Figure 3.4. Scatterplot of pre- to post-condition changes in state anxiety scores and the H/M ratio across the quiet rest and low and high intensity exercise conditions.

CHAPTER 4

EFFECTS OF ACUTE EXERCISE ON SELF-REPORTED ANXIETY AND THE H- REFLEX AFTER CAFFEINE INGESTION²

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Abstract

The effects of moderate intensity cycling exercise on state anxiety and the H-reflex were examined among 16 individuals whose anxiety was experimentally manipulated by consumption of a large dose of caffeine. State anxiety and the H-reflex in the soleus and flexor carpi radialis (FCR) muscles were measured before and 1 h after consuming caffeine or placebo, and then again 10 min after 30 min of either cycling at an intensity of 60% $\dot{V}O_{2peak}$ or quiet rest. We found that (1) caffeine consumption increased state anxiety, but it did not influence the amplitude of the soleus H-reflex; (2) acute exercise reduced state anxiety only after consumption of caffeine, but it reduced the soleus H-reflex after consumption of either caffeine or placebo; (3) there was no evidence of a relationship between changes in state anxiety and soleus H-reflex; and (4) neither caffeine nor acute exercise influenced the FCR H-reflex. Exercise-induced anxiolysis does not appear to underlie the post-exercise reduction of the soleus H-reflex.

Keywords: Hoffmann reflex, anxiety, caffeine, exercise

Introduction

Many researchers have examined the anxiolytic effects of acute exercise (Dishman, 1998; O'Connor, Raglin, & Martinsen, 2000). The mean effect of acute exercise on self-reported anxiety has approximated $\frac{1}{4}$ - $\frac{1}{2}$ standard deviation (SD; Landers & Petruzzello, 1994; Petruzzello, Landers, Hatfield, Kubitz, & Salizar, 1991). Yet, there are several limitations of previous research into effects of acute exercise on anxiety. One limitation has been that study participants were characterized by low pre-exercise state anxiety scores (O'Connor et al., 2000). This "floor effect" has resulted in small effects of acute exercise on anxiety (O'Connor et al., 2000; Tieman, Peacock, Cureton, & Dishman, 2001). Another limitation has been that researchers generally have ignored the concurrent effects of acute exercise on symptoms of anxiety and neuromuscular variables that might be correlates of anxiety. This is surprising as muscle tension, trembling, twitching, feeling shaky, and muscle aches and soreness are symptoms of anxiety disorders (American Psychiatric Association, 2000).

The Hoffmann reflex (i.e., H-reflex) has been viewed as a neuromuscular substrate of anxiety that is altered by acute exercise (Bulbulian & Darabos, 1986; deVries, Wiswell, Bulbulian, & Moritani, 1981; Petruzzello et al., 1991). Seven published studies have reported that bouts of cycling or jogging exercise reduced the amplitude of the H-reflex recorded in the soleus muscle (Avela, Kyröläinen, Komi, & Rama, 1999; Bulbulian, 2002; Bulbulian & Bowles, 1992; Bulbulian & Darabos, 1986; deVries et al., 1981, deVries, Simard, Wiswell, Heckathorne, & Carabetta, 1982; Mimasa, Matsumoto, & Moritani, 1990). Five of the 7 studies interpreted the reduced H-reflex as a "tranquilizing" effect (Bulbulian, 2002; Bulbulian &

Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990), but none of those studies included a concurrent self-report measure of anxiety when recording the H-reflex.

Recently, we examined the effects of acute exercise on self-reported anxiety and the H-reflex among males differing in trait anxiety scores (Motl, O'Connor, & Dishman, 2002). Males who reported low ($n = 20$) or high ($n = 20$) trait anxiety completed a measure of state anxiety and underwent recording of the soleus H-reflex immediately before and 10-minutes after 20 minutes of quiet rest, low intensity cycling (40% $\dot{V}O_{2peak}$), and high intensity cycling (70% $\dot{V}O_{2peak}$). We found that (1) cycling and quiet rest similarly reduced self-reported anxiety, and the magnitude of the reduction was smaller for males having low trait anxiety than high trait anxiety; (2) cycling, but not quiet rest, reduced the H-reflex; the magnitude of the reduction did not differ between low or high trait anxious males; and (3) reductions of self-reported anxiety were unrelated to reductions of the H-reflex. Those results implied that the post-exercise reduction in the H-reflex was unrelated to self-reported anxiety after exercise, but the relationship was examined across a truncated distribution of state anxiety change scores, despite pre-screening for high trait anxiety. Hence, experimentally increasing and then decreasing anxiety and measuring the concurrent effects on the H-reflex would provide a stronger test of the relationships among exercise, anxiety, and the H-reflex.

Anxiety can be experimentally increased using a caffeine model of anxiogenesis (Nickell & Uhde, 1994; Youngstedt, O'Connor, Crabbe, & Dishman, 1998). The consumption of a high dose of caffeine has been associated with increases in self-reported anxiety (e.g., Charney, Galloway, & Heninger, 1984) and muscle tension (e.g., Pritchard, Robinson, deBethizy, Davis, & Stiles, 1995). The consumption of caffeine has influenced neuromuscular variables such as

resting EMG and physiological tremor (Hasenfratz & Bättig, 1992; James, 1990; Miller, Lombardo, & Fowler, 1998), but has had mixed positive and null influences on the soleus H-reflex (Eke-Okoro, 1982; Kalmar & Cafarelli, 1999).

Previous research from our lab (Youngstedt et al., 1998) has employed the caffeine model of angiogenesis when examining the anxiolytic effect of acute exercise. Eleven physically active, moderately fit males completed four, 60 minute conditions: (1) cycling at 60% $\dot{V}O_{2peak}$ after consuming 800 mg of caffeine; (2) cycling at 60% $\dot{V}O_{2peak}$ after consuming 800 mg of lactose; (3) quiet rest after consuming 800 mg of caffeine; and (4) quiet rest after consuming 800 mg of lactose. The consumption of caffeine resulted in a large increase in pre-condition state anxiety (~1 SD). State anxiety was reduced by 1.31 SD 20-minutes after cycling only in the caffeine condition.

Another possible explanation for the post-exercise reduction in the H-reflex involves the cyclical and repetitive activation of the leg musculature during cycling or jogging exercise. Cyclical and repetitive activation of the leg musculature might result in a post-exercise inhibition of the Ia afferents and/or alpha motoneurons involved in the soleus H-reflex through four spinal pathways: (1) Ib inhibitory interneurons which are co-activated by Ia afferents from the soleus muscle; (2) Renshaw cells activated by discharge of alpha motoneurons projecting to the soleus muscle (i.e., recurrent inhibition); (3) reciprocal Ia inhibition of alpha motoneurons through activation of the tibialis anterior (i.e., antagonist muscle); and (4) presynaptic inhibition of Ia terminals through activation of the tibialis anterior muscle (Capaday, 1997; Pierrot-Deseilligny & Mazevet, 2000). This possibility can be indirectly examined by comparing the effect of

cycling exercise on the H-reflex recorded in the soleus (i.e., leg) and flexor carpi radialis (i.e., arm) muscles.

The present study further examined whether exercise-induced anxiolysis was a cause of the post-exercise reduction of the H-reflex. The primary purpose involved examining the effect of acute cycling exercise on changes in self-reported anxiety and the soleus H-reflex in individuals whose anxiety was increased by consumption of a high dose of caffeine. If the soleus H-reflex is a neuromuscular substrate of anxiety, then consumption of caffeine would be expected to increase self-reported anxiety and the soleus H-reflex, and cycling exercise would be expected to reduce caffeine-induced alterations of self-reported anxiety and the soleus H-reflex.

The secondary purpose of this study was a comparison of the effects of acute cycling exercise on the H-reflex recorded in the soleus and FCR muscles. If the post-exercise reduction of the soleus H-reflex is related to the cyclical and repetitive activation of the leg musculature rather than anxiety, then cycling exercise would be expected to result in a reduction of the H-reflex recorded in the soleus muscle, but not the FCR muscle.

Methods

Participants

Participants ($N = 16$) were male students who reported normal caffeine sensitivity and low daily caffeine consumption (i.e., $< 100 \text{ mg}\cdot\text{d}^{-1}$), and who were non-smokers and of average body weight. Only males were recruited because caffeine clearance is slowed during the luteal phase of the menstrual cycle (Lane, Steege, Rupp, & Kuhn, 1992) and oral contraceptives can reduce clearance and extend the half-life of caffeine (Abernathy & Todd, 1985). Subjects who

reported normal caffeine sensitivity and low daily caffeine consumption were recruited to minimize the potential of panic-like reactions to caffeine (Charney et al., 1982) and avoid the effects of habitual caffeine consumption on anxiogenic responses to caffeine (Fredholm, Bättig, Holmén, Nehlig, & Zvartau, 1999; Nehlig, 1999; Nehlig, Daval, & Debry, 1992). Only non-smokers of average body weight were recruited to avoid the effects of cigarette smoking (Joeres et al., 1988) and obesity (Kamimori, Somani, Knowlton, & Perkins, 1987) on the rate of caffeine metabolism. Based on the subject characteristics provided in Table 4.1, the males were low in trait anxiety and moderately activity and physically fit.

Experimental Design

This study was conducted using a 2 (Drug: caffeine and placebo) \times 2 (Condition: exercise and quiet rest) \times 3 (Time: pre-drug, post-drug/pre-condition, post-condition) within subjects, repeated measures factorial design. The order of Condition was counter-balanced within a counter-balanced presentation of Drug. Hence, every participant completed an exercise and a quiet rest session after consuming caffeine or placebo. Caffeine was administered using a double-blind procedure to protect against possible subject (Christensen, White, Krietsch, & Steele, 1990) and experimenter expectancy effects. An individual who was not involved in data collection placed gelatin capsules containing the appropriate content and dosage in coded, zip-lock bags. The order of drug administration was provided to the first author after the data were collected.

Power Analysis

Statistical power analysis indicated that a sample of 16 participants was adequate to detect a large (0.80 SD) effect of the Drug \times Condition \times Time interaction on self-reported

anxiety and the H-reflex (Power = 0.80, $p < 0.05$, ICC = 0.80; Potvin & Schutz, 2000). An even larger effect of exercise on anxiety (1.31 SD) was reported with caffeine-induced angiogenesis (Youngstedt et al., 1998). The mean effect size calculated from six studies examining the influence of acute exercise on the H-reflex approximated 1 SD (90% CI = 0.63 - 1.37).

Measures

Daily caffeine consumption. Daily caffeine consumption was estimated using a self-report measure. The measure required participants to report consumption of common dietary sources of caffeine (e.g., coffee, tea, cocoa, & soft drinks) on a daily basis across a seven-day period. The amount of caffeine in the common dietary sources was based on the following estimates: 125 mg per cup of brewed coffee, 90 mg per cup of instant coffee, 4.5 mg per cup of decaffeinated coffee, 60 mg per cup of tea, 5 mg per cup of cocoa or chocolate milk, 20 mg per glass of cola and 40 mg per can of cola, and 1 mg per gram of chocolate (Fredholm et al., 1999; James, Bruce, Lader, & Scott, 1989; Kennedy, von Moltke, Harmatz, Engelhardt, & Greenblatt, 1991).

State-Trait Anxiety Inventory. The 40-item State-Trait Anxiety Inventory (STAI) was used to measure state and trait anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). Twenty items measured state anxiety and 20 items measured trait anxiety. The items were rated on a 4-point scale anchored by Not at all (1), Somewhat (2), Moderately so (3), and Very much so (4). The STAI has acceptable internal consistency and test-retest reliability (Spielberger et al., 1983). There is an abundance of correlational and experimental evidence

supporting the validity of the inference that scores on the STAI reflect anxiety (Spielberger et al., 1983).

Seven-day physical activity recall. Weekly energy expenditure was estimated using a seven-day physical activity recall interview (Blair, 1984) for descriptive purposes. Evidence supports the reliability and validity of scores from the seven-day physical activity recall interview for college students (Dishman & Steinhardt, 1988).

Perceptions of exertion. Perceptions of exertion were measured using Borg's (1998) 15-point, 6-20 scale. The scale was anchored by Very, very light (7) and Very, very hard (19). Evidence supports the reliability and validity of this measure (Borg, 1998).

Peak oxygen consumption ($\dot{V}O_{2peak}$). Participants performed an incremental exercise test on an electronically-braked, computer-driven cycle ergometer (Lode BV, Groningen, The Netherlands) to estimate $\dot{V}O_{2peak}$. Initially, participants were fitted to the cycle ergometer, and provided with standardized instructions for the perceived exertion scale (Borg, 1998). After inserting a mouthpiece for collecting expired gases, the participants undertook a 5-min warm-up at 25 W. The initial workrate for the exercise test was 50 W, and the workrate continuously increased at a rate of 24 W·min⁻¹. Using an open-circuit spirometry system (SensorMedics Metabolic Cart, model 2900), ventilation (\dot{V}_E), oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and respiratory exchange ratio (RER) were measured every 20 s. Heart rate was continuously displayed using a Polar Vantage XL heart rate monitor (Polar Electro Oy, Kempele, Finland). Heart rate, perceptions of exertion, and workrate were recorded every minute. $\dot{V}O_{2peak}$ was defined by three criteria: (1) heart rate within 10 beats·min⁻¹ of age-predicted maximum (i.e., ~1 SD); (2) respiratory exchange ratio ≥ 1.10 ; or (3) perceived

exertion > 18. Ventilatory threshold ($\dot{V}_T^{\textcircled{a}}$) was estimated based on plots of $\dot{V}_E^{\textcircled{a}} / \dot{V}O_2^{\textcircled{a}}$ and $\dot{V}_E^{\textcircled{a}} / \dot{V}CO_2^{\textcircled{a}}$ as a function of time (Davis, Frank, Whipp, & Wasserman, 1979).

H-reflex. Participants were prepared for skin surface measurements of soleus and FCR muscle activity using electromyography (EMG) and percutaneous electrical stimulation of the tibial and median nerves in the right leg and arm, respectively. The skin surface was shaved, and abraded and cleaned using fine grain sand-paper and alcohol swabs. Two 1-cm Ag-AgCl electrodes (MED associates, Georgia, VT) with Grass EC2 cream (Astro-Med, Inc., West Warwick, RI) were attached along the soleus muscle 2-3 cm below the heads of the gastrocnemius muscles; another 1-cm AG-AgCl electrode was attached superior to the lateral malleolus. Two 1-cm Ag-AgCl electrodes with Grass EC2 cream were attached along the right FCR muscle $\frac{1}{2}$ of the distance between the medial epicondyle and the radial styloid; another 1-cm Ag-AgCl electrode was attached superior to the ulnar styloid. Those electrodes were marked with semipermanent marker and connected to GRASS P511 amplifiers (Astro-Med, Inc., West Warwick, RI). The amplifiers were connected to an oscilloscope (Kenwood CS-8010; Kenwood TMI, Corp., Yokohama, Japan) and a data acquisition system (GRASS PolyVIEW; Astro-Med, Inc., West Warwick, RI).

The tibial and median nerves were located using stimulus probe electrodes. Round (2.5 cm) and rectangular (5 cm \times 3.5 cm) pre-gelled, self adhering carbon rubber electrodes (900ST series TENS/NMES electrodes; EMPI, St. Paul, MN) were placed above the tibial nerve in the popliteal fossa and superior to the patella, respectively. Two round (2.5 cm) pre-gelled, self-adhering carbon rubber electrodes (900ST series TENS/NMES electrodes; EMPI, St. Paul, MN) were placed in-line and above the median nerve in the cubital fossa. The

electrodes were marked with semipermanent marker, secured with 3M Micropore tape and 3M Coban, and connected to a constant current unit (GRASS CCU1A; Astro-Med, Inc., West Warwick, RI) in-line with a stimulus isolation unit (GRASS SIU8TB; Astro-Med, Inc., West Warwick, RI) and a somatosensory stimulation unit (GRASS S10DSCM; Astro-Med, Inc., West Warwick, RI). There were Velcro® circumferential bandage-type electrodes placed between the stimulating and recording electrodes (GRASS F-E10SG1 & F-E10SG2; Astro-Med, Inc., West Warwick, RI).

Impedance of the recording and stimulating electrodes was measured using an electrode impedance meter (GRASS EZM 4; Astro-Med, Inc., West Warwick, RI). The average impedance of the recording electrodes across Drug, Condition, and Time was 1.10 ± 0.46 kO and 1.56 ± 0.60 kO for the soleus and FCR muscles, respectively. The average impedance of the stimulating electrodes was 1.70 ± 0.28 kO and 2.88 ± 0.50 kO for the tibial and median nerves, respectively.

The H-reflex was measured in a thermoneutral (23 ± 1 EC, ~ 40% relative humidity), sound dampened (100 db less than ambient), electrically shielded, earth-grounded chamber. Participants sat on a custom-designed chair that supported the head and controlled body and joint positions. The hip and knee joint angles were 120E and 160E, respectively. The chair was equipped with a rotating platform for the right foot. The rotating platform was connected to a pneumatic device (RLF06A-SAP-AA00 Round Line Actuator, Norgren, Littleton, CO) with an air pressure regulator (R21 Dial Air™ Regulator; Wilkerson, Englewood, CO) set at 15 psi to control the activity of the soleus muscle. The rotating platform also was connected to a potentiometer (WPM 18-09, Servo Pot; Omega, Stamford, CT) in-line with a digital display

(DP25-E Process Panel Meter; Omega, Stamford, CT) to monitor the ankle joint angle. The ankle joint angle was maintained between 88-92°. There was a stable platform for the right arm, and the participant's arm was placed in a prone position (Baldissera, Bellani, Cavalleri, & Lalli, 2000). The angle of the elbow joint angle 160°.

Rectangular 1-ms and 0.8-ms impulses were delivered to the tibial and median nerves every 8 s (Panizza, Nilsson, & Hallett, 1989). The resulting muscle activity was recorded using EMG. The EMG signal was sampled at a rate of 1 kHz, bandwidth filtered from 3 Hz to 1 kHz, and amplified by 1,000. The strength of the impulse was progressively increased by ¼ unit increments on the constant current unit to locate the maximal H-reflex and M-wave responses. Ten electrical impulses then were provided at the stimulus increment corresponding to the maximal H-reflex and M-wave responses. Ten electrical impulses yielded reliable measures of the soleus H-reflex (range of Intraclass Correlation Coefficients [ICCs] = .87 - .98, \underline{M} = .95), soleus M-wave (range of ICCs = .94 - .97, \underline{M} = .96), FCR H-reflex (range of ICCs = .96 - .98, \underline{M} = .97), and FCR M-wave (range of ICCs = .93 - .96, \underline{M} = .95) across Drug, Condition, and Time.

The 10 consecutive recordings were averaged to form maximal H-reflexes and M-waves for the soleus and FCR muscles. The maximal H-reflex and M-wave then were employed to compute the H/M ratio. The H/M ratio represents the magnitude of the reflex (i.e., H-reflex) relative to the recruitment of all motor axons (i.e., M-wave). Hence, the H/M ratio represents an estimate of the proportion of the motoneuron pool recruited by the muscle reflex (Pierrot-Deseilligny & Mazevet, 2000).

The actual current being applied during nerve stimulation was measured using a current probe amplifier (Tektronix AM 503A; Tektronix, Inc., Beaverton, OR) connected to an oscilloscope (Kenwood CS-8010). The average current across Drug, Condition, and Time for the maximal soleus H-reflex and M-wave were 36.83 ± 2.36 mA and 98.79 ± 6.78 mA, respectively. The average current for the maximal FCR H-reflex and M-wave were 16.96 ± 2.49 mA and 60.46 ± 3.00 mA, respectively.

Procedures

The procedures were approved by the University of Georgia Institutional Review Board. Participants completed one day of baseline testing and four days of experimental testing. The four days of experimental testing were separated by ~1 wk. Experimental testing was conducted in the morning (0700 h) and the time of day was standardized within and between subjects (± 1 h). Participants were asked to (1) avoid caffeine consumption during the entire week before beginning the experimental testing; (2) abstain from eating and exercising for 12 h before experimental testing; and (3) abstain from consuming alcohol and caffeine for 24 h before experimental testing.

Baseline day. On the baseline day, all participants signed an informed consent document and completed a pre-exercise medical history questionnaire, seven-day recall of daily caffeine consumption, and the trait portion of the STAI. The researcher performed the seven-day physical activity recall interview. Participants then performed the incremental exercise test.

After the exercise test, participants were prepared for recording the H-reflex and moved to an environmental chamber and positioned on a custom-designed chair. Participants completed the measure of state anxiety, and then underwent measurements of the H-reflex in

the soleus and FCR muscles. The data from the baseline day were not analyzed, and testing only was performed to familiarize subjects with the protocol.

Experimental days. On the experimental days, participants underwent 1 of 4, 30-minute conditions: (1) cycling at 60% $\dot{V}O_{2peak}$ after consuming caffeine; (2) cycling at 60% $\dot{V}O_{2peak}$ after consuming placebo; (3) quiet rest after consuming caffeine; and (4) quiet rest after consuming placebo. Caffeine and placebo were delivered in gelatin capsules (No. 1, Lilly, Eli Lilly & Company, Indianapolis, IN). The dose of caffeine (Caffeine Anhydrous, USP/NF, Gallipot, St. Paul, MN) was 10 mg·kg⁻¹ body weight based on consistent observations of elevated anxiety (e.g., Charney et al., 1984; Dagar et al., 1999; Mattila, Seppala, & Mattila, 1988). The dose of placebo was an equal number of gelatin capsules containing white, all-purpose flour. The order of the conditions was counter-balanced; otherwise the procedures were identical.

Initially, participants were prepared for recording the H-reflex and moved to the environmental chamber and positioned on a custom-designed chair. Participants then completed the measure of state anxiety and underwent measurements of the H-reflex in the soleus and FCR muscles. Subjects consumed the gelatin capsules containing either caffeine or placebo with 500 ml of water, and sat and read quietly in the environmental chamber.

One hour after ingesting the capsules, which has been reported to coincide with peak plasma caffeine concentrations (Kamimori et al., 1987, 1995; Kaplan et al., 1997), participants again completed the measure of state anxiety. Participants then underwent measurements of the H-reflex in the soleus and FCR muscles.

Participants were moved to another room and either (1) cycled on an ergometer for 30 min at 60% $\dot{V}O_{2peak}$ or (2) sat and read quietly for 30 min. Heart rate and perceptions of exertion were recorded every 5 minutes. Expired gases were analyzed using open-circuit spirometry after 5, 15, and 25 minutes to verify the exercise intensity. Minor adjustments to the workrate were made to maintain the exercise intensity. The physiological and perceptual responses to the conditions are provided in Table 4.2.

After exercise or quiet rest, participants returned to the environmental chamber and sat on the custom-designed chair. Beginning 10 minutes after exercise or quiet rest, participants completed the measure of state anxiety and underwent measurements of the H-reflex in the soleus and FCR muscles.

Exercise condition. The exercise condition consisted of 30 min of cycling at an intensity corresponding to 60% $\dot{V}O_{2peak}$. Research has indicated that both the exercise mode, duration, and intensity are adequate to reduce anxiety (Landers & Petruzzello, 1994; Petruzzello et al., 1991) and the H-reflex (e.g., deVries et al., 1981; Bulbulian & Darabos, 1986).

Data Analysis

The data were analyzed with 2 (Drug: caffeine and placebo) \times 2 (Condition: exercise and quiet rest) \times 3 (Time: pre-drug, post-drug/pre-condition, post-condition) repeated measures ANOVAs based on the multi-variate F-statistic (Pillai-Bartlett) (Keselman, 1998). Effect sizes associated with F-statistics were expressed as eta-squared (η^2). Effect sizes based on mean differences were expressed as Cohen's d (Cohen, 1988). The Greenhouse-Geisser epsilon (ϵ) was reported when the sphericity assumption was violated (i.e., if Mauchly's test of sphericity was statistically significant at $p < .05$). The family-wise error rate was controlled

using the Bonferroni adjustment when tests of simple effects were conducted (Keselman, 1998).

The relationship between changes in state anxiety and the H/M ratio was examined using a Drug \times Condition repeated measures ANCOVA on H/M ratio change scores with state anxiety change scores as a time varying covariate (Winer, Brown, & Michels, 1991). The result of that analysis was compared with a Drug \times Condition repeated measures ANOVA on only H/M ratio change scores. Changes in the univariate F-statistic and η^2 were indicative of a difference between models, and hence an effect of state anxiety on the H-reflex; the univariate F-statistic was compared across models (Winer et al., 1991) as the multi-variate F-statistic was unavailable with the repeated measures ANCOVA that included the time varying covariate. Those analyses were performed on change scores computed for pre-post drug and then pre-post condition.

Results

State Anxiety

There was a significant Drug \times Condition \times Time interaction on state anxiety scores, $F(2, 14) = 5.12, p < .05, \eta^2 = .42, \epsilon = .68$. As illustrated in Figure 4.1A, state anxiety scores were significantly increased from before to after consumption of caffeine in both the exercise ($d = 0.67$) and quiet rest ($d = 1.36$) conditions; scores were unchanged from before to after consumption of placebo in the exercise ($d = -0.07$) and quiet rest ($d = -0.04$) conditions. State anxiety scores were significantly decreased from before to after cycling exercise in the caffeine condition ($d = -0.34$), but were unchanged after quiet rest in the caffeine condition ($d = 0.05$).

There were no changes in anxiety scores from before to after cycling exercise ($d = 0.04$) or quiet rest ($d = 0.04$) in the placebo condition.

There also was a significant Drug \times Time interaction on state anxiety scores, $F(2, 14) = 27.06$, $p < .0001$, $\eta^2 = .79$. As illustrated in Figure 4.1B, state anxiety scores were significantly increased from before to after consumption of caffeine ($d = 1.04$), but were unchanged from before to after consumption of placebo ($d = -0.06$). Anxiety scores remained significantly elevated above pre-drug values after exercise and quiet rest in the caffeine condition ($d = 0.86$). Anxiety scores were unchanged after exercise and quiet rest combined in the placebo condition ($d = -0.02$).

Soleus Muscle: H-reflex, M-Wave, and H/M Ratio

Maximal H-reflex. There was not a significant Drug \times Condition \times Time interaction on maximal H-reflex values, $F(2, 14) = 0.35$, $p = .71$, $\eta^2 = .05$. There was a significant Condition \times Time interaction, $F(2, 14) = 20.68$, $p < .0001$, $\eta^2 = .75$, $\epsilon = .72$. As illustrated in Figure 4.2A, the soleus H-reflex did not change from before to after the consumption of caffeine and placebo in the exercise ($d = 0.04$) and quiet rest ($d = 0.06$) conditions. The H-reflex was significantly decreased from before to after exercise ($d = -1.09$), but not quiet rest ($d = 0.11$), after consumption of caffeine and placebo.

Maximal M-wave. There was not a significant Drug \times Condition \times Time interaction, $F(2, 14) = 0.69$, $p = .52$, $\eta^2 = .09$, nor was there a significant Condition \times Time interaction, $F(2, 14) = 0.11$, $p = .90$, $\eta^2 = .02$, on maximal M-wave values. As illustrated in Figure 4.2B, the M-wave did not change from before to after the consumption of caffeine and placebo in the exercise ($d = 0.02$) or quiet rest ($d = 0.05$) conditions. The M-wave also did not change from

before to after exercise ($d = 0.10$) or quiet rest ($d = 0.07$) after consumption of caffeine and placebo.

H/M ratio. There was not a significant Drug \times Condition \times Time interaction on H/M ratio values, $F(2, 14) = 1.85$, $p = .19$, $\eta^2 = .21$. There was a significant Condition \times Time interaction, $F(2, 14) = 54.05$, $p < .0001$, $\eta^2 = .89$, $\epsilon = .69$. As illustrated in Figure 4.2C, the soleus H/M ratio did not change from before to after the consumption of caffeine and placebo in the exercise ($d = 0.06$) or quiet rest ($d = 0.09$) conditions. The H/M ratio was significantly decreased from before to after exercise ($d = -1.40$), but not quiet rest ($d = 0.06$) after consumption of caffeine and placebo.

Flexor Carpi Radialis (FCR) Muscle: H-reflex, M-Wave, and H/M Ratio

Maximal H-reflex. There was not a significant Drug \times Condition \times Time interaction, $F(2, 14) = 0.46$, $p = .64$, $\eta^2 = .06$, nor was there a significant Condition \times Time interaction, $F(2, 14) = 2.83$, $p = .09$, $\eta^2 = .29$, $\epsilon = .74$, on maximal H-reflex values. As illustrated in Figure 4.3A, the FCR H-reflex did not change from before to after the consumption of caffeine and placebo in the exercise ($d = 0.02$) or quiet rest ($d = 0.05$) conditions. The H-reflex also did not change significantly from before to after exercise ($d = -0.07$) or quiet rest ($d = 0.03$) after consumption of caffeine and placebo.

Maximal M-wave. There was not a significant Drug \times Condition \times Time interaction, $F(2, 14) = 0.54$, $p = .59$, $\eta^2 = .07$, nor a significant Condition \times Time interaction, $F(2, 14) = 2.38$, $p = .13$, $\eta^2 = .25$, on maximal M-wave values. As illustrated in Figure 4.3B, the M-wave did not change from before to after the consumption of caffeine and placebo in the exercise (d

= 0.05) or quiet rest ($d = -0.03$) conditions. The M-wave also did not change from before to after exercise ($d = -0.07$) or quiet rest ($d = -0.02$) after consumption of caffeine and placebo.

H/M ratio. There was not a significant Drug \times Condition \times Time interaction, $F(2, 14) = 0.75$, $p = .49$, $\eta^2 = .10$, $\epsilon = .60$, nor a significant Condition \times Time interaction, $F(2, 14) = 1.60$, $p = .24$, $\eta^2 = .19$, on FCR H/M ratio values. As illustrated in Figure 3C, the H/M ratio did not change from before to after the consumption of caffeine and placebo in the exercise ($d = -0.03$) or quiet rest ($d = 0.06$) conditions. The FCR H/M ratio also did not change from before to after exercise ($d = 0.00$) or quiet rest ($d = 0.05$) after consumption of caffeine and placebo.

Relationship Between Changes in Anxiety and the Soleus H-reflex

Pre-post drug. The 2×2 repeated measures ANCOVA on pre-post drug soleus H/M ratio change scores, with pre-post drug state anxiety change scores as a time varying covariate, indicated a non-significant Condition main effect, $F(1, 14) = 0.30$, $p = .59$, $\eta^2 = .02$. The 2×2 repeated measures ANOVA on only pre-post drug soleus H/M ratio change scores also indicated a non-significant Condition main effect, $F(1, 15) = 0.33$, $p = .57$, $\eta^2 = .02$. The magnitude of the univariate F-statistic and η^2 for the Condition main effects did not differ between analytic models (Winer et al., 1991). Hence, changes in self-reported anxiety were unrelated to changes in the H/M ratio from before to after drug consumption.

Pre-post condition. The 2×2 repeated measures ANCOVA on pre-post condition soleus H/M ratio change scores, with pre-post condition state anxiety change scores as a time varying covariate, indicated a significant Condition main effect, $F(1, 14) = 114.18$, $p < .0001$, $\eta^2 = .89$. The 2×2 repeated measures ANOVA on only pre-post condition soleus H/M ratio

change scores also indicated a significant Condition main effect, $F(1, 15) = 104.83$, $p < .0001$, $\eta^2 = .88$. There were no differences in the magnitude of the univariate F-statistic and η^2 for the Condition main effects between analytic models (Winer et al., 1991). Again, changes in self-reported anxiety were unrelated to changes in the H/M ratio from before to after exercise and quiet rest.

Scatter-plots. The scatter-plots of pre-post drug and pre-post condition change scores for state anxiety and the soleus H/M ratio with lines-of-best-fit per condition are presented in Figures 4.4A and 4.4B, respectively. The scatter-plots support the lack of an association between changes in anxiety and the soleus H/M ratio. Overall, the changes in self-reported anxiety were unrelated to the changes in the soleus H/M ratio across Drug and Condition.

Discussion

Consumption of caffeine resulted in a large increase of state anxiety, but it did not influence the amplitude of the soleus H-reflex. Acute exercise resulted in a reduction of state anxiety only after the consumption of caffeine, but it reduced the soleus H-reflex after consumption of either caffeine or placebo. There was no evidence linking changes in state anxiety with changes in the soleus H-reflex. Neither caffeine nor acute exercise influenced the amplitude of the FCR H-reflex. These results do not support exercise-induced anxiolysis as a cause of the post-exercise reduction of the soleus H-reflex.

Caffeine, Exercise, and Anxiety

As expected, consumption of a large dose of caffeine ($10 \text{ mg}\cdot\text{kg}^{-1}$ body weight) was effective for increasing pre-condition anxiety scores. We observed a large effect of caffeine on pre-condition state anxiety scores ($d = 1.04$) in the present study. Youngstedt et al. (1998)

observed a similar effect of caffeine (800 mg) on pre-condition anxiety scores (~ 1 SD). Hence, the caffeine-model of anxiogenesis is useful for manipulating pre-condition anxiety scores. This is important because “floor” effects commonly have been observed in studies of exercise-induced anxiolysis (O’Connor et al., 2000; Tieman et al., 2001).

Similar to the results of Youngstedt et al. (1998), we found that 30 minutes of moderate intensity cycling exercise resulted in a reduction of state anxiety, but only after consuming caffeine; there was no effect of exercise on anxiety in the placebo condition. The magnitude of the reduction in anxiety was moderate ($d = -0.34$), but consistent with the average effect ($\sim \frac{1}{4}$ - $\frac{1}{2}$ SD) reported in previous meta-analyses (Landers & Petruzzello, 1994; Petruzzello et al., 1991).

Our results might have implications for the adenosine neuromodulatory system as a mechanism for exercise-induced anxiolysis (O’Connor et al., 2000; Youngstedt et al., 1998). Adenosine is present throughout the brain and acts as a neuromodulator by inhibiting the release of excitatory neurotransmitters and regulating neuronal firing rates (Fredholm et al., 1999). Receptors for adenosine, particularly A_1 receptors, are widely distributed in brain areas involved in anxiety (e.g., cortex, hypothalamus, locus coeruleus, & amygdala; Fredholm et al., 1999; Nehlig et al., 1992). The primary central action of caffeine is the competitive blockade of A_1 receptors; this is the presumed cause of caffeine-induced anxiety (Nehlig et al., 1992). Therefore, if caffeine blocks the post-exercise reduction of anxiety, then indirect evidence would support the adenosine neuromodulatory system as a mechanism for exercise-induced anxiolysis (O’Connor et al., 2000; Youngstedt et al., 1998). Our data do not support this

hypothesis because anxiety was reduced after exercise even though A₁ receptors were presumably blocked by caffeine.

Caffeine, Exercise, and H-reflex

The soleus H/M ratio was not influenced by caffeine, but was significantly decreased after exercise ($d = -1.40$). Those findings were consistent with previous research interpreting the reduction as a “tranquilizing” effect of acute exercise (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Previous research has demonstrated that 20 minutes of low to high intensity cycling or jogging exercise resulted in approximately 13-22% reductions of the H/M ratio. We found that 30 minutes of moderate intensity cycling exercise resulted in a 44% reduction of the soleus H/M ratio. Clearly, cycling and jogging exercise reduce the amplitude of the H-reflex in the soleus muscle.

There were no effects of caffeine or exercise on the FCR H-reflex. To our knowledge, no other studies have examined the effect of acute cycling exercise on the H-reflex recorded in the arm. Hence, we have provided initial evidence that a bout of lower body cycling exercise does not influence the H-reflex in the upper body.

We observed that the effect of acute exercise on the H-reflex was specific to the muscle group being exercised. Cycling exercise reduced the H-reflex in the leg, but not the arm. This indirectly suggests that the H-reflex is modulated after exercise by local and/or spinal cord processes rather than brain regions involved in anxiety. There also is a possibility that brain-regions involved in motor control exert a modulation of the H-reflex pathway after exercise.

Exercise, Anxiety, and H-reflex

Previous researchers have interpreted the post-exercise reduction of the soleus H-reflex as a “tranquilizing” effect of acute exercise (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990). Our results do not support this interpretation. We observed that experimentally increasing and decreasing anxiety with caffeine and acute exercise were not statistically or graphically (Figures 4A and 4B) associated with concurrent changes in the soleus H/M ratio. The lack of an association is consistent with our previous results (Motl et al., 2002). We previously reported that reductions of self-reported anxiety were unrelated to reductions of the H-reflex across three conditions for both low and high trait anxious males (Motl et al., 2002). Hence, the post-exercise reduction in the soleus H-reflex, reported by previous researchers (Bulbulian & Darabos, 1986; deVries et al., 1981, 1982; Mimasa et al., 1990) and observed in the present study, appears to be unrelated to changes in self-reported anxiety after exercise.

Explanations for the Post-exercise Attenuation of the Soleus H-reflex

There are several possible alternative explanations for the post-exercise reduction in the soleus H-reflex. One possibility is that the cyclical and repetitive activation of the leg musculature during cycling or jogging exercise results in a prolonged post-exercise inhibition of the Ia afferents and/or alpha motoneurons involved in the soleus H-reflex. Four spinal pathways that are involved in the inhibition of Ia afferents and/or alpha motoneurons are good candidates for such an effect (Capaday, 1997; Pierrot-Deseilligny & Mazevet, 2000). These pathways include (1) Ib inhibitory interneurons which are co-activated by Ia afferents from the soleus muscle; (2) Renshaw cells activated by discharge of alpha motoneurons projecting to the soleus

muscle (i.e., recurrent inhibition); (3) reciprocal Ia inhibition of alpha motoneurons through activation of the tibialis anterior (i.e., antagonist muscle); and (4) presynaptic inhibition of Ia terminals through activation of the tibialis anterior muscle.

Another possibility is that cycling or jogging exercise activates Type III and IV afferent nerve endings and fibers originating in the soleus and other leg muscles. Type III and IV myelinated and unmyelinated afferent fibers originate from nociceptive and non-nociceptive nerve endings located primarily in the walls of arterioles and the surrounding connective tissue of skeletal muscles. Type III nerve endings are primarily responsive to mechanical pressure; Type IV nerve endings are polymodal and responsive to temperature, mechanical pressure, and biochemical by-products of muscle metabolism. Cycling exercise near ventilatory threshold likely activates Type III and IV nerve endings (Mitchell & Schmidt, 1996), and the associated afferent fibers have powerful inputs to terminals of Ia afferents and to Ib inhibitory interneurons within the spinal cord (Rossi, Decchi, Ginanneschi, 1999; Rossi, Decchi, Dami, Della Volpe, & Groccia, 1999). Activation of type III and IV nerve endings and fibers during exercise might lead to presynaptic inhibition of the Ia afferent terminals or activation of Ib inhibitory interneurons involved in the soleus H-reflex that lasts into the post-exercise period.

Cycling or jogging exercise might reduce the H-reflex through influences on interneurons and neurons within the motor cortex. Perhaps cycling or jogging exercise leads to an inhibition of interneurons and neurons within the motor cortex that provide excitatory inputs to soleus alpha motoneurons (Mercuri, Wassermann, Ikoma, Samii, & Hallett, 1997).

Conclusions

In summary, we found that (1) caffeine consumption increased state anxiety, but it did not influence the amplitude of the soleus H-reflex; (2) acute exercise reduced state anxiety only after consumption of caffeine, but it reduced the soleus H-reflex after consumption of either caffeine or placebo; (3) there was no statistical or graphical evidence linking changes in both state anxiety and the soleus H-reflex; and (4) neither caffeine nor acute exercise influenced the H-reflex recorded in the FCR muscle. The present results, in combination with our previous findings (Motl et al., 2002), do not support that exercise-induced anxiolysis is a cause of the post-exercise reduction of the soleus H-reflex. Hence, the post-exercise reduction of the H-reflex should not, as yet, be interpreted as a “tranquilizing” effect of acute exercise.

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Table 4.1

Characteristics of the 16 male volunteers.

Characteristic	Mean \pm standard deviation
Age (y)	21.38 \pm 2.33
Height (cm)	179.06 \pm 7.62
Mass (kg)	72.75 \pm 7.04
Trait Anxiety (STAI Form Y-2)	31.00 \pm 9.14
Daily caffeine consumption (ml·d ⁻¹)	36.06 \pm 28.18
Physical Activity (7-d PAR; kJ·kg ⁻¹ ·wk ⁻¹)	136.28 \pm 46.68
$\dot{V}O_{2peak}^@$ (ml·kg ⁻¹ ·min ⁻¹)	47.48 \pm 8.03
$\dot{V}O_{2peak}^@$ (l·min ⁻¹)	3.46 \pm 0.73
HR _{peak} (beats·min ⁻¹)	187.06 \pm 5.95
RER _{peak}	1.17 \pm 0.07
RPE _{peak}	19.19 \pm 0.54
$\dot{V}_T^@$ (% $\dot{V}O_{2peak}^@$)	63.63 \pm 4.40

Note. STAI Form Y-2 = State-Trait Anxiety Inventory Form Y-2 (Trait portion). 7-d PAR = Seven-day Physical Activity Recall. $\dot{V}O_{2peak}^@$ = Peak oxygen consumption. HR_{peak} = Peak heart rate. RER_{peak} = Peak respiratory exchange ratio. RPE_{peak} = Peak rate of perceived exertion. $\dot{V}_T^@$ = Ventilatory threshold.

Table 4.2

Physiological and perceptual responses to quiet rest and cycling exercise across the placebo and caffeine drug administrations.

Condition	Drug	% $\dot{V}O_{2peak}$	Heart Rate	RPE
Quiet rest	Placebo	8.39 ± 1.78	64.26 ± 6.43	6.00 ± 0.00
	Caffeine	9.20 ± 1.92	64.66 ± 9.21	6.00 ± 0.00
60% $\dot{V}O_{2peak}$	Placebo	61.19 ± 4.58	141.60 ± 10.69	12.73 ± 1.13
	Caffeine	63.09 ± 4.70	141.90 ± 6.68	12.12 ± 1.38

Note. Tabled values are mean ± standard deviation. $\dot{V}O_{2peak}$ = Peak oxygen consumption. RPE = Rate of perceived exertion.

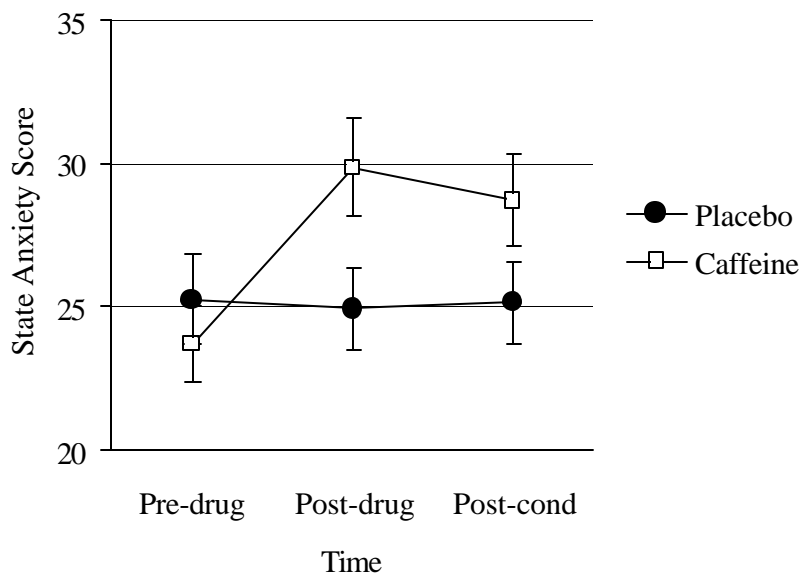
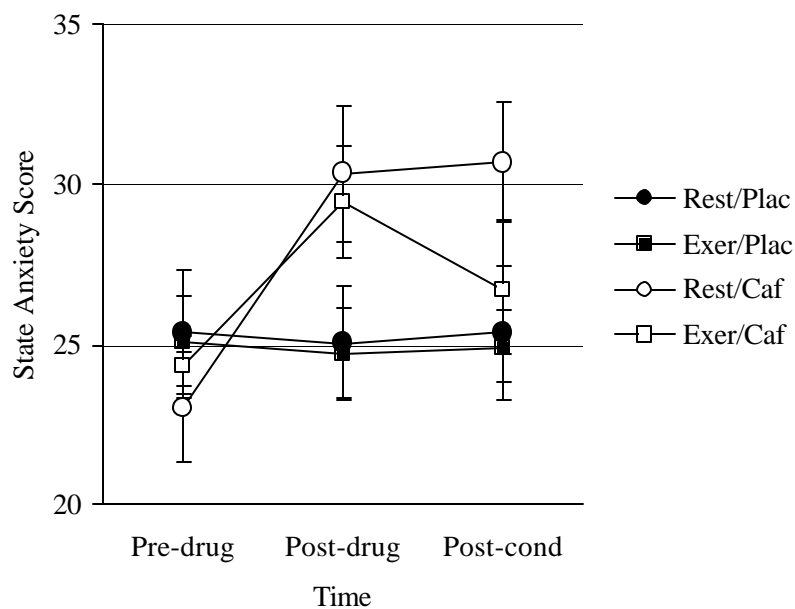


Figure 4.1. State anxiety scores as a function of time after exercise and quiet rest following both caffeine and placebo consumption (A) and as a function of time following caffeine and placebo consumption (B). Values in the figure are mean \pm standard error.

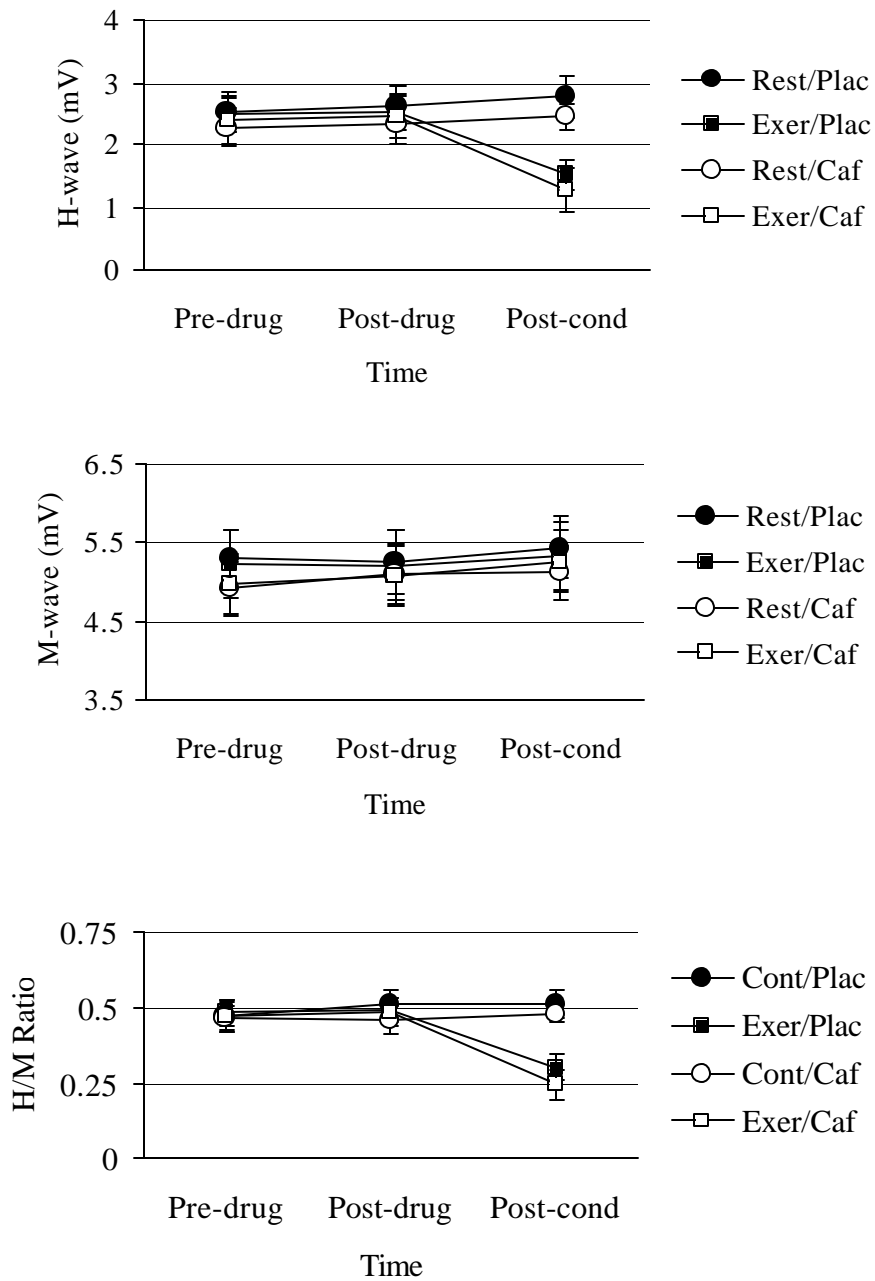


Figure 4.2. Soleus H-reflex (A), M-wave (B), and H/M ratio (C) values as a function of time after exercise and quiet rest following both caffeine and placebo consumption. Values in the figure are mean \pm standard error.

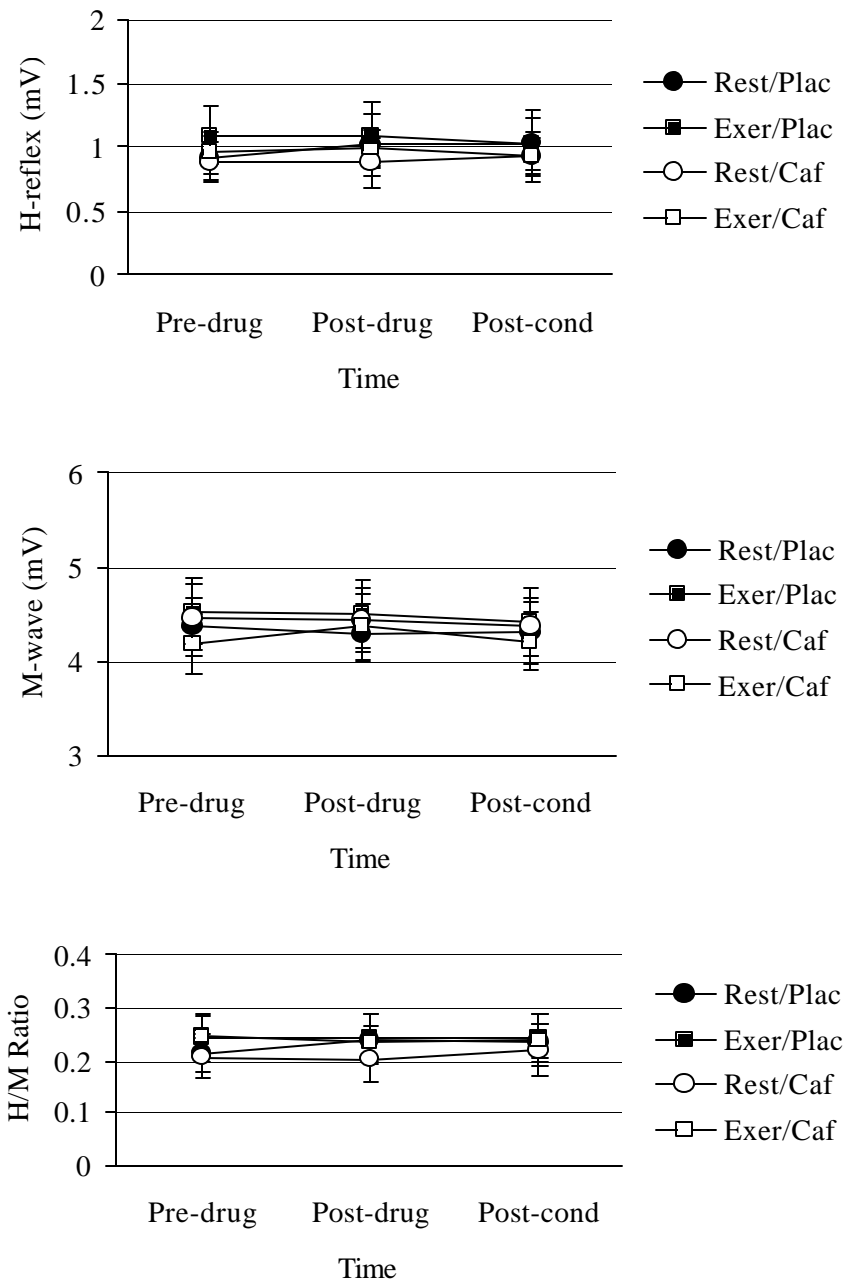


Figure 4.3. Flexor carpi radialis H-reflex (A), M-wave (B), and H/M ratio (C) values as a function of time after exercise and quiet rest following both caffeine and placebo consumption. Values in the figure are mean \pm standard error.

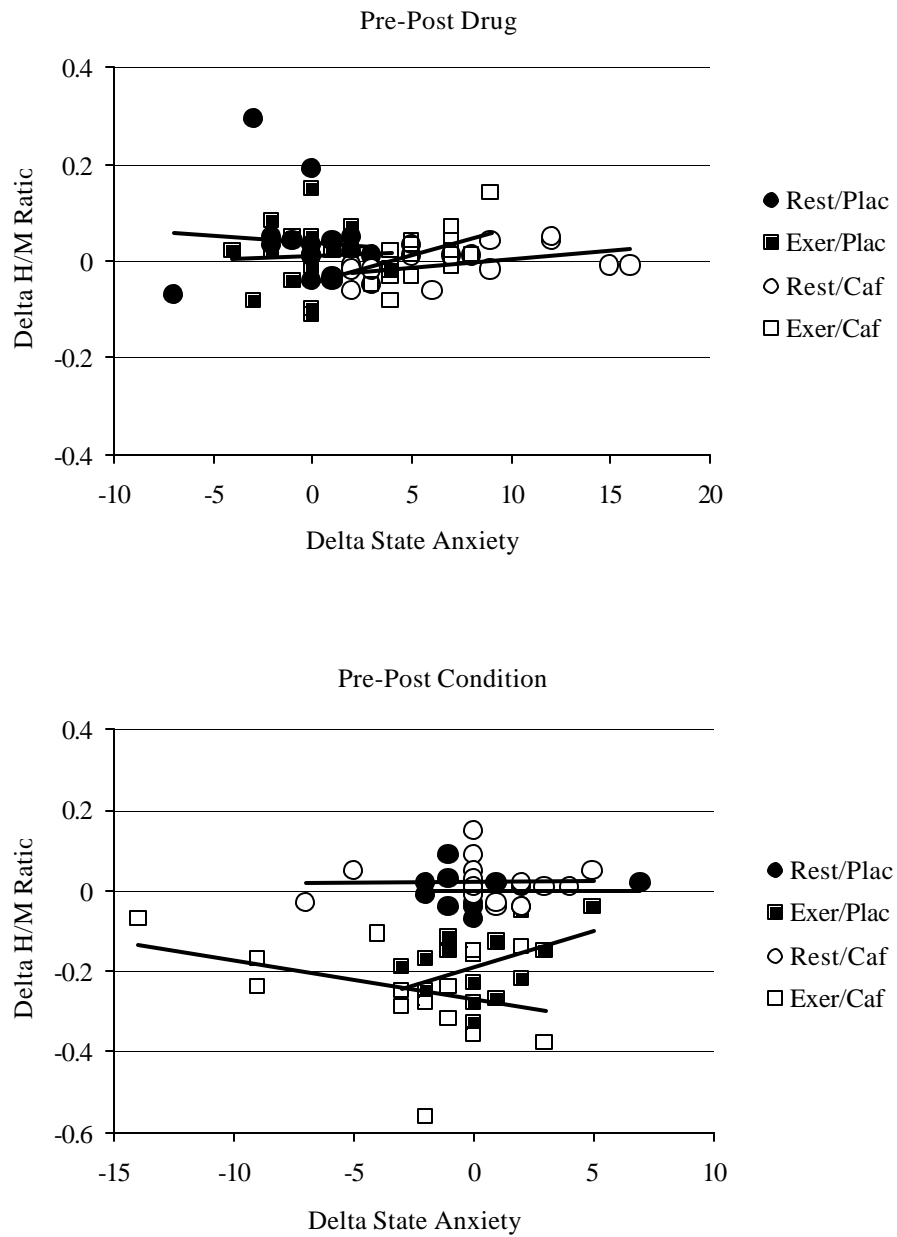


Figure 4.4. Scatter-plot of pre-post drug (A) and pre-post condition (B) changes scores for state anxiety and the soleus H/M ratio as a function of exercise and quiet rest following caffeine and placebo consumption.

CHAPTER 5

CONCLUSIONS

Anxiety disorders are a concern in modern society. Anxiety disorders pose a financial burden and the symptoms detract from an individual's quality life. Moreover, anxiety disorders have been implicated in the etiology of other diseases (e.g., cardiovascular disease).

Preventing anxiety disorders is important from a public health perspective. Pharmacological and psychological therapies are effective for treating symptoms of anxiety disorders. Yet, few individuals who report symptoms of anxiety seek help from a mental health professional. Exercise may be an important adjuvant for treating symptoms of anxiety and enhancing mental hygiene.

Acute exercise consistently has reduced symptoms of anxiety. But, few researchers have examined the concurrent effects of acute exercise on symptoms of anxiety and physiological variables that might be correlates of anxiety. Those who have focused on blood pressure and electrocortical activity, but generally have ignored neuromuscular measures. The Hoffmann or H-reflex has been considered to be a neuromuscular substrate of anxiety that is altered by acute exercise.

Two studies were conducted to evaluate the relationship between exercise-induced changes in anxiety and the H-reflex. The first study examined the effects of low and high intensity cycling exercise on state anxiety and the H-reflex among males having low or high trait anxiety. We found that (1) exercise and quiet rest resulted in similar reductions of state anxiety,

and the magnitude of the reductions was larger for males having high trait anxiety than low trait anxiety; (2) exercise, but not quiet rest, resulted in a reduction of the H-reflex; the magnitude of the reduction did not differ between males having low or high trait anxiety; and (3) reductions of self-reported anxiety were unrelated to reductions of the H-reflex across all three conditions. These results implied that the post-exercise reduction in the H-reflex was unrelated to self-reported anxiety after exercise. But the relationship was examined across a truncated distribution of state anxiety change scores, despite pre-screening for high trait anxiety.

Experimentally increasing and then decreasing anxiety and measuring the concurrent effects on the H-reflex would provide a stronger test of the relationships among exercise, anxiety, and the H-reflex. The second study examined the effects of moderate intensity cycling exercise on state anxiety and the H-reflex in individuals whose anxiety was experimentally manipulated by a large dose of caffeine. We found that (1) caffeine consumption increased state anxiety, but it did not influence the amplitude of the soleus H-reflex; (2) acute exercise reduced state anxiety only after consumption of caffeine, but it reduced the soleus H-reflex after consumption of either caffeine or placebo; (3) there was no evidence of a relationship between changes in state anxiety and soleus H-reflex; and (4) neither caffeine nor acute exercise influenced the flexor carpi radialis H-reflex. These results do not support the notion that exercise-induced anxiolysis is a cause of the post-exercise reduction of the soleus H-reflex.

As a whole, the findings indicated that the post-exercise reduction in the H-reflex is unrelated to self-reported anxiety after exercise. Hence, the post-exercise reduction of the H-reflex should not, as yet, be interpreted as a “tranquilizing” effect of acute exercise.

Researchers should examine the influence of processes originating in the spinal cord and brain on the post-exercise reduction of the soleus H-reflex. Some of the processes within the spinal cord that might cause a reduced H-reflex after exercise include presynaptic Ia inhibition, homosynaptic depression, reciprocal inhibition, recurrent inhibition, and Ib interneuron inhibition. Another possible explanation for a reduction in the H-reflex after exercise is increased inhibition of interneurons and neurons within the motor cortex of the brain. Researchers should consider examining neurobiological influences on the post-exercise reduction of the H-reflex, including GABA, endogenous opioids, norepinephrine, and serotonin. Future research ultimately will elucidate the nature of the relationship between acute exercise and the H-reflex.

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