EMOTION AND THE DEFENSE CASCADE: MODULATION OF VOLUNTARY AND INVOLUNTARY MOVEMENT

By

STEPHEN A. COOMBES

A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

2006

ACKNOWLEDGMENTS

I thank Dr. Christopher Janelle for his continued support and supervision of my academic development as well as his invaluable wisdom on matters of real life. Likewise, I thank Dr. Jim Cauraugh whose continued enthusiasm and keen interest have been hugely appreciated. I also thank my committee members, Dr. Mark Tillman and Dr. Ira Fischler for their patience, input, and support.

Finally I thank my family, the wonderful Christine, and my great friends on both sides of the Atlantic.

TABLE OF CONTENTS

page

LIST OF FIGURES

Abstract of Dissertation Presented to the Graduate School
of the University of Florida in Partial Fulfillment of the
Requirements for the Degree of Doctor of Philosophy

EMOTION AND THE DEFENSE CASCADE: MODULATION OF VOLUNTARY AND INVOLUNTARY MOVEMENT

By

Stephen A. Coombes

August 2006

Chair: Christopher M. Janelle
Major Department: Applied Physiology and Kinesiology

Evidence indicates that voluntary and involuntary movements are altered by affective context, the characteristics of an initiating stimulus, as well as the duration between affective context onset and initiating cue. The purpose of the present study was to delineate the central and peripheral mechanisms that contribute to this phenomenon. During the presentation of attack, erotic, household object and blank images, participants (N = 35) were instructed to respond to auditory stimuli (startle,107dB; or probe, 80dB) presented at varying time intervals following picture onset (500, 1500, 3000-5000 msec) by initiating a bimanual isometric contraction of the wrist and finger extensor muscles against two independent load cells. The startle blink response was also measured to provide an index of how valence and probe interval modulate involuntary movement. Analyses of electromyography and force measures revealed that (1) voluntary and involuntary movements are sensitive to short lead interval prepulse effects, (2) the intensity of an acoustic startle stimulus accelerates temporal components and strengthens

magnitude components of voluntary movement, (3) faster and stronger voluntary movements occurred approximately 1500 msec post image onset, when initiated to startle cues with a strong trend indicating that this pattern was accentuated during exposure to attack images. Collectively, these findings carry significant implications for those seeking to facilitate the speed and force of voluntary movement (i.e., movement rehabilitation), and for those seeking to regulate emotional input so as to optimize the quality of intended movements.

CHAPTER 1
INTRODUCTION

Emotion and Movement

Rapidly identifying emotionally salient information in threatening and dangerous contexts, and demonstrating the ability to translate that information into successful and appropriate behaviors is critical to survival. A primary function of emotion, therefore, is the preparation for action (Schupp, Junghofer, Weike, & Hamm, 2003a). The link between primitive emotions and overt motor actions was first noted by (Cannon, 1929), who suggested that when confronted with a dangerous situation, an organism elicits an "emergency reaction" composed of either a fight or flight survival response. The basic principle of Cannon's work remains intact today. Modulated by the threat from predators, defensive behaviors have been classified into three categories that traverse the entire animal kingdom: freezing, fleeing, and fighting (defensive attack: Eilam, 2005). Demonstrating the impact these defensive predispositions have on voluntary and involuntary movement is the primary purpose of this proposal.

The utility of understanding defensive predispositions is two fold. First, activating emotional circuits that predispose humans to execute specific motor actions may be an effective method to forge new pathways between intention and movement for those suffering motor impairment (e.g., stroke). For example, despite increased research efforts and rehabilitation options, over 65% of individuals with stroke have residual motor impairments one-year post (Wade, Langton-Hewer, Wood, Skilbeck, & Ismail, 1983). As such, understanding how emotions modulate movement may lead to emotional

manipulations being fused into existing rehabilitation techniques to enhance their effectiveness.

Second, within a wide range of performance contexts, movements have to be executed during dynamic states of emotional flux. In consequence, predisposed movements may be incongruent with intentional movements. Understanding how emotions predispose movement, therefore, will be essential in tailoring regulatory strategies to combat emotion driven dispositions. In short, understanding how active defensive circuitry alters overt motor behavior holds considerable promise for emotion regulation as well as movement rehabilitation.

Defensive Behavior

Animal models indicate that the amygdala and the dorsal and ventral periaqueductal gray (PAG) mediate the expression of defensive behaviors according to the nature of the threat, including its 1) type (i.e., immediate/innate/ conditioned), 2) proximity, and 3) complexity. The defense cascade model, conceptualized within an evolutionary perspective of the relative position of predator and prey (Bradley & Lang, 2000; Fanselow, 1994; Lang, Bradley, & Cuthbert, 1997; Wade et al., 1983), proposes three distinct defensive phases: pre-encounter, post-encounter (freezing), and circa-strike/defensive fighting/fleeing.

Within picture-viewing paradigms, exposure to an unpleasant cue results in a stable pre-encounter condition that is then superseded by a post-encounter state reflected in an initial “orienting of attention” and a rapid increase in skin conductance response (arousal). Oriented attention typically manifests in strong inhibition of the startle blink reflex for highly arousing visual stimuli (Bradley, Cuthbert, & Lang, 1993), cardiac deceleration (Bradley, Codispoti, Cuthbert, & Lang, 2001), and a reduction in postural

sway (Azevedo et al., 2005). Cardiac acceleration and potentiation of the startle blink reflex (accentuated in unpleasant contexts) signal the transition from a post encounter freezing phase to defensive mobilization (approx. 800 msec).

Orienting of Attention: Valence or Arousal?

Although activation of defensive circuitry (e.g., startle blink potentiation) has been demonstrated early in the viewing period when phobic's view objects relating to their phobias (Globisch, Hamm, Esteves, & Öhman, 1999), startle blink inhibition among controls typically coincides with highly arousing affective foregrounds, independent of valence (Bradley et al., 1993). The notion, however, that attention rather than valence modulates the early blink reflex (<800 msec) has recently been contested. Specifically, Stanley and Knight (2004) demonstrated that relative to positive and neutral contexts, blink potentiation occurred at both early (300msec) and late (2-5 s) probe times during exposure to threat images. Conversely, exposure to disgust images only resulted in a main effect of blink potentiation relative to positive contents. As such, averaging across "unpleasant" foregrounds rather than analyzing specific categories (i.e., threat, disgust) within broad time windows may prevent threat-related blink potentiation from emerging. Consequently, acute specification of emotional context, as well as probe interval duration, are essential in understanding the time course of active defensive circuitry. The primary goal of this proposal, therefore, is to confirm threat related startle blink potentiation across freezing and defense mobilization phases, and to determine how this progression simultaneously alters voluntary movement.

The innate predisposition to protect oneself from danger (active defensive system) is complemented by the instinctive tendency to approach pleasant stimuli (active appetitive system). Capturing the polarity between approach and avoidance, Lang,

Bradley and colleagues (Lang et al., 1997) have proposed the Biphasic Theory of emotion. The extent to which emotions alter the direction (approach/withdrawal), speed, magnitude, and accuracy of voluntary movements has been captured within a number of behavioral protocols. Specifically, relative to activation of appetitive circuitry, activation of defensive circuitry accelerates avoidance movements (i.e., pushing a lever away from the body, Chen and Bargh, 1999; Duckworth et al., 2002; Marsh et al., 2005), accelerates the speed and decreases the accuracy of a controlled motor task (Coombes, Janelle, & Duley, 2005), and leads to greater force production during a sustained isometric contraction without sacrificing movement variability (Coombes, Cauraugh, & Janelle, 2006).

In addition to force production, EMG measures are routinely used to index voluntary (Carlsen, Chua, Inglis, Sanderson, & Franks, 2004a; Valls-Solé, Rothwell, Goulart, Cossu, & Munoz, 1999; Valls-Solé et al., 1995) and involuntary movements (Hillman et al., 2004; Stanley and Knight 2004). Combining EMG and force measures offers a unique approach to indexing the effect of emotion on movement. Indeed, understanding the physiology of EMG and force production ensures that findings can be interpreted according to physiological mechanisms.

EMG and Force Measures

Amplitude of surface EMG is routinely used to quantify voluntary and involuntary muscular contraction (Bolton, Cauraugh, & Hausenblas, 2004; Hillman, Rosengren, & Smith, 2004; Moore, Drouin, Gansneder, & Shultz, 2002; Rau, Schulte, & Disselhorst-Klug, 2004; Stanley & Knight, 2004). Surface EMG amplitude and latency is sensitive to the number and rate of motor unit contractions (Andreassi, 2000), as well as the size and location of motor unit activation relative to the position of the corresponding sensors

(Keenan, Farina, Merletti, & Enoka, 2005). In addition, the size of the evoked muscle potential is influenced by sarcolemmal conduction velocity, axonal conduction velocity, variability in the activation times of motor neurons, and shape of the intracellular action potential (Keenan et al., 2005).

Although numerous variables alter EMG amplitude, startle elicited blink amplitudes consistently vary according to affective valence. For example, greater peak EMG amplitude, reflecting a stronger muscular contraction, has been associated with startle elicited blink reflexes during exposure to threat images (relative to neutral and pleasant) at early (300msec: Stanley & Knight, 2004) and late probe intervals (> 2000msec: Lang, Bradley, & Cuthbert, 1990; Stanley & Knight, 2004). In addition, we (Coombes et al., in review) have demonstrated a similar effect on voluntary movement, such that exposure to unpleasant images interacts with the presentation of movement initiating startle cues (relative to an 80db tone) resulting in greater peak amplitude relative to all valence tone probe conditions. Further, peak EMG voluntary and involuntary latencies attenuate when movements are executed to startle cues during exposure to unpleasant images (Lipp, Siddle, & Dall, 1997). Collectively, EMG indices of voluntary and involuntary movement have been interpreted as indicating that an evolutionary/survival advantage maybe gained from the execution of strong, rapid muscle contractions.

The force produced by a muscle depends on the number and size of active motor units and the rate at which those units discharge action potentials (Macefield, Fuglevand, & Bigland-Ritchie, 1996; Moritz, Barry, Pascoe, & Enoka, 2005). Specifically, two mediating mechanisms have been proposed to account for muscular force production

(Kamen & Du, 1999); the “size principle” and “rate coding.” By sequentially increasing the number of active motor units within the motoneuron pool, from the smallest motor units to the largest, the total force output increases (size principle) (Aimonetti, Vedel, Schmied, & Pagni, 2000; Henneman, 1979; Schmied, Aimonetti, & Vedel, 2002; Schmied, Morin, Vedel, & Pagni, 1997). This recruitment order has been confirmed for isometric contractions with a high correlation between recruitment force threshold and twitch force (Riek & Bawa, 1992). Second, although motor unit discharge rates have been associated with variations in force production (rate coding: (Milner-Brown, Stein, & Yemm, 1973), given that motor units vary according to threshold and spike amplitude, it is not a simple linear relationship between discharge rate and force production (Hamada, Kimura, & Moritani, 2004; Klein, Ivanova, Rice, & Garland, 2001). Nevertheless, we have previously demonstrated that indices of force are modulated according to initiating stimulus and valence. Specifically, peak forces are accentuated, onset to peak force slopes are steeper, and latencies are shorter when ballistic wrist and finger extensions are executed to startle relative to tone cues (Coombes et al., in review). Further, force onset slopes are steeper, and latencies are shorter when ballistic movements are executed during unpleasant relative to pleasant and blank exposure conditions. These data suggest that startle initiating cues and activation of defensive circuitry increase the size and/or number of active motor units.

Acoustic Initiated Movements

The acoustic startle reflex is a short-latency behavior elicited by a sudden and intense acoustic stimulus (Grillon & Baas, 2003). Considered a primitive defensive reflex, the acoustic startle serves as an interrupt of ongoing behavior (Lang et al., 1990). The probable chain of activation of the primary acoustic startle reflex is generally

considered to consist of 3 synapses: (1) cochlear root neurons; (2) PnC neurons; and (3) motor neurons in the spinal cord (Lang, Davis, & Ohman, 2000; Y. Lee, Lopez, Meloni, & Davis, 1996). Direct links between the amygdala and the nucleus reticularis pontis caudalis (PnC) and PAG are critical in potentiation for the startle reflex (Davis & Whalen, 2001; Zhao & Davis, 2004).

Accelerating premotor reaction times by replacing “go” signals with startle cues has been consistently replicated (Carlsen et al., 2004b; Valls-Solé et al., 1999; Valls-Solé et al., 1995). To account for these findings the subcortical triggering hypothesis has been proposed, and contends that startle cues initiate movements that are stored subcortically within the reticular formation (Carlsen, Chua, Inglis, Sanderson, & Franks, 2004a). Should this be the case, given that amygdala (via PAG) projections to the PnC are responsible for potentiation of the startle blink, there is reason to believe that voluntary movements executed from the PnC will be altered by emotion in a similar fashion to involuntary movements. As such, we will determine how the characteristics of voluntary and involuntary movements are altered according to varying initiating cues, affective contexts, and probe intervals.

Participants will be exposed to attack, erotica, neutral, and blank images. Picture onset will be a cue for participants to ready themselves to move. During image presentation, participants will be instructed to initiate a simple RT ballistic movement at the presentation of acoustic stimuli (either a startle, 107dB; or tone, 80dB). The presentation period will run for 6 seconds, during which startle and tone cues will be equally represented at 3 predetermined time intervals during the exposure period (500msec, 1500msec, 3000-5000msec). Voluntary movements of the wrist and finger

extensors will be indexed via force transducers and EMG sensors on the fore-arms. An index of the involuntary blink reflex will be captured via EMG sensors beneath the left eye. Three hypotheses are offered.

Hypotheses

1a) We predict that if valence modulates movement at all time intervals, movements to acoustic cues during exposure to threat images will be significantly different from erotica, neutral, and blank exposures (attack = accelerated times, accentuated peaks, steeper slopes. [1])

1b) However, if arousal modulates movement early in the exposure period (500msec), movements during exposure to attack and erotica images will be similar, and each will be different compared to neutral and blank images (attack and erotica = decelerated times, attenuated peaks, shallower slopes).

2) Relative to tone initiated voluntary movements, startle initiated movements at all probe intervals will be significantly different from all tone initiated movements (startle = accelerated times, accentuated peaks, steeper slopes. [1])

3) Significant positive correlations between corresponding voluntary and involuntary dependent variables during startle trials will permit the interpretation that voluntary and involuntary movements share similar subcortical pathways.

---

[1] **Accelerated times**: faster voluntary and blink PMTs; faster voluntary and involuntary EMG risetime; faster force risetime; faster peak blink EMG latency; **Accentuated peaks**: greater peak voluntary and blink EMG; greater voluntary peak force; **Steeper slopes**: steeper slope to voluntary and blink peak EMG; steeper slope to voluntary peak force

CHAPTER 2
EMOTION AND MOVEMENT

Overt coordinated motor behavior is the culmination of a complex interaction between various functioning neural structures. To better understand the controlling mechanisms of movement related decision making, movement preparation, movement execution, and movement feedback, the major cortical and subcortical structures involved in movement will be addressed. Specific attention will be paid to areas where emotion may impact the motor system. The primary motor area (M1), the supplementary motor area (SMA), the dorsal premotor area (PMd), and the cingulated motor areas (CMA) are included in a section concerning the role of the cortex in movement production. Following a summary of the cortical regions, the basal ganglia and reticular formation are evaluated in terms of their role in motor behavior.

Two major improvements have been made in the evolution of human motor control; the capability to maintain an erect posture and the ability to move the fingers independently (Canedo, 1997). While bipeds and quadrupeds boast neural mechanisms that integrate bodily movement and associated postural adjustments, the postural constraints imposed by bipedal locomotion are more demanding (Canedo, 1997). The activity of distal, proximal, and axial muscles have to be controlled by some structure or structures able to coordinate medial and lateral motor systems. Specific cortical and subcortical regions, coupled with descending spinal tracts collectively permit the necessary simultaneous activation of distal and postural muscles (e.g., Picard & Strick,

1996; Vulliemoz, Raineteau, & Jabaudon, 2005). Details of the cortical and subcortical structures that permit such motor control are presented below.

Cortical Control of Movement

Large regions of the brain located on the lateral surface and on the medial wall of each hemisphere participate in the generation and control of movement. Four distinct areas have been identified: 1) Primary motor area (M1, the precentral gyrus), 2) Supplementary motor area (SMA, adjacent to the premotor area, but on the medial surface of the hemisphere), 3) Premotor area (anterior to M1, on the lateral aspect of the hemisphere), and 4) Cingulate motor area (in the anterior part of the cingulate sulcus, adjacent to the inferior end of the SMA).

Primary Motor Cortex (M1)

Located along the precentral gyrus in Brodmans area 4, the M1 houses considerable pyramidal neurons that directly link (via the corticospinal tract) with the spinal cord. In consequence, the M1 is considered a key structure in the execution of voluntary movement (Canedo, 1997; Cunnington, Windischberger, Deecke, & Moser, 2002; Lee, Chang, & Roh, 1999; Wildgruber, Erb, Klose, & Grodd, 1997). Traditionally, the MI was thought to be exclusively involved in the execution of movements (Richter, Andersen, Georgopoulos, & Kim, 1997). However, this conventional view was challenged by the discovery of higher-order motor components in the MI of monkeys (Georgopoulos, Taira, & Lukashin, 1993). Preparatory activity in the M1 in monkeys stimulated corresponding questions to be asked of the M1 in humans. During completion of a delayed cued finger movement task (i.e., a warning signal followed by a delay, followed by a go signal) Richter et al. (1997) collected event-related fMRI data from M1, PM, and SMA and reported activity in all three areas during movement preparation and

movement execution. As predicted, activity in M1 was weaker during movement preparation than during movement execution; and although activity was of similar intensity during preparatory and execution periods in the secondary motor areas, during the execution phase M1 activity was greater relative to activity in the secondary areas. Although M1 activity during preparatory periods has been corroborated elsewhere (Crammond & Kalaska, 2000; Mushiake, Inase, & Tanji, 1991), it should be noted that the M1 cells sensitive to movement preparation have been located close to the dorsal PM area (Crammond & Kalaska, 2000).

To date, however, M1 activity continues to be closely associated with movement execution, best exemplified by the consequences of M1 lesions which result in impaired voluntary movements of associated body parts (Lang & Schieber, 2003). Specifically, the ability to move and control one body part exclusively of all others (e.g., the fingers) is severely impaired, with attempted individual movements often accompanied by considerable involuntary movements of adjacent body parts (Lang & Schieber, 2003; Schieber & Poliakov, 1998). Additional support of the M1's acute control of movement is demonstrated in subtle finger movements; movements that can be temporarily unattainable by reversible inactivation of small portions of the hand representation area in M1 (Brochier, Boudreau, Pare, & Smith, 1999; Schieber & Poliakov, 1998).

M1 activation is not essential or alone, however, in its control of voluntary movement as evidenced by the very limited involvement of the cat M1 during routine locomotion across a regular surface (Beloozerova & Sirota, 1993; Marple-Horvat, Amos, Armstrong, & Criado, 1993). Investigations into the many basic neuronal networks regulating somatic movement have, in consequence, successfully focused on the

brainstem (Canedo, 1997). Under circumstances when automated movements have to be modified online (i.e., traversing undulating surfaces), and alterations in exact placement of the foot are demanded, the discharge of the pyramidal neurons in the motor cortex are considerably accentuated; the more difficult the placement, the greater the discharge (Beloozerova & Sirota, 1993). In consequence movements that demand acute online adjustment, or the use of individual proximal body parts, require M1 input if successful execution is to be realized.

A redeeming quality of the M1 that emanates across the majority of literature concerns its physiological make-up. Evidence suggests that rather than specific portions of the M1 unilaterally controlling specific movements, the diversity and overlapping nature of the distributed network of neurons within each portion of the M1 ensure that damage to one area can often be compensated for by adjacent areas (Donoghue & Sanes, 1988; Sanes & Donoghue, 2000). A considerable advantage of such a distributed network permits the immense storage capability and richness of function as well as providing a basis for network flexibility (Elbert, Pantev, Wienbruch, Rockstroh, & Taub, 1995; Sanes & Donoghue, 2000). As such, the amount of brain matter devoted to any particular body part is dynamic and flexible, with neural representations waxing or waning according to use; in turn altering the level of control the associated portion of the M1 has over that body part (Elbert et al., 1995).

The increase and decrease in limb specific cortical representation is termed *neural plasticity* (Sanes & Donoghue, 2000). Maintaining or enhancing the cortical representation of any body part is reliant upon continued use; a severe infarction or lesion that prevents the flow of necessary information within the neural structures that permit

movement typically leads to catastrophic consequences (Wilson, Gandevia, Inglis, Gracies, & Burke, 1999). If a limb cannot be used, its cortical representation diminishes via cortical reorganization, sometimes with alarming consequences (Woodhouse, 2005). On the opposite end of the continuum, however, the alternative is that neural representation increases the more use a specific limb gets; the larger the corresponding cortical representation, the finer the control one has over that specific limb (Elbert et al., 1995).

This reciprocal cause and effect neural plasticity relationship has been elegantly demonstrated in rats (Donoghue & Sanes, 1988). Following the amputation of a rats forelimb at birth, 2-4 months following amputation the authors noted the occurrence of 3 organizational differences: 1) intact muscle groups had enlarged cortical representations, 2) normally weak connections from MI to the proximal musculature were strengthened, and 3) muscles were grouped in unusual combinations in the reorganized cortical maps. Evolving from work in rat models, observation of the dynamic substrate of the human motor cortex is a relatively new phenomena, but one that warrants considerable optimism within the movement rehabilitation domain. Indeed, current knowledge portrays M1 as a distributed network of neurons that collectively demonstrate an innate ability to reorganize according to physiological circumstance.

In conclusion, given an intact network between the cortex and limb, the M1 is essential to the initiation and control of volitional movement. **If emotion has the capacity to alter movements, which one assumes it does, one must consequently ask, exactly which part of the process does emotion modulate? Given the physiological make-up, anatomical connections, and function of M1, there appears to be no direct**

route via which emotion can alter the initiation of movements within the M1. Although other brain regions were thought to influence motor output only by way of efferent projections to M1, recent evidence suggests that the secondary and cingulate motor areas also have direct access to corticospinal tracts and the lower brain mechanisms essential in the realization of volitional movement (Dum & Strick, 1991).

The Supplementary Motor Area (SMA)

Located in Brodman's area 6 the SMA lies medial to the premotor area and projects to M1 and to the corticospinal and corticobulbar tracts. Removing portions of the SMA produces specific deficits in bimanual coordination (Brinkman, 1984) or internally guided or instructed movements (Kazennikov et al., 1998; Kermadi, Liu, Tempini, & Rouiller, 1997), whereas chemical inactivation results in an inability to sequentially execute multiple movements (Shima & Tanji, 1998). Likewise, clinical SMA lesion studies have corroborated impairments similar to those induced via inactivation: the failure of sequential motor performance (Laplane, Talairach, Meininger, Bancaud, & Bouchareine, 1977; Laplane, Talairach, Meininger, Bancaud, & Orgogozo, 1977) and a reduction in spontaneous movements (Krainik et al., 2001). The SMA therefore appears to be charged with guiding sequential movements based on internal cues, and is often associated with the performance of pre-learned motor sequences (Jenkins, Brooks, Nixon, Frackowiak, & Passingham, 1994), or self paced motor behaviors (e.g., self paced finger movements: (Larsson, Gulyas, & Roland, 1996).

Subcomponents of the SMA

The SMA may not function as a single unit, and the functions charged to the SMA as a whole may be housed within independent functionally distinct regions. Specifically, whereas lesions of the SMA lead to deficient sequential motor performance (Laplane,

Talairach, Meininger, Bancaud, & Bouchareine, 1977) and a reduction in spontaneous movements (Krainik et al., 2001), lesions of the pre-SMA manifest in deficits in updating sequential movements (Shima & Tanji, 1998) and the acquisition of sequential procedures (Nakamura, Sakai, & Hikosaka, 1999). The functional difference between different portions of the SMA emerged from the notion that cognitive demand(s) associated with the motor task modulate regional SMA activity (Deiber et al., 1991).

In monkeys first, and more recently in humans, anatomical and functional data (Geyer, Matelli, Luppino, & Zilles, 2000; Picard & Strick, 1996) have resulted in the SMA being split into two distinct portions: 1) pre-supplementary motor area (caudal portion of area 6), and 2) supplementary motor area proper (rostral portion of area 6). The connectivity, physiology, and function of the pre-SMA suggest that it is more closely aligned with prefrontal areas than with motor areas (Picard & Strick, 2001). **Prefrontal areas provide cognitive, sensory, and motivational inputs for motor behavior** (Walton, Devlin, & Rushworth, 2004), whereas the motor areas are concerned more with the core fabric of movement (e.g. muscle patterns). The notion of splitting the SMA into two separate areas is founded in two distinct differences in the anatomical connections of the pre-SMA and SMA proper: 1) only the SMA proper is directly connected to M1 and to the spinal cord (Dum & Strick, 1991; Wang, Shima, Sawamura, & Tanji, 2001), and 2) only the pre-SMA is interconnected with the prefrontal cortex (Lu, Preston, & Strick, 1994; Luppino, Matelli, Camarda, & Rizzolatti, 1993). Notably, these distinct anatomical characteristics are reflected in variations in task specific activity (Geyer et al., 2000).

Given increases in activation of the SMA with the acquisition of a motor sequence task, the interpretation until recently, was that the SMA is associated with

learned sequential movements (Hikosaka et al., 1996). Recent accounts of task specific pre-SMA activity, however, have altered the inferred role the SMA plays in the motor domain. (Sakai et al., 1999) recently compared pre-SMA activation in closely matched tasks requiring visuo–motor associations, but varied in motor and perceptual sequence components. Activation of the pre-SMA occurred in all tasks that required visuo–motor associations relative to tasks that required sequential processes. Moreover, pre-SMA activation was greatest in the conditional task, in which non-sequential responses were randomly determined by the color of visual cues. **These data indicate that activation of the pre-SMA has little to do with motor sequence learning, rather, that pre-SMA activation reflects the establishing or retrieving of visuo–motor associations.**

Functional differences between the SMA proper and pre-SMA have been further corroborated (in monkeys) during the performance of a reaching task in which two visual instruction cues were presented: 1) target location, and 2) reaching arm, separated with a delay between the cues (Hoshi & Tanji, 2004a, 2004b, 2004c). The authors identified four major differences in pre-SMA and SMA proper activation: 1) neuronal activity preceding the appearance of visual cues was more frequent in the pre-SMA, 2) a considerable portion of pre-SMA neurons (relative to SMA proper neurons) responded to the first and second cue, reflecting the processing of visual stimuli and their associated meaning (i.e., coupling target location and arm use), 3) during the motor planning period, activity in the pre-SMA reflected target location, while activity in the SMA reflected which arm to use, and 4) during movement execution, increased activity occurred in SMA and was selective for the use of either the ipsilateral or contralateral arm. In contrast, activity of the pre-SMA was suppressed. These findings provide further evidence for the

functional dissection of the SMA, corroborating previous claims that **the pre-SMA is more concerned with processing and integrating relevant internal and external related stimuli (supported by its links to the prefrontal cortex; (Lu et al., 1994; Luppino et al., 1993), while the SMA proper is integral to the motor planning period, reflecting which limbs are being readied for movement, in addition to the execution of movement those limbs.**

Additional studies have extended the involvement of the pre-SMA to associations based on auditory stimuli (Kurata, Tsuji, Naraki, Seino, & Abe, 2000). Visual and auditory versions of a conditional choice reaction time paradigm generated pre-SMA activations equal in magnitude (Sakai et al., 2000). The contribution of the pre-SMA to sensory–motor associations, therefore, maybe considered modality-independent as well as effector-independent, given that similar regions are activated in unimanual left and right limb conditional motor tasks (Kurata et al., 2000; Sakai et al., 2000). This supports the view that the pre-SMA operates at a more abstract level and is more closely related to the processing, integration, and maintenance of relevant sensory information than response selection or execution (Cunnington et al., 2002; Kurata et al., 2000; K. M. Lee et al., 1999; Sakai et al., 2000). In stark contrast, SMA proper activation only occurs during movement-related components of visual or auditory tasks, and appears to be more involved with the pure movement portions of specified tasks (Boecker et al., 1998; Cunnington et al., 2002; Stephan et al., 1995).

The Premotor Cortex (PM)

The premotor cortex lies anterior to the M1 in Brodman's area 6 and the lower part of area 8 (See Figure 2-1). PM receives afferents from the thalamus and projects onto portions of the corticospinal and corticobulbar tracts as well as to the M1

(Dum & Strick, 1991). Dum and Strick also note that the total number of corticospinal neurons in the arm representations of the PM equals or exceeds the total number in the arm representation of the M1. PM collectively comprise more than 60% of the cortical area in the frontal lobe that projects to the spinal cord, and consequently, is the origin of a substantial portion of the corticospinal system. Each of the PM areas has direct access to the spinal cord, and as such, each has the potential to influence the generation and control of movement independently of M1.

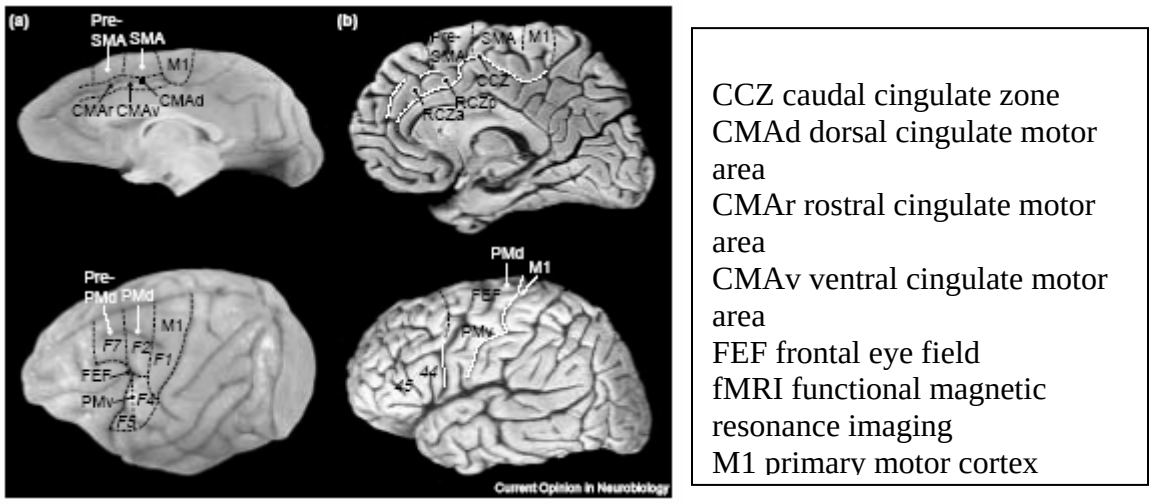

Figure 2-1. Imaging the premotor areas. Motor areas of the frontal lobe in monkeys (a) and homologous areas in the human (b). In humans, the border between areas 6 and 4 on the lateral surface is located in the anterior bank of the central sulcus. For illustration, the border is drawn on the surface of the hemisphere along the central sulcus (bottom, white dotted line). Except for the most medial portion, M1 does not occupy the precentral gyrus.

The premotor cortex controls proximal and trunk muscles in addition to controlling voluntary movement of the eyes via the frontal eye fields (Dum & Strick, 1991). Damage to the premotor areas in humans leads to a syndrome termed “apraxia” in which patients are unable to perform skilled motor tasks (Hanna-Pladdy, Heilman, & Foundas, 2001; Leiguarda & Marsden, 2000). The premotor area is activated during movements that are primarily guided by visual, auditory, or somatosensory stimuli (Jenkins et al., 1994;

Larsson et al., 1996). Van Mier and colleagues (van Mier, Tempel, Perlmutter, Raichle, & Petersen, 1998) reported increased activation in the dorsal premotor cortex (PMd) during a battery of maze-tracing tasks (right- and left-handed) and suggested that PMd activation was involved with the temporal aspects of movement planning (Halsband, Ito, Tanji, & Freund, 1993), as well as the temporal aspects of the acquisition, execution (Middleton & Strick, 2001; Seitz et al., 1994), and retention of motor tasks (Middleton & Strick, 2001). Similar to pre-SMA activation patterns noted above (Kurata et al., 2000; K. M. Lee et al., 1999; Sakai et al., 2000), van Mier et al. reported that PMd cortex activity was similar for right- and left-handed performance, suggesting that activity in the PMd is involved in abstract processes of complex tasks, rather than processes directly related to the execution of those tasks. Research concerning the functioning PM in monkeys, however, has guided more recent human research which has further distinguished anatomical, physiological, and functional subdivisions within the area.

Subcomponents of PM cortex

Founded on anatomical and physiological differences, the dorsal part of the PMd in primates has been divided into rostral (PMd_r or pre-PMd) and caudal (PMd_c or PMd proper) subdivisions (Matelli, Luppino, & Rizzolatti, 1991). These differences are comparable to those that determine the pre-SMA/SMA proper distinction noted above. Indeed, the PMd_c (PMd proper) shares three primary characteristics with the SMA proper: 1) both areas project to the M1 and directly to the spinal cord (Dum & Strick, 1991; He, Dum, & Strick, 1993), 2) neither area has substantial interconnections with prefrontal cortex (Lu et al., 1994), and 3) neurons in both regions are primarily involved in aspects of motor control (Geyer et al., 2000). Likewise, the PMd_r (pre-PMd) has much in common with the pre-SMA, specifically: 1) neither of these areas project to the M1 or

to the spinal cord (Dum & Strick, 1991; He et al., 1993), rather 2) both regions are interconnected with areas of prefrontal cortex and with the reticular formation (Geyer et al., 2000; Lu et al., 1994) and finally, 3) results of neuronal recording and functional imaging studies suggest that the pre-SMA and the PMd_r are more involved in cognitive than in motor processes. In short, the PMd_c contains a high proportion of neurons that display set- and movement-related activity whereas neurons in the PMd_r are more responsive to sensory cues, and fewer are active in relation to movement.

Functional PMd predictions founded in animal data have guided human research. For example, Simon et al. (2002) predicted that the PMd_r would primarily activate during attention and/or memory processes whereas activity of the PMd_c would correspond with motor preparation/execution. Developed from the monkey reaching task noted above (Hoshi & Tanji, 2004a, 2004b, 2004c) in which a first cue guided the focus of spatial attention and memory, and the second instructed an arm movement, Simon et al. modified the protocol to produce two tasks, during which fMRI data was collected. To maximize spatial attention and memory demands the first task presented a series of 4, 8, or 12 white squares. At the end of the series, motor execution was signaled by the appearance of 1 red and 1 green square and a central fixation cross turning from white to either green or red. At this point, one of two possible button presses was required (middle finger = green/ index finger = red). For the experimental condition of task 1, the correct response was determined by which execution cue held the same position as the last white square in the sequence of 2, 8, or 12 white squares. The color of the square in the matching position determined the correct response. For the control condition, the response was determined by the color of the fixation cross.

The second task extended the motor preparation phase by lengthening and varying the delay (between 1 and 5.5 s) between the instructional cue and movement execution. Presentation of a single white square was followed by a fixed delay. Then the 2 execution squares were presented for variable durations together with a green or red fixation cross. For both the experimental and control conditions of task 2, the correct response was determined by the color of the square that occupied the location of the final stimulus (green in this example). However, for the experimental condition, subjects were required to withhold their response until offset of the execution squares (and concomitant return of the white cross), whereas, for the control, they were asked to respond immediately following directional cue onset.

As expected, subjects' displayed significantly slower reaction times in the experimental condition of the spatial/memory task (task 1: control – experiment = -137 ms) given the required spatial matching that preceded movement execution. Alternatively, but again in line with prediction, the manipulation of motor preparation length in task 2 resulted in faster reaction times (control – experiment = 283 ms) suggesting that motor preparation did occur during the extended delay period, and resulted in the manifestation of faster RTs. Concerning the pre-motor areas, as expected the spatial attention/memory paradigm preferentially activated the PMd_r, whereas the motor preparation paradigm engaged the PMd_c. Interpretations corroborated previous evidence from both monkey and human studies. **Similar to the pre-SMA and SMA proper distinction, it appears that the human PMd_r participates in spatial attention and working memory (Coull & Nobre, 1998; Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; Petit et al., 1996; Stern et al., 2000), while the PMd_c is central to the**

execution of movement. The simultaneous activation of other cortical areas also confirmed expectation; findings will be discussed later in a summary section addressing the nature of interactive activity across all cortical motor areas.

Cingulate Motor Areas

The majority of natural actions are selected voluntarily from many possible options. Actions are often chosen based on their predicted consequences; predictions that are based on the internal and external state of the organism. As stated, emotions influence action and typically emerge in circumstances where adaptive control is required (Ekman & Davidson, 1994). As such, all eyes point towards a structure or set of structures that bridge emotion and action. The M1, SMA, and PM, however, do not appear to be the motor structures that directly link the emotion and movement domains. **Motor control research has been and continues to be successful in determining the complex network of structures that plan, control, and execute movement (Simon et al., 2002), but knowledge of the human motor system for the most part has developed independently of the interacting influence that emotions may play.** In terms of the motor cortex, the progression that has been made in alleviating this issue has focused on the cingulate motor area (CMA).

In addition to its role in movement execution, evidence suggests that it is the CMA, given its anatomical position and functional connections with surrounding brain areas (Vogt & Pandya, 1987), that decides, directs, and assesses the appropriateness of motor function (Picard & Strick, 1996). The CMA is located within regions lining the cingulate sulcus in the medial surface of the cerebral hemisphere and has been dissected into rostral (CMAr) and caudal (CMAc) portions (Matelli et al., 1991). Distinguishing itself from the primary, pre, and supplementary motor areas, the CMA receives

considerable afferent input from limbic structures (as well as the prefrontal cortex), ensuring a flow of information to the CMA concerning motivation, the internal state of the organism, as well as cognitive evaluation of the environment (Bates & Goldman-Rakic, 1993; Lu et al., 1994; Morecraft & Van Hoesen, 1998).

With regard to the limbic system, the amygdala and ventral striatum project to the anterior cingulate cortex and the cingulate gyrus, which in turn project to the CMAr (Vogt & Pandya, 1987). These projections deliver information about reward values that are directly connected to the goals of motor acts. In addition, the pathways that link the prefrontal cortex to the CMAr (Lu et al., 1994) transmit information held in short-term memory about the occurrence of events during the performance of previously performed motor tasks (Goldman-Rakic, 1995). The CMA therefore, has access to affective information that if processed correctly can influence the appropriate selection of a voluntary motor action that is consistent with the current motivational state (Picard & Strick, 1996). Once a selection has been made the CMAs send efferents to the primary and secondary motor areas as well as brainstem structures that in turn help plan, coordinate, and then via projection to the spinal cord, execute the movement (Dum & Strick, 1991; He, Dum, & Strick, 1995).

Task specific activity of the monkey brain has advanced understanding of the role of the CMA in decision making, planning, execution, and the control of motor action. For example, Shima & Tanji (1998) trained three monkeys to either push or turn a handle, in response to a visual trigger signal. The animals voluntarily selected one of the two movements based on the amount of reward (grape juice) anticipated. During a series of constant-reward trials, the monkeys continually selected a particular movement in

anticipation of its beneficial consequences. If the reward was reduced, conditioned training was such that the monkeys learned to perform the alternate movement, and as such, a cyclical process developed, with the monkeys altering their movements in an effort to always obtain maximum reward. Event-related single-cell recording techniques were used to record cellular activity from the CMAr, CMAc and M1. CMAr and CMAc activity was found to relate to movement initiation and movement preparation, while only the CMAr showed activity specific to the occurrence of a reward. Shima and Tanji concluded that the monkey CMAr plays a key role in choosing the most appropriate action (given internal and external information garnered from the situation) in an effort to achieve the greatest consequential gain from that action. The CMAc, however, was exclusively involved in the execution of the chosen movement (Isomura, Ito, Akazawa, Nambu, & Takada, 2003; Takada et al., 2001).

Transitional research into the human CMA has attracted considerable interest in recent years (Isomura et al., 2003; Jenkins et al., 1994; Posner, Petersen, Fox, & Raichle, 1988; Ullsperger & von Cramon, 2004; Walton et al., 2004). Considered a possible homolog of the rostral cingulate motor area (CMAr) in monkeys (Walton et al., 2004) the human rostral cingulate zone (RCZ) of the dorsal anterior cingulate cortices (ACd) is closely connected to the motor system, and is involved in monitoring self-generated movements and in signaling the need for immediate changes of behavior (Jenkins et al., 1994; Picard & Strick, 1996; Ullsperger & von Cramon, 2004).

The RCZ is thought to be intricately involved in focusing an individual's attention to necessary cues. Specifically, attention for action, response selection, motor preparation, and motor execution are all processes charged to the RCZ (Isomura et al.,

2003). Further justification has been found in evidence that lesions of cingulate areas result in impairments of motor performance in human patients (Turken & Swick, 1999). Corroboration of motor and cognitive related RCZ activity was reported by (Cunnington et al., 2002), who compared brain activation during internally guided and externally triggered finger movements. During each condition, predominant cingulate cortex activation (in addition to SMA activation) was identified in the posterior end of the CMAr, which is thought to be involved in motor tasks requiring internal movement selection (Picard & Strick, 1996). Indeed, as with the pre-SMA, the CMAr shows greater activation during internally generated movements (Deiber, Honda, Ibanez, Sadato, & Hallett, 1999; Wessel, Zeffiro, Toro, & Hallett, 1997), is involved in early processes of movement preparation (Ball et al., 1999) and in the internal representation or imagination of movement (Stephan et al., 1995). Both the CMAr and the pre-SMA therefore appear to be commonly involved in making the decision as to the most appropriate movement to make given the circumstances. Analogous to the different portions of the SMA and PM areas, the cingulate motor areas have been contrasted with the orbitofrontal cortex (OFC) in terms of their anatomical connections and varying but related functions. In contrast to the RCZ, the OFC is a rich recipient of afferents from sensory regions and is not directly connected with the motor system. Functionally, the OFC appears to be involved in more general monitoring of sensory events with respect to their significance to the individual (Ullsperger & von Cramon, 2004).

Recent evidence has sought to further disentangle processes that culminate in overt movement. Similar in fashion to the monkey reward task (Shima & Tanji, 1998), Walton et al. (2004) required human participants to complete a number of response-

switching tasks that varied according to the extent to which participants had to make choices and monitor feedback.[1] By varying whether participants needed to make choices and monitor feedback, the authors demonstrated (with event related fMRI data) a reciprocal relationship between the RCZ and OFC during the evaluation of the outcome of a choice (See Figure 2-2). The nature of the relationship varied according to whether the action was freely selected by the participant or guided by the experimenter, with activation increasing in the RCZ and decreasing in the OFC when the action was freely selected, and the reverse occurring when the action was selected by the experimenter. As such, the neural mechanisms responsible for movement and appraisal of movement consistently vary according to whether or not the performed movement is selected internally or is forced externally.

The issue of how emotion modulates free-willed versus externally instructed motor actions is attracting a growing interest and has been singled out as a goal of future research across a broad array of disciplines (Ullsperger & von Cramon, 2004). **The goal, however, of eliciting real life quantifiable free-willed movements in response to an emotive cue remains essential to the progression of our understanding of the emotion-movement relationship.**

Self- Versus Externally-Paced Movements

Functional brain imaging data in humans and single cell recordings in monkeys have generally shown preferential involvement of the supplementary motor area (SMA)

[1] GUESS condition: after a "switch" cue, participants had both to decide upon an appropriate response and to monitor the resultant feedback to determine which set of response rules was in place. FIXED condition: participants were told always to make a particular finger press response on the first trial after the switch cue. Unaware of which response set was subsequently in place, participants still had to monitor the feedback from the instructed action (which was correct on 50% of trials) and use the information to work out which set to use. INSTRUCTED condition: participants were informed by the switch cue which response set was in place meaning they could switch sets without needing to monitor their responses.

in self-initiated movement (Deiber et al., 1999; Wessel et al., 1997) and strong bilateral activation of lateral premotor areas for externally triggered movements (Catalan et al., 1998; Van Oostende et al., 1997; Wessel et al., 1997).

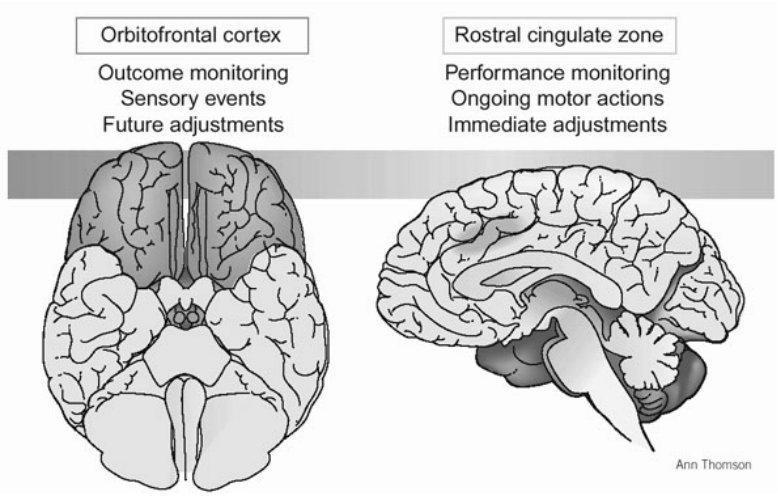

Figure 2-2. Schematic of the two frontal regions implicated in monitoring functions. Taken from Nature Neuroscience 7, 1173 - 1174 (2004). Decision making, performance and outcome monitoring in frontal cortical areas. (Ullsperger & von Cramon, 2004).

Identifying the temporal sequalea of the activating motor areas during specific tasks has been integral to better understanding the contribution(s) offered by each distinctive portion of the motor cortex. For example, in a delayed cued movement task, Richter et al. (1997) evidenced (via event-related fMRI) increased activity within both the SMA and lateral premotor areas during the movement preparation period (delay between a warning and GO signal), while the M1 showed only minimal activation during the preparation period and greatest activation during movement execution. Likewise, during self-paced movements Wildgruber et al. (1997) showed that the peak activation within pre-SMA precedes activation within M1 and therefore pre-SMA activity most likely reflects movement preparation.

In related works, Cunnington et al. (2002) used rapid event-related fMRI to investigate the spatial location and relative timing of activation for self-initiated versus externally triggered finger sequence movements. Each movement condition involved similar strong activation of the pre-SMA, SMA proper, CMAr, and the contralateral M1. Although levels of SMA and CMAr activation did not differ significantly between movement conditions, the timing of the hemodynamic response within the pre-SMA was significantly earlier for self-initiated compared with externally triggered movements, further confirming the notion that pre-SMA is involved in early processes associated with the preparation of voluntary movement (Lee et al., 1999; Picard & Strick, 1996). Given the lack of choice concerning which movement to make, differences in the cingulate areas are not surprising as the CMA/RCZ has been associated with making reward driven decisions when a number of possible movements are available. The lack of any activity at all in the premotor cortex during either task, however, was reported, and stands as contrary to other evidence collected in the same lab (Cunnington et al., 2002). (Cunnington et al., 2002) offered task variations between this and other studies as a potential explanation for this finding. Specifically, in Cunnington et al. (2002) the same movement was always planned and executed; the only varying factor was the internal versus external initiation of the task. As such the sequential nature of the movements required (three alternating finger taps) demanded preparation and/or preprogramming, and given that the movements were similarly accurate between initiation conditions, the SMA and CMA were clearly capable of preparing, controlling, and executing the necessary movements without assistance from the PMd. Given that performance accuracy was high, it seems that exceptions to the sweeping generalizations concerning internally

(SMA) and externally (PMd) guided movements exist and are the result of what may seem minor differences in experimental protocol. Rather than undermining previous research, therefore, these data highlight how flexible and effective the human motor system is.

Summary: Cortical Control of Movement

In recent years, the development of new techniques/methodologies has considerably advanced our knowledge of the role the cortex plays in motor control. Indeed, considerable progression has been made in attempting to understand which cortical areas are involved in the numerous discrete processes that precede and then accompany overt movement.

M1. The diversity and overlapping nature of the distributed network of neurons within each portion of the M1 permits cortical reorganization; neural plasticity in M1 has been evidenced following extended periods of training (Elbert et al., 1995) or following injury (Donoghue & Sanes, 1988; Sanes & Donoghue, 2000). Although traditionally considered to be exclusively involved in, and absolutely essential to the execution of motor tasks, present day evidence concerning activity in the human brain suggests that not only is the M1 active during the preparatory phase of movement, but also that voluntary movements can be executed directly by secondary brain regions and perhaps also sub-cortically. Nevertheless, the wealth of evidence is such that the M1 is primarily involved in motor execution, and specifically, in permitting manipulation of distal musculature.

SMA. The magnitude and temporal activation of the pre-SMA relative to the SMA proper during a range of tasks are such that one can be considered as fundamentally different from the other (Picard & Strick, 2001). The pre-SMA operates at a more

abstract level and is more closely related to the processing, integration, and maintenance of relevant sensory information than response selection or execution (Cunnington et al., 2002; Kurata et al., 2000; Lee et al., 1999; Sakai et al., 2000). Alternatively, SMA proper activation only occurs during movement-related components of visual or auditory tasks, and appears to be more involved with the pure movement portions of specified tasks (Boecker et al., 1998; Cunnington et al., 2002; Stephan et al., 1995). Functionally and anatomically distinct from the SMA proper, overt behavioral data coupled with anatomical data suggest that the pre-SMA may be functionally considered as a region of the prefrontal cortex (Picard & Strick, 2001). In conclusion, the two portions of the SMA are such that the pre-SMA and SMA proper combined may well be capable of planning and executing voluntary movements independent of M1.

PMd. Human data has corroborated evidence from animal research suggesting a functional segregation within the premotor cortex (Picard & Strick, 2001). Attention to the short-term storage and processing of visuospatial information engages the PMd_r (Coull & Nobre, 1998; Courtney et al., 1998; Petit et al., 1996; Stern et al., 2000), whereas motor planning, initiation, and execution engage the PMd_c (Grafton et al., 1998; Lee et al., 1999; Simon et al., 2002).

CMA/RCZ. Human movements are altered via the internal and external state of the organism (including the emotional state of the organism via amygdala projections). Considered a possible homolog of the CMAr in monkeys (Walton et al., 2004) the human RCZ of the ACd is closely connected to the motor system, and is involved in monitoring self-generated movements and in signaling the need for immediate changes of behavior (Jenkins et al., 1994; Picard & Strick, 1996; Ullsperger & von Cramon, 2004).

Specifically, the CMAr/RCZ plays a key role in choosing the most appropriate action (given internal and external information and the potential of freely choosing a number of alternatives) in an effort to achieve the greatest consequential gain from that action. In contrast, the CMAc (CCZ) is primarily involved in the execution of the chosen movement (Isomura et al., 2003; Takada et al., 2001) thereby aligning itself more with the SMA proper and the PMd_c.

Subcortical Control of Movement

Basal Ganglia

The basal ganglia (BG) works in concert with the cortex to orchestrate and execute planned motivated behaviors that require motor, cognitive, and limbic circuits (Haber, 2003). Intricately involved in several aspects of goal-directed behaviors, BG function bridges the emotion, motivation, cognition, and planning processes that lead to movement, as well as performing a critical role in the expression of movement (Boecker et al., 1998; Brown & Marsden, 1998; Haber, 2003). Deficits in motor behavior have been associated and correlated with basal ganglia dysfunction (Greenberg, 2002). Although a broad range of processes have since been pinned onto the BG [e.g., cognitive sequence planning, Graybiel, (1997); learning, Jueptner et al., (1997); habit learning & acquisition of non-motor dispositions and tendencies, Knowlton et al., (1996); executive function, Peigneux et al., (2000); and creativity, Cotterill, (2001)] this review will focus on the specific role that BG has on movement and emotion.

The basal ganglia are several groups of nuclei in each cerebral hemisphere which include the striatum (caudate nucleus, putamen, and ventral striatum) and the pallidum or globus pallidus (see Figure 2-3; internal and external segment GPi, GPe, and ventral

pallidum) (Greenberg, 2002). Closely related structures include the substantia nigra pars reticulate (SNr), the ventral tegmental area, and the subthalamic nucleus (Haber, 2003).

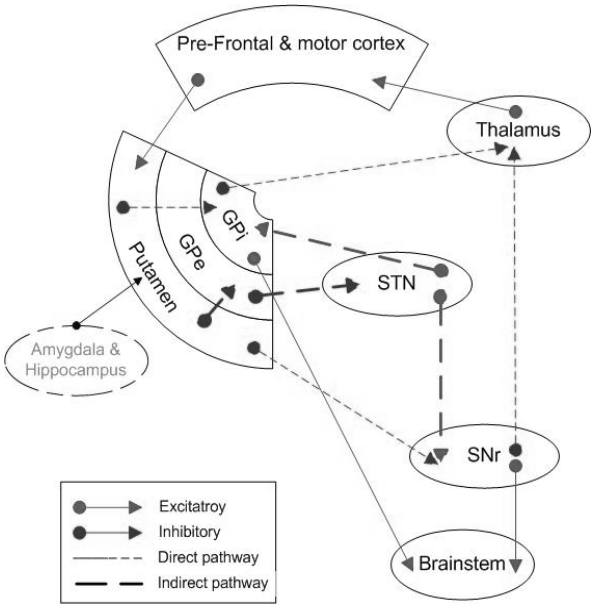

Figure 2-3. Motor circuit of the basal ganglia. The indirect and direct pathways are presented along, with how the cortex communicates with BG. GPi = internal segment of the globus pallidus; GPe = external segment of the globus pallidus STN, = subthalamic nucleus; SNr = substantia nigra pars reticularis

The striatum is the main target of cortical, thalamic, and brainstem input to the basal ganglia. In addition, the ventral striatum receives input from the limbic regions, including the amygdala and hippocampus (Fudge et al., 2002), and in addition the CMA/RCZ has been closely linked to the development of reward-based learning (Hassani et al., 2001). The striatum projects to the GPi and GPe, and in turn the GPi projects to the thalamus. The internal section is one of two main output nuclei of the basal ganglia, along with the SNr, which also outputs to the thalamus (Wichmann & DeLong, 1993). Outputs from these two structures are passed via the thalamus, back to the cortex (primarily the SMA, and possibly also to the PM cortex; (Brotchie et al., 1991a, 1991b, 1991c), completing

what is referred to as the “direct” cortico-basal ganglia pathway. The GPe is connected to the STN, which in turn projects back to the GPi; this connectivity is the “indirect” cortico-basal ganglia pathway (Haber, 2003; Middleton & Strick, 2002). The motor circuit of the BG and its associated direct and indirect pathways are displayed in Figure 2-3. Information cycles from the cortex, to the basal ganglia and thalamus, and back to the cortex again, forming a functional loop that modulates movement. The collective summation of activation/inhibition of these pathways modulates movement. Stimulation of the direct pathway leads to increased inhibition of the GPi, which consequently reduces the inhibitory tone on the thalamus, in turn facilitating excitation of the cortex and facilitating movement. In contrast, stimulation of the indirect pathway leads to increased inhibition of the GPe, which in turn leads to excitation of the STN; this activates the GPi and so increases the inhibition of the thalamus and reduces excitation of the motor cortex, inhibiting movement (Lewis et al., 2003). Appropriate balance between these two pathways is essential for typical everyday movements; PD, for example, results from a loss of the natural balance within this motor loop. Specifically, a decrease in dopamine levels results in increased activity in GPi and SNr which prevents inhibition of the thalamus, resulting in under-activation of motor cortical areas, as displayed overtly in hypokinesis (Chase et al., 1998; Haber, 2003).

From an input-output analysis, therefore, the basal ganglia do not appear to generate motions directly; they take input from the cortical and subcortical regions, process this information and then pass it back to the cortex via the thalamus, for execution (Cummings, 1993). Nevertheless, the importance of an intact BG system is substantiated by the array of symptoms that manifest following damage or disease in the

BG: (1) hypokinesias: impairment of initiation, velocity, and amplitude of movement, increase in muscle tension or hypertonia [e.g., Parkinson's Disease; Haber, (2003)]: (2) hyperkinesia: disorganized or excessive movement (e.g., Huntington's Disease) and, (3) dementias: cognitive and emotional dysfunctions.

Varying cortical structures have been offered as key to movement preparation (see above; CMA, pre-SMA, PMCr). However, preparatory activity has been demonstrated at several other sites outside the cerebral hemispheres, including the globus pallidus (Turner & Anderson, 1997), the striatum (Alexander & Crutcher, 1990), and the pallidal-receiving areas of the thalamus (Anderson et al., 1993). Motor preparation in much the same way as motor execution (Sanes & Donoghue, 1997) should therefore be considered a distributed phenomenon not limited to the cerebral cortex (Prut et al., 2001).

Given the range of motor dysfunctions that arise from or are related to BG malfunction (e.g., Parkinson 's & Huntington's disease), substantial efforts have sought to determine the exact role that BG play in motor function. Positron emission tomography (PET) studies have reported increased regional blood flow prior to voluntary movements not only in the SMA, M1, and other cortical areas, but also thalamus, and the BG (Deiber et al., 1996; Deiber et al., 1991; Jahanshahi et al., 1995; Wessel et al., 1997). BG appear to be activated similarly preceding voluntary movements that are internally generated and externally triggered (Cunnington et al., 2002; Jahanshahi et al., 1995; Jenkins et al., 2000).

Corroboration of BG involvement in motor preparation has been echoed by (Paradiso et al., 2004) who reported data from scalp and surgically implanted electrodes in the subthalamic nucleus of Parkinson's patients while they completed wrist extension

movements. Readiness potentials in the subthalamic nucleus were present before contralateral and ipsilateral hand movements. The authors thereby affirmed that in parallel with the cortex, BG circuitry was activated during movement preparation.

A more detailed explanation of BG involvement in movement preparation has been offered by (Nambu, Tokuno, & Takada, 2002) who have associated the initiation, execution, and termination pattern of movement with varying BG circuits. Immediately prior to cortically driven movement execution (planning = CMAr, pre-SMA, PMdr; execution = CMAc, SMA proper, PMdc) an accompanying signal is sent from SMA and

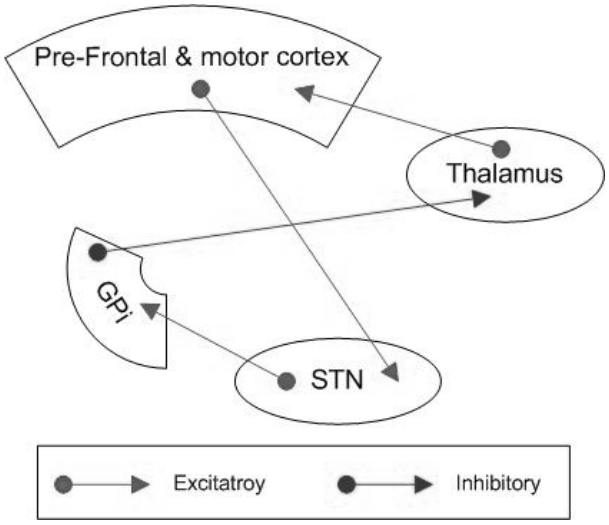

Figure 2-4. The cortico-STN-pallidal “hyperdirect” pathway as proposed by (Nambu et al., 2002). STN = Subthalamic nucleus; GPi – external portion of the globus pallidus. The additional pathway from the cortex to the STN is the cornerstone of the hyperdirect pathway.

M1 to the GPi through a cortico-STN-pallidal “hyperdirect” pathway that comprehensively activates GPi neurons. Consequently, large areas of the thalamus and cortex related to the selected and competing motor program are inhibited (see Figure 2-4). Next, a second signal is passed via the direct pathway (see Figure 2-3 above) to the GPi to inhibit the specific set of pallidal neurons, dis-inhibiting the pathway between thalamus and cortex; leading to the execution of the selected movement. Finally, a third

signal, passed via the “indirect” pathway (see Figure 2-3) broadly activates GPi neurons, suppressing their targets and terminating the movement. As such, only the selected motor program is initiated, executed, and terminated at the appropriate time, whereas other competing programs in the surrounding area are quashed. Figure 2-5 outlines two BG related systems that account for the phenomena that voluntary movements are always associated

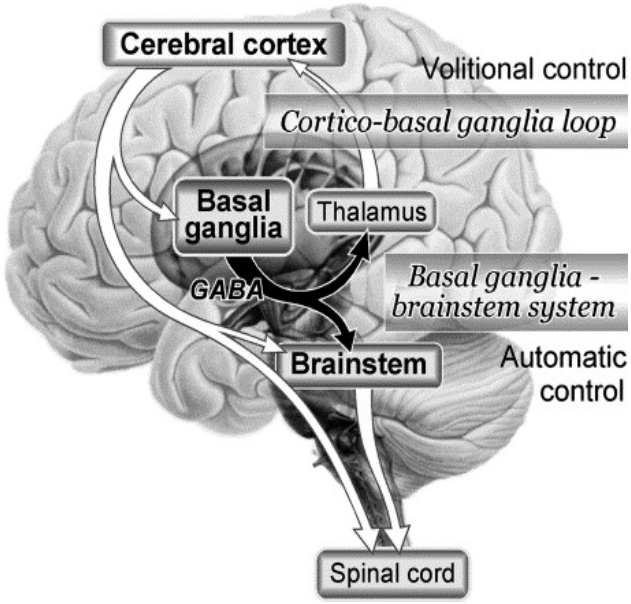

Figure 2-5. Volitional and automatic control of locomotor movements. GABAergic basal ganglia output to the thalamocortical neurons and the brainstem neurons integrate volitional and automatic control processes of movements (Takakusaki et al., 2004).

with automatic control processes which are performed unconsciously (Grillner & Wallen, 2004). (Hikosaka, Takikawa, & Kawagoe, 2000) propose that BG have two ways to control movements using three output systems (direct, indirect, and hyperdirect thalamocortical) to amalgamate the volitional control of movement with automatic control processes (e.g. saccade: (Isa, 2002); locomotion: (Grillner & Wallen, 2004) which are controlled via networks in the brainstem and spinal cord (Takakusaki, Saitoh, Harada, & Kashiwayanagi, 2004). BG circuits, therefore, appear to be essential: 1) during the

preparatory state prior to movement, suppressing all movements, 2) during the execution of movement, allowing only the desired movement to be executed, and 3) during movement termination when all movements are completed and a resting state is desired. Affective modulations of psychopysiological measures correspond with phases 1 and 2 of this progression and have lead to the formulation of the defense cascade model.

The Defense Cascade

Emotions have the capacity to elicit a myriad of varying behavioral responses in human beings. Evolved from primitive circuits in which a stimulus was typically followed by a response in a very standardized fashion, the human brain has developed the ability to *use time*. That is, humans can permit, suppress, accentuate, or abolish overt behavioral responses to emotional cues (Lang et al., 1997). The complex interaction of the neural circuitry that process emotions is such that a single response indicating activation of the appetitive or defensive motivational system is not necessarily reflected in a parallel way by all measures (i.e., HR, SCR, ERP). Instead as activation levels associated with the eliciting stimulus increase, a cascade of different response events occur ("defense cascade" see Figure 2-6; (Lang et al., 1997). Specific to activation of defensive circuitry, a three stage sequence has been proposed, based on the relative position of predator and pray (Bradley & Lang, 2000; Fanselow, 1994; Lang et al., 1997): pre-encounter, post-encounter, and circa-strike. Circa-strike refers to defensive actions when threat is proximal.

An important issue therefore, is to determine how movements are altered at varying stages through the progression of the defense cascade. That is, will movement be facilitated/debilitated monotonically as *arousal* increases across time,

or will movement be more affected by duration and proximity to *valenced* cues carrying different affective quality?

As evident in Figure 2-6, overt action (i.e., a defensive response) follows stimulus identification and then a freezing period. Following initial perception, as threat and arousal simultaneously increase, SCR climbs, startle potentiation increases reflecting defensive priming (via amygdala to PnC, to be discussed), and then immediately before movement, cardiac acceleration signals a classic defensive response. **Determining how the fundamental structures governing this sequence of events alter the resulting movement should be addressed in future research efforts. Once again, as is the case in the majority of affective research, little is known beyond the processes that precede "overt action" and consequently little is known concerning how affect modulated movement increases an organism's chances of survival (LeDoux, 1998).** Considerable advances may be made in movement rehabilitation if emotional circuitry can serve as a movement facilitator.

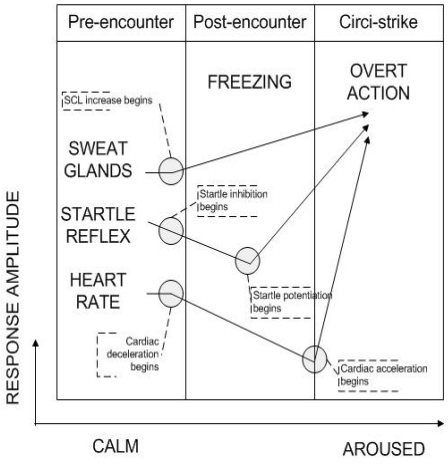

Figure 2-6. A schematic presentation of the defense response cascade underlying processing of increasingly arousing aversive stimuli. The arousal or intensity dimension is viewed here as analogous to a dimension of predator imminence that has been implemented in studies of animal fear. Reproduced from (Lang et al., 1997).

Cross referencing the defense cascade with BG activity, it is possible that the progression from “freezing” to defensive action maybe reflected in BG activation. As noted above, Nambu et al. (2002) suggest that BG control initial inhibition of movement (e.g., freezing) via the hyperdirect pathway, while a decision is made concerning the most appropriate movement to make (CMA/RCZ), followed by mobilization of the chosen motor action (e.g., defensive response stimulated by an external motivationally relevant stimulus) via the direct pathway, followed by final movement termination once the threat has passed. **In highly emotive situations the ability to control unnecessary movements, to then execute the most appropriate movement at the most appropriate time are essential within all movement domains.**

Further support for converging emotion and movement systems comes from reports concerning Parkinson’s disease. Given the typical slowness of movement that often signals PD (Haber, 2003), emotionally charged situations have been reported to override bradykinesia and result in patients exhibiting “paradoxical kinesia”; a sudden transient remission of bradykinesia when confronted with a life threatening emergency (Zigmond, Stricker, & Berger, 1987). It is possible therefore, that intense emotions can result in the intense focusing of attention, and thus motivation towards completing the necessary movement(s) to ensure survival. The BG, therefore, maybe viewed as an attentional center that can alter the flow of information from sensory input to motor output, and in turn, simultaneously suppress and permit specific movements according to situations (Brown & Marsden, 1998). **To re-iterate, it seems that without directly deciding, planning, or executing movements, the BG has enormous influence on which movement, from a number of potential options, is amplified and executed,**

and which movement(s) are inhibited to allow the primary movement(s) to execute without interference. Such reports that intertwine the largely independent research lines of emotion and movement beautifully exemplify the benefit of multi-disciplinary research, and serve as motivation to further investigate the complex relationship between emotion and movement. Focus will now turn to how emotionally rich information reaches the BG.

Basal Ganglia and Emotion

The nucleus acccumbens is a dominant part of the ventral striatum and is the leading sub-cortical candidate for the hub that integrates emotion, motivation, and cognition with action (Greenberg, 2002). Divided into two principal parts, the nucleus accumbens is composed of a central core that is associated with the extrapyramidal motor system, and a peripheral shell that links with the limbic system (Sturm et al., 2003). Receiving input from the hippocampus and the amygdala (Maclean, 1990) and projecting onto the ventral pallidum, substantia nigra, thalamus, and cingulate cortex, the nucleus accumbens is ideally located to serve as the key limbic-motor interface (Sturm et al., 2003). (Graybiel, 1997) echoed the importance of the such a hub, stating that the "…limbic basal ganglia system has a key function in translating action plans related to drive states and homeostatic control into action repertoires" (p. 460). **It seems appropriate, therefore, to ask whether processes within the NA translate fear into defensive action or positive affect into approach behavior?**

Stimulation of different areas in the basal forebrain can evoke different types of goal directed behaviors (Grillner, Georgopoulos, & Jordan, 1997); see Biphasic Theory section). An important component of these motivated behaviors concerns the direction of

the resulting movements; movements that will transport an organism towards or away from a given situation/cue depending on the valence of the stimuli (Grillner et al., 1997).

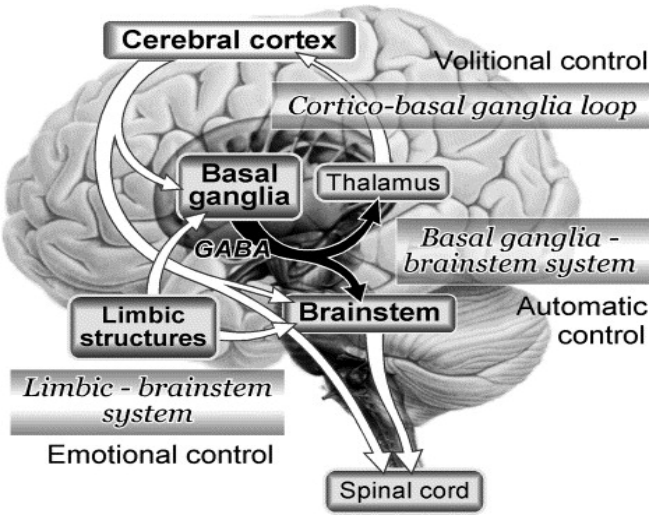

Figure 2-7. Possible neuronal mechanisms of integration of volitional, emotional and automatic control of motor behaviors.

One underlying issue concerns whether such movement patterns are executed with similar vigor; that is, are approach behaviors executed with the same speed and force as defensive behaviors? Are attack behaviors executed as quickly, forcefully, and accurately as escape behaviors? If emotion primes movement, do movements vary according to valence, to arousal, or to a combination of each?

The concept of emotions serving as action dispositions continues to gain support. de Gelder and colleagues (de Gelder, Snyder, Greve, Gerard, & Hadjikhani, 2004), for example, exposed participants to affective images while simultaneously recording fMRI activity. Along with amygdala and visual cortex activity, activity was also reported in the RCZ as well as the nucleus accumbens. **The burning question therefore is: exactly what role, and to what extent do emotions alter the probability of specific action dispositions leading to the execution of specific behaviors?**

Traditionally the dopamine (DA) systems in the nucleus accumbens were thought to directly mediate the rewarding or primary motivational characteristics of natural stimuli such as food, water, and sex (Salamone, Correa, Mingote, & Weber, 2003; Salamone, Correa, Mingote, & Weber, 2005; Salamone, Wisniecki, Carlson, & Correa, 2001). In terms of the link between emotion and action, however, rather than attenuating the primary motivation for natural rewards such as food, obstructing DA transmission within the NA disturbs the inclination of animals to engage in effortful responding to obtain food. That is, rats with accumbens DA depletions remain directed towards the acquisition and consumption of food. When not securing the food, however, the rats display a less vigorous, more cautious set of behaviors (Cardinal, Pennicott, Sugathapala, Robbins, & Everitt, 2001; Correa, Carlson, Wisniecki, & Salamone, 2002; Salamone et al., 2003; Salamone et al., 2001). **DA systems in the nucleus accumbens, therefore, appear to be critically involved in activational aspects of motivation, and a key modulator of response speed, vigor, and persistence in directed behavior; functions that enable organisms to exert effort in reward-seeking behavior** (Salamone et al., 2005). Analogous to a gate, filter, or amplifier, the NA can be promoted to the role previously given to the BG in general; that of altering emotion related information as it travels from various cortical or limbic areas on its way to motor areas of the brain (Everitt et al., 1999). An active NA, therefore, is thought to encode information related to the predictive value of environmental stimuli and the specific behaviors required to respond to them (Nicola, Yun, Wakabayashi, & Fields, 2004). That is, accumbens DA is necessary for modulating the electrophysiological and the behavioral responses to environmental cues (Yun, Wakabayashi, Fields, & Nicola, 2004).

In summary, although the role of the NA is becoming clearer in the rat brain, study of NA activity in the human brain has continued to follow psychopathologies, with the motor components taking a subsidiary role. If indeed the NA acts as a hub between the emotional limbic system and the motor system, it is of paramount importance to investigate how the NA may be used to facilitate movement.

Brainstem Reticular Formation

Extending into the spinal cord and diencephalons, the reticular formation refers to a region of neural tissue in the brainstem (medulla, pons, and midbrain) consisting of small areas of gray matter among fibers of white matter (Tortora & Grabowski, 2003). Traditionally the reticulospinal system (reticular formation, reticulospinal tract) has been charged with modulating automatic movements including the initiation and regulation of locomotion (Matsuyama & Drew, 2000a, 2000b; Matsuyama et al., 2004), postural control, vestibular reactions (Bolton et al., 1992; Matsuyama & Drew, 2000a, 2000b), and head movements that permit gaze control (Cowie & Robinson, 1994; Cowie, Smith, & Robinson, 1994). Without disputing the severe impairment of postural control that results from lesioned reticulospinal fibers, such lesions also manifest behaviorally in the impairment of gross limb movements (Lawrence & Kuypers, 1968).

More recently, the reticular formation (medial pontomedullary reticular formation (mPMRF)) has been associated with the preparation and performance of voluntary movements. Specifically, Buford & Davidson (2004) published single neuron data collected from the mPMRF of monkeys while performing a two-dimensional reaching task that included an instructed delay interval based on a color coded visuospatial cue. Monkeys were positioned in a primate chair which limited postural movements, thus allowing cells involved in preparatory activity to be distinguished from those involved in

movement-related activity. Given that preparatory areas of the secondary and cingulated motor cortex (Pre-SMA, PMdr, CMAr) project to the reticulospinal system (Keizer & Kuypers, 1989) the authors sought to determine whether or not cells within the reticular formation may be sensitive to movement preparation. The authors reported that of the 176 neurons with movement-related activity, 109 (62%) displayed pure-movement activity and 67 (38%) exhibited both preparatory and movement activity. Although lower than ratios reported in SMA, PMd, and CMAd (Alexander & Crutcher, 1990; Backus, Ye, Russo, & Crutcher, 2001), these data suggest that the **reticular formation houses cells that are sensitive to the planning of upper limb reaching movements, and as such, the reticular formation may prove to be an alternative pathway for the voluntary control of gross movement.**

Given that subcortical regions maybe involved in motor planning, applying this knowledge to situations where planning regions of the cortex have been damaged (i.e., stroke) holds considerable promise. However, consistently activating cells in the reticular formation that are sensitive to preparing movements with a view to strengthening their ability to compensate for damaged cortical regions, remains unknown. Further, activating cells in the reticular formation may be reliant on descending signals from the cortex. Furthermore, spatially cued, temporally specific planned movements originating in the reticular formation seem unlikely given the myriad of processes preceding movement preparation (e.g., stimulus perception/interpretation, rule learning). Overt displays of planned movement in decerebreated primates would clarify whether activation of the reticular formation can compensate for damaged cortical regions.

Summary: The Motor System

The cortical and subcortical structures that elegantly interact to produce motor function are complex, flexible, and comprehensively integrated. Regardless of its novelty and complexity, the planning, initiation, and execution of a motor task appears to be a distributed process, requiring cortical, subcortical and intact spinal tracts if appropriate motor actions are to be realized. Identifying hubs within the motor system where emotion may potentially impact this complex network offers a tremendously fascinating task for movement scientists. The cingulated motor areas, and the nucleus accumbens have emerged as two potential candidates. With this in mind, the following section offers a synopsis of the emotional system, with an emphasis placed on the structures that interact with motor areas.

Emotion

Emotion is a mental state that arises subjectively, via activation of primitive circuits that have been conserved throughout mammalian evolution (LeDoux, 2000) rather than through conscious effort. Emotions are often accompanied by physiological changes. Emotions, therefore, are held to be functional products of Darwinian evolution, developed from primitive actions that facilitated the continued survival of living organisms. Echoing this basic premise, Öhman, Hamm, & Hugdahl (p. 538, 2000) eloquently state:

> Evolution has primed organisms to be responsive to stimuli that more or less directly relate to the overall task of promoting ones genes to prosper in subsequent generations…. Stimuli of these types are embedded within emotional systems that help regulate behavior within critical functional domains

Emotion-related behavioral and psychophysiological data have been interpreted as reflecting approach/avoidance behaviors (Chen & Bargh, 1999; Duckworth, Bargh,

Garcia, & Chaiken, 2002; Hillman et al., 2004). Interpretations of self-report data have resulted in the suggestion that many discrete emotions exist, ranging from sadness, happiness, loss, and guilt (Lazarus, 2000). Imaging data continues to map the cortical and subcortical neural circuitry of the emotional system including these discrete states. Identifying the time course and physiological map of the startle reflex provides a fine example of the emotion-related successes garnered from animal research (Davis, Gendelman, Tischler, & Gendelman, 1982; Davis, Parisi, Gendelman, Tischler, & Kehne, 1982, to be discussed). Suffice to say, the emotion system is investigated with a divergent array of methodologies.

Systems impacted via emotion are wide ranging, both in terms of when and how the system is altered. That is, following onset of an emotional cue, demonstration of affective modulation occurs at varying times according to the measure being used; affective modulation of the startle blink response occurs 500msec following exposure; Skin conductance responses are altered according to arousal level, and can be illustrated physiologically 1-2 sec following initial exposure (Coombes, Janelle, & Duley, 2005); Affective modulation in heart rate response is visible 1500msec post emotional cue onset (Lang, Greenwald, Bradley, & Hamm, 1993). As such, depending on which branch of the sympathetic NS is being monitored, the time frame within which emotion driven changes will occur varies. In line with active lines of research concerning the temporal characteristics of emotion modulated P3 responses, HR, and SCR (Schupp, Junghofer, Weike, & Hamm, 2003a; 2003b), **quantifying the emotional modulation of overt voluntary motor function across time is a promising avenue for future research (Coombes et al., 2005).** Further, the robustness and validity of the Biphasic theory of

emotion lends itself well to the study of such phenomena (e.g., Coombes et al., 2005; Hillman et al., 2004).

Biphasic Theory of Emotion

Biphasic theory (Lang et al., 1990; Lang et al., 1997; Lang, Bradley, & Cuthbert, 1998a, 1998b) posits that the broad array of emotions experienced and displayed by human beings can be organized according to valence (i.e., appetitive or defensive) and intensity (i.e., arousal level). When engaged, each system (appetitive, defensive) impacts the functioning brain (including motor circuits), priming specific representations, associations, and action programs that correspond to the immediate environmental context. Hence, while not actions in themselves (Lang et al., 1997), emotions do influence action and typically emerge in circumstances where adaptive control is required (Ekman & Davidson, 1994). **Thus, when conceptualizing affects as motivationally tuned states of readiness (Lang et al., 1998b), Schupp and colleagues propose that a key function of emotion is the preparation for action** (Schupp et al., 2003a). In addition to valence and arousal, motor activation has also been noted as a third factor particularly helpful in describing primary emotions (Heilman & Gilmore, 1998). One commonly used measure that provides an index of the modulatory impact of emotion on involuntary motor function is the startle blink response.

Emotional Circuitry

The limbic system

The limbic system concept, an anatomical abstraction for an arched shape group of structures, first emerged in the mid 1950's (Maclean, 1949, 1952), and since its inception has been synonymous with efforts to explain and understand human emotion. The roots of a limbic system are grounded in an evolutionary explanation of mind and

behavior (Isaacson, 1982; Maclean, 1952, 1954, 1955a, 1955b, 1972). Sometimes referred to as the ancient, archicortex or primordial cortex (as opposed to the cerebral cortex that is referred to as the neocortex or new cortex) the limbic region is located on the medial border of the cerebral hemispheres.

The neocortex, found only in mammals, has been associated with thinking, reasoning, problem solving, and memory, leaving hunger, thirst, and other primitive internal urges to be attributed to the ancient cortex which is found in all vertebrates (LeDoux, 2000; Panksepp, 2003). As such, independent anatomical regions were traditionally paired with corresponding independent processes; emotion and cognition (Maclean, 1952, 1955a, 1955b). Scoville & Milner (1957), however, reported that damage to a central structure in the limbic system -the hippocampus- had a debilitating effect on long-term memory rather than on emotional processes. In consequence, the polarization of separate systems for cognition and emotion began, which in turn brought into question components of, and hence, the existence of the limbic system.

Caution, therefore, should be exercised when associating the limbic system exclusively with emotion. Indeed, with the fear system often bypassing the hippocampus, LeDoux (2000) suggests that a "limbic system" grounded in tradition rather than data, is a flawed and inadequate account of the emotional brain, and provides no more than an "…off-the-shelf explanation of how the brain works" (p.159). Aside from issues concerning its authenticity, for those who support the limbic system account of emotion, widespread agreement has yet to be reached concerning exactly which nuclei compose the limbic system (Patterson & Schmidt, 2003). For example, given the abundant two-

way connections between limbic structures and the hypothalamus and thalamus, some have included these later structures within the limbic system (Andreassi, 2000).

Nevertheless, widespread use of the term “limbic system” has permitted the concept to remain prominent in contemporary discourse, with credible support for such a system continuing undiminished (Panksepp, 2003). Revisiting the vertebrate/mammal brain distinction, Panksepp (2003) retains and supports the notion that emotional responses, including their intrinsic affective attributes, most likely emerge from "limbic" regions that are more evolutionarily conserved in vertebrates than those that mediate cognitive capacities (Maclean, 1990). Resolving the issue concerning whether or not a “limbic system” exists is not the focus of this discourse, and hence, whether considered to be, or not to be, components of the limbic system the following section outlines the amygdala and the periacqueductal central grey given the integral role they play in the physiological and behavioral manifestations of emotion.

Amygdala

The amygdala is a nuclear complex in the forebrain, positioned in the anterior medial section of the temporal lobe consisting of about ten distinct nuclei that are grouped into four regions: basolateral, lateral, central, and basomedial. The amygdala receives highly processed sensory input from the neocortex and hippocampus via the lateral and basolateral nuclei; in turn these nuclei project to the central nucleus which then project (via the stria terminalis) to a variety of hypothalamic sites, the nucleus accumbens (Graybiel, 1997; Maclean, 1990) and periaqueductal gray (Fendt & Fanselow, 1999), the cingulated motor areas (Morecraft & Van Hoesen, 1998; Vogt & Pandya, 1987), as well as the PnC (Davis, Gendelman, Tischler, & Gendelman, 1982; Lang et al.,

1990). These functional links collectively mediate the manifestation of emotion modulated voluntary and involuntary movements.

Potentiation of the startle blink reflex according to emotional context provides evidence of how emotion alters the execution of involuntary motor action; the rostral part of the medial subdivision of the central nucleus of the amygdala contains cells that project to the PnC, a nucleus in the acoustic startle circuit [Rosen, Hitchcock, Sananes, Miserendino, & Davis, (1991); emotion and startle to be discussed later]. In a similar fashion, the amygdala projects directly and indirectly to the nucleus accumbens and CMA respectively, altering voluntary movements according to an organism's affective context and the consequences of varying actions within that affective context. The amygdala is involved in complex cognitive and behavioral functions, and serves to process somatic states that emerge from primary unconditional or learned inducers (Bechara, Damasio, & Damasio, 2003).

LeDoux defines the amygdala as a center for emotional evaluation (LeDoux, 1994, 2003; LeDoux, Cicchetti, Xagoraris, & Romanski, 1990), specifically involved in the detection and manifestation of fear. In addition to reports that continue to support the essential role of the amygdala in the fear system, this association should not be considered unilateral. Indeed, when exposed to affective content, fMRI data have, in addition to coupling amygdala activation with fear, also associated the processing of positively valenced stimuli with significant amygdala activity (e.g., Garavan, Pendergrass, Ross, Stein, & Risinger, 2001). Conflicting data exist, however, concerning the link between amygdala activation and pleasant stimuli. For example, fMRI data reported by (de Gelder et al., 2004) indicated significant amygdala activation during

exposure to unpleasant/fearful images relative to neutral images, but not during exposure to pleasant as compared to neutral images. It is interesting to note though, that de Gelder et al. did not report a direct statistical comparison between activation patterns during exposure to unpleasant and pleasant stimuli.

The amygdala has a dual sensory input system. Information is taken in via sensory channels and is streamed to the thalamus, at which point the inputs diverge; one pathway leads directly to the amygdala (fast channel) while the other projects to the cortex (slow channel). Providing the amygdala with raw sensory threat-related information via this specialized fast channel circuit may offer distinct advantages in the interest of promoting survival. (LeDoux, 1995) has described this fast channel route as a “quick and dirty” subcortical pathway that allows for very rapid, but crude, analysis of stimulus features from the incoming visual stream (LeDoux, 1995, 1996; Shi & Davis, 2001). This route, involves direct thalamo-amygdala pathways allowing for a cursory but rapid analysis of visual objects passing from the retina into the fear centers of the brain. The alternate ascending route to the cortex permits acute processing of the sensory input to determine if the sensory input is real, perceived, dangerous, or harmless. Although delayed, the result of this more comprehensive cortical evaluation of sensory stimuli is projected back to the amaygdala, reinforcing or suppressing initial amygdala activity.

Although not actions themselves, emotions may be considered action dispositions, and while it is clear that the amygdala are central in the interpretation and evaluation of emotion, it is the efferent amygdala projections that result in the covert and overt consequences of an experienced emotion. Indeed, lesions of the central nucleus of the amygdala block all conditional fear responses including behavioral, autonomic,

cardiovascular, and hormonal responses, whereas lesions of the pariacqueductal gray (PAG) block only the automated behavioral responses to fear (LeDoux, 1996). It is believed, therefore, that the central nucleus of the amygdala may be the final common pathway of conditional fear responses and that its efferent targets, including the PAG, mediate specific automated responses (see BG and CMA section above for information concerning emotion and voluntary movement). Specifically, circastrike attack (overt defensive action) is not initiated by direct stimulation of the central nucleus of the amygdala (De Oca, DeCola, Maren, & Fanselow, 1998). In consequence, to understand the chain reaction that begins with activation of emotional circuitry and leads to involuntary overt movement, attention must turn to the periacqueductal gray.

Periacqueductal central grey

The periaqueductal grey (PAG) is a large structure in the midbrain (surrounding the aqueduct of silvus) thought to be involved in two contrary patterns of defensive action, one related to freezing, in which ongoing behavior is halted leading to complete immobility except for that required for breathing (De Oca et al., 1998), and another related to escape responses (Vianna, Graeff, Landeira-Fernandez, & Brandao, 2001). The PAG receives afferents from the amygdala, nucleus stria terminalis, dorsal hypothalamus, midline thalamus, periventricular grey and the dorsolateral and ventrolateral midbrain tegmentum. In turn, the majority of efferent fibers leaving the PAG terminate in the reticular formation, parabrachial nuclei, trigeminal motor nucleus, and nucleus ambiguous. With regard to defensive freezing, evidence suggests that such behaviors are modulated by afferent projections that the ventral PAG (vPAG) receives from forebrain structures, especially from the amygdala (Bandler & Shipley, 1994; Carrive, 1993;

Fanselow, 1991; Fendt & Fanselow, 1999), while the dorsal portion of the PAG (dPAG) appears to mediate both active and inhibitory behavioral patterns of defensive responses.

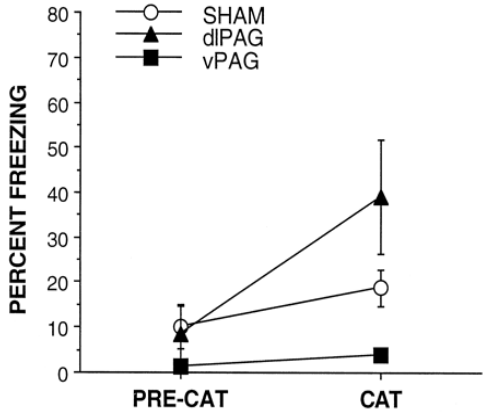

Figure 2-8. Rats with lesions of the dPAG or the vPAG in comparison with sham-lesioned rats showed enhanced or decreased levels of freezing, respectively, when presented with a cat. Adpated from (De Oca et al., 1998)

In rats, lesions of the dPAG enhanced conditioned freezing (De Oca et al., 1998) and reduced escape reactions to electrical footshock (Fanselow, 1991). Alternatively, stimulating the dPAG by increasing current in a stepwise fashion elicits a freezing response followed by vigorous escape reactions (Coimbra & Brandao, 1993; Schenberg, Costa, Borges, & Castro, 1990). Vigorous escape reactions are not elicited by direct stimulation of the central nucleus of the amygdala. Indeed, stimulation of the lateral and central nucleus of the amygdala produces long-lasting, opioid-mediated inhibition of the affective defensive response elicited by dPAG stimulation in the cat (Shaikh, Lu, & Siegel, 1991a, 1991b). Importantly, this inhibition is selective to defensive behavior; circling behavior (in cats) elicited by dPAG stimulation was unaffected by amygdala stimulation. Thus, it may be necessary for the amygdala to be inhibited in order to engage in active defensive behaviors.

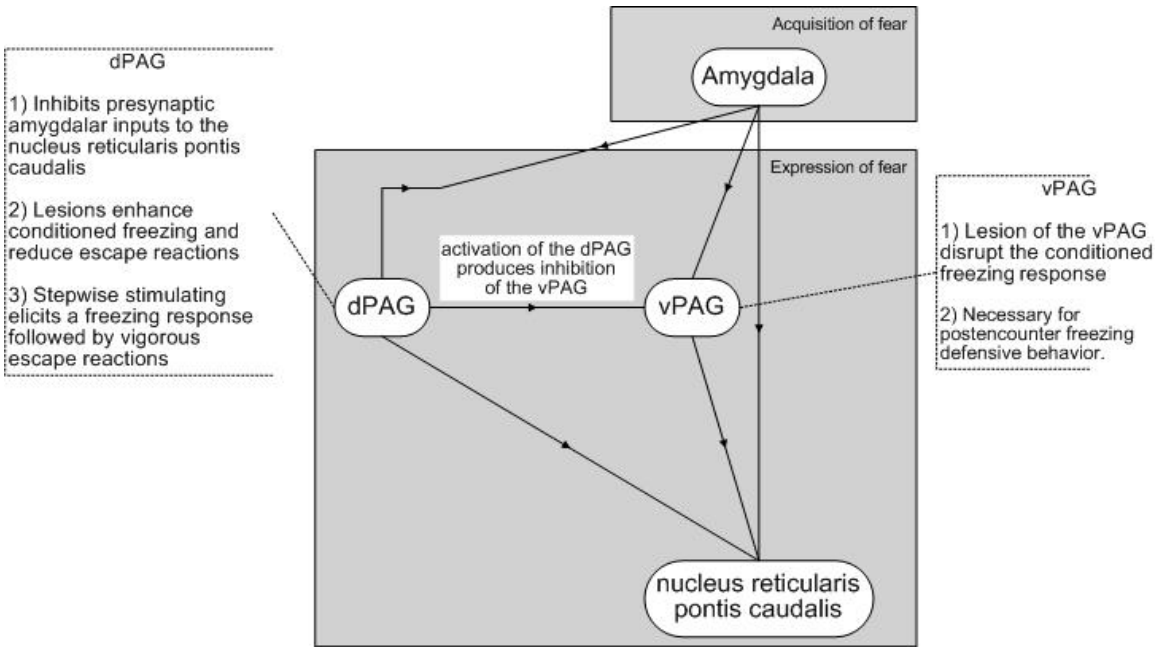

Figure 2-9. Linking the Amygdala, reticular formation, and the Periacqueductal Central Grey in a functional circuit that interact to modulate the overt involuntary behavioral manifestation of emotion.

Anatomical connections between the vPAG, dPAG, and the amygdala maybe key to the inhibition of a freezing response (see Figure 2-9). Specifically, activation of the dPAG may briefly inhibit the amygdala and vPAG to interfere with the processing of incoming sensory information, while also permitting active defensive behaviors. Specifically, Walker & Davis (1997) suggest that an active dPAG inhibits presynaptic amygdalar inputs to the PnC, a critical component in the execution of reflexive and voluntary motor function (to be discussed), indicating an involvement of the dPAG in the transition from freezing to defensive movements as threat levels increase. Concerning the interconnectivity of the ventral and dorsal portions of the PAG, freezing and escape responses induced by dPAG stimulation do not depend on the integrity of the vPAG (Vianna et al., 2001), so whereas initial stimulation of the dPAG leads to an initial freezing behavior, continued stimulation inhibits amygdala and vPAG, leading to active

defensive behaviors. The vPAG, alternatively, is specifically involved in post encounter conditioned freezing response. The majority of efferent fibers leaving the PAG terminate in the PnC (in addition to the parabrachial nuclei, trigeminal motor nucleus, and nucleus ambiguous), likewise, coupled with amygdala afferents that also terminate in the PnC, the inhibition/activation triumvirate pathway patterns between PAG, amygdala, and PnC all contribute to the execution of overt emotionally driven behaviors. (Ratner, 1967) proposed a description of defensive response topography that varied as a function of the distance between predator and prey. Defensive behaviors varied between freezing, flight, fight, and tonic immobility as the predatory distance decreased. Tonic immobility is a prone, immobile position elicited in wild prey animals thought to inhibit further attack by removing movement as an attack-eliciting cue (Sargeant & Eberhardt, 1975). Drawing on the evolutionary strains of Biphasic theory and the defense cascade (see above), when assessing the rate of approach of threat, a freeze-attack/escape-freeze may be the appropriate dynamic sequalea for the continued survival of living organisms. Specifically, when faced with threat, forebrain activity mediating freezing leads to immobility as the animal freezes (activation of the sympathetic nervous system: decreased HR, increased SCR), then as the threat draws nearer and physical contact is made between predator and prey, the defensive needs of the animal may be best served by complete midbrain control and activation of circastrike behaviors (inhibition of vPAG and amygdala, activation of dPAG). Safe from the threat of direct physical attack, forebrain activity (reduction in activation of dPAG with a simultaneous activation of vPAG and amygdala) mediates the return to immobility and a second freezing response that continues until safety is restored (Sargeant & Eberhardt, 1975). When the situation

alters to become non-threatening, homeostasis is realized via activation of the parasympathetic system. The parasympathetic system returns the body back to a relaxed state, culminating in the resumption of preferred activity within a safe environment (Fanselow, Lester, & Helmstetter, 1988).

Acoustic Startle and Movement

Startle Circuit

The acoustic startle reflex is a short-latency behavior elicited by a sudden and intense acoustic stimulus. Considered a primitive defensive reflex, the acoustic startle serves as an interrupt of ongoing behavior (Lang et al., 1990). The subcortical neural circuitry of the startle reflex has been mapped via techniques that focus on specific nuclei in an effort to either eliminate (electrolytic lesion) or illicit (single pulse electrical stimulation) a startle response.

Given the temporal characteristics of the acoustic startle (8ms in rats, from startle to EMG activity) Davis and colleagues (Davis et al., 1982a; Davis et al., 1982b) initially mapped what was then considered a simple pathway through four synapses, three in the brainstem (ventral cochlear nucleus; an area medial and ventral to the ventral nucleus of the lateral lemniscus; nucleus reticularis pontis caudalis [PnC]) and one synapse onto motorneurons in the spinal cord. However in the intervening years since this 4-synapse route was evidenced, re-evaluation (e.g., Lee et al., 1996) has suggested that cochlear root neurons proceed directly too, and then terminate in the PnC. Accordingly, given that cochlear root neurons terminate onto reflex critical PnC cells that in turn project to motor neurons in the spinal cord (Lingenhohl & Friauf, 1994) the previously identified synapse at the lemniscus is now bypassed (Lee et al., 1996). In summary, the chain of probable activation of the primary acoustic startle reflex is generally considered to consist of 3

rather than 4 synapses: (1) cochlear root neurons; (2) PnC neurons; and (3) motor neurons in the spinal cord (Lang et al., 2000; Lee et al., 1996).

Having established the central components of startle circuitry in animals (Davis et al., 1982a; Davis et al., 1982b), more recent efforts have sought to decipher the transient variables that contribute to, and the overt behavioral repercussions of, the human startle reflex (Lang et al., 1990). In human subjects, early research concerning startle elicited defensive movements identified a generalized bodily reflex following exposure to a gun shot (Landis & Hunt, 1939). Contemporary startle research, however, typically centers on neuroelectric activity (ERP) and/or electromyographic (EMG) indices of eye blink, neck, shoulder, trunk, and/or leg flexion.

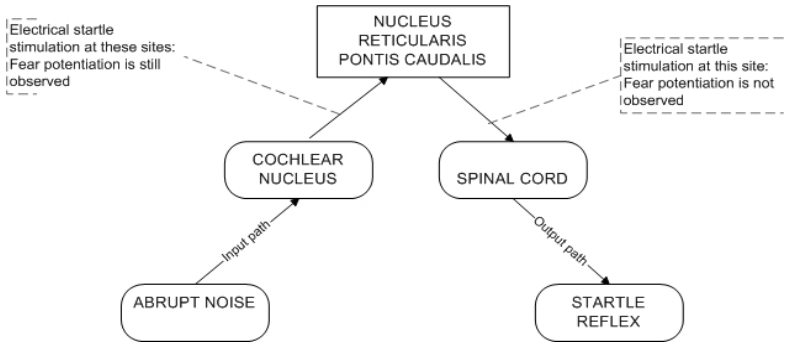

Figure 2-10. The primary acoustic startle reflex is generally considered to consist of 3 synapses: (1) cochlear root neurons; (2) PnC neurons; and (3) motor neurons in the spinal cord

Due to its sensitivity and slow habituation rate, the eye-blink has captured considerable attention. For example, guided by the biphasic theory of emotion, Hillman and colleagues (Hillman, Hsiao-Wecksler, & Rosengren, 2005), reported a positive association between the eye-blink reflex and postural reactions to an acoustic startle. Likewise, in addition to homeostatic reflexive motor functions, a similar paradigm has

been used in a number of laboratories worldwide to study the impact of active startle circuitry on voluntary motor function (e.g., Carlsen, Chua, Inglis, Sanderson, & Franks, 2003; Carlsen et al., 2004a, 2004b; Carlsen, Hunt, Inglis, Sanderson, & Chua, 2003; Valls-Solé et al., 1999; Valls-Solé et al., 1995).

Acoustic Startle and Involuntary Movement

Hillman and colleagues (Hillman et al., 2005), reported evidence concerning the impact of an acoustic startle on blink magnitude and postural sway, permitting conclusions concerning the association between the magnitude and latency of the startle blink, with the magnitude and latency of whole body postural movements. Specifically, Hillman et al. required participants to stand passively on a force platform. Postural adjustments (measured by changes in center of foot pressure) and the eye blink reflex were time-locked to the presentation of an acoustic startle (96dB). Relative to a baseline condition, beginning approximately 100 ms following the acoustic startle, participants displayed an initial anterior movement followed by a posterior movement. A positive association was reported between blink magnitude and the amount of movement in the posterior direction only. The authors postulate that the acoustic startle probe triggered a defensive reaction, and the resulting anterior-posterior response was an overt sign of postural flexion, an evolutionary reaction promoting survival (Hillman et al., 2005).

The notion that an acoustic startle elicits involuntary movement is an often validated phenomena specifically in terms of the blink reflex. Startle and movement literature, however, has developed this relationship to include voluntary movement also. The following section will detail the growing body of literature concerning acoustic startle initiated voluntary movements.

Acoustic Startle and Voluntary Movement

Dependent on uniqueness and complexity, varying cortical and subcortical areas of the brain have been charged with planning, executing, and controlling movement. Evidence indicates however, that once a movement has been planned, movement maybe initiated and completed significantly faster when an unexpected acoustic startle (approx 124dB) replaces or accompanies a visual GO signal (Valls-Solé et al., 1995). Valls-Solé and colleagues (1995) implemented a simple RT task requiring participants to respond to a visual GO signal. A visual warning signal (5 seconds before the GO signal) readied participants to the imminent GO signal. However, during a portion of the experimental trials, an unexpected acoustic startle (estimated at 150dB) was delivered at fixed time intervals of 0, 25, 50, 75, 100 and 150 ms following the visual GO signal. For interval durations between 0-75 ms post the GO signal, the acoustic startle resulted in faster pre-motor and motor time, as well as faster task completion. Pre-motor, motor, and task completion time increased monotonically as the time between the GO signal and the startle increased. Acoustic startles were also presented preceding the GO signal, and although the net result was movement initiation, the recorded RT was not as short as trials in which the startle stimulus unexpectedly accompanied the visual GO signal. These early reports suggest that pairing or replacing the GO signal with an acoustic startle leads to faster PMT, MT, and overall task completion.

Given that voluntary movement was the focus of the Valls-Solé (1995) paper and is the focus of this review, the factors that composed the speeded response deserve attention. To determine whether the EMG signal underlying startle speeded RTs were similar to normal RTs, Valls-Solé et al. (1999) modified their 1995 protocol to include task related EMG activity and a second simple RT task. Two similar experiments were

reported, the only difference between them being the required behavioral response to the GO signal (wrist flexion/extension or stand on tiptoe). As in the 1995 paper, a warning signal preceded a 5 second silence, leading to a visual GO signal that was presented alone or accompanied by a 130dB acoustic startle. Results corroborated previous findings (Valls-Solé et al., 1995) indicating that regardless of the response (wrist, tiptoe), the acoustic startle sped up the execution of the voluntary movement. However, the comparison made between EMG patterning of movement with and without the startle indicated that although a time shift was observed, as far as muscle activation was concerned, the patterning was near identical. **Hence, the voluntary reaction was driven at the speed of a startle reaction while maintaining the characteristics of the motor program**. In light of identical EMG patterns between conditions, the authors concluded that faster reaction times were the consequence of a rapid initiation of the movement pattern rather than an early startle reflex coupled with a later voluntary response. **Therefore, having established a similarity between the EMG patterning of startle and non-startle triggered movements, what and where is the mechanism driving the facilitation of the pre-EMG phase of startle initiated preplanned movements?**

When the subject is prepared to react, the excitability of the motor pathway to the muscles involved in the planned reaction may be facilitated. As such Valls-Solé et al. (1999) suggested that because the startle and GO signals were in different modalities, the acoustic startle stimulus may not have been promoted into the thalamo-cortical sensory motor system, but rather, could have been integrated into the bulbar reticular formation. Coupled with a reduced threshold in the motor system, the startle may have triggered the motor system at a level further downstream from where the visual GO would normally

initiate the same movement. The reticular formation, where the startle response originates, logically becomes one potential candidate. Consequently, something akin to a motor program maybe stored in brainstem and spinal centers, allowing the program to be triggered (via startle) independently of the usual descending GO command from the motor cortex. **The issue of subcortical initiated movement remains an interesting one, although to date, the mechanisms that permit an acoustic startle to initiate subcortically stored voluntary movement have not been directly tested and are therefore unknown.**

In a series of related follow up studies Carlsen and colleagues (Carlsen et al., 2004a, 2004b; Carlsen, Nagelkerke, Garry, Hodges, & Franks, 2000) have replicated and extended the findings of Valls-Solé et al. (Valls-Solé et al., 1999; Valls-Solé et al., 1995). Although the major premise of Valls-Solé et al.'s work has not been significantly altered, a number of papers provide EMG, kinematic, simple and choice RT evidence that further validate a startle elicited speeded RT. One potential explanation of the startle elicited speeded RT is that the startle may increase neural excitability, decrease motor system neural thresholds, summating to voluntary movement with shorter PMT. Accordingly, any movement that is elicited via an acoustic startle should be characterized by shorter PMT's.

To address this issue (Carlsen et al., 2004a) modified the Valls-Solé protocol, adding two and four choice RT tasks to the simple RT task. Participants heard a warning signal, followed by a short pause, and then at the onset of a visual target were required to extend or flex the wrist to move a lever (represented by a cursor on a viewing screen) to reposition the cursor on the target (also visible on viewing screen) as quickly and

accurately as possible. Onset of the target was randomly accompanied by a 127dB acoustic startle, with potential target locations varying between 1, 2, and 4 potential positions within each trial block, respectively. Again, if facilitated PMT were the result of neural excitability, then during each trial block, PMT for target plus startle trials should be faster than target alone trials. This, however, was not the case. As the number of potential targets increased (1, 2, 4) PMT increased, however, only simple PMTs were facilitated during startle compared to non startle trials, with no differences emerging between control and startle conditions for either the 2 or 4 choice RT tasks (Carlsen et al., 2004b). The authors proposed that the cortical processes of response selection inherent in a choice reaction time task barred a preplanned motor program from being formulated and stored, and subsequently initiated subcortically. In consequence, Carlsen et al. argued that cortically initiated movements, relative to subcortical initiated movement, take considerably longer to materialize. However, these data simply suggest that a preplanned movement will be initiated faster if initiation is accompanied by a startle.

Speculating from these data, that a preplanned movement cannot be initiated from the cortex so rapidly should be treated with considerable caution. Realistically, PMT's of a preplanned cortically stored motor program cannot be inferred from performance on a choice reaction time task because the PMT during a CRT task involves response selection *and* movement execution rather than just movement execution. The second argument offered by the authors to support the subcortical initiation of SRT's was that some PMT's < 60ms. Fixed amounts of time are required for sensory transduction and neural conduction to the cortex, and for neural conduction from the cortex to the arm. The first volley of neural activity caused by acoustic stimuli takes 35 ms to reach the auditory

cortex (Erwin & Buchwald, 1986). In turn, the time it takes for the motor cortex to communicate with the arm is 20-25 ms (Jones, Calancie, Hall, & Bawa, 1996; Valls-Solé et al., 1999), suggesting a combined total of 60 ms. Given that Carlsen et al. reported average times of 80ms for the startle initiated SRT condition, they infer that the 20ms differential (80 – 35 – 25 = 20) is not adequate for the necessary cortical processing that is required for cortical initiated movement. Further, given that only three startle trials were included within each response category, variability and inherent error must be taken into account. For example, when discussing issues on the scale of milliseconds across a small number of trials, one must be certain that (among other technical issues) the acoustic stimulus is recorded in the physiological trace at the exact point the stimulus was actually presented. Error in the range of $\pm$10ms per trial will have considerable consequences.

Methodological issues are also noted regarding the inclusion/exclusion criteria concerning participants; from the 20 participants tested, 2 did not display a startle response [as indexed by activity in the sternocleidomastiod (SCM) muscle, Carlsen et al., (2003a); Carlsen et al., (2003b)] and 4 failed to show decreased RTs during startle trials. All 6 participants were removed from analysis. Although Carlsen et al. were specifically interested in participants who showed facilitated RTs due to the presence of a startle response, it is perhaps no surprise that startle and control initiated movements were statistically differentiated, given that participants who did not display faster PMTs, although demonstrating a startle response, were removed from the analysis. One must ask: **Is it ethical to remove participants who did not show rapid startle initiated**

movements relative to a control tone, and then go onto conclude that startle initiation of a preplanned movement results in speeded PMTs?

A second point of interest concerns the use of the SCM activity to infer a startle response. (Carlsen et al., 2003a) suggest that the blink reflex is not an accurate measure of the startle response (the SCM provides a more accurate representation) and as such, the reliance on a modulated blink reflex in affective research should potentially be discarded? **Two important questions result: 1) Is the startle response an all or nothing phenomena simply reliant on a stimulus threshold to be realized? Indexing the behavioral impact of varying stimulus intensities offers a protocol via which this issue can be evaluated. 2) Are the behavioral manifestations that occur in response to a 127dB startle probe considerably different from those observed following a 95-105dB startle?**

Summary: Acoustic Startle and Movement

Carlsen et al.'s efforts to build an argument for the subcortical storage of movement programs and the speeded startle initiation of subcortical movements (Carlsen et al., 2004a) is weakened by indirect assumptions, and the exclusion of data that does not support the hypothesized mechanism. Nevertheless, in the majority of participants, the fact remains that PMTs are speeded if an acoustic startle acts as or accompanies a GO signal. Further, evidence suggests that the speeded voluntary movement that is initiated via startle is similar in EMG burst duration and timing, kinematic patterning (Carlsen et al., 2004b; Valls-Solé et al., 1999) and accuracy (Carlsen et al., 2004b; Carlsen et al., 2000), as the same movement performed in the absence of the startling stimulus. **In short the same voluntary movement occurs regardless of the initiating stimulus, the**

difference being that an acoustic startle results in a voluntary movement being completed at the more rapid rate of a startle reflex (Carlsen et al., 2004a, 2004b; Valls-Solé et al., 1999; Valls-Solé et al., 1995).

Acoustic Startle, Emotion, and Movement

Acoustic Startle, Emotion, and Involuntary Movement

The influence of emotion on involuntary movements has attracted significant interest in recent years. Below, the potential mechanism for such a relationship will first be outlined, followed by data supporting the notion that emotions are capable of modulating the magnitude and latency of involuntary movements.

Considerable data supports the notion that a direct pathway linking the amygdala and PnC mediates fear potentiated startle (see Figure 2-10; Rosen et al., 1991). However, the exact route(s) via which signals from the amygdala reach the PnC (a crucial relay in the primary acoustic startle circuit: (Lee et al., 1996; Rosen et al., 1991) are yet to be resolved. The issue has emerged because in addition to the PnC, the amygdala also projects to the rostral midbrain (Fendt, Koch, & Schnitzler, 1994b; Rosen et al., 1991) including deep layers of the superior colliculus/deep mesencephalic nucleus (deep SC/DpMe), the periaqueductal gray (PAG), and the lateral mesencephalic reticular formation MRF), which all in turn project onto the PnC (Meloni & Davis, 1999). Lesions within rostral midbrain regions block fear-potentiated startle (Fendt, Koch, & Schnitzler, 1994a; Yeomans & Frankland, 1996), suggesting that these areas serve as a relay between the amygdala and the PnC. To determine the critical output relay between the amaygdala and the PnC, Zhao & Davis (2004) locally infused an equal dose of a glutamate non-NMDA receptor into the areas of interest within the rostral midbrain. In short fear-potentiated startle was blocked following infusion of the receptor into the deep

SC/DpMe before testing but had no effect on baseline startle amplitude. The same dose infused into the dorsalolateral PAG, the lateral MRF, or the superficial layers of the SC did not affect fear-potentiated startle, although the treatment did reduce contextual freezing when infused into the dorsal/lateral PAG. The authors concluded therefore, that of the three potential candidates that act as the critical output relay between the amaygdala and the PnC, the most likely mediating site for fear-potentiated startle is the SC/DpMe, and furthermore, that glutamatergic transmission is required for this action (Zhao & Davis, 2004).

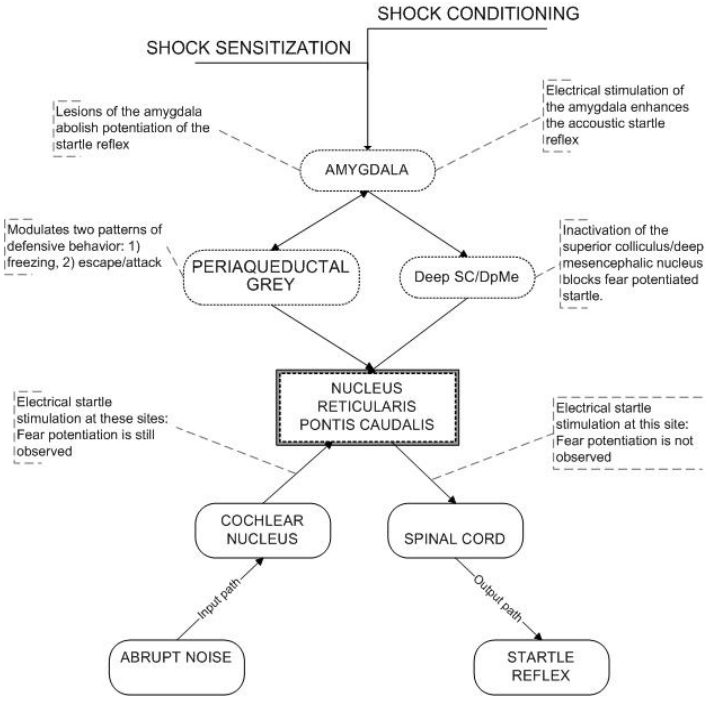

Figure 2-11. Affective modulation of startle circuitry: priming motor function. Reciprocal activation/inhibition between the periaqueductal grey and amygdala modulate PnC activity which in turn modulates startle potentiation and voluntary motor function.

Animal literature has shown that startle reflex circuitry is directly influenced by amygdala projections (assuming an intact SC/DpMe, Zhao & Davis, 2004). Crossing into the human domain, evidence indicates that a localized lesion of the right amygdala results

in an inhibited reflex contralateral to the lesion (Angrilli et al., 1996). Furthermore, the typical startle potentiation induced by an aversive emotive background does not manifest, furthering the belief that the amygdala is involved with human startle and emotional responses (Angrilli et al., 1996).

To determine whether the amygdala's role in affective processing extends beyond negative stimuli, Garavan and colleagues (Garavan et al., 2001) collected fMRI data while exposing subjects to high and low arousing pleasant and unpleasant pictures, in addition to neutral control pictures. Amygdala activation, relative to a neutral picture baseline, was significantly increased for both affective stimuli and did not differ for pleasant and unpleasant categories. Furthermore, whereas arousal level appeared to modulate the amygdala response for negative stimuli (increased arousal was associated with increase in activity), regardless of arousal level, pleasant pictures produced significant amygdala responses, suggesting that the amygdala plays a significant role in the processing of affective stimuli indiscriminate of the motivational system activated (Garavan et al., 2001). Increased activation of the amygdala, therefore, does not necessarily increase startle blink reflex magnitude; increased amygdala activity merely represents the modulatory impact the amygdala has on response characteristics, potentially via its connections with the PAG. As such, Walker and Davis postulate that **the role of the dPAG in potentiated startle is during the performance of fear-motivated behaviors and not during the acquisition and processing of fearful stimuli.**

The notion that affect, via activation of the amygdala, modulates startle has been extensively examined (e.g., Schupp, Junghofer, Weike, & Hamm, 2004). According to a

motivational priming pattern of affective modulation, associated startle reflexes are primed by the affective context well in advance of when a secondary probe is actually presented. The magnitude of the eye-blink response (in addition to other physiological processes, e.g., ERP) is modulated according to the affective valence of the context, while the polarity of the response is influenced by arousal. For example, the startle blink reflex is potentiated when humans are exposed to threat and violent death images, and is inhibited when humans are exposed to erotica scenes. This pattern of blink magnitude is robust across varying pleasant and unpleasant categories, with arousal levels controlling the polarization of the response (Bradley, Cuthbert, & Lang, 1999).

Typical protocols present the startle stimulus between 2-4 s after image onset, and indeed, the pattern of affective modulation is robust. However, blink magnitude is sensitive to the length of time an individual is exposed to the image before the startling stimulus occurs (Bradley et al., 1999). Specifically; (1) strong inhibitory effects are obtained when blink reflexes are elicited immediately after picture onset, (2) at the point of maximum inhibition (300 msec after picture onset), reflex inhibition is significantly larger for arousing pictures, compared with neutral pictures, (3) 500 msec post picture onset, reflexes are significantly augmented for unpleasant versus pleasant foregrounds, suggesting affective modulation by this point. (4) inhibited reflexes characterize the first 3 s following picture onset, and following 3 s of exposure, the reflex magnitude appears to asymptote for all conditions.

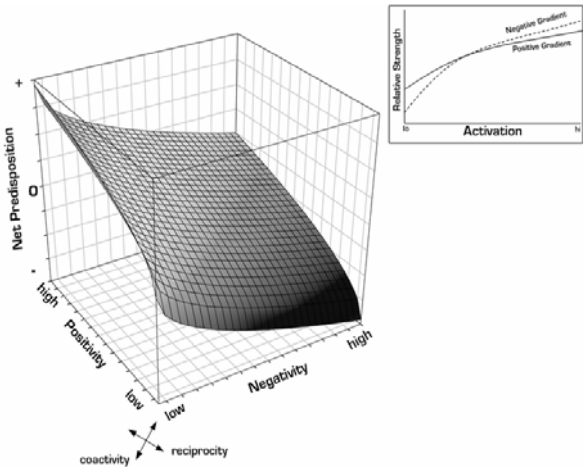

Figure 2-12. The Evaluative Space Model (Cacioppo et al., 1994, 1999) is useful to illustrate how various local conditions may influence the dispositional attributes of an organism.

Taking into account the temporal properties of the defense cascade (freeze response to circastrike) the temporal sensitivity of emotion and attention processes appear to directly influence the magnitude and latency of an involuntary movement. Consequently, one can also predict that a similar pattern maybe evidenced concerning the execution of voluntary movements. Therefore, indexing the characteristics of a preplanned movement to an acoustic probe at varying intervals during a fixed exposure period (in addition to or rather than just indexing the blink reflex) appears to be one among many exciting future directions. Optimizing stimulus intensity and the lead interval of an initiating stimulus as well as identifying the most appropriate affective context for the execution of particular movements are critical manipulations that could drive the investigation of alternative unique mechanisms that may ultimately benefit movement rehabilitation domains (e.g., stroke, Parkinson's). Notwithstanding the interacting impact of initiating stimulus, a growing body of literature has indexed the overt behavioral consequences of affective context.

Cacioppo's Evaluative Space Model

Appropriately reacting to variable conditions in the environment is key to survival. Biphasic theory posits that an organism will initiate approach or avoidance behaviors when confronted with pleasant or unpleasant circumstances, respectively. Related to this biphasic notion, Cacioppo and colleagues (Cacioppo, 1994; Cacioppo & Berntson, 1999; Cacioppo, Crites, Gardner, & Bernston, 1994; Cacioppo & Gardner, 1999; Cacioppo, Uchino, & Berntson, 1994) predict that an organism's affect system may be organized to achieve a dynamic balance between appetite and defense *(*Evaluative Space Model, ESM; see Figure 2-12). The ESM suggests that positive and negative information initiates the activation of two functionally separate evaluative processors (i.e., positivity and negativity). Together, the summation of these processors equate to a net predisposition to move toward or away from a given stimulus. Because these processors are relatively distinct, each has the flexibility for the local environment to shape its activation function (Cacioppo & Berntson, 1999). In the top-right corner of the figure, each function's activation pattern is characterized. At a net predisposition of zero, a small offset towards positivity can be noticed. Additionally, as activation increases for either function, it can be seen that the slope for negativity increases faster than for positivity. Together, these functions express what has been called a *positive offset* and *negativity bias*.

According to Cacioppo & Bernston (1999), "the process of natural selection may also have sculpted a propensity to react more strongly to negative than positive stimuli" (p.136). As the Evaluative Space model suggests, humans possess a fundamental orientation to rapidly shift into defense at lower levels of activation than for positivity. This predisposition, however, can be shaped by the local environment in the interest of

survival. The net effect of this movement bias has been investigated in a number of situations across a range of motor actions [posture, Hillman et al., (2004); pinch grip, Noteboom, Fleshner, & Enoka, (2001); lever pulling, Chen & Bargh, (1999); square tracing, Coombes, Janelle, & Duley, (2005)].

Emotion and Voluntary Movement

Rapid conscious and non-conscious processing has been shown to influence overt movement speed and direction. Chen and Bargh (1999) exposed participants to stimulus words and instructed one group of participants with incongruent instructions by requiring them to push a lever away from them (avoidance behavior) if the stimulus word presented was positive (activation of appetitive circuitry), and to pull the lever toward them (approach behavior) if the stimulus word was negative (activation of defensive circuitry); the second group received opposite congruent instructions. Results indicated that faster pulling of the lever coincided with positive initiating cues, while negative initiating cues were associated with significantly faster responses when pushing the lever. In a second experiment, participants were exposed to positive and negative stimuli and were instructed to only pull (group 1) or push (group 2) the lever to pleasant and unpleasant initiating cues. Again, results confirmed that negative stimuli resulted in faster pushing movements, while positive stimuli led to significantly quicker pulling movements. These valence effects are notable, given that negatively valenced cues resulted in faster movement time, as compared to positively valenced cues, regardless of movement direction (i.e., push or pull).

Interpreting these data within the Biphasic theory (Lang, 2000), it can be argued that in the face of negative or threatening cues, activation of defensive circuitry primes the human organism to move with greater haste. That is, when

exposed to negative cues, speeded movement may increase survival rate, permitting notions that this functional relationship has, and may continue to provide an evolutionary advantage to the human organism. Replication of movement speed findings have been reported with stimuli being novel words rather than familiar words, corroborating the notion that emotions can and will differentially impact movement speed and direction (Duckworth et al., 2002). **This sequence of studies draws attention to a number of important issues: Is there different motor circuitry underlying defensive and appetitive motivated behavior? Perhaps, alternatively, neural thresholds are decreased throughout the motor system, or the basal ganglia amplifies movements in unpleasant or threatening contexts?**

Alterations in center of pressure (i.e., postural adjustments) resulting from exposure to affective pictures were recorded by Hillman, Rosengren, & Smith (2004) in an effort to determine whether activation of motivational systems alter the magnitude and direction of postural movements. The authors reported gender-differences for postural responses to unpleasant pictures; an effect not found for pleasant and neutral pictures. In line with approach-avoidance predictions, females exhibited increased postural movement away from the unpleasant cue, but contrary to prediction males exhibited increased movement towards unpleasant pictures. Although gender differences in postural sway corroborated the findings of Bradley and Colleagues (Bradley, Codispoti, Sabatinelli, & Lang, 2001) who suggested that females have a broad disposition to react with a greater defensive set during unpleasant, highly arousing pictures, **testing broad predictions of avoidance behaviors whenever an organism is faced with unpleasant, threatening, or dangerous situations appears problematic. Revisiting the fight or**

flight response, it is reasonable to assume that when coupling certain threatening or dangerous situations (i.e., no escape route) with certain temperaments (i.e., aggression) whereas one individual may flee another may fight. Consequently, although in each case safety may ultimately be reached, the means by which safety is achieved contrasts significantly. The question therefore remains: do fight and flight responses differ in terms of movement direction but remain identical in terms of neural circuitry and movement force, speed, and accuracy?

With regard to stable sustained muscle activation, Noteboom and colleagues (e.g., Noteboom, Barnholt, & Enoka, 2001) required participants to perform a pinch grip task across a 10 min period, asking only that their pinch remain constant; while error was recorded and reported, time was not an issue within the protocol. The authors reported associations between increased impairment of steadiness on a pinch grip task with increases in arousal, trait anxiety, and intensity of a noxious stimulus (electric shock to the hand). Conversely, protocols that include the lever pulling task mentioned previously (Chen & Bargh, 1999) have not incorporated movement accuracy, but rather have recorded speed of pulling or pushing the lever, with movement direction and time being the dependent measures of interest.

As such, there is considerable data suggesting that the temporal and spatial characteristics of voluntary movement are influenced by the affective state of the individual, and that the speed and magnitude of startle elicited reflexive movements (e.g., blink reflex) vary according to affective states. Furthermore evidence suggests that voluntary movements can be achieved at the pace of a reflexive movement if the voluntary movement is initiated via an acoustic startle. To date however, startle initiated

voluntary movement and manipulated affective states have never been collectively examined in a systematic fashion. Linking emotion driven behavioral alterations with an underlying neural mechanism remains a formidable but exciting challenge for movement scientists.

Acoustic Startle, Emotion, and Voluntary Movements

Overt behavioral movements that accompany the startle reaction are considered reflexive (homeostatic) and are therefore typically considered to be exempt from voluntary control (Valls-Solé et al., 1995). Startle reflex pathways, however, require neural structures that are also intricately involved in voluntary motor action (e.g., reticulospinal system). Evidence for the facilitation of voluntary movement via manipulation of affective context and initiating stimulus has been reported. For example, Bradley, Drobes, & Lang (1996) exposed participants to pleasant, unpleasant, and neutral images; at varying intervals during the exposure period participants were required to make a simple button press following the presentation of an acoustic startle or tone. Faster reaction times coincided with startle probes and RT were accelerated later in the viewing period (i.e., at longer startle lead intervals). Specifically, longer RTs emerged early in the viewing period (maximal at 300msec) and decreased as the exposure period progressed. Similar to eye-blink magnitude (see above), RTs leveled off following 2-3 s of exposure and remained relatively constant for the duration of the 6 s exposure period. These findings (coupled with startle blink modification data presented above) represent varying attentional and emotional processes in picture perception (Bradley et al., 1999).

In discussing the Bradley et al. (1996) abstract, Bradley et al. (1999) suggest that following picture onset, processing resources were automatically allocated to stimuli that

engaged appetitive or defensive motivational systems, resulting in inhibited blink magnitude and lengthy RT's, relative to neutral pictures. As such, an initial orientating response may inhibit overt behavior, a phenomena magnified with activation of defensive circuitry (i.e., freezing). During the continuing exposure period, once initial processing has occurred attentional resources maybe freed up resulting in greater blink potentiation and faster RT.

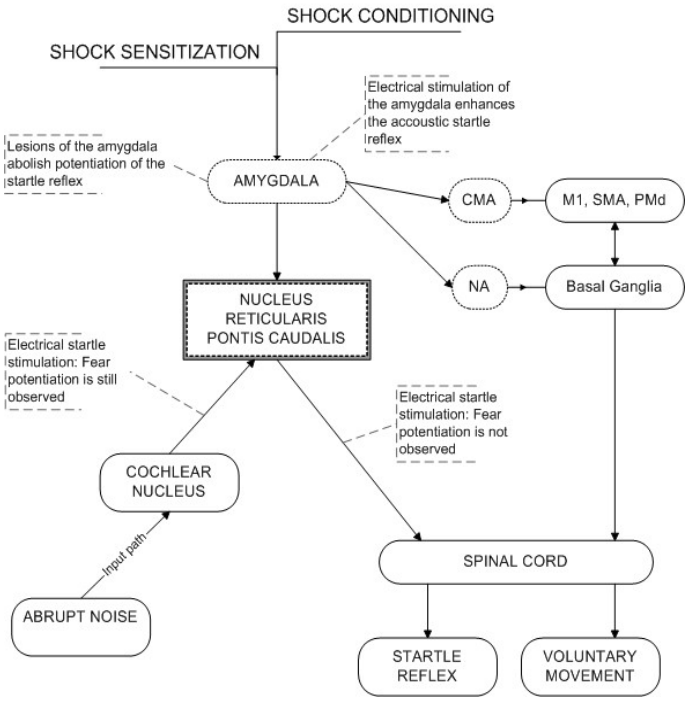

Figure 2-13. Priming motor function: Amygdala activity projects to the PnC and nucleus accumbens (NA) which in turn modulate reflexive and voluntary motor function. CMA = cingulated motor area, NA = nucleus accumbens, M1 primary motor area, SMA = supplementary motor area, PMd dorsal premotor cortex.

Conclusion

Aside from one abstract (Bradley et al., 1996) and a brief synopsis of that abstract (Bradley et al., 1999), startle elicited movements have not been systematically investigated within varying affective contexts. The above review, however, amalgamates

largely independent but complementary bodies of literature that summate to provide strong inference concerning the means by which the emotional system primes motor actions, and the varying impact initiating cues have on overt movements (See Figure 2-13). In closing, the above review justifies the necessity and importance of developing a research line that can successfully delineate the mechanisms underlying how and if affective states coupled with initiating cues impact the characteristics of voluntary motor function.

CHAPTER 3
METHODS

Participants

Thirty five (females = 17; males = 18) undergraduate students from the University of Florida were recruited to participate in this study, and received extra credit as compensation. Participants reported no hearing loss or central nervous system disorders that could affect movement. Written informed consent was obtained from all participants prior to beginning the study. All Participants' self-reported dominant hand use. All left handed participants (3, male) were excluded from the analyses to prevent confound due to handedness. In addition, data points 3 SDs from the mean were considered extreme scores and were removed prior to analysis. The repeated measures analyses were such that participants missing one (or more) score(s) were completely removed from each separate analysis. Consequently, 29 participants were included in the PRT, EMG peak, EMG risetime, and peak force analyses; 28 participants were included in the EMG slope and force risetime analyses; and 25 participants were included in the force slope analysis. With regard to analyses of the startle blink reflex, 26 participants were included in each analysis.

Instrumentation

Affective Stimuli

Participants viewed a total of 64 digitized photographs selected from the International Affective Picture System (IAPS; NIMH Center for the Study of Emotion and Attention, 2005) representing three affective categories (16 erotic couples, 16 attack,

16 household objects[1]). Sixteen blank black images were also presented. All pictures were visible for 6 seconds. Images were selected according to affective normative ratings (CSEA) to ensure that erotic and attack images were similarly arousing, and that each were significantly more arousing than neutral images (P = 6.57; U = 6.64; N = 2.56). For valence, each category significantly differed from each other (P = 6.75; U = 2.4; N = 4.97). Each participant viewed each picture only once. Stimulus presentation order was randomized and counterbalanced.

Task

While viewing each picture, participants were required to respond as quickly as possible to any acoustic stimulus by initiating an isometric bimanual contraction of the wrist and finger extensor muscles against two independent load cells (left/right limb).

Acoustic Stimuli

Created with custom built Labview software (7.1; National Instruments, Austin, TX), the tone cue consisted of a 50 ms tone delivered at 80 dB. In contrast, the startle cue stimulus was a 50 ms burst of white noise delivered at 107 dB with near instantaneous rise time. Acoustic stimuli were presented binaurally through a set of calibrated headphones (Radio Shack digital sound level meter: 33-2055, Fort Worth, TX). Acoustic stimuli were presented at set intervals of 500, 1500, and between 3000-5000 msec post picture onset (*M* = 4011.88, *SD* = 153.11, range = 3645.50-4345.25). Tone and startle cues were equally represented within each picture category at each time period (2 startle/tones per category per time period). As such, each valence by acoustic cue by time

[1] IAPS images: **erotic couples:**,4647, 4607, 4652, 4656, 4658, 4659, 4660, 4664, 4670, 4681, 4687, 4689, 4694, 4695, 4800, 4810; **attack:** 3530, 3500, 6260, 6540, 6313, 6550, 6243, 6370, 6510, 6200, 6560, 6360,6230, 6250, 6300, 6244; **household objects:** 7002, 7004, 7006, 7009, 7010, 7025, 7035, 7041, 7050, 7052, 7055, 7059, 7080, 7090, 7150, 7175.

period combination was experienced twice. To prevent habituation and anticipation, catch trials (no sound) occurred four times within each valence category. Intertrial intervals varied from 10-14 s.

Voluntary Movement

Participants were prepared for measurement in accordance with the Society for Psychophysiological Research guidelines (Putnam, Johnson, & Roth, 1992). EMG surface electrodes (silver–silver chloride electrodes, 1 cm in diameter and 2 cm apart with an epoxy-mounted preamplifier) were placed over the extensor communis digitorum and extensor carpi ulnaris muscles of left and right arms. To index force generation during each isometric wrist/finger extension, two 34.1 kg load cells embedded in cushioned platforms were altered in height to accommodate individual hand sizes (see Figure 3-1). Upper limb EMG (bandpass filter 1-500 Hz) and force data were amplified by 5 K and collected at 1000 Hz via Biopac software (3.8.1, Biopac Systems Inc, Goleta, CA, USA).

Blink reflex

The eye-blink response to the acoustic startle probe was recorded by placing two Biopac shielded 4 mm Ag/AgCl electrodes (ELS204S) over the orbicularis oculi muscle beneath the left eye. The raw EMG signals were amplified by 5,000 using a Biopac bioamplifier (EMG100B) and bandpass filtered from 90 to 250 Hz.

Trial onset and offset, and visual and auditory stimulus presentation were controlled via a custom Labview program. The custom-written program simultaneously sent a 5-volt digital marker into the physiological trace to indicate picture onset and acoustic stimulus onset. Each separate 10 s trial (2 s baseline; 6 s picture presentation; 2 s buffer) was streamed to disk for offline analyses.

Procedure

After all questions had been answered and informed consent had been obtained, participants were seated in a comfortable chair positioned 1.0 m from a 19" LCD presentation screen. Next, height of the force platforms was adjusted, load cells were calibrated, and EMG sensors were attached to the forearms and beneath the left eye (see Figure 3-1). Following calibration, participants were familiarized with the protocol via a 4 trial practice session (all blank images, 1 startle, 2 tone, and 1 catch trial). Participants were instructed to (1) "look at each picture for the entire time it is on the screen", (2) "consider picture onset as a cue to prepare to make the required wrist and finger extension", and (3) "respond as quickly as possible to an acoustic stimuli by initiating a short duration bimanual isometric contraction of the wrist and finger extensor muscles." Following picture offset, participants were instructed to continue viewing the blank screen as the next image would appear after a short break. At the conclusion of all trials, hands were removed from the customized force platform, EMG sensors were removed, and the participants were debriefed. From participant arrival to departure, the experiment lasted approximately 30 minutes.

Data Reduction

Voluntary movement

EMG and force data were analyzed offline via a custom LabVIEW program. EMG signals were rectified and filtered with a 25-Hz lowpass elliptic filter (Carlsen et al., 2004b). Baseline EMG and force scores were calculated for each trial (mean score during 150 ms preceding acoustic stimulus onset). Eight dependent measures were calculated for each trial: (1) premotor reaction time: PRT, (2) force onset: F_{onset}, (3) EMG amplitude: EMG_{amp}, (4) force amplitude: F_{amp}, (5) force risetime: $F_{risetime}$, (6) EMG

Figure 3-1**.** Experimental setup. **Top**: postures of arms, forearms, and shoulders before and during the bimanual task. **Bottom left:** posture of hands relative to load cells during movement preparation and ITI. **Bottom right:** posture of hands relative to load cells during ballistic movement execution.

risetime: $EMG_{risetime,}$ (7) force slope: F_{slope}**,** and (8) EMG slope: EMG_{slope}**,** (see Figure 3 for specific details and calculations). For each trial for each limb, the semi-automated analysis program superimposed force and filtered EMG data over the digital trigger signal. Visible on a computer monitor, the program automatically identified and then inserted cursors at F_{amp} and EMG_{amp} locations within specified windows after acoustic stimulus onset (EMG: 40-500 msec; Force: 40-800 msec). Baseline corrected normalized F_{amp} and EMG_{amp} T-scores were calculated for each trial within each participant's data prior to statistical analysis. Onset of muscle action was identified by locating the first time point where EMG signal amplitude was greater than double the baseline value (Wong & Ng, 2005). Likewise, onset of force production was identified as the first time point where force data exceeded double the force baseline value (see Figure 3). Given the

strictness of the detection algorithm, coupled with intermittent intermediary EMG and/or force noise between stimulus onset and movement onset, the location of each of these threshold locations was visually verified and manually adjusted if necessary. Because of excessive noise and/or no visible peak in EMG or Force within the specified windows, a total of 19 trials were removed from 9 participants' data sets (range 1-4 trials per subject; 97.8% of the trials were included in the analysis). For each participant, no more than 1 trial was removed from each acoustic stimulus by valence condition. Summary statistics were created by averaging left and right limb data for each dependent variable.

Blink reflex

The raw EMG signals were rectified and low pass filtered (25Hz) offline via a custom built LabVIEW program. The semi-automated program identified and inserted a cursor at peak EMG amplitude within a 20-150 ms window after startle stimulus onset. Onset of muscle contraction was identified by locating the time point where EMG signal amplitude first equaled and then surpassed double the baseline value (Wong & Ng, 2005) 2005). A cursor was displayed at this location. Baseline corrected peak t-scores were then calculated for each trial within each participant's data prior to statistical analysis. Four

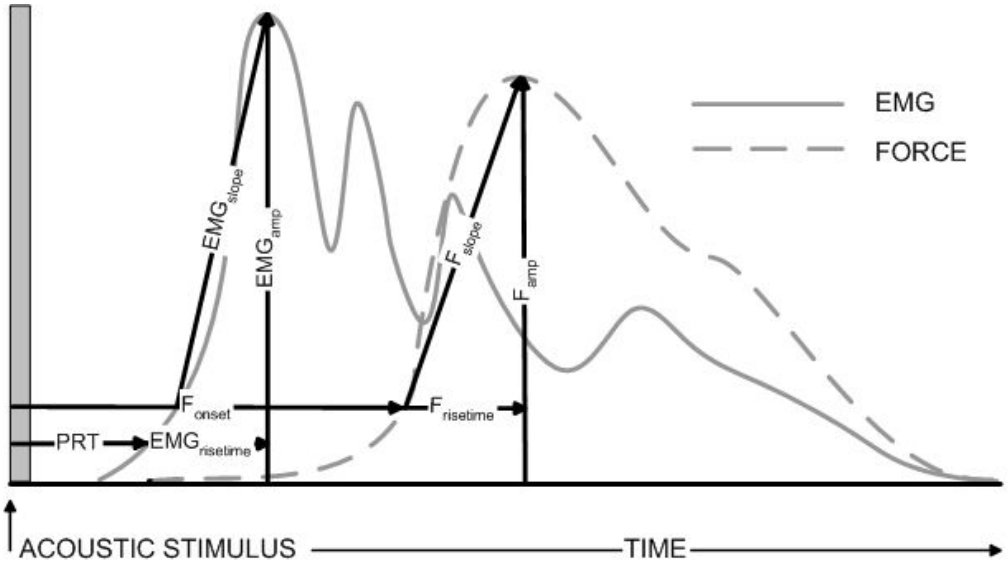

Figure 3-2. Calculation of dependent variables, voluntary movement. **PRT:** Delay between acoustic stimulus onset and EMG threshold. **F_{onset}:** Delay between acoustic stimulus onset and Force onset. **EMG_{amp}:** Peak amplitude within a 40-500ms window following acoustic stimulus onset. **F_{amp}:** Peak amplitude within a 40-800ms window following acoustic stimulus onset. **$EMG_{risetime}$:** Latency between EMG onset and peak. **$F_{risetime}$:** Latency between Force onset and peak. **EMG_{slope}:** EMG amplitude change from threshold to peak, divided by time from threshold to peak. **F_{slope}:** Force amplitude change from threshold to peak, divided by time from threshold to peak.

dependent variable scores were calculated for each startle trial: premotor time, peak force latency, peak amplitude, EMG slope (see figure 3-3). For each participant, data from accepted trials were averaged for each level of valence for each level of probe interval.

Statistical Analyses

To establish whether startle initiated movements and activation of appetitive and/or defensive circuitry alter voluntary and involuntary motor function, each dependent variable was analyzed in 2 (ACOUSTIC STIMULUS: startle, tone) × 4 (VALENCE: erotica, attack, household objects, blank) × 3 (PROBE INTERVAL: 500ms, 1500ms, 3000-5000ms) analysis of variance (ANOVA), with repeated measures on all three factors.

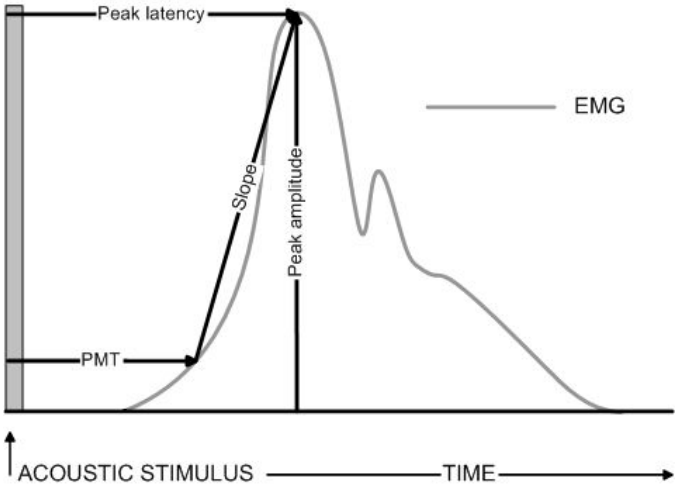

Figure 3-3. Calculation of dependent variables, blink reflex. Threshold refers to the location and amplitude in the EMG trace where values are greater than double the corresponding baseline value. **PMT:** Delay between acoustic stimulus onset and EMG threshold. **Peak amplitude**: Peak amplitude within a 20-150ms window following acoustic stimulus onset. **Peak latency**: acoustic stimulus onset to peak EMG amplitude. **Slope**: EMG amplitude change from threshold to peak, divided by time from threshold to peak.

For *F* - ratio interactions with valence and probe interval, if the sphericity assumption was violated, then Geisser-Greenhouse corrections were used to obtain the critical *p*-value. Follow-up analyses were conducted using simple effects tests and the Tukey HSD procedure for significant interactions and main effects, respectively.

To illustrate the relationship between voluntary and involuntary startle triggered movements, Pearson correlation coefficients were computed between corresponding variables (voluntary and involuntary: PMT, EMG peak, peak EMG latency, EMG slope) matched for valence, probe interval, and limb. For all analyses, the probability value was set at $p < .05$.

CHAPTER 4
RESULTS

Voluntary Movement

Premotor Reaction Time (PRT)

A significant main effect of time (F (2, 56) = 28.82, $p < .001$) evidenced that PRTs were faster following longer probe intervals (1500 and 3000-5000 msec) relative to shorter probe intervals (500 msec). A significant main effect of acoustic stimulus indicated that when movements were initiated following startle relative to tone cues, premotor times were accelerated (F (1, 28) = 44.67, $p < .001$). Additionally, a significant main effect of valence indicated that relative to erotic images, exposure to attack and household object images resulted in faster PRT, F (3, 84) = 9.98, $p < .001$. Further, PRT during exposure to scenes of household objects was faster as compared to attack and blank conditions.

These significant main effects, however, were superseded by a Time x Valence interaction (F (6, 168) = 3.55, $p = .002$). Follow-up analyses indicated that PRTs initiated to cues 500 msec following erotic image onset were slower than all other Valence x Time conditions aside from attack and blank conditions at 500 msec. In addition, exposure to attack images at 500 msec resulted in slower PRT relative to blank conditions at 1500 and 3000-5000 msec intervals. Finally, PRTs to cues at 500 msec during blank exposure periods were greater than during household object exposure periods with probe intervals of 1500 and 3000-5000 msec. (see Figure 4-1). Remaining interactions did not reach significance (p's > .05).

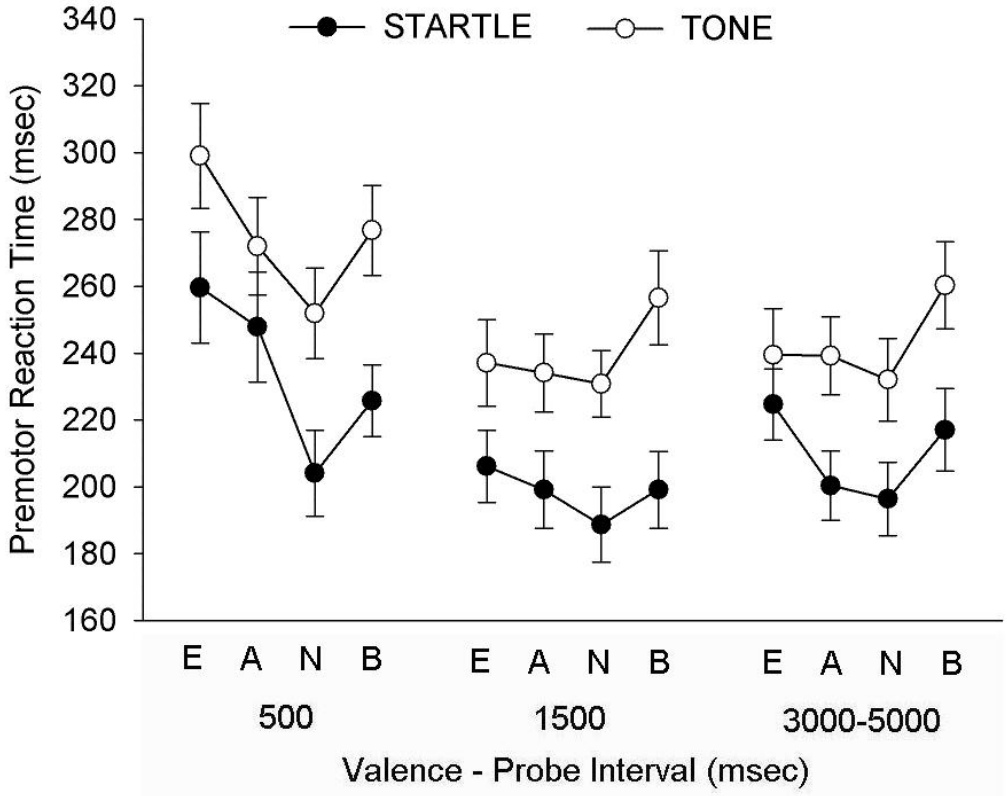

Figure 4-1. PRT (± 1SE) for startle and tone cues for each valence category for each probe interval. E = erotica, A = attack, N = household objects, B = blank

EMG Risetime ($EMG_{risetime}$)

EMG onset to peak was significantly altered by initiating stimulus (F (1, 28) = 7.50, p = .012) with inspection of the means indicating that rise times were shorter to startle relative to tone cues ([msec] Startle: M = 69.86, SE = 5.32; Tone: M = 80.60, SE = 8.90). Main effects of time, valence and remaining interactions did not reach significance (p's > .05).

EMG Peak Normalized T-scores (EMG_{amp})

A significant main effect of acoustic stimulus was evidenced, indicating that EMG_{amp} was greater to startle relative to tone cues, F (1, 28) = 66.08, p < .001. This main effect, however, was superseded by a significant Time x Acoustic Stimulus interaction (F (2, 56) = 3.79, p = .029), and Time x Valence interaction (F (6, 168) = 3.55, p = .002)

(see Figure 4-2). Follow-up tests for the Time x Acoustic Stimulus interactions revealed that peaks to startle cues at 1500 and 3000-5000 msec were greater than tone conditions at the same intervals. In addition, peaks to startle cues at the 1500 msec interval were greater than all tone conditions. Post-hoc tests to identify specific Time x Valence differences were not significant. Main effects of time and valence did not reach significance (*p's* > .05).

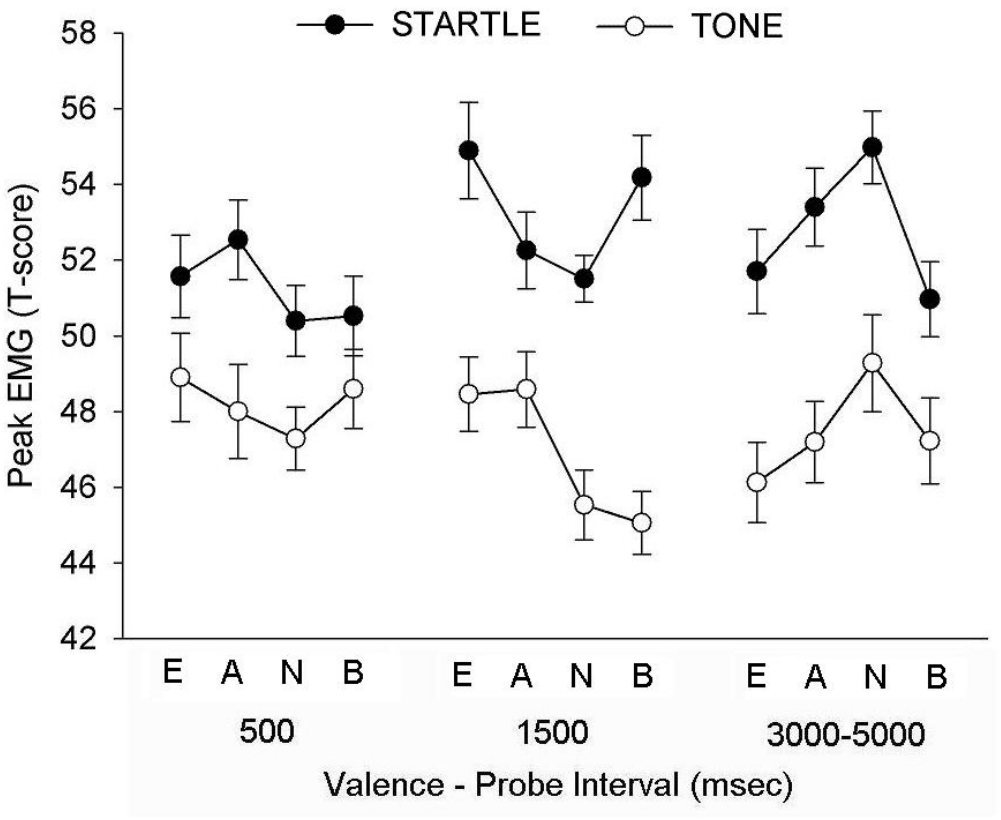

Figure 4-2. EMG_{amp} (normalized T-scores, + 1SE) for startle and tone cues for each valence category for each probe interval. E = erotica, A = attack, N = household objects, B = blank

EMG Slope (EMG_{slope})

Analyses revealed that EMG_{slope} was significantly altered by acoustic stimulus, such that slopes were of a steeper gradient when movements were initiated to startle relative to tone cues (F (1, 27) = 7.28, p = .012) ([msec] Startle: M = .93, SE = .05; Tone:

M = .76, *SE* = .05). Main effects of time and valence and all higher order interactions did not reach significance (*p's* > .05).

Force Risetime ($F_{risetime}$)

Analyses revealed a significant effect of acoustic stimulus on the latency between force onset and peak force (*F* (2, 56) = 3.97, *p* = .024), indicating that risetimes were more rapid to startle relative to tone cues ([msec] Startle: *M* = 147.78, *SE* = 12.49; Tone: *M* = 155.34, *SE* = 13.35).

Peak Force Normalized T-scores (F_{amp})

Analysis of normalized F_{amp} scores evidenced a significant main effect of acoustic stimulus (*F* (1, 28) = 97.19, *p* < .001), indicating that peaks were greater following startle relative to tone cues. Analysis of F_{amp} also revealed a significant Time x Acoustic Stimulus interaction (*F* (2, 56) = 4.86, *p* = .011) with follow-up tests revealing greater peaks following startle cues at 1500 and 3000-5000 msec probe intervals relative to tone cues at the same intervals. In addition, peaks to startle cues at 1500 msec were greater than tone conditions at 500 msec. (see Figure 4-3). Finally, a significant interaction between time and valence was evidenced (*F* (6, 168) = 2.50, *p* = .025), although follow-up tests including planned comparisons for attack images were not significant. Main effects of time and valence and remaining interactions were not significant (*p's* > .05).

Force Slope (F_{slope})

Gradient of slope between F_{onset} and F_{amp} was significantly affected by Acoustic Stimulus (*F* (1, 24) = 33.75, *p* < .001). Follow-up analyses indicated that steeper slopes coincided with all startle conditions (*M* = .42, *SE* = .04) relative to tone conditions (*M* = .36, *SE* = .03). Neither main effects for time, valence, nor the remaining interactions reached significance (*p's* > .05).

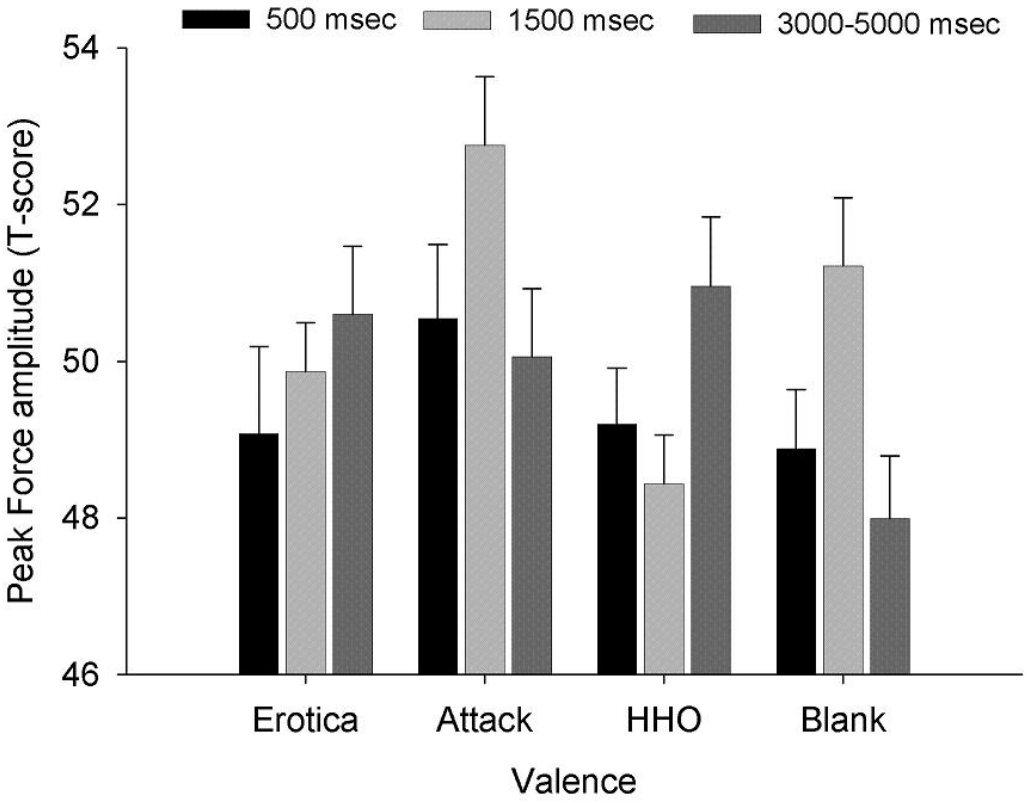

Figure 4-3. $Force_{amp}$ (normalized T-scores, $\pm$ 1SE) collapsed across initiating stimulus (startle, tone) for each valence category for each probe interval.

Involuntary Movement (Blink Reflex)

Premotor Reaction Time (PRT)

Significant main effects of time (F (2, 42) = 12.73, $p < .001$) and valence (F (3, 63) = 7.26, $p < .001$) evidenced that PRT was longer at probe intervals of 500 msec relative to all later probe intervals, and longer during exposure to pleasant stimuli relative to all other categories. The time by valence interaction was not significant (F (6, 126) = .39, p = .88).

Peak EMG T score

Analyses revealed that peak EMG of the startle blink reflex was significantly altered by affective context (F (3, 63) = 5.86, p = .001), with follow-up analyses evidencing smaller peaks during exposure to pleasant images relative to all other

categories. In addition, a significant main effect of time was also evidenced (F (2, 42) = 23.15, $p < .001$), with follow up analyses confirming that smaller peak scores at 500 msec relative to peaks at 1500 msec and 3000-5000 msec. The time by valence interaction was not significant (F (6, 126) = .93, $p = .47$).

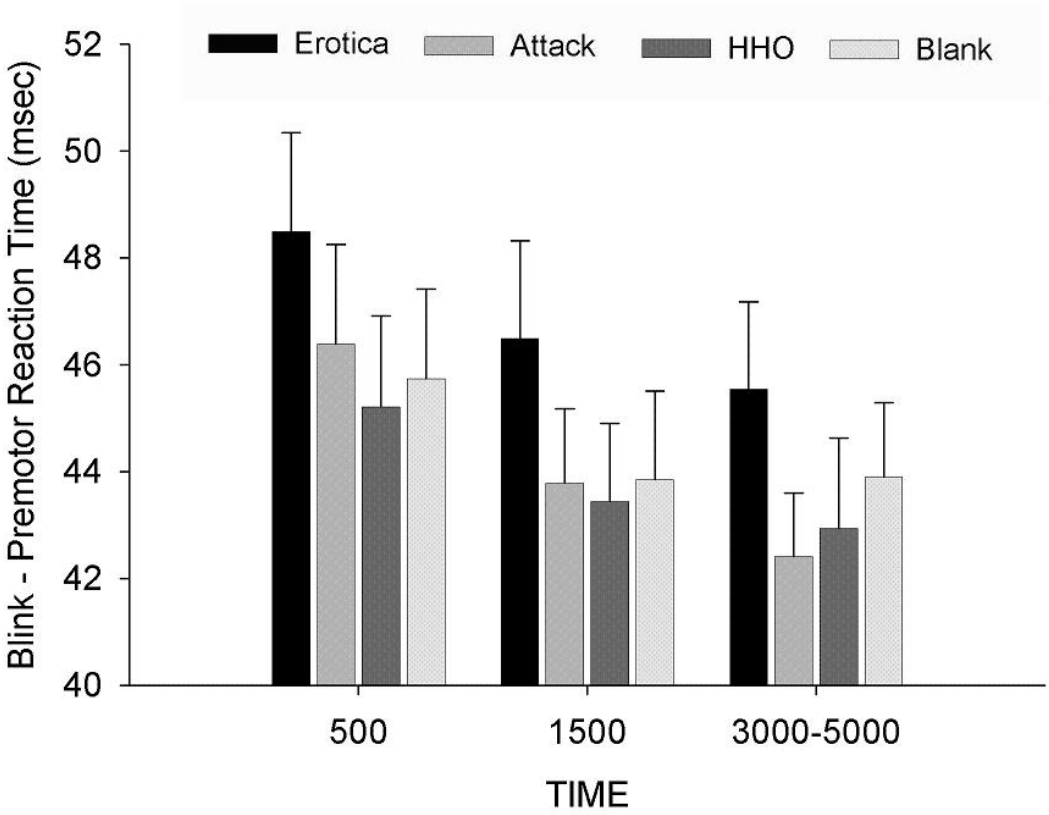

Figure 4-4. Blink reflex premotor reaction time for each probe interval for each valence category. PRT's were longer at probe intervals of 500 msec relative to all later probe intervals, and longer during exposure to pleasant relative to all other stimuli.

Peak latency

Peak EMG latency of the startle blink reflex was not altered by time (F (2, 42) = 2.97, $p = .062$), valence (F (3, 63) = .30, $p = .83$), or from an interaction between these two factors (F (6, 126) = .93, $p = .47$).

EMG slope

EMG slope of the startle blink reflex was not altered by time (F (2, 42) = 2.10, p = .136), valence (F (3, 63) = .28, p = .84), or from an interaction between these two factors (F (6, 126) = .76, p = .61).

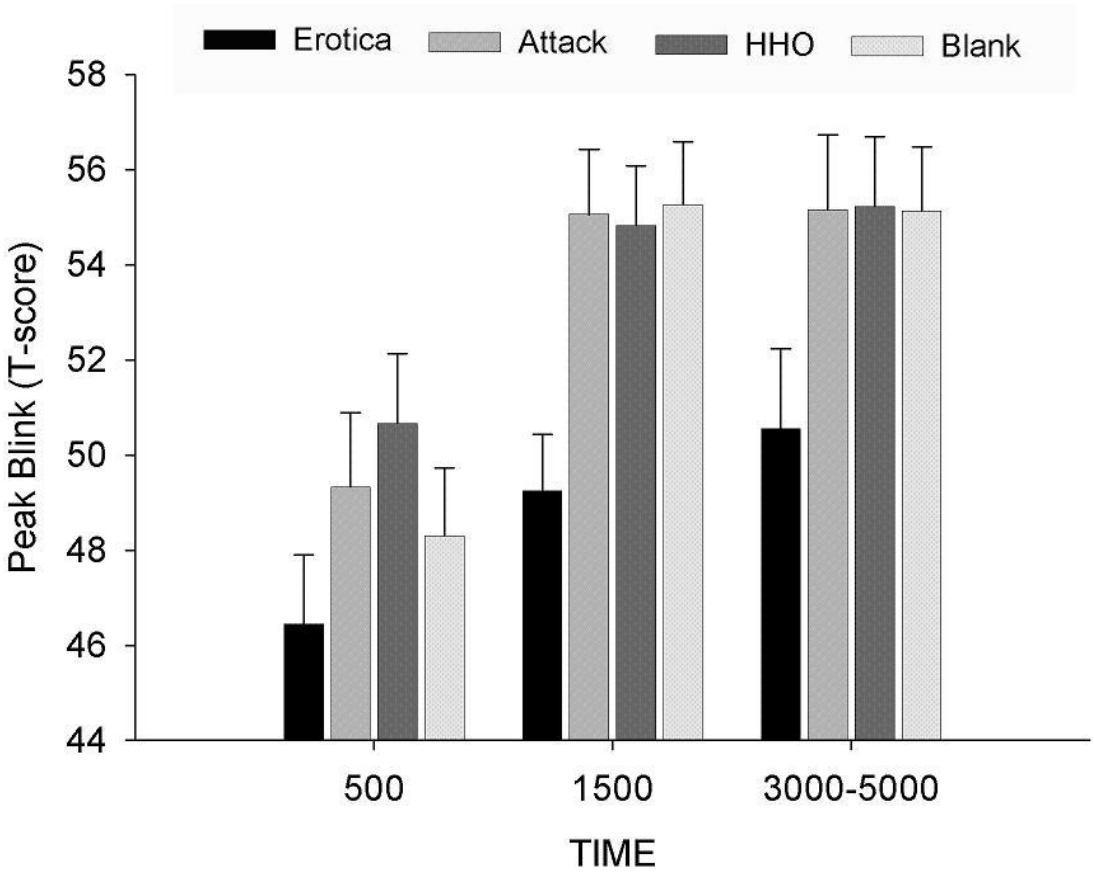

Figure 4-5. Mean blink peak T score for each probe interval for each valence category. Attenuated peaks coincided with exposure to erotic images relative to all other categories, and smaller peak scores were evidenced at 500 msec relative to peaks at later probe intervals.

Correlations: Voluntary and Involuntary Movement

To investigate the relationship between voluntary and involuntary startle triggered movements, Pearson correlation coefficients were computed between corresponding voluntary and involuntary variables matched for valence and probe interval.

Premotor Reaction Time (PRT)

No significant correlations were evidenced between voluntary and involuntary PRTs (*p's* > .05).

Peak EMG T score

Significant positive correlations were obtained between peak EMG of voluntary movement and peak EMG of the startle blink reflex during exposure to attack and during exposure to household object images with probe intervals of 500 msec (attack: $N = 26$, $.r = .420$, $p = .037$; household objects: $N = 26$, $r = .401$, $p = .042$).

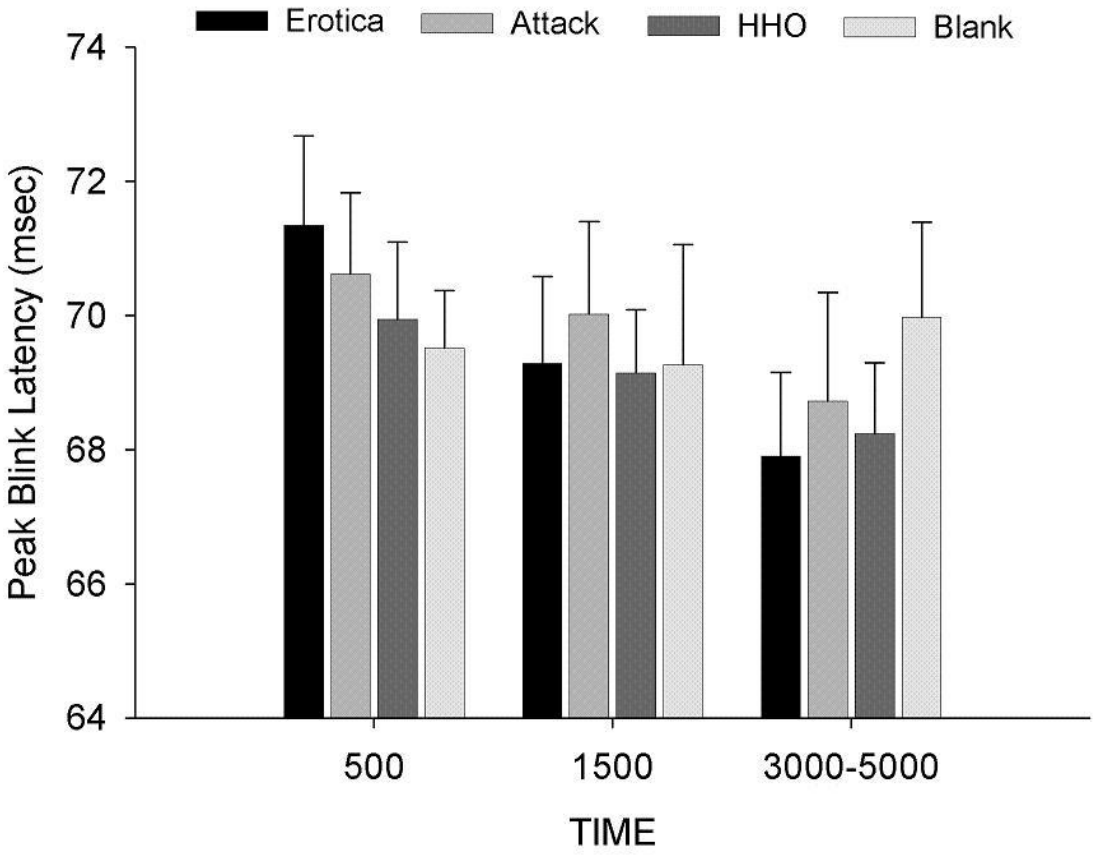

Figure 4-6. Peak EMG latency of the blink reflex for each probe interval for each valence category. No main effects or interactions were evidenced.

EMG slope

Analyses revealed a significant positive correlation between voluntary and involuntary movements for EMG slope. Specifically, the variations in EMG slope of the blink reflex positively correlated with corresponding voluntary movements at probe intervals of 500 msec during exposure to erotic images (N = 26, r = .440, p = .028).

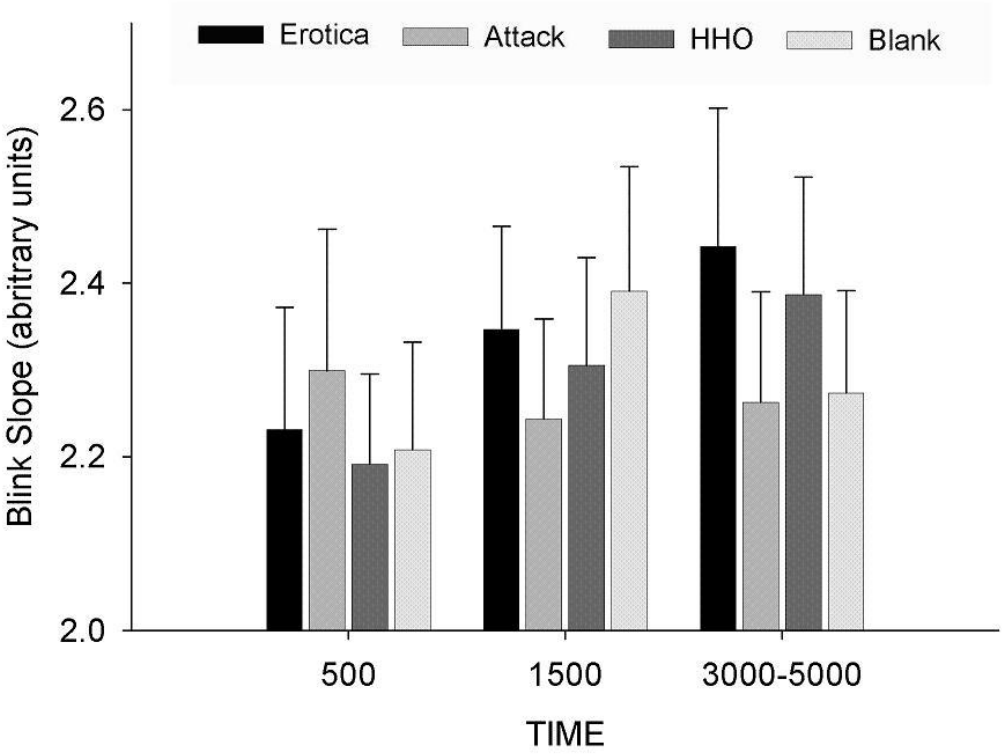

Figure 4-7. EMG slope of the startle blink reflex for each probe interval for each valence category. No main effects or interactions were evidenced.

CHAPTER 5
DISCUSSION

The present experiment extended a previous protocol (Coombes, Cauraugh, & Janelle, in review) to determine the impact of probe interval (500-5000 msec), initiating cue (80dB tone, 107dB startle), and affective context (erotic, attack, household object, blank images) on preplanned voluntary ballistic movement and the involuntary startle blink reflex. The aim of the present study was three-fold: (1) to index the impact of arousal and valence on voluntary and involuntary movement at various intervals during a 6 second viewing period, (2) to corroborate previous evidence that faster and stronger voluntary movements are initiated to startle, relative to tone cues, and (3) to determine whether or not startle triggered voluntary and involuntary movements are positively correlated. To address these aims, participants were required to execute voluntary movements to the onset of acoustic stimuli while viewing a range of scenes. In the discussion that follows I will argue that (1) central and peripheral motor processes of voluntary and involuntary movements are differentially altered by varying combinations of time, acoustic stimulus, and valence; (2) that voluntary and involuntary movements are sensitive to short lead interval prepulse effects, and (3) faster and stronger voluntary movements occur approximately 1500 msec post image onset when initiated to startle cues, with a trend that this combination is accentuated during exposure to attack images. Having addressed my findings, limitations of the present study will be outlined, and recommendations for future research will be offered.

Voluntary Movement

Premotor Reaction Time

Hypotheses 1a and 1b posited potential differences in the temporally sensitive impact of emotional valence and emotional arousal on central (and peripheral) motor processes. Corroborating previous evidence, voluntary premotor RTs were altered by emotional valence such that relative to erotic images, faster premotor RTs coincided with exposure to attack (Chen & Bargh, 1999; Coombes et al., 2005) and household object images (Coombes et al., in review; Coombes et al., 2005). These data support the notion that faster overall movement times during or following exposure to attack/unpleasant and household object/neutral images partially result from expedited centrally driven motor processes (Coombes et al., in review). Additionally, central processing times during exposure to household images were faster than attack and blank conditions. Neutral conditions have rarely been employed in emotion-movement protocols (Chen & Bargh, 1999; Marsh, Ambady, & Kleck, 2005), however, when they have been included, their impact on motor related processes have been difficult to interpret (Schimmack, 2005). This issue will be addressed in detail later.

Time periods also modulated premotor RT; with speeded premotor RTs evidenced following longer probe intervals (1500 and 3000-5000 msec) relative to shorter probe intervals (500 msec). These data exemplify a prepulse effect, such that attentional capture to visual stimuli (regardless of the arousal/valence properties of the foreground image) inhibited premotor RT at 500 msec intervals (see Figure 4-1).

Superseding independent effects of valence and time, follow-up analyses demarcating the interactive effect of time and valence on premotor RT indicated that movements initiated to cues presented 500 msec following erotic image onset were

slower than all other conditions aside from attack and blank conditions at the same time interval. In addition, exposure to attack images at 500 msec resulted in slower premotor RTs relative to blank conditions at 1500 and 3000-5000 msec intervals. Finally, Premotor RTs to cues at 500 msec during blank exposure periods were greater than during neutral exposure periods with probe intervals of 1500 and 3000-5000 msec.

These data corroborate previous emotion-startle blink evidence (Bradley et al., 1993) but in the *voluntary movement domain*, demonstrating that more arousing foregrounds (erotic, attack) inhibit the speed of movement execution at early relative to late probe intervals. As these arousing stimuli also draw attention to them, an attentional explanation likely accounts for inhibition in 2 of the 3 short lead interval findings (Bradley et al., 1993; Filion, Dawson, & Schell, 1998). However, blank foregrounds resulted in inhibition of premotor RT, which cannot be directly attributed to arousal or valence. One potential explanation is that during exposure to blank images, participants were expecting the blank picture to be replaced by an IAPS scene; as such, anticipation resulted in maintenance of attention on the blank screen, resulting in a relative delay in premotor RT. The notion that expectation may alter response times can be easily controlled in future studies by varying pictures that are included within each image sequence, a suggestion that will be further addressed in the limitations/future research sections later.

Premotor RTs elicited later in the viewing period were not significantly altered by valence. Consequently, the motivational priming hypothesis, which accounts for valence effects following long lead intervals was not supported (Bradley et al., 1993). Previous evidence indicates that exposure to unpleasant and neutral images speeds central

processing when movements are initiated between 2-4 s post picture onset (Coombes et al., in review). I predicted that faster and stronger movements would manifest later (1500, 3000-5000) in the viewing period during exposure to attack images relative to other affective contexts at the same time interval. The expected progression from freezing to a fight/flight pattern was not demonstrated in the temporal modulation of voluntary movement. A number of potential explanations may account for this unexpected finding. First, psychophysiological indices that act as the foundation for the defense cascade model (Lang et al., 1997) were garnered from participants while they passively viewed images. The anticipated pattern of behavior, therefore, does not take into account the planning or execution of overt motor action; processes that alter the pattern of a typical psychophysiological response (e.g., HR, Coombes et al., 2005). In the present case, planning, anticipation, and execution processes directly related to the motor task may have suppressed or masked activation of the emotion circuits; thereby preventing emotion from maximally impacting movement. A second and more plausible (and testable) explanation concerns the nature of the movement. Specifically, research on the monkey brain has demonstrated that the CMA areas are essential in decision making, planning, execution, and the control of motor action only when rewards are offered for specific movements (Shima & Tanji, 1998). In the present case, the movement was not linked to any functional consequence associated with the affective foreground, and likewise, no accuracy component was incorporated permitting a feedback loop (i.e., success/failure). As such, the impact of emotion may be accentuated when movement accuracy (rather than just movement speed) is a core component of the task. Hence, it is plausible that the emotion network and the movement networks were not maximally integrated in the

current protocol. For example, it has been demonstrated that offering choices for the treatment activities and incorporating functional goals to therapeutic tasks can enhance response rate and movement efficiency in stroke patients (Wu, Wong, Lin, & Chen, 2001). Likewise, Volman and colleagues (Volman, Wijnroks, & Vermeer, 2002) reported that providing a functional context to perform a task (i.e., turning a light switch off versus reaching to a marker) enhances the quality of reaching movements (speed, smoothness, control) of the affected arm in children with spastic hemiparesis. Further discussion of these potential explanations along with future solutions are offered in the limitations and future research sections below.

In line with the second hypothesis, an effect of initiating cue emerged for premotor RT. Specifically, relative to the 80dB tone cue, the 107dB startle initiating cue resulted in speeded premotor RTs, corroborating prior startle triggered premotor RT findings (Carlsen et al., 2004a, 2004b; Rothwell, 2006; Valls-Solé et al., 1999; Valls-Solé et al., 1995), and further validating the notion that startle initaiting cues expidite central motor processes. Additionally, the nature of the initiating cue impacted all peripheral voluntary movement indices. That is, the intensity of the 107dB startle initiating cue resulted in speeded EMG risetimes, force risetimes, greater peak EMG and force amplitudes, and steeper EMG and force slope gradients.

Two complementary explanations are offered to account for the impact of acoustic stimulus on movement: (1) subcortical triggering and (2) stimulus intensity. The reticular formation has been implicated as a central structure within the startle circuit (Grillon & Baas, 2003), ensuring rapid overt behavioral responses to abrupt startling stimuli (i.e., startle blink response). In addition to the role of the reticular formation in the

manifestation of involuntary movements, emerging evidence indicates that neurons within the reticular system are sensitive to voluntary motor planning and initiation (Buford & Davidson, 2004). As such, although our premotor RT's were not fast enough to rule out cortical processing (cf., Carlsen et al., 2004a; Valls-Solé et al., 1999), the possibility that movements were subcortically initiated cannot be discarded.

To bridge the affective and motor literature, the protocol used herein presented startle cues at a volume of 107dB through headphones (within the common range of that used in the emotion-startle blink literature, (e.g., Lang et al., 1990; Stanley & Knight, 2004) rather than the 124 dB presented through speakers behind the subjects head (as used by Carlsen et al., 2004a; Valls-Solé et al., 1999). The disparity between startle stimulus volume potentially slowed response times in the present data set, while also leading to questions concerning the volume at which a stimulus intensity effect gives way to activation of startle circuitry. For example, can the startle circuit be activated at varying stimulus intensities? is the startle response an all or nothing response? if the startle circuit is not activated, what are the pathways that permit a stimulus intensity effect on voluntary movement? what are the conditions necessary for a startle response to occur? These questions aside, results showed strong effects of acoustic stimulus, supporting previous evidence that voluntary reaction times to auditory stimuli are inversely correlated with stimulus intensity (Pascual-Leone et al., 1992).

The majority of the startle-voluntary movement literature to date has contrasted premotor RTs following cues at 80dB and 124dB without the presence of a concurrent visual stimulus. A promising future research direction, therefore, is to gauge the impact of a concurrent visual emotional stimulus while also identifying the parameters that

separate a stimulus intensity effect from activation of the startle circuit (e.g., stimulus volume, environmental context), and ultimately, how these factors alter overt voluntary movement. Although blink reflex data were collected in this experiment via activity of the left orbicularis oculi muscle, activity of the sternocleidomastoid (SCM) muscle was not recorded (viewed as an index of the presence of a startle response; (Valls-Solé et al., 1999) preventing strong inferences that modulation of central and peripheral indices were driven by an active startle circuit rather than a stimulus intensity effect. Activation of the startle circuit aside, these data confirm the finding that increasing the intensity of an auditory stimulus expedites movement initiation and execution. Furthermore, stimulus volume and the concurrent viewing task used in the present study are the most likely explanations to account for the slowing of premotor RTs relative to other stimuli used (124dB startle; Carlsen et al., 2004a).

Peak EMG and Peak Force Amplitude

With regard to peak peripheral motor processes, we observed a similar interacting effect of time and acoustic stimulus for both EMG and force, such that EMG and force peaks to startle cues at 1500 and 3000-5000 msec intervals were greater than tone conditions at the same intervals. Interpreting these results while viewing Figure 4-2 (peak EMG), it is clear that whereas peak responses to tone cues remained relatively constant across varying time intervals, significant findings were predominantly the result of greater peripheral activity to startle cues later in the viewing period, with maximal activation occurring at 1500 msec to startle cues. Similar to the interpretation offered above to account for the modulation of premotor RTs, it is conceivable that in addition to slowing central motor processes, a prepulse effect also inhibited peripheral motor activity at the 500 msec time interval (Bradley et al., 1993) relative to the later probe intervals.

With regard to probe interval and initiating cue, faster and stronger movements were executed 1500 msec post visual stimulus onset and to a startle rather than a tone cue. This finding is important for those who seek to facilitate the speed and strength of movement, and likewise, for those who seek to control or attenuate movement speed and force.

Although initial analyses offered support to the notion that the affective foreground and the exposure length preceding movement initiation impact movement execution, further analyses did not reveal specific differences between pairings of affective context and time period for peak EMG or peak force. Viewing Figure 4-3 this finding (at least for peak force) is surprising given the sharp contrast between scores at 1500 msec relative to early and late time periods during exposure to attack images. Ad-hoc tests implemented to delineate the effect of time and activate defensive circuitry failed to reach significance.

Summary

To summarize, central and peripheral motor processes of voluntary and involuntary movements are differentially altered by varying combinations of time, acoustic stimulus, and valence. Specifically, (1) voluntary movements are sensitive to short lead interval prepulse effects (i.e., attention; Bradley et al., 1993), (2) the intensity of an acoustic startle stimulus accelerates temporal components and strengthens magnitude components of voluntary movement, (3) Bridging the prepulse effect, stimulus intensity effect, and the motivational priming hypothesis, faster and stronger voluntary movements occurred 1500 msec post image onset, when initiated to startle cues with a strong trend indicating that this pattern was accentuated during exposure to attack images.

Involuntary Movement

Human startle modification research is divided into two primary areas: short and long lead interval effects. Short lead interval effects refer to startle modification by lead stimuli occurring between 0 and 500 to 800 ms and long lead interval effects of approximately greater than 800 ms (Filion et al., 1998). However, it is has been demonstrated that when viewing pictures of their own feared object, phobics show startle potentiation as early as 300 ms relative to control pictures, while controls do not display valence driven differences until around 800 ms (Globisch et al., 1999). In the involuntary domain (startle blink potentiation/inhibition) the work of Stanley and Knight suggests otherwise (Stanley & Knight, 2004), however, with startle blink potentiation noted at early lead intervals (300 msec) but only to specific threat related cues, as opposed to a broad range of unpleasant stimuli.

Predictions for modulation of involuntary movement were similar to those concerning voluntary movement, and were driven by previous evidence of startle blink potentiation during exposure to unpleasant foregrounds (e.g., Lang et al., 1990; Stanley & Knight, 2004). Main effects of valence on premotor RT and peak EMG indicated that time to movement initiation was shorter, and EMG peaks larger during exposure to attack, household object, and blank images relative to erotic images, and at each of the late intervals relative to the 500 msec time interval. As such, hypotheses concerning latency and amplitude were corroborated in terms of the comparison between appetitive and defensive circuitry (Stanley and Knight, 2004). However, analogous to premotor RTs of voluntary movement, responses during exposure to attack, household object and blank images were indistinguishable. The salient issue therefore, is whether erotic images

inhibit the latency and amplitude of the startle blink, whether attack, household object and blank images potentiate the startle blink, or a combination of both. Either way the similar scores during exposure to attack, household object and blank images are difficult to interpret given the valence and arousal disparity between the stimuli. Potential explanations, however, are offered next.

Unpleasant and Neutral Stimuli Similarly Modulate Movement?

Similarity in the blink reflex responses between neutral and unpleasant images at late intervals has not been reported to date. However, similar movements following unpleasant and neutral images have been reported in the emotion-voluntary movement literature (e.g., Coombes et al., in review; Schimmack, 2005). The requirement, therefore, to execute an overt motor response is one explanation to account for the similarity between unpleasant and neutral images demonstrated in the present study. Schimmack (2005) for example, elegantly pitted arousal, general negativity, and evolutionary threat hypotheses against each other within an interference protocol. Participants were required to solve a math problem (study 1) and to detect the location of a line (study 2) during the simultaneous presentation of varying emotional images. Findings indicated that although arousal was a significant predictor of response latency, no significant differences in response latencies between neutral and snake pictures were evidenced in either study. Schimmack suggested that a threat detection system (in our case, reflected as a component of the voluntary movement), may not be hardwired, but may be under voluntary control and open to the influence of learning experiences. A flexible system that is open to learning would certainly be consistent with functional theories of emotion (Nelson, Shelton, & Kalin, 2003), and functionally adaptive.

Given that explanations are lacking, and the majority of previous protocols addressing emotion and movement have not yielded data from neutral conditions (Chen & Bargh, 1999; Duckworth et al., 2002), this issue remains key to the continued progression of emotion and movement research and demands further attention. To this point, however, predictions driven by emotional valence or emotional arousal cannot alone offer an adequate and comprehensive interpretation of the relationship between emotion and overt motor behavior.

Voluntary and Involuntary Movements: Is there a relationship?

Premotor RT

Premotor time findings for voluntary and involuntary movements were each modulated by valence and by time, such that times were longer during exposure to erotic images and longer at the 500 msec interval. Correlation analyses, however, did not yield significant relationships between voluntary and involuntary movement, suggesting that although similar patterns emerged, these patterns did not present in a linear fashion within each subject. In consequence, it is unlikely that startle cues of 107dB trigger voluntary and involuntary movements via similar subcortical pathways.

Peak EMG

Significant positive correlations were obtained between peak EMG of voluntary and involuntary movement during exposure to attack and household object images with probe intervals of 500 msec, respectively. Together these data provide some evidence for a link between voluntary and involuntary movements, but only within specific conditions. The few correlations that were significant, however, and the arbitrariness with which they emerged prevent firm conclusions from being drawn regarding a relationship between reflexive and voluntary movements (i.e., why would peak EMG between the limb and

eye only be related at 500 msec to unpleasant and neutral images, and not other intervals, or valence conditions?)

EMG Slope

Similar in nature to peak EMG findings, only a single positive correlation was evidenced between the slopes of voluntary and involuntary movement at probe intervals of 500 msec during exposure to erotic images, suggesting again that voluntary and involuntary movements are not significantly correlated, and likely therefore, do not share similar pathways. The hypothesis that voluntary and involuntary movements share similar pathways cannot be completely discarded, however, given that variations downstream of the subcortex contribute to movement execution (e.g., spinal thresholds, motor unit size, recruitment, and firing frequency)

Summary

If voluntary and involuntary movements do indeed share similar pathways within the subcortex, one would assume that voluntary and involuntary movements would be positively correlated, which was not demonstrated within the present experiment. Although there are mechanisms downstream of the subcortex that by default must be unique to eye blinks and limb movements and that these factors could potentially alter movements in varying fashions, the conclusion drawn from these correlation data is that voluntary and involuntary movements to 107dB startle cues share few if any neurological pathways.

Limitations

Previous evidence indicates that emotions alter voluntary (Coombes et al., in review) and involuntary (Stanley and Knight, 2005) movement. In addition it has previously been established that the intensity of an initiating cue alters the speed and

force with which voluntary movements are initiated and executed. Furthermore, within the emotion-blink reflex literature, the time course of emotion modulation suggests that the blink reflex is differentially modulated by a two-way interaction between time and valence (Stanley and Knight, 2004). The experimental parameters manipulated in the present study involved replication of a previous voluntary movement study that evaluated the impact of variations in valence and acoustic stimulus (Coombes et al., in review). However, three notable changes were made to the present protocol. First, valence categories were restricted to attack, erotic, and household object images (as opposed to a broad array of unpleasant, pleasant, and neutral images). Second, acoustic stimuli were randomly presented at varying time intervals (500 msec, 1500 msec, 3000-5000 msec) during the 6 second viewing period (rather than between 2000-4000 msec). Finally, the magnitude and latency of the startle blink reflex response was added as a dependent variable to chart involuntary movement characteristics. Despite encouraging results, two limitations potentially hindered firmer conclusions from being drawn. Specifically, it is plausible that by adding the Time factor (with 3 levels), fewer individual trials were averaged into each condition. Furthermore, to accommodate the Time factor, the number of total trials was more than doubled (30 to 70), which may have potentially resulted in extraneous factors confounding results (i.e., boredom, fatigue, habituation)

The endeavor to replicate previous emotion and movement protocols was coupled with an effort to imitate the typical emotion-startle blink protocol. Accordingly, acoustic cues were delivered at a volume of 80dB (tone) and 107dB (startle) as opposed to the 124dB used within the startle-movement literature (Rothwell, 2006; Valls-Solé et al., 1999). Coupled with this attenuation of startle stimulus intensity, EMG activity was not

collected from the SCM, preventing a dichotomy of the data into trials where startle responses were and were not present. Nevertheless, strong effects of stimulus intensity did emerge within central and peripheral measures. Although attenuation of stimulus volume and not collecting data from the SCM prevented inferences concerning the subcortical triggering hypothesis, in no way did this diminish the efficacy and salience of our stimulus intensity findings.

A second methodological issue concerns the affective images used. Although a range of valenced images have traditionally been used in emotion and startle blink paradigms, recent reports have narrowed the specific categories of images (e.g., threat, Stanley& Knight, 2004). Likewise, in the emotion and movement literature, researchers have typically only used pleasant and unpleasant stimuli. In doing so, the relative effects of pleasant and unpleasant states have not been compared to neutral and blank conditions. Indeed, Marsh et al. (2005) recently reported motor responses to fear and anger cues only, and drew inferences from differences between them (outlined previously). In consequence, comparing two arousal matched emotions similar in valence (e.g., threat, anger) or polarized by valence (fear/erotic) would limit the number of trials (i.e., not including neutral and blank condition) within the protocol, resulting in a cleaner design which may permit firmer conclusions, albeit at the expense of being unable to control for the impact of affective arousal.

One final issue that may have limited the impact of emotion on movement, is that the movement required by participants had no functional significance. Further, their was neither an accuracy component or a reward manipulation included in the protocol, which may have attenuated the impact of emotional context on movement.

Future Research

Upon considering future adjustments to the present protocol, limiting the number of conditions by comparing specific appetitive and/or defensive systems, (i.e., fear versus anger) will ensure that results are more easily interpreted. Doing so will also provide a stronger indication that the effects reported to date are not the consequence of multi-valenced image sequences. In addition, removing either the startle or tone condition (given the robust stimulus intensity effect already demonstrated) would permit fewer over all trials, and greater emphasis on emotion modulation. Further, within a picture viewing paradigm, increasing the startle stimulus intensity and recording EMG from the SCM would be a logical progression to permit conclusions concerning the subcortical triggering hypothesis and the impact that affective context has on subcortically triggered movements. In addition, a simple movement-startle protocol in which startle cues are presented at varying intensities (80dB-124dB) while simultaneously collecting EMG activity from multiple locations would offer insight into the parameters that separate stimulus intensity from activation of the startle circuit. A simple modification to the protocol used herein, would be to alter instructions to require participants to move as hard as possible, rather than as quickly as possible. The goal oriented emphasis of the task may alter the interaction effect between emotion and central and peripheral motor processes.

The present protocol may benefit from the introduction of goal oriented movements, the result of which would dictate a subsequent administration of reward/punishment. By overlaying greater functional meaning to the task, and relevant consequences to its execution, the cingulate areas may be preferentially involved, and would by default potentially magnify the interaction of the emotion and movement

systems. In addition, altering the task and offering post-hoc or real time feedback would add to the ecological validity of understanding how emotions alter movement.

Developing the notion that real world functional movements are executed differently from more abstract movements, response rate and movement efficiency are facilitated following stroke when patients are offered choices in terms of which treatment activities to participate in and by incorporating functional goals into the rehabilitation protocol (Wu et al., 2001). Furthermore, the functional consequence of performing a task has been shown to alter the speed, control, and quality of movement in the affected arm of children with spastic hemiparesis (Volman et al., 2002). Specifically, subjects made fast reaching movements with the affected arm in three context conditions: (a) reach to press a light switch to turn on a red light (functional), (b) reach to press the light switch; no light (semi-functional), and (c) reach to a marker (nonfunctional). The authors concluded that the functional condition (i.e., condition “a”) elicited better quality movements of the affected arm. As such, the interaction of emotion and movement systems is receiving greater attention across a broad range of disciplines. Future research is clearly required to identify the pathways that result in emotion modulating movement.

In addition to protocol changes, understanding the impact of emotion on ballistic movement will benefit greatly from layering other methodologies onto protocols similar to the one used herein. For example, a more precise understanding of how emotions alter central and peripheral control systems would be achieved by including measures derived from single motor unit techniques (peripheral), spectral analyses of SEMG (peripheral), as well as brain imaging (central) techniques. For example, mapping the central neural pathways preceding, and charting the peripheral activity during movement under varying

emotional states would offer considerable insight into how and why attack and household object central processing times are similar. In addition, the use of transcranial magnetic stimulation during movement preparation/planning (i.e., following picture onset but preceding the initiating cue) would permit conclusions concerning whether or not emotions alter the excitability of cortical motor areas.

The use of converging methodologies and complimentary instrumentation will permit a number of important questions to be answered: Do emotions alter the size, number, and/or frequency of firing motor units? Do emotions alter the "size principle" or "rate coding" mechanisms? Do startle cues trigger movements stored in the subcortex? Do amygdala-reticular formation connections offer a "fast-track" pathway to ensure rapid voluntary movement initiation in aversive contexts? Are the basal ganglia/CMA essential to the expression of emotion modulated movement?

Conclusion

Levels of overt aggression have declined with the advancement of civilization such that on a daily basis one rarely has to move forcefully and/or quickly to survive. As such, the evolutionary notion that emotions are essential for survival, at first glimpse, appears outdated within the relatively safe contemporary society. However, for those suffering motor deficits (e.g., bradykinesia: stroke, Parkinson's disease, affective disorders), supplementing existing or developing new rehabilitation protocols to take advantage of primitive brain circuits appears to be a promising noninvasive avenue for future research. In addition, for those striving to regulate the impact of emotion (e.g., police officers, military personnel) the present findings highlight the innate disposition of the human to move more rapidly in aversive contexts, strengthening the notion that innate movement dispositions may not always be congruent with intended movement plans. With continued

empirical effort, researchers will be able to provide recommendations to harness the benefits and alleviate the costs associated with emotion modulated movement.

LIST OF REFERENCES

Aimonetti, J. M., Vedel, J. P., Schmied, A., & Pagni, S. (2000). Inhibition versus facilitation of the reflex responsiveness of identified wrist extensor motor units by antagonist flexor afferent inputs in humans. *Exp. Brain Res., 133*(3), 391-401.

Alexander, G. E., & Crutcher, M. D. (1990). Neural representations of the target (goal) of visually guided arm movements in three motor areas of the monkey. *J. Neurophysiol., 64*(1), 164-178.

Anderson, M. E., Inase, M., Buford, J., & Turner, R. (1993). Movement and preparatory activity of neurons in pallidal-receiving areas of the monkey thalamus. In N. Mano, I. Hamada & M. R. DeLong (Eds.), *Role of the cerebellum and basal ganglia in voluntary movement.* (pp. 163-170). Amsterdam: Elsevier.

Andreassi, J. (2000). *Psychophysiology human behavior and physiological response* (4th ed.). Mahwah, NJ: L. Erlbaum Publishers.

Angrilli, A., Mauri, A., Palomba, D., Flor, H., Birbaumer, N., Sartori, G., et al. (1996). Startle reflex and emotion modulation impairment after a right amygdala lesion. *Brain, 119 (Pt 6)*, 1991-2000.

Azevedo, T. M., Volchan, E., Imbiriba, L. A., Rodrigues, E. C., Oliveira, J. M., Oliveira, L. F., et al. (2005). A freezing-like posture to pictures of mutilation. *Psychophysiology, 42*(3), 255-260.

Backus, D. A., Ye, S., Russo, G. S., & Crutcher, M. D. (2001). Neural activity correlated with the preparation and execution of visually guided arm movements in the cingulate motor area of the monkey. *Exp. Brain Res., 140*(2), 182-189.

Ball, T., Schreiber, A., Feige, B., Wagner, M., Lucking, C. H., & Kristeva-Feige, R. (1999). The role of higher-order motor areas in voluntary movement as revealed by high-resolution EEG and fMRI. *Neuroimage, 10*(6), 682-694.

Bandler, R., & Shipley, M. T. (1994). Columnar organization in the midbrain periaqueductal gray: modules for emotional expression? *Trends Neurosci., 17*(9), 379-389.

Bates, J. F., & Goldman-Rakic, P. S. (1993). Prefrontal connections of medial motor areas in the rhesus monkey. *J. Comp. Neurol., 336*(2), 211-228.

Beloozerova, I. N., & Sirota, M. G. (1993). The role of the motor cortex in the control of accuracy of locomotor movements in the cat. *J. Physiol., 461*, 1-25.

Boecker, H., Dagher, A., Ceballos-Baumann, A. O., Passingham, R. E., Samuel, M., Friston, K. J., et al. (1998). Role of the human rostral supplementary motor area and the basal ganglia in motor sequence control: investigations with H2 15O PET. *J. Neurophysiol., 79*(2), 1070-1080.

Bolton, D. A., Cauraugh, J. H., & Hausenblas, H. A. (2004). Electromyogram-triggered neuromuscular stimulation and stroke motor recovery of arm/hand functions: a meta-analysis. *J. Neurol. Sci., 223*(2), 121-127.

Bolton, P. S., Goto, T., Schor, R. H., Wilson, V. J., Yamagata, Y., & Yates, B. J. (1992). Response of pontomedullary reticulospinal neurons to vestibular stimuli in vertical planes. Role in vertical vestibulospinal reflexes of the decerebrate cat. *J. Neurophysiol., 67*(3), 639-647.

Bradley, M. M., Codispoti, M., Cuthbert, B. N., & Lang, P. J. (2001). Emotion and motivation I: defensive and appetitive reactions in picture processing. *Emotion, 1*(3), 276-298.

Bradley, M. M., Codispoti, M., Sabatinelli, D., & Lang, P. J. (2001). Emotion and motivation II: sex differences in picture processing. *Emotion, 1*(3), 300-319.

Bradley, M. M., Cuthbert, B. N., & Lang, P. J. (1993). Pictures as prepulse: attention and emotion in startle modification. *Psychophysiology, 30*(5), 541-545.

Bradley, M. M., Cuthbert, B. N., & Lang, P. J. (1999). Affect and the startle reflex. In M. E. Dawson, A. M. Schell & A. H. Böhmelt (Eds.), *Startle modification: Implications for neuroscience, cognitive science, and clinical science.* (pp. 157-183). Cambridge, UK: Cambridge University Press.

Bradley, M. M., Drobes, D. J., & Lang, P. J. (1996). A probe for all reasons: Reflex and RT measures in perception. *Psychophysiology, 33*, S25.

Bradley, M. M., & Lang, P. J. (2000). Affective reactions to acoustic stimuli. *Psychophysiology, 37*(2), 204-215.

Brinkman, C. (1984). Supplementary motor area of the monkey's cerebral cortex: short- and long-term deficits after unilateral ablation and the effects of subsequent callosal section. *J. Neurosci., 4*(4), 918-929.

Brochier, T., Boudreau, M. J., Pare, M., & Smith, A. M. (1999). The effects of muscimol inactivation of small regions of motor and somatosensory cortex on independent finger movements and force control in the precision grip. *Exp. Brain Res., 128*(1-2), 31-40.

Brotchie, P., Iansek, R., & Horne, M. K. (1991a). Motor function of the monkey globus pallidus. 1. Neuronal discharge and parameters of movement. *Brain, 114 (Pt 4)*, 1667-1683.

Brotchie, P., Iansek, R., & Horne, M. K. (1991b). Motor function of the monkey globus pallidus. 2. Cognitive aspects of movement and phasic neuronal activity. *Brain, 114 (Pt 4)*, 1685-1702.

Brotchie, P., Iansek, R., & Horne, M. K. (1991c). A neural network model of neural activity in the monkey globus pallidus. *Neurosci. Lett., 131*(1), 33-36.

Brown, P., & Marsden, C. D. (1998). What do the basal ganglia do? *Lancet, 351*(9118), 1801-1804.

Buford, J. A., & Davidson, A. G. (2004). Movement-related and preparatory activity in the reticulospinal system of the monkey. *Exp. Brain Res., 159*(3), 284-300.

Cacioppo, J. T. (1994). Social neuroscience: autonomic, neuroendocrine, and immune responses to stress. *Psychophysiology, 31*(2), 113-128.

Cacioppo, J. T., & Berntson, G. G. (1999). The affect system: Architecture and operating characteristics. *Current Directions in Psychological Science, 8*, 133-137.

Cacioppo, J. T., Crites, S. L., Jr., Gardner, W. L., & Bernston, G. G. (1994). Bioelectrical echoes from evaluative categorizations: I. A late positive brain potential that varies as a function of trait negativity and extremity. *J. Pers. Soc. Psychol., 67*(1), 115-125.

Cacioppo, J. T., & Gardner, W. L. (1999). Emotion. *Annu. Rev. Psychol., 50*, 191-214.

Cacioppo, J. T., Uchino, B. N., & Berntson, G. G. (1994). Individual differences in the autonomic origins of heart rate reactivity: the psychometrics of respiratory sinus arrhythmia and preejection period. *Psychophysiology, 31*(4), 412-419.

Canedo, A. (1997). Primary motor cortex influences on the descending and ascending systems. *Progress in Neurobiology, 51*(3), 287-335.

Cannon, W. (1929). *Bodily changes in pain, hunger, fear and rage. Researches into the function of emotional excitement.* NY: Harper and Row.

Cardinal, R. N., Pennicott, D. R., Sugathapala, C. L., Robbins, T. W., & Everitt, B. J. (2001). Impulsive choice induced in rats by lesions of the nucleus accumbens core. *Science, 292*(5526), 2499-2501.

Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2003a). Startle response is dishabituated during a reaction time task. *Exp. Brain. Res., 152*(4), 510-518.

Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2004a). Can prepared responses be stored subcortically? *Exp. Brain. Res., 159*(3), 301-309.

Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2004b). Prepared movements are elicited early by startle. *J. Mot. Behav., 36*(3), 253-264.

Carlsen, A. N., Hunt, M. A., Inglis, J. T., Sanderson, D. J., & Chua, R. (2003b). Altered triggering of a prepared movement by a startling stimulus. *J. Neurophysiol., 89*(4), 1857-1863.

Carlsen, A. N., Nagelkerke, P., Garry, M., Hodges, N., & Franks, I. M. (2000). Using the startle paradigm to investigate the nature of a prepared response. *J. Sport & Exercise Psychol., 22S*, S24.

Carrive, P. (1993). The periaqueductal gray and defensive behavior: functional representation and neuronal organization. *Behav. Brain Res., 58*(1-2), 27-47.

Catalan, M. J., Honda, M., Weeks, R. A., Cohen, L. G., & Hallett, M. (1998). The functional neuroanatomy of simple and complex sequential finger movements: a PET study. *Brain, 121 (Pt 2)*, 253-264.

Chase, T. N., Oh, J. D., & Blanchet, P. J. (1998). Neostriatal mechanisms in Parkinson's disease. *Neurology, 51*(2 Suppl 2), S30-35.

Chen, M., & Bargh, J. A. (1999). Nonconcious approach and avoidance behavioral consequences of the autonomic evaluation effect. *Personality and Social Psychology Bulletin, 25*, 215-224.

Coimbra, N. C., & Brandao, M. L. (1993). GABAergic nigro-collicular pathways modulate the defensive behaviour elicited by midbrain tectum stimulation. *Behav. Brain Res., 59*(1-2), 131-139.

Coombes, S. A., Cauraugh, J. H., & Janelle, C. M. (2006). Emotion and movement: Activation of defensive circuitry alters the magnitude of a sustained muscle contraction. *Neurosci. Lett., 396*(3), 192-196.

Coombes, S. A., Cauraugh, J. H., & Janelle, C. M. (in review). Emotional state and initiating cue alter central and peripheral motor processes. *Emotion*.

Coombes, S. A., Janelle, C. M., & Duley, A. R. (2005). Emotion and motor control: movement attributes following affective picture processing. *J. Mot. Behav., 37*(6), 425-436.

Correa, M., Carlson, B. B., Wisniecki, A., & Salamone, J. D. (2002). Nucleus accumbens dopamine and work requirements on interval schedules. *Behav. Brain Res., 137*(1-2), 179-187.

Cotterill, R. M. (2001). Cooperation of the basal ganglia, cerebellum, sensory cerebrum and hippocampus: possible implications for cognition, consciousness, intelligence and creativity. *Progress in Neurobiology, 64*(1), 1-33.

Coull, J. T., & Nobre, A. C. (1998). Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. *J. Neurosci., 18*(18), 7426-7435.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279*(5355), 1347-1351.

Cowie, R. J., & Robinson, D. L. (1994). Subcortical contributions to head movements in macaques. I. Contrasting effects of electrical stimulation of a medial pontomedullary region and the superior colliculus. *J. Neurophysiol., 72*(6), 2648-2664.

Cowie, R. J., Smith, M. K., & Robinson, D. L. (1994). Subcortical contributions to head movements in macaques. II. Connections of a medial pontomedullary head-movement region. *J. Neurophysiol., 72*(6), 2665-2682.

Crammond, D. J., & Kalaska, J. F. (2000). Prior information in motor and premotor cortex: activity during the delay period and effect on pre-movement activity. *J. Neurophysiol., 84*(2), 986-1005.

Cummings, J. L. (1993). Frontal-subcortical circuits and human behavior. *Arch. Neurol., 50*(8), 873-880.

Cunnington, R., Windischberger, C., Deecke, L., & Moser, E. (2002). The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. *Neuroimage, 15*(2), 373-385.

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

Davis, M., Parisi, T., Gendelman, D. S., Tischler, M., & Kehne, J. H. (1982). Habituation and sensitization of startle reflexes elicited electrically from the brainstem. *Science, 218*(4573), 688-690.

de Gelder, B., Snyder, J., Greve, D., Gerard, G., & Hadjikhani, N. (2004). Fear fosters flight: a mechanism for fear contagion when perceiving emotion expressed by a whole body. *Proc. Natl. Acad. Sci., U S A, 101*(47), 16701-16706.

De Oca, B. M., DeCola, J. P., Maren, S., & Fanselow, M. S. (1998). Distinct regions of the periaqueductal gray are involved in the acquisition and expression of defensive responses. *J. Neurosci., 18*(9), 3426-3432.

Deiber, M. P., Honda, M., Ibanez, V., Sadato, N., & Hallett, M. (1999). Mesial motor areas in self-initiated versus externally triggered movements examined with fMRI: effect of movement type and rate. *J. Neurophysiol., 81*(6), 3065-3077.

Deiber, M. P., Ibanez, V., Sadato, N., & Hallett, M. (1996). Cerebral structures participating in motor preparation in humans: a positron emission tomography study. *J. Neurophysiol., 75*(1), 233-247.

Deiber, M. P., Passingham, R. E., Colebatch, J. G., Friston, K. J., Nixon, P. D., & Frackowiak, R. S. (1991). Cortical areas and the selection of movement: a study with positron emission tomography. *Exp. Brain Res., 84*(2), 393-402.

Donoghue, J. P., & Sanes, J. N. (1988). Organization of adult motor cortex representation patterns following neonatal forelimb nerve injury in rats. *J. Neurosci., 8*(9), 3221-3232.

Duckworth, K. L., Bargh, J. A., Garcia, M., & Chaiken, S. (2002). The automatic evaluation of novel stimuli. *Psychol. Sci., 13*(6), 513-519.

Dum, R. P., & Strick, P. L. (1991). The origin of corticospinal projections from the premotor areas in the frontal lobe. *J. Neurosci., 11*(3), 667-689.

Eilam, D. (2005). Die hard: A blend of freezing and fleeing as a dynamic defense-implications for the control of defensive behavior. *Neurosci. Biobehav. Rev., 29*(8), 1181-1191.

Ekman, P., & Davidson, R. J. (1994). Afterword: Can we control our emotions? In P. Ekman & R. J. Davidson (Eds.), *The nature of emotion: Fundamental questions* (pp. 280-281). NY: Oxford University Press.

Elbert, T., Pantev, C., Wienbruch, C., Rockstroh, B., & Taub, E. (1995). Increased cortical representation of the fingers of the left hand in string players. *Science, 270*(5234), 305-307.

Erwin, R. J., & Buchwald, J. S. (1986). Midlatency auditory evoked responses: differential recovery cycle characteristics. *Electroencephalogr. Clin. Neurophysiol., 64*(5), 417-423.

Everitt, B. J., Parkinson, J. A., Olmstead, M. C., Arroyo, M., Robledo, P., & Robbins, T. W. (1999). Associative processes in addiction and reward. The role of amygdala-ventral striatal subsystems. *Ann. N Y Acad. Sci., 877*, 412-438.

Fanselow, M. S. (1991). The midbrain periaqueductal gray as a coordinator of action in response to fear and anxiety. In A. Despaulis & R. Bandler (Eds.), *The midbrain periaqueductal gray matter: functional, anatomical, and neurochemical organisation* (pp. 151-175). NY: Plenum.

Fanselow, M. S. (1994). Neural organization of the defensive behavior system responsible for fear. *Psychonomic Bulletin & Review, 1*, 429-438.

Fanselow, M. S., Lester, L. S., & Helmstetter, F. J. (1988). Changes in feeding and foraging patterns as an antipredator defensive strategy: a laboratory simulation using aversive stimulation in a closed economy. *J. Exp. Anal. Behav., 50*(3), 361-374.

Fendt, M., & Fanselow, M. S. (1999). The neuroanatomical and neurochemical basis of conditioned fear. *Neurosci. Biobehav. Rev., 23*(5), 743-760.

Fendt, M., Koch, M., & Schnitzler, H. U. (1994a). Lesions of the central gray block the sensitization of the acoustic startle response in rats. *Brain Res., 661*(1-2), 163-173.

Fendt, M., Koch, M., & Schnitzler, H. U. (1994b). Sensorimotor gating deficit after lesions of the superior colliculus. *Neuroreport, 5*(14), 1725-1728.

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

Fudge, J. L., Kunishio, K., Walsh, P., Richard, C., & Haber, S. N. (2002). Amygdaloid projections to ventromedial striatal subterritories in the primate. *Neuroscience, 110*(2), 257-275.

Garavan, H., Pendergrass, J. C., Ross, T. J., Stein, E. A., & Risinger, R. C. (2001). Amygdala response to both positively and negatively valenced stimuli. *Neuroreport, 12*(12), 2779-2783.

Georgopoulos, A. P., Taira, M., & Lukashin, A. (1993). Cognitive neurophysiology of the motor cortex. *Science, 260*(5104), 47-52.

Geyer, S., Matelli, M., Luppino, G., & Zilles, K. (2000). Functional neuroanatomy of the primate isocortical motor system. *Anat. Embryol. (Berl), 202*(6), 443-474.

Globisch, J., Hamm, A. O., Esteves, F., & Öhman, A. (1999). Fear appears fast: temporal course of startle reflex potentiation in animal fearful subjects. *Psychophysiology, 36*(1), 66-75.

Goldman-Rakic, P. S. (1995). Cellular basis of working memory. *Neuron, 14*(3), 477-485.

Grafton, S. T., Fagg, A. H., & Arbib, M. A. (1998). Dorsal premotor cortex and conditional movement selection: A PET functional mapping study. *J. Neurophysiol., 79*(2), 1092-1097.

Graybiel, A. M. (1997). The basal ganglia and cognitive pattern generators. *Schizophr. Bull., 23*(3), 459-469.

Greenberg, N. (2002). Adaptive functions of the corpus striatum: The past and future of the r-complex. In G. A. Cory, R. Gardner & NetLibrary Inc. (Eds.), *The evolutionary neuroethology of Paul MacLean convergences and frontiers.* (pp. 45-81). Westport, CT: Praeger.

Grillner, S., Georgopoulos, A. P., & Jordan, L. M. (1997). Selection and initiation of motor behaviour. In P. S. G. Stein, S. Grillner, A. Selverston & D. G. Stuart (Eds.), *Neurons, networks and motor behavior* (pp. 4-19). Cambridge, MA: MIT.

Grillner, S., & Wallen, P. (2004). Innate versus learned movements--a false dichotomy? *Prog. Brain Res., 143*, 3-12.

Grillon, C., & Baas, J. (2003). A review of the modulation of the startle reflex by affective states and its application in psychiatry. *Clin. Neurophysiol., 114*(9), 1557-1579.

Haber, S. N. (2003). The primate basal ganglia: parallel and integrative networks. *J. Chem. Neuroanat., 26*(4), 317-330.

Halsband, U., Ito, N., Tanji, J., & Freund, H. J. (1993). The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. *Brain, 116 (Pt 1)*, 243-266.

Hamada, T., Kimura, T., & Moritani, T. (2004). Selective fatigue of fast motor units after electrically elicited muscle contractions. *Journal of Electromyography and Kinesiology, 14*(5), 531-538.

Hanna-Pladdy, B., Heilman, K. M., & Foundas, A. L. (2001). Cortical and subcortical contributions to ideomotor apraxia: analysis of task demands and error types. *Brain, 124*(Pt 12), 2513-2527.

Hassani, O. K., Cromwell, H. C., & Schultz, W. (2001). Influence of expectation of different rewards on behavior-related neuronal activity in the striatum. *J. Neurophysiol., 85*(6), 2477-2489.

He, S. Q., Dum, R. P., & Strick, P. L. (1993). Topographic organization of corticospinal projections from the frontal lobe: motor areas on the lateral surface of the hemisphere. *J. Neurosci., 13*(3), 952-980.

He, S. Q., Dum, R. P., & Strick, P. L. (1995). Topographic organization of corticospinal projections from the frontal lobe: motor areas on the medial surface of the hemisphere. *J. Neurosci., 15*(5 Pt 1), 3284-3306.

Heilman, K. M., & Gilmore, R. L. (1998). Cortical influences in emotion. *J. Clin Neurophysiol., 15*(5), 409-423.

Henneman, E. (1979). Functional organization of motoneuron pools: the size-principle. In H. Asanuma & V. J. Wilson (Eds.), *Integration in the Nervous System* (pp. 13-25). Tokyo: Igaku-Shoin.

Hikosaka, O., Sakai, K., Miyauchi, S., Takino, R., Sasaki, Y., & Putz, B. (1996). Activation of human presupplementary motor area in learning of sequential procedures: a functional MRI study. *J. Neurophysiol., 76*(1), 617-621.

Hikosaka, O., Takikawa, Y., & Kawagoe, R. (2000). Role of the basal ganglia in the control of purposive saccadic eye movements. *Physiol. Rev., 80*(3), 953-978.

Hillman, C. H., Hsiao-Wecksler, E. T., & Rosengren, K. S. (2005). Postural and eye-blink indices of the defensive startle reflex. *Int. J. Psychophysiol., 55*(1), 45-49.

Hillman, C. H., Rosengren, K. S., & Smith, D. P. (2004). Emotion and motivated behavior: postural adjustments to affective picture viewing. *Biol. Psychol., 66*(1), 51-62.

Hoshi, E., & Tanji, J. (2004a). Area-selective neuronal activity in the dorsolateral prefrontal cortex for information retrieval and action planning. *J. Neurophysiol., 91*(6), 2707-2722.

Hoshi, E., & Tanji, J. (2004b). Differential roles of neuronal activity in the supplementary and presupplementary motor areas: from information retrieval to motor planning and execution. *J. Neurophysiol., 92*(6), 3482-3499.

Hoshi, E., & Tanji, J. (2004c). Functional specialization in dorsal and ventral premotor areas. *Prog. Brain Res., 143,* 507-511.

Isa, T. (2002). Intrinsic processing in the mammalian superior colliculus. *Curr. Opin. Neurobiol., 12*(6), 668-677.

Isaacson, R. L. (1982). *The limbic system* (2nd ed.). NY: Plenum Press.

Isomura, Y., Ito, Y., Akazawa, T., Nambu, A., & Takada, M. (2003). Neural coding of "attention for action" and "response selection" in primate anterior cingulate cortex. *J. Neurosci., 23*(22), 8002-8012.

Jahanshahi, M., Jenkins, I. H., Brown, R. G., Marsden, C. D., Passingham, R. E., & Brooks, D. J. (1995). Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. *Brain, 118 (Pt 4)*, 913-933.

Jenkins, I. H., Brooks, D. J., Nixon, P. D., Frackowiak, R. S., & Passingham, R. E. (1994). Motor sequence learning: a study with positron emission tomography. *J. Neurosci., 14*(6), 3775-3790.

Jenkins, I. H., Jahanshahi, M., Jueptner, M., Passingham, R. E., & Brooks, D. J. (2000). Self-initiated versus externally triggered movements. II. The effect of movement predictability on regional cerebral blood flow. *Brain, 123 (Pt 6)*, 1216-1228.

Jones, K. E., Calancie, B., Hall, A., & Bawa, P. (1996). Comparison of peripheral Ia and corticomotoneuronal composite EPSPs in human motoneurons. *Electroencephalogr. Clin. Neurophysiol., 101*(5), 431-437.

Jueptner, M., Frith, C. D., Brooks, D. J., Frackowiak, R. S., & Passingham, R. E. (1997). Anatomy of motor learning. II. Subcortical structures and learning by trial and error. *J. Neurophysiol., 77*(3), 1325-1337.

Kamen, G., & Du, D. C. C. (1999). Independence of motor unit recruitment and rate modulation during precision force control. *Neuroscience, 88*(2), 643-653.

Kazennikov, O., Hyland, B., Wicki, U., Perrig, S., Rouiller, E. M., & Wiesendanger, M. (1998). Effects of lesions in the mesial frontal cortex on bimanual co-ordination in monkeys. *Neuroscience, 85*(3), 703-716.

Keenan, K. G., Farina, D., Merletti, R., & Enoka, R. M. (2005). Influence of motor unit properties on the size of the simulated evoked surface EMG potential. *Exp. Brain Res.*, 1-13.

Keizer, K., & Kuypers, H. G. (1989). Distribution of corticospinal neurons with collaterals to the lower brain stem reticular formation in monkey (Macaca fascicularis). *Exp. Brain Res., 74*(2), 311-318.

Kermadi, I., Liu, Y., Tempini, A., & Rouiller, E. M. (1997). Effects of reversible inactivation of the supplementary motor area (SMA) on unimanual grasp and bimanual pull and grasp performance in monkeys. *Somatosens. Mot. Res., 14*(4), 268-280.

Klein, C. S., Ivanova, T. D., Rice, C. L., & Garland, S. J. (2001). Motor unit discharge rate following twitch potentiation in human triceps brachii muscle. *Neurosci. Lett., 316*(3), 153-156.

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science, 273*(5280), 1399-1402.

Krainik, A., Lehericy, S., Duffau, H., Vlaicu, M., Poupon, F., Capelle, L., et al. (2001). Role of the supplementary motor area in motor deficit following medial frontal lobe surgery. *Neurology, 57*(5), 871-878.

Kurata, K., Tsuji, T., Naraki, S., Seino, M., & Abe, Y. (2000). Activation of the dorsal premotor cortex and pre-supplementary motor area of humans during an auditory conditional motor task. *J. Neurophysiol., 84*(3), 1667-1672.

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

Lang, C. E., & Schieber, M. H. (2003). Differential impairment of individuated finger movements in humans after damage to the motor cortex or the corticospinal tract. *J. Neurophysiol., 90*(2), 1160-1170.

Lang, P. J. (2000). Emotion and motivation: Attention, perception, and action. *Journal of Sport and Exercise Psychology, 22*, 122-140.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1990). Emotion, attention, and the startle reflex. *Psychol. Rev., 97*(3), 377-395.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). Motivated attention: Affect, activation and action. In Lang, R. F. Simons & M. T. Balaban (Eds.), *Attention and orienting: sensory and motivational processes* (pp. 97-135). NJ: Lawrence Erlbaum Associates.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1998a). Emotion and motivation: measuring affective perception. *J. Clin Neurophysiol., 15*(5), 397-408.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1998b). Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. *Biol. Psychiatry, 44*(12), 1248-1263.

Lang, P. J., Davis, M., & Ohman, A. (2000). Fear and anxiety: animal models and human cognitive psychophysiology. *J. Affect. Disord., 61*(3), 137-159.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30*(3), 261-273.

Laplane, D., Talairach, J., Meininger, V., Bancaud, J., & Bouchareine, A. (1977). Motor consequences of motor area ablations in man. *J. Neurol. Sci., 31*(1), 29-49.

Laplane, D., Talairach, J., Meininger, V., Bancaud, J., & Orgogozo, J. M. (1977). Clinical consequences of corticectomies involving the supplementary motor area in man. *J. Neurol. Sci., 34*(3), 301-314.

Larsson, J., Gulyas, B., & Roland, P. E. (1996). Cortical representation of self-paced finger movement. *Neuroreport, 7*(2), 463-468.

Lawrence, D. G., & Kuypers, H. G. (1968). The functional organization of the motor system in the monkey. II. The effects of lesions of the descending brain-stem pathways. *Brain, 91*(1), 15-36.

Lazarus, R. S. (2000). How emotions influence performance in competitive sports. *Sport Psychologist, 14*(3), 229-252.

LeDoux, J. E. (1994). Emotion, memory and the brain. *Sci. Am., 270*(6), 50-57.

LeDoux, J. E. (1995). Emotion: clues from the brain. *Annu. Rev. Psychol., 46*, 209-235.

LeDoux, J. E. (1996). Emotional networks and motor control: a fearful view. *Prog. Brain Res., 107*, 437-446.

LeDoux, J. E. (1998). Fear and the brain: where have we been, and where are we going? *Biol. Psychiatry, 44*(12), 1229-1238.

LeDoux, J. E. (2000). Emotion circuits in the brain. *Annu. Rev. Neurosci., 23*, 155-184.

LeDoux, J. E. (2003). The emotional brain, fear, and the amygdala. *Cell Mol. Neurobiol., 23*(4-5), 727-738.

LeDoux, J. E., Cicchetti, P., Xagoraris, A., & Romanski, L. M. (1990). The lateral amygdaloid nucleus: sensory interface of the amygdala in fear conditioning. *J. Neurosci., 10*(4), 1062-1069.

Lee, K. M., Chang, K. H., & Roh, J. K. (1999). Subregions within the supplementary motor area activated at different stages of movement preparation and execution. *Neuroimage, 9*(1), 117-123.

Lee, Y., Lopez, D. E., Meloni, E. G., & Davis, M. (1996). A primary acoustic startle pathway: obligatory role of cochlear root neurons and the nucleus reticularis pontis caudalis. *J. Neurosci., 16*(11), 3775-3789.

Leiguarda, R. C., & Marsden, C. D. (2000). Limb apraxias: higher-order disorders of sensorimotor integration. *Brain, 123 (Pt 5)*, 860-879.

Lewis, S. J., Caldwell, M. A., & Barker, R. A. (2003). Modern therapeutic approaches in Parkinsons disease. *Expert Rev. Mol. Med., 2003*, 1-20.

Lingenhohl, K., & Friauf, E. (1994). Giant neurons in the rat reticular formation: a sensorimotor interface in the elementary acoustic startle circuit? *J. Neurosci., 14*(3 Pt 1), 1176-1194.

Lipp, O. V., Siddle, D. A., & Dall, P. J. (1997). The effect of emotional and attentional processes on blink startle modulation and on electrodermal responses. *Psychophysiology, 34*(3), 340-347.

Lu, M. T., Preston, J. B., & Strick, P. L. (1994). Interconnections between the prefrontal cortex and the premotor areas in the frontal lobe. *J. Comp. Neurol., 341*(3), 375-392.

Luppino, G., Matelli, M., Camarda, R., & Rizzolatti, G. (1993). Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. *J. Comp. Neurol., 338*(1), 114-140.

Macefield, V. G., Fuglevand, A. J., & Bigland-Ritchie, B. (1996). Contractile properties of single motor units in human toe extensors assessed by intraneural motor axon stimulation. *J. Neurophysiol., 75*(6), 2509-2519.

Maclean, P. D. (1952). Some psychiatric implications of physiological studies on frontotemporal portion of limbic system (visceral brain). *Electroencephalogr. Clin. Neurophysiol. Suppl., 4*(4), 407-418.

Maclean, P. D. (1954). The limbic system and its hippocampal formation; studies in animals and their possible application to man. *J. Neurosurg*, 11(1), 29-44.

Maclean, P. D. (1955a). The limbic system ("visceral brain") and emotional behavior. *AMA Arch. Neurol. Psychiatry.,* 73(2), 130-134.

Maclean, P. D. (1955b). The limbic system (visceral brain) in relation to central gray and reticulum of the brain stem; evidence of interdependence in emotional processes. *Psychosom. Med.,* 17(5), 355-366.

Maclean, P. D. (1972). Cerebral evolution and emotional processes: new findings on the striatal complex. *Ann. N Y Acad. Sci.,* 193, 137-149.

Maclean, P. D. (1990). *The triune brain in evolution: role in paleocerebral functions.* NY: Plenum.

Marple-Horvat, D. E., Amos, A. J., Armstrong, D. M., & Criado, J. M. (1993). Changes in the discharge patterns of cat motor cortex neurones during unexpected perturbations of on-going locomotion. *J. Physiol.,* 462, 87-113.

Marsh, A. A., Ambady, N., & Kleck, R. E. (2005). The effects of fear and anger facial expressions on approach- and avoidance-related behaviors. *Emotion,* 5(1), 119-124.

Matelli, M., Luppino, G., & Rizzolatti, G. (1991). Architecture of superior and mesial area 6 and the adjacent cingulate cortex in the macaque monkey. *J. Comp. Neurol.,* 311(4), 445-462.

Matsuyama, K., & Drew, T. (2000a). Vestibulospinal and reticulospinal neuronal activity during locomotion in the intact cat. I. Walking on a level surface. *J. Neurophysiol.,* 84(5), 2237-2256.

Matsuyama, K., & Drew, T. (2000b). Vestibulospinal and reticulospinal neuronal activity during locomotion in the intact cat. II. Walking on an inclined plane. *J. Neurophysiol.,* 84(5), 2257-2276.

Matsuyama, K., Mori, F., Nakajima, K., Drew, T., Aoki, M., & Mori, S. (2004). Locomotor role of the corticoreticular-reticulospinal-spinal interneuronal system. *Prog. Brain Res.,* 143, 239-249.

Meloni, E. G., & Davis, M. (1999). Muscimol in the deep layers of the superior colliculus/mesencephalic reticular formation blocks expression but not acquisition of fear-potentiated startle in rats. *Behav. Neurosci.,* 113(6), 1152-1160.

Middleton, F. A., & Strick, P. L. (2001). Cerebellar projections to the prefrontal cortex of the primate. *J. Neurosci.,* 21(2), 700-712.

Middleton, F. A., & Strick, P. L. (2002). Basal-ganglia 'projections' to the prefrontal cortex of the primate. *Cereb. Cortex,* 12(9), 926-935.

Milner-Brown, H. S., Stein, R. B., & Yemm, R. (1973). Changes in firing rate of human motor units during linearly changing voluntary contractions. *The Journal Of Physiology,* 230(2), 371-390.

Moore, B. D., Drouin, J., Gansneder, B. M., & Shultz, S. J. (2002). The differential effects of fatigue on reflex response timing and amplitude in males and females. *J. Electromyogr. Kinesiol.,* 12(5), 351-360.

Morecraft, R. J., & Van Hoesen, G. W. (1998). Convergence of limbic input to the cingulate motor cortex in the rhesus monkey. *Brain Res. Bull.,* 45(2), 209-232.

Moritz, C. T., Barry, B. K., Pascoe, M. A., & Enoka, R. M. (2005). Discharge Rate Variability Influences the Variation in Force Fluctuations Across the Working Range of a Hand Muscle. *J. Neurophysiol.,* 93(5), 2449-2459.

Mushiake, H., Inase, M., & Tanji, J. (1991). Neuronal activity in the primate premotor, supplementary, and precentral motor cortex during visually guided and internally determined sequential movements. *J. Neurophysiol.,* 66(3), 705-718.

Nakamura, K., Sakai, K., & Hikosaka, O. (1999). Effects of local inactivation of monkey medial frontal cortex in learning of sequential procedures. *J. Neurophysiol.,* 82(2), 1063-1068.

Nambu, A., Tokuno, H., & Takada, M. (2002). Functional significance of the cortico-subthalamo-pallidal 'hyperdirect' pathway. *Neurosci. Res.,* 43(2), 111-117.

Nelson, E. E., Shelton, S. E., & Kalin, N. H. (2003). Individual differences in the responses of naive rhesus monkeys to snakes. *Emotion,* 3(1), 3-11.

Nicola, S. M., Yun, I. A., Wakabayashi, K. T., & Fields, H. L. (2004). Cue-evoked firing of nucleus accumbens neurons encodes motivational significance during a discriminative stimulus task. *J. Neurophysiol.,* 91(4), 1840-1865.

Noteboom, J. T., Barnholt, K. R., & Enoka, R. M. (2001). Activation of the arousal response and impairment of performance increase with anxiety and stressor intensity. *J. Appl. Physiol.,* 91(5), 2093-2101.

Noteboom, J. T., Fleshner, M., & Enoka, R. M. (2001). Activation of the arousal response can impair performance on a simple motor task. *J. Appl. Physiol.,* 91(2), 821-831.

Öhman, A., Hamm, A., & Hugdahl, K. (2000). Cognition and the autonomic nervous system: Orienting, anticipation, and conditioning. In J. Cacioppo, L. Tassinary & G. G. Berntson (Eds.), *Handbook of psychophysiology* (pp. 533-575). NY: Cambridge University Press.

Panksepp, J. (2003). At the interface of the affective, behavioral, and cognitive neurosciences: decoding the emotional feelings of the brain. *Brain Cogn.,* 52(1), 4-14.

Paradiso, G., Cunic, D., Saint-Cyr, J. A., Hoque, T., Lozano, A. M., Lang, A. E., et al. (2004). Involvement of human thalamus in the preparation of self-paced movement. *Brain,* 127(Pt 12), 2717-2731.

Pascual-Leone, A., Valls-Sole, J., Wassermann, E. M., Brasil-Neto, J., Cohen, L. G., & Hallett, M. (1992). Effects of focal transcranial magnetic stimulation on simple reaction time to acoustic, visual and somatosensory stimuli. *Brain,* 115 (Pt 4), 1045-1059.

Patterson, D. W., & Schmidt, L. A. (2003). Neuroanatomy of the human affective system. *Brain Cogn.,* 52(1), 24-26.

Peigneux, P., Maquet, P., Meulemans, T., Destrebecqz, A., Laureys, S., Degueldre, C., et al. (2000). Striatum forever, despite sequence learning variability: a random effect analysis of PET data. *Hum. Brain Mapp.,* 10(4), 179-194.

Petit, L., Orssaud, C., Tzourio, N., Crivello, F., Berthoz, A., & Mazoyer, B. (1996). Functional anatomy of a prelearned sequence of horizontal saccades in humans. *J. Neurosci.,* 16(11), 3714-3726.

Picard, N., & Strick, P. L. (1996). Motor areas of the medial wall: a review of their location and functional activation. *Cereb. Cortex,* 6(3), 342-353.

Picard, N., & Strick, P. L. (2001). Imaging the premotor areas. *Curr. Opin. Neurobiol.,* 11(6), 663-672.

Posner, M. I., Petersen, S. E., Fox, P. T., & Raichle, M. E. (1988). Localization of cognitive operations in the human brain. Science, 240(4859), 1627-1631.

Prut, Y., Perlmutter, S. I., & Fetz, E. E. (2001). Distributed processing in the motor system: spinal cord perspective. *Prog. Brain Res.,* 130, 267-278.

Ratner, S. C. (1967). Comparative aspects of hypnosis. In J. E. Gordon (Ed.), *Handbook of clinical and experimental hypnosis* (pp. 550-587). NY: Macmillan.

Rau, G., Schulte, E., & Disselhorst-Klug, C. (2004). From cell to movement: to what answers does EMG really contribute? *J. Electromyogr. Kinesiol.,* 14(5), 611-617.

Richter, W., Andersen, P. M., Georgopoulos, A. P., & Kim, S. G. (1997). Sequential activity in human motor areas during a delayed cued finger movement task studied by time-resolved fMRI. *Neuroreport,* 8(5), 1257-1261.

Riek, S., & Bawa, P. (1992). Recruitment of motor units in human forearm extensors. *J. Neurophysiol.,* 68(1), 100-108.

Rosen, J. B., Hitchcock, J. M., Sananes, C. B., Miserendino, M. J., & Davis, M. (1991). A direct projection from the central nucleus of the amygdala to the acoustic startle pathway: anterograde and retrograde tracing studies. *Behav. Neurosci.,* 105(6), 817-825.

Rothwell, J. C. (2006). The startle reflex, voluntary movement, and the reticulospinal tract. *Suppl. Clin. Neurophysiol.,* 58, 223-231.

Sakai, K., Hikosaka, O., Miyauchi, S., Sasaki, Y., Fujimaki, N., & Putz, B. (1999). Presupplementary motor area activation during sequence learning reflects visuo-motor association. *J. Neurosci.,* 19(10), RC1.

Sakai, K., Hikosaka, O., Takino, R., Miyauchi, S., Nielsen, M., & Tamada, T. (2000). What and when: parallel and convergent processing in motor control. *J. Neurosci.,* 20(7), 2691-2700.

Salamone, J. D., Correa, M., Mingote, S., & Weber, S. M. (2003). Nucleus accumbens dopamine and the regulation of effort in food-seeking behavior: implications for studies of natural motivation, psychiatry, and drug abuse. *J. Pharmacol. Exp. Ther.,* 305(1), 1-8.

Salamone, J. D., Correa, M., Mingote, S. M., & Weber, S. M. (2005). Beyond the reward hypothesis: alternative functions of nucleus accumbens dopamine. *Curr. Opin. Pharmacol.,* 5(1), 34-41.

Salamone, J. D., Wisniecki, A., Carlson, B. B., & Correa, M. (2001). Nucleus accumbens dopamine depletions make animals highly sensitive to high fixed ratio requirements but do not impair primary food reinforcement. *Neuroscience,* 105(4), 863-870.

Sanes, J. N., & Donoghue, J. P. (1997). Static and dynamic organization of motor cortex. *Adv. Neurol.,* 73, 277-296.

Sanes, J. N., & Donoghue, J. P. (2000). Plasticity and primary motor cortex. *Annu. Rev. Neurosci.,* 23, 393-415.

Sargeant, A. L., & Eberhardt, R. T. (1975). Death feigning by ducks in response to predation by red foxes. *The American Midland Naturalist,* 94, 109-119.

Schenberg, L. C., Costa, M. B., Borges, P. C., & Castro, M. F. (1990). Logistic analysis of the defense reaction induced by electrical stimulation of the rat mesencephalic tectum. *Neurosci. Biobehav. Rev.,* 14(4), 473-479.

Schieber, M. H., & Poliakov, A. V. (1998). Partial inactivation of the primary motor cortex hand area: effects on individuated finger movements. *J. Neurosci.,* 18(21), 9038-9054.

Schimmack, U. (2005). Attentional interference effects of emotional pictures: threat, negativity, or arousal? *Emotion,* 5(1), 55-66.

Schmied, A., Aimonetti, J. M., & Vedel, J. P. (2002). Presynaptic and disynaptic inhibition induced by group I muscle afferents. *Adv. Exp. Med. Biol.,* 508, 179-185.

Schmied, A., Morin, D., Vedel, J. P., & Pagni, S. (1997). The "size principle" and synaptic effectiveness of muscle afferent projections to human extensor carpi radialis motoneurones during wrist extension. *Exp. Brain Res.,* 113(2), 214-229.

Schupp, H. T., Junghofer, M., Weike, A. I., & Hamm, A. O. (2003a). Emotional facilitation of sensory processing in the visual cortex. *Psychol. Sci.,* 14(1), 7-13.

Schupp, H. T., Junghofer, M., Weike, A. I., & Hamm, A. O. (2003b). Attention and emotion: an ERP analysis of facilitated emotional stimulus processing. *Neuroreport,* 14(8), 1107-1110.

Schupp, H. T., Junghofer, M., Weike, A. I., & Hamm, A. O. (2004). The selective processing of briefly presented affective pictures: an ERP analysis. *Psychophysiology,* 41(3), 441-449.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *J. Neurochem.,* 20(1), 11-21.

Seitz, R. J., Canavan, A. G., Yaguez, L., Herzog, H., Tellmann, L., Knorr, U., et al. (1994). Successive roles of the cerebellum and premotor cortices in trajectorial learning. *Neuroreport,* 5(18), 2541-2544.

Shaikh, M. B., Lu, C. L., & Siegel, A. (1991a). Affective defense behavior elicited from the feline midbrain periqueductal gray is regulated by mu and delta opioid receptors. *Brain Res.,* 557(1-2), 344-348.

Shaikh, M. B., Lu, C. L., & Siegel, A. (1991b). An enkephalinergic mechanism involved in amygdaloid suppression of affective defence behavior elicited from the midbrain periaqueductal gray in the cat. *Brain Res.,* 559(1), 109-117.

Shi, C., & Davis, M. (2001). Visual pathways involved in fear conditioning measured with fear-potentiated startle: behavioral and anatomic studies. *J. Neurosci.,* 21(24), 9844-9855.

Shima, K., & Tanji, J. (1998). Role for cingulate motor area cells in voluntary movement selection based on reward. *Science,* 282(5392), 1335-1338.

Simon, S. R., Meunier, M., Piettre, L., Berardi, A. M., Segebarth, C. M., & Boussaoud, D. (2002). Spatial attention and memory versus motor preparation: premotor cortex involvement as revealed by fMRI. *J. Neurophysiol.,* 88(4), 2047-2057.

Stanley, J., & Knight, R. G. (2004). Emotional specificity of startle potentiation during the early stages of picture viewing. *Psychophysiology,* 41(6), 935-940.

Stephan, K. M., Fink, G. R., Passingham, R. E., Silbersweig, D., Ceballos-Baumann, A. O., Frith, C. D., et al. (1995). Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *J. Neurophysiol.,* 73(1), 373-386.

Stern, C. E., Owen, A. M., Tracey, I., Look, R. B., Rosen, B. R., & Petrides, M. (2000). Activity in ventrolateral and mid-dorsolateral prefrontal cortex during nonspatial visual working memory processing: evidence from functional magnetic resonance imaging. *Neuroimage,* 11(5 Pt 1), 392-399.

Sturm, V., Lenartz, D., Koulousakis, A., Treuer, H., Herholz, K., Klein, J. C., et al. (2003). The nucleus accumbens: a target for deep brain stimulation in obsessive-compulsive- and anxiety-disorders. *J. Chem. Neuroanat.,* 26(4), 293-299.

Takada, M., Tokuno, H., Hamada, I., Inase, M., Ito, Y., Imanishi, M., et al. (2001). Organization of inputs from cingulate motor areas to basal ganglia in macaque monkey. *Eur. J. Neurosci.,* 14(10), 1633-1650.

Takakusaki, K., Saitoh, K., Harada, H., & Kashiwayanagi, M. (2004). Role of basal ganglia-brainstem pathways in the control of motor behaviors. *Neurosci. Res.,* 50(2), 137-151.

Tortora, G. J., & Grabowski, S. R. (2003). *Principles of anatomy and physiology* (10th ed.). New York: Wiley.

Turken, A. U., & Swick, D. (1999). Response selection in the human anterior cingulate cortex. *Nat. Neurosci.,* 2(10), 920-924.

Turner, R. S., & Anderson, M. E. (1997). Pallidal discharge related to the kinematics of reaching movements in two dimensions. *J. Neurophysiol.,* 77(3), 1051-1074.

Ullsperger, M., & von Cramon, D. Y. (2004). Decision making, performance and outcome monitoring in frontal cortical areas. *Nat. Neurosci.,* 7(11), 1173-1174.

Valls-Solé, J., Rothwell, J. C., Goulart, F., Cossu, G., & Munoz, E. (1999). Patterned ballistic movements triggered by a startle in healthy humans. J. Physiol, 516 (Pt 3), 931-938.

Valls-Solé, J., Sole, A., Valldeoriola, F., Munoz, E., Gonzalez, L. E., & Tolosa, E. S. (1995). Reaction time and acoustic startle in normal human subjects. *Neurosci. Lett.,* 195(2), 97-100.

van Mier, H., Tempel, L. W., Perlmutter, J. S., Raichle, M. E., & Petersen, S. E. (1998). Changes in brain activity during motor learning measured with PET: effects of hand of performance and practice. *J. Neurophysiol.,* 80(4), 2177-2199.

Van Oostende, S., Van Hecke, P., Sunaert, S., Nuttin, B., & Marchal, G. (1997). FMRI studies of the supplementary motor area and the premotor cortex. *Neuroimage,* 6(3), 181-190.

Vianna, D. M., Graeff, F. G., Landeira-Fernandez, J., & Brandao, M. L. (2001). Lesion of the ventral periaqueductal gray reduces conditioned fear but does not change freezing induced by stimulation of the dorsal periaqueductal gray. *Learn. Mem.,* 8(3), 164-169.

Vogt, B. A., & Pandya, D. N. (1987). Cingulate cortex of the rhesus monkey: II. Cortical afferents. *J. Comp. Neurol.,* 262(2), 271-289.

Volman, M. J., Wijnroks, A., & Vermeer, A. (2002). Effect of task context on reaching performance in children with spastic hemiparesis. *Clin. Rehabil.,* 16(6), 684-692.

Vulliemoz, S., Raineteau, O., & Jabaudon, D. (2005). Reaching beyond the midline: why are human brains cross wired? *Lancet Neurol.,* 4(2), 87-99.

Wade, D. T., Langton-Hewer, R., Wood, V. A., Skilbeck, C. E., & Ismail, H. M. (1983). The hemiplegic arm after stroke: measurement and recovery. *J. Neurol. Neurosurg. Psychiatry,* 46(6), 521-524.

Walker, D. L., & Davis, M. (1997). Involvement of the dorsal periaqueductal gray in the loss of fear-potentiated startle accompanying high footshock training. *Behavioral Neuroscience,* 111(4), 692-702.

Walton, M. E., Devlin, J. T., & Rushworth, M. F. (2004). Interactions between decision making and performance monitoring within prefrontal cortex. *Nat. Neurosci.,* 7(11), 1259-1265.

Wang, Y., Shima, K., Sawamura, H., & Tanji, J. (2001). Spatial distribution of cingulate cells projecting to the primary, supplementary, and pre-supplementary motor areas: a retrograde multiple labeling study in the macaque monkey. *Neurosci. Res.,* 39(1), 39-49.

Wessel, K., Zeffiro, T., Toro, C., & Hallett, M. (1997). Self-paced versus metronome-paced finger movements. A positron emission tomography study. J. *Neuroimaging,* 7(3), 145-151.

Wichmann, T., & DeLong, M. R. (1993). Pathophysiology of parkinsonian motor abnormalities. *Adv. Neurol.,* 60, 53-61.

Wildgruber, D., Erb, M., Klose, U., & Grodd, W. (1997). Sequential activation of supplementary motor area and primary motor cortex during self-paced finger movement in human evaluated by functional MRI. *Neurosci. Lett.,* 227(3), 161-164.

Wilson, L. R., Gandevia, S. C., Inglis, J. T., Gracies, J., & Burke, D. (1999). Muscle spindle activity in the affected upper limb after a unilateral stroke. *Brain,* 122 (Pt 11), 2079-2088.

Wong, Y. M., & Ng, G. Y. (2005). The double peak-to-peak analysis for determining EMG onset of muscle contraction. *Electromyogr. Clin. Neurophysiol.,* 45(5), 267-271.

Woodhouse, A. (2005). Phantom limb sensation. *Clin. Exp. Pharmacol. Physiol.,* 32(1-2), 132-134.

Wu, C. Y., Wong, M. K., Lin, K. C., & Chen, H. C. (2001). Effects of task goal and personal preference on seated reaching kinematics after stroke. *Stroke,* 32(1), 70-76.

Yeomans, J. S., & Frankland, P. W. (1996). The acoustic startle reflex: neurons and connections. *Brain Research Reviews,* 21, 301-314.

Yun, I. A., Wakabayashi, K. T., Fields, H. L., & Nicola, S. M. (2004). The ventral tegmental area is required for the behavioral and nucleus accumbens neuronal firing responses to incentive cues. *J. Neurosci.,* 24(12), 2923-2933.

Zhao, Z., & Davis, M. (2004). Fear-potentiated startle in rats is mediated by neurons in the deep layers of the superior colliculus/deep mesencephalic nucleus of the rostral midbrain through the glutamate non-NMDA receptors. *J. Neurosci.,* 24(46), 10326-10334.

Zigmond, M. J., Stricker, E. M., & Berger, T. W. (1987). Parkinsonism: insights from animal models utilizing neurotoxic agents. In A. R. Liss (Ed.), *Animal models of dementia*, (pp. 1-38). NY.

BIOGRAPHICAL SKETCH

Stephen Coombes was born in Bristol, England, on April 7th, 1977. After receiving his Bachelor of Science Degree in applied psychology and sports science from Liverpool John Moores University, he relocated to Gainesville (Florida) in 2000 and in 2002 received a Master of Science degree in applied physiology and kinesiology (APK) with a concentration in motor learning and control from the University of Florida. Stephen continued in the APK doctoral program with a concentration in motor learning and control, and under the guidance of Dr. Christopher Janelle, received his PhD in August 2006.