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Central and peripheral nervous system interactions: From mind to brain to body

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Abstract

The hierarchical organization of the nervous system allows for the control of peripheral functions such as sweating and glucocorticoid release to be under the exquisite control of the brain. These peripheral responses, in turn, regulate themselves through interactions at various levels of the brain. The nature of these interactions, and how they coalesce to influence, guide, and change higher-order functions such as attention and emotion, is the topic of the ten reports presented in this special issue of the *International Journal of Psychophysiology*. Using a variety of techniques, these reports demonstrate the state of the science of mind-body interactions, and they also showcase the prominent role that psychophysiological measurements continue to play in understanding these interactions.

That the brain and peripheral nervous systems interact is no surprise to anyone who has ever found themselves sweating in front of an audience while trying to remember the lines from a play that had, until recently, been firmly committed to memory. This serves as a dramatic (pun intended) example of how emotional experience can affect the function of the peripheral nervous system—through sympathetic innervation of sweat glands—as well as the function of the central nervous system—in this case, reduced mnemonic retrieval. Appreciation of these interactions between central and peripheral nervous systems is not new, but the level of interest in these interactions is higher than ever, as reflected by the contributions to this special issue of the *International Journal of Psychophysiology*. We have assembled a group of reports that illustrate the wide variety of methodologies, topics, and physiological systems that are currently used to understand the interactions between the workings of the brain and peripheral nervous and chemical response systems.

What is perhaps most noteworthy about this collection of reports is the breadth of approaches used to address central and peripheral interactions. Many of the traditional methods of psychophysiology—ERPs, skin conductance, heart rate—are represented, of course. But in addition, there are several approaches that are less commonly reported in the usual pages of the *International Journal of Psychophysiology*, for instance, measures of immune function, analysis of drug effects, and studies of patients undergoing the WADA test. Although emotion is the primary topic of many of the papers, issues such as meditation, memory, interoception, and visual imagery are also represented. Across such disparate methods and topics, all these

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studies share the goal of better understanding the relationships among the brain, peripheral responses, and behavior. The work not only illustrates the mutually productive cross-fertilization between psychophysiology and neuroscience, but it also depicts the ways in which psychophysiology has remained firmly centered as one of the important experimental methods to understand how the mind works, how the brain works, how the body works, and how these entities interact.

An issue that has long been of interest to cognitive neuroscience, psychophysiology, and psychology more generally is nonconscious information processing. One of the most commonly cited examples of nonconscious influences on behavior is blindsight, which refers to preserved visual capabilities in patients who have frank cortical blindness—e.g., such patients can respond above chance to light flashes presented in hemianopic fields (Weiskrantz, Warrington, Sanders, & Marshall, 1974). Physiological measures such as skin conductance (Bechara et al., 1995) and blood flow in the amygdala (Morris, deGelder, Weiskrantz, & Dolan, 2001) have often been employed to demonstrate intact implicit processing in the absence of conscious awareness. One such example is the case of covert facial recognition, first demonstrated more than two decades ago by Bauer (Bauer, 1984) and by Tranel and colleagues (Tranel & Damasio, 1985). In patients with prosopagnosia (the inability to recognize previously familiar faces), Tranel et al. showed that the patients had intact skin conductance responses to well known faces (e.g., family members, famous persons). Using a similar methodology, Denburg and colleagues (this issue) describe a new example of the influence of nonconscious processing on physiology and behavior. The investigators report a patient with damage to occipitoparietal cortices resulting in simultanagnosia. The patient displays limited conscious awareness of the contents of emotionally provocative scenes, but shows normal skin conductance responses to these scenes. These findings provide another example of the influence of nonconscious processing on behavior and further demonstrate the dissociable nature of emotional responses (indexed by skin conductance responses) and conscious awareness.

Rudrauf and colleagues (this issue) have addressed head-on the question of how the brain and periphery work together in the integrated experience of emotion, using a combined MEG-heart rate study. Participants were presented with a series of movies, which depicted pleasant, unpleasant, and neutral scenes. Throughout the stimulus presentation, brain activity was recorded with MEG and peripheral physiological responses (heart rate) and subjective reports were measured concomitantly. The stimuli were presented in such a way as to allow for the visualization of neural responses as they unfolded in real time, taking full advantage of the superior temporal resolution capabilities of MEG. Results showed activity in the orbitofrontal cortex as early as 200–350 ms after the onset of both pleasant and unpleasant stimuli, but not in response to neutral stimuli. Heart rate showed the prototypical slowing during the first 500 ms of stimulus presentation, which was most pronounced for the unpleasant stimuli. Correlation analyses between subjective reports of arousal and activity across the brain during the processing of emotional stimuli demonstrated strong associations between arousal and activity in the insula, primary and secondary somatosensory cortices, as well as areas of the medial prefrontal cortex. The authors suggest that these findings demonstrate the representation of feeling states in the brain as they unfold at a millisecond level. This work corroborates previous studies that have suggested a role for the somatosensory and insular cortices in the experience of emotion (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000) (Craig, 2002). Additionally, the time course of the response in the medial prefrontal cortex and the heart rate response suggest a mapping of the bodily state engendered by the emotional stimuli in the medial prefrontal region. (Critchley, Elliott, Mathias, & Dolan, 2000) have previously suggested such a mapping of electrodermal responses in the medial PFC. Rudrauf and colleagues have demonstrated the correspondence among central, peripheral, and subjective responses using an innovative methodology that allows for the measure of these responses on the order of milliseconds.

Music exerts profound effects on emotional responses. Listening to music can alter our physiological responses as well as our subjective emotional state. These two emotional response systems do not always go hand-in-hand. Research on the cognitive neuroscience of emotion has demonstrated different neural substrates for physiological responses evoked by emotion versus the recognition of emotion (Adolphs et al., 2000) (Tranel & Damasio, 1985). Johnsen et al. (this issue) have demonstrated a similar dissociation in the experience and recognition of emotion from music stimuli. In their study, Johnsen and colleagues found that patients with damage to the ventromedial prefrontal cortex (VMPFC) do not produce skin conductance responses to emotionally arousing music, although the patients rate the music as emotionally provocative. Patients with damage to the somatosensory cortex show the converse pattern: intact skin conductance responses, but reduced subjective experience of the emotional experience. These results provide another example of the dissociable nature of different facets of emotional experience. The brain is normally able to seamlessly integrate our affective experiences and recognition. Damage to one of the brain areas necessary for this integration results in a disjointed emotional experience, and science has capitalized on this to learn about how the independent components typically work together.

The perception of internal events (or interoception) is a key issue in understanding the relationships among central and peripheral states and emotional experience. The primary method for assessing interoception has been the heart beat perception/detection task. In this task, participants are asked to match an external stimulus with their own heart rate. However, this task is only performed at above-chance levels by around 40% of normal participants, or less (Wiens, 2005). These limitations led Khalsa et al. (this issue) to develop a new methodology to assess interoception. Using a double blind, placebo-controlled drug study, these authors show that the infusion of isoproterenol (a beta adrenergic agonist) elicits increased heart rate and increased measures of interoception (as measured by ratings of heart beat and respiration sensations). Further, these authors show that the location of the feelings of heart beat perception is centered in the anterior chest region overlaying the heart, although there was considerable variability in this measure. Some participants, for instance, reported feeling the heart beat in the arm, neck, or gut. These findings are interesting in relation to one of the broad questions addressed in the current issue: how does the central nervous system map activity that is occurring in the periphery? The Khalsa et al. study (as the authors note) cannot provide a final answer to this question, but the methodology developed by these authors may provide a tool to better address the question.

Vianna and colleagues (this issue) used measures of peripheral autonomic function, skin conductance and electrogastrogram (EGG) activity, to examine the bodily states engendered by imagery of emotional autobiographical events. Both skin conductance and EGG were correlated with the rated arousal of the imagery. By contrast, they found that vividness ratings were negatively correlated with EGG. The authors suggest from these findings that the recollection of highly vivid events may be accomplished by the actions of the central nervous system and in the case of these highly vivid memories, peripheral measures do not seem to make much of a contribution. In the case of memories that are not vividly recalled, peripheral physiological activity may be necessary to bring these events back to awareness. We know from studies of mood-dependent and mood-congruent memory that affective experience at retrieval may serve as a facilitative cue, increasing the likelihood of retrieval (Bower, 1981) (Bower & Forgas, 2000). Exposure to cues of an emotional event, be they internal or external, can trigger an emotional state similar to that experienced during that event. This cueing, which may call on both central and peripheral mechanisms, may facilitate the recollection of events that are less available for vivid re-experience (Buchanan, 2007). Vianna et al suggest that for

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certain memories that are not vividly recollected, peripheral physiology can serve as an additional cue, perhaps facilitating recollection in spite of the diminished vividness of these experiences.

Another area of inquiry that has gained momentum in recent years is the investigation of how persons who are highly experienced meditators may develop enhanced ability to introspect their bodily functions (cf. Khalsa et al., in press), or to process exteroceptive stimuli. In an exploration of the latter of these issues, Cahn and Polich (this issue) studied the neural activity (event-related potentials) of experienced Vipassana meditators in response to various auditory stimuli, while the participants were either meditating or not. The idea was that meditation would reduce the "automatic" processing of attention-demanding (but task irrelevant) stimuli, processing which normally happens in fairly mandatory fashion and is difficult to voluntarily suppress. The results supported this prediction, inasmuch as the meditators showed an attenuated P3a component during meditation when exposed to attention-demanding auditory stimuli; moreover, the meditation-induced reduction in P3a amplitude was strongest in participants reporting more hours of daily mediation practice. The authors suggest that their data support the notion that the practice of Vipassana meditation is effective in reducing cognitive and emotional reactivity to distracting external stimuli, which is of course one of the fundamental goals of the practice in the first place. This finding puts empirical teeth in at least some of the claims about what meditation practice can accomplish, although the Cahn and Polich study is limited by the fact that there was no non-meditator comparison group. Nonetheless, this investigation adds to a growing set of studies that have attempted to put meditation practices on more solid scientific footing (e.g., Davidson et al., 2003; Khalsa et al., in press).

Emotion-modulated startle (EMS) has been a popular paradigm because of its sensitivity to valence (differential responses to positive versus negative affective manipulations (Lang, Bradley, & Cuthbert, 1990) and the ubiquity of the response across species (Lang & Davis, 2006). Driscoll and colleagues (this issue) describe a study using the EMS paradigm, but with a new wrinkle: participants attempted to *regulate* their emotional responses within the EMS paradigm. Disorders involving deficits in emotion regulation are widespread, and this has helped push the study of this topic to the forefront of affective science (Gross, 2002); (Taylor & Liberzon, 2007). The ability to regulate our emotions is a key skill in adaptive social and emotional functioning. Driscoll et al show that attempted down-regulation of emotion decreased startle magnitude, skin conductance responses, and heart rate. These results were found overlaid on the typical EMS response pattern (unpleasant > neutral > pleasant), but they also demonstrate the power of self-regulation in controlling emotional responses. Something as basic as the startle reflex is influenced both by our current environment (e.g., unpleasant visual scenes) as well as by our response to it (e.g., emotional regulation).

The secretion of cortisol in humans follows a diurnal cycle, and shows a characteristic spike after awakening. This increase has been termed the cortisol awakening response (CAR), and this is the focus of a review article by Fries et al. (this issue). The authors discuss the relevance of the CAR to psychophysiology and behavioral medicine research, and they provide an up to date review of the CAR, its biological and central nervous systems origins, the influence of factors such as age, gender, smoking, and sleep, and relationships with health and stress. The authors conclude that the CAR is strongly influenced by the anticipation of the upcoming day. The exact function of the CAR, however, remains unknown, although Fries et al. offer the intriguing speculation that the CAR may reflect a person's expectation of preparing for the events of the day—a sort of blend of self reflection and prospective memory that helps one prepare physiologically for anticipated demands. This idea is consistent with some of our own findings in amnesic patients with hippocampal damage, who do not show the characteristic increase in cortisol after awakening and who—because of their amnesia—do not have the kind of prospective memory and self reflection that would allow them to contemplate their upcoming day (Buchanan et al., 2004). No matter the function of the CAR, though, the review by Fries et al. provides important background information for researchers who plan to use cortisol as a dependent measure in their studies, as the diurnal cycle and influence of many attribute and behavioral variables need to be taken into account in the design of such studies.

Cortisol elevation following stress can have important effects on various target tissues in the body, including the central nervous system and the immune system. In the study reported by Rohleder et al. (this issue), the investigators assayed glucocorticoid sensitivity in the periphery by measuring production of interleukin-6 (IL-6), and correlated this with participants' retrieval of previously learned emotional versus neutral words. It was found that relative suppression of IL-6 production was correlated with weaker retrieval of emotional words, but not with retrieval of neutral words, suggesting a possible association of peripheral glucocorticoid sensitivity with memory for emotional but not neutral material. The authors link this finding to research on post-traumatic stress disorder (PTSD), which has shown that PTSD patients tend to show enhanced peripheral glucocorticoid sensitivity and heightened alteration of memory performance in response to acute glucocorticoid administration (e.g., Yehuda et al., 2004). The Rohleder et al. study also underscores the importance of individual differences in assessing relationships between stress, cortisol, and central and peripheral glucocorticoid sensitivity. An important issue that cannot be decisively addressed in this study is that of sex differences. Several studies by these authors and others have demonstrated sex differences in glucocorticoid sensitivity (Buchanan & Tranel, 2008; Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001). Although the study leaves many questions unanswered, it highlights the wide-ranging effects that glucocorticoids may have on central and peripheral function.

Aging is a topic that has gained increasing importance and relevance in recent years, although this has received relatively little attention in the psychophysiology literature. Thayer and colleagues (this issue) present a reanalysis of data that involved looking at heart rate responses during internal carotid injections of sodium amobarbital (what is known clinically as the Wada test, where one cerebral hemisphere is anesthetized to allow clinicians to determine speech and memory laterality). The focus in the data analyzed by Thayer et al. was on aging effects, and the authors found several interesting results that demonstrate significant age-related effects for participants between 20 and 47 years old, on average. During sodium amobarbital injections, the younger participants tended to show HR increases that were similar for left and right hemispheres, whereas the older participants showed HR increases that were (1) smaller overall than in younger participants, and (2) larger in the right hemisphere than in the left hemisphere. Although limited by the relatively young age of the overall sample (no participant was older than 65), these findings hint that there are important age-related differences in cortical inhibitory control of heart rate. The results contribute to a growing body of data that has suggested age-related changes in the manner in which the two hemispheres interact and "dominate" different aspects of cognitive, behavioral, and—in light of the current findings—even psychophysiological outputs (e.g., Cabeza, 2002; Dolcos et al., 2002).

In conclusion, the reports presented in this special issue of the *International Journal of Psychophysiology* highlight the multifaceted connections between the central and peripheral nervous systems at their many points of intersection. The results of these studies provide a nice update to so-called "mind-body" issues that have been the focus of psychology from its inception. Hopefully, these collected works will spur others to address this important topic in new and exciting ways. We continue to be impressed by the power of the many classic and innovative experimental approaches entailed under the rubric of "psychophysiology," and how these have continued to allow scientists to elucidate how the mind, brain, and body operate.

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