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MODULATION AND EXPERIENCE OF EXTERNAL STIMULI: TOWARD A SCIENCE OF EXPERIENCE AND INTEROCEPTION*

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The concept of interoception can be found in various writing over the past 100 or more years dating back to Sherrington, James and Lange. Professor György Ádám that made American scientists increasingly aware of the importance of interoception with his 1967 book Interoception and Behavior. In this article we want to discuss two areas of research from out laboratory that have been influenced from this perspective. First, we will focus on electrocortical correlates of error detection during visuo-motor task and examine the manner in which an individual becomes aware of making an error as well as the way in which this awareness directs behavior on an ongoing basis. Second, we will examine hypnotic modulation of the pain experience and describe the manner in which electrocortical processes reflect the modulation and experience of pain. In this discussion, we suggest the importance of the anterior cingulate in not only modulating these processes in particular but also in its more general role as an interface between the limbic system and the neocortex and the integration of cognitive with emotional stimuli.

Keywords: Interoception – EEG – error detection – pain – hypnosis

INTRODUCTION

The concept of interoception can be found in various writing over the past 100 or more years [6]. Sherrington used the word "interoceptor" to describe sensory nerve receptors that originate within the body. The fact that changes in visceral systems can be perceived lies at the heart of both James [17] and Lange [21]. This in turn has fostered the idea that the experience of changes in visceral organs lies at the heart of emotionality. The important idea is that there exists a system that is capable of perceiving changes within visceral systems which relates not only to the establishment of a healthy internal environment within changing systems, but also allows for physiological information to be perceived by conscious systems. As critical as this idea is, given the hierarchical nature of the study of biological processes, many of the important questions that reached across biological levels were often ignored. Some years ago it was Professor György Ádám that made American scientists increasing-

* Dedicated to Professor György Ádám on the occasion of his 80th birthday.

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ly aware of the importance of these cross level questions with his 1967 book *Interoception and Behavior* [1]. It is currently encouraging to see a new generation of scientists being influenced by his more recent book *Visceral Perception* [2]. For many of us Professor Ádám showed how to understand the manner in which visceral perceptions may influence a variety of cognitive processes including our experience and report of emotion. Additionally, in our own work using electrocortical process, Professor Ádám always made us think twice, once to consider how the physiological processes observed in our research reflect the processing of events from the external world and once to consider how they reflect those of the internal world which in turn modifies our experiences. The existence and modification of the body's internal feedback system lies at the heart of the research from our laboratory.

One of the critical questions for any theory of self-regulation is the manner in which higher level processes such as planning and volition can be derived from our current scientific understanding of physiological processing. A great variety of research from the 20th century emphasized the role of the frontal lobes in the organization, evaluation, and planning of behavioral responses in including error correction, execution of novel actions, inhibition of behavior and alerting to danger. Evidence has also grown to show the importance of the role of emotional processes from the limbic areas in modulating the frontal evaluative aspects. Patients with damage to the frontal lobe, although able to accurately describe environmental situations, lack the ability to formulate action plans that move beyond these environmental demands. Nauta [27] gives a clue as to the mechanism involved in these deficits when he refers to these patients as having interoceptive agnosia. That is to say, these individuals lack the internal feelings that give an evaluative component to actions. In our own work we have sought to determine marker variables associated with these internal feelings especially on an electrocortical level. In this article we want to discuss two areas of research from our laboratory that have contributed to this search. Specifically, we will focus on electrocortical correlates of error detection during visuo-motor tasks and hypnotic modulation of the pain experience. As can be determined these areas have benefited greatly from a visceral perception perspectives.

SUCCESSFUL PERFORMANCE AND THE EEG

An intriguing question involves the manner in which an individual becomes aware of making an error as well as the manner in which this awareness directs behavior on an ongoing basis. We have studied electrophysiological markers associated with successful and failed performance [e.g. 34]. In this study individuals performed a visuomotor task contained within the computer game, "Frustrated Maze". The basic task was to drag a ball using the mouse along a narrow mazelike path from the starting point to the goal without touching the "maze wall" and other obstacles. We had subjects play the game both under time pressure and non-time pressure conditions. During the games we recorded EEG activity from 15 electrode sites (Fp1, Fp2, Fz,

F3, F4, Cz, C3, C4, Pz, P3, P4, T7, T8, O1, O2) referenced to linked mastoids. Comparing the successful with the unsuccessful trials, we found three major results. First, there was a widely distributed reduction of *fast* alpha (peak of approximately 10.5 Hz) over frontal-central and parietal areas and centrally localized reduction of "mu" over the somatomotor cortex during successful trials. Second, there was localized enhancement of frontal midline theta (Fm theta) and midline gamma in conjunction with successful trials. And third, these findings were more pronounced in the time pressure condition. We assume that the reduction in alpha, especially during the time pressure conditions, reflects an increase in task demands and complexity as has been noted in other studies. Theta, on the other hand, showed an increase in power during successful trials. Given that an increase in frontal Fm theta activity has also been observed during successfully simulated driving tasks [20], the question arises as to the aspect of successful performance that is associated with this increase in EEG theta activity.

Frontal midline theta was initially noted during the continuous performance of mental tasks such as mental arithmetic and that it increases with task difficulty [16]. Theta has also been linked to an event related potential, that of error-related negativity or ERN that peaks approximately 100 ms after an individual makes an error [10, 24]. This activity appears related to error monitoring in relation to action regulation. In terms of its source, a variety of studies suggest that the anterior cingulate is the source of this 4–7 Hz midline activity. Broca in the 1870s first described the "le grand lobe limbique" or limbic system with the dorsal part being the cingulated cortex. Papez [28] in the 1930s saw this structure as the receptive organ for the experience of emotion. The anterior cingulate receives information from the amygdala which is assumed to be fear related as well as show neuronal activity in relation to performance reward and error. Currently, the anterior cingulated is seen to monitor performance, including errors and reward, and to adjust behavior to optimize payoff [3]. The purpose of the 4–7 Hz theta activity appears to be that of fostering entrainment in an interregional manner that allows for limbic circuits to exert regulatory control on cortical networks and thus facilitate the reestablishment of executive control following an error condition [24]. The anterior cingulate has also been shown to be involved in the emotional experience of pain.

PAIN AND ITS EXPERIENCE

Pain has evolved as a critical process for the survival of the organism. Its systems allow for immediate awareness concerning potential injury. Current research has demonstrated that the experience of pain is more than the resultant of a simple stimulus response mechanism involving the sensory system. It is now viewed as involving a complexity of systems involving at least affective evaluation, attention, cognitive appraisal and arousal systems [18, 26] which require the integrated activity of widely distributed networks that include cortical as well as subcortical structures. Some of this evidence has been integrated in theoretical accounts of the hypotheti-

cal, parallel brain processes involved in pain [25]. From the interoception perspective, a crucial question involves the manner in which these various systems supply information to one another in both a temporal and spatial manner.

Electrophysiological approaches (e.g. ERPs, EEG) and brain imaging techniques (e.g. fMRI, PET, dense array EEG and MEG) allow one to monitor cerebral functioning in the human as related to pain (see 4 for a review). Using a variety of stimulation techniques, painful events have been shown to produce an early contralateral response in the primary somatosensory cortex (S1), followed by a more distributed contralateral activity in the 120–170 ms range that may also include ipsilateral components. Late responses display a bilateral pattern of activation. Since these later components are correlated with subjective reports of pain and only appear if the pain is felt, they are assumed to be related to cognitive or affective evaluation of the painful stimulus [12]. Anatomically, a variety of regions have been implicated in pain perception including primary and secondary somatosensory cortex, anterior cingulate cortex, basal ganglia and anterior frontal cortex [22, 36]. Additionally, Ploghaus and coworkers were able to differentiate regions associated with the experience of pain (anterior cingulate, mid-insula, and anterior cerebellum) from those associated with the expectation of pain (anterior medial frontal cortex, anterior insula, and posterior cerebellum). In terms of mechanisms which modify the experience of pain, found early event-related magnetic fields (ERF) that showed a contralateral maximum (M1), and later evoked potentials maximal at vertex with a latency of 200–270 ms (N240) and 320–380 ms (P340) in response to painful laser stimulation. In this study distraction tasks did not affect the M1 components but did reduce the peak-to-peak amplitude of the EEG evoked potentials. Thus, a crucial question is the manner in which sensory and emotional aspects of pain can be modulated in a variety of situations.

We chose to use hypnosis to modulate pain since it is a well known behavioral intervention [7, 13, 14, 15]. Previous clinical reports have shown hypnotically induced reductions of pain under a variety of both chronic (e.g. cancer) and acute (e.g. painful medical procedures) conditions. In our study [32] we worked with carefully screened high and low hypnotically susceptible individuals and measured electrocortical activity using a dense array (129 electrode) EEG procedure. We presented electroshocks to either the left or right finger under two different hypnotic suggestions [1] to dissociate (hypoalgesia) either the hand receiving the shock or the other one and [2] to sensitize (hyperalgesia) a particular hand for pain perception. In the study we examined [1] initial self-report and psychophysiological differences in relation to hypnotic susceptibility; and [2] differential pain experiences and electrocortical indicators of hypo- and hyper-algesia suggestions in relation to hypnotic susceptibility. In order to reduce the data available and to describe the topography of the ERPs, we utilize a procedure to determine the spatiotemporal structure of the signal as described in other studies [9, 35]. Basically, a Principal Components Analysis (PCA) was performed on the cortical source data in response to the pain stimuli to determine the spatial patterns in the data. A second PCA was performed on these data

to describe the temporal patterns present. The resulting spatiotemporal factor scores were used to describe the electrocortical activity in response to the pain stimuli.

In examining the overall pain-related evoked potential, the most striking feature was a drop in amplitude for the P250 component during the hypnosis condition for the high susceptible individuals and an increase in amplitude for the lows as compared to baseline. This was true for the spatial factor showing high loading at central sites. The earlier N140 component, on the other hand, showed fewer and less specific changes during the hypnotic condition consistent with previous pain research showing these components to be more stimulus oriented [e.g. 11]. In particular, this component was decreased non-specifically during both hypnosis conditions in the high susceptible subjects during left stimulation, at right temporal locations. In terms of the later components, low susceptible individuals show an increase in power for both the hypo- and hyper-algesia conditions whereas high susceptible individuals display a decrease in power with the dissociation condition showing the greatest decrease. A variety of studies suggest that the later components are related to the painfulness of the stimuli and that these components may even be lacking when the stimuli are not experienced as painful [e.g. 11]. These findings are consistent with our results in that during the dissociation condition the high susceptible individuals show smaller later components. This clearly suggests an inhibitory process for the high susceptible individuals associated with the hypnotic suggestions. This inhibitory process may be more of a global than specific nature in that the P250 amplitude in high hypnotically susceptible individuals decreased rather than increased. Thus, it is possible that hypnosis may activate inhibitory processes regardless of the direction of the hypnotic suggestion. This finding is also consistent with the regional cerebral blood flow studies of Rainville et al. [30, 31] in which hypnotic suggestions to increase or decrease pain were not found in the primary sensory regions but only the anterior cingulate.

Comparison of the early N140 and the later P250 in high and low susceptible subjects under pre-hypnosis and dissociation supports the idea that at earlier stages, the lateralized (i.e. contralateral) response is modulated by unspecific effects of the hypnosis procedure, showing no group by condition interaction. These early effects may be related to differences in arousal in the relevant circuitry that may be mediated by structures such as the parts of the ascending reticular arousal system [33] or the intralaminar nuclei of the thalamus [19]. At the later stages, the high hypnotic susceptible individuals showed a significant decrease in the P250 amplitude in response to the dissociation suggestion whereas the low susceptible individuals displayed an increase during both the hypoalgesia and hyperalgesia conditions. The center of gravity of these later activations appeared to be at the central regions, showing a bilateral distribution. A variety of possible explanations may account for this result. For instance, affective evaluation of the incoming painful stimulus may be altered by the hypnosis procedure. Given that the spatial factors showing these effects for the P250 in our study show a wide distribution over central areas, it seems possible that brain areas that are activated as parts of the aversive response include the anterior

cingulate or prefrontal cortex. Both structures are highly connected to subcortical structures known to be involved in defensive affective processing, such as the amygdaloid nuclei. Future work may try to shed light on these questions by obtaining correlates of emotional state such as subjective ratings, skin conductance or facial EMG data, an approach recently initiated by De Pascalis and his colleagues [8].

In our study, self-report data displayed differential patterns of responding with low susceptible individuals showing little differentiation between the baseline, hypoalgesia, and hyperalgesia conditions whereas high susceptible individuals showed greater spread in the instructed direction. This result gives support to the suggestion that any differential responding to the pain stimuli by the high and low susceptible participants were the influence of the hypnotic suggestions. Additionally, high and low susceptible individuals during baseline did not differ in their ratings of the painful stimuli, which suggest that high and low hypnotically susceptible people rate external stimuli in a similar way.

SUMMARY

In this article we sought to emphasize *two processes,* that of error detection and that of pain perception, which can be considered from a visceral perception perspective. We further sought to suggest the importance of the anterior cingulate in not only modulating these processes in particular but also in its more general role as an interface between the limbic system and the neocortex and the integration of cognitive with emotional stimuli. We are just beginning to gain some perspective of the manner in which the anterior cingulate is involved in self-regulation including error detection, mood regulation, attention and pain [e.g. 5, 23]. Further, our work with the experience of pain using hypnotic suggestions points to the importance of considering temporal factors as reflected in electrocortical measures to help decouple sensory from emotional coding. A crucial question for future research is the manner in which such procedures as hypnosis are able to modulate the actual feel of an emotional experience. As we understand more concerning the "feel of experience", perhaps, we will be able to approach the questions Professor Ádám raised in his books and articulate the manner in which internal processes come into consciousness.

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