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Commentary

What does the prefrontal cortex "do" in affect: perspectives on frontal EEG asymmetry research

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Abstract

This commentary provides reflections on the current state of affairs in research on EEG frontal asymmetries associated with affect. Although considerable progress has occurred since the first report on this topic 25 years ago, research on frontal EEG asymmetries associated with affect has largely evolved in the absence of any serious connection with neuroscience research on the structure and function of the primate prefrontal cortex (PFC). Such integration is important as this work progresses since the neuroscience literature can help to understand what the prefrontal cortex is "doing" in affective processing. Data from the neuroscience literature on the heterogeneity of different sectors of the PFC are introduced and more specific hypotheses are offered about what different sectors of the PFC might be doing in affect. A number of methodological issues associated with EEG measures of functional prefrontal asymmetries are also considered.

Keywords: Frontal EEG asymmetry; Emotion; Prefrontal cortex; Neuroimaging

1. Introduction

It is very gratifying for me personally to be writing this commentary since the publication of this Special Issue marks the fact that there now exists a substantial corpus of scientific literature investigating methodological and conceptual issues surrounding the use of measures of asymmetric prefrontal electrical signals recorded from the scalp surface to make inferences about emotional processes. With my colleagues and students at the time, I first reported 25 years ago on the use of asymmetries in scalp-recorded frontal brain

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electrical activity to make inferences about emotional processes (Davidson et al., 1979). At the time, it was a lonely field though there were investigators from other domains of neuroscience who underscored the important role played by the prefrontal cortex in different aspects of emotional processes (e.g., Nauta, 1971). This Special Issue has brought together the best of current research using these non-invasive measures to investigate different aspects of the methodology and construct validity of these measures. When I began to work in this area, research on the central nervous system substrates of emotional processes was largely restricted to studies in non-human species that focused on the role of subcortical structures in emotional and motivational processes, leading to a view, still championed by some (e.g., Panksepp, 2003; but see Davidson, 2003a for a rebuttal), that the fundamental circuitry for emotion and motivation lies in subcortical zones and that cortical tissue has little if anything directly to do with emotion. The only exceptions to this view at the time came from observations of patients with localized cortical brain damage (e.g., Gainotti, 1972) and from early studies on the role of prefrontal lesions on the socioemotional behavior of monkeys (e.g., Myers, 1972). The research featured in this Special Issue is part of a larger body of work (see e.g., Rolls, 1999 for a modern example) that forcefully underscores the importance of prefrontal cortex for emotional and motivational processes.

However, the work represented in this Special Issue has, for the most part, evolved with little connection to the core neuroscience research on the structure and function of the prefrontal cortex. I will argue that this state of affairs must change if this work is to become an accepted part of the influential body of neuroscientific research on the prefrontal cortex. Just what specific role the primate prefrontal cortex (PFC) might be playing in emotion still remains elusive and will be one of the several issues I will address in some detail below. The substantive portions of this commentary will be divided into two parts. The first part will address some of the fundamental conceptual issues that lie at the core of this work, most of which were not addressed in the articles in this Special Issue. I will focus on what the PFC is “doing” in emotion and will draw on other neuroscience literature on PFC from which insights about its role in emotion might be gleaned. In this section, I will also emphasize the fact that the PFC is heterogeneous, both anatomically and functionally and any serious discussion of PFC function must make distinctions among the sub-territories of the PFC. Also to be emphasized is the fact that the PFC is part of a larger overall circuit and that other components of the circuitry are crucial for understanding how the brain implements emotional and motivation processes. It cannot be solely through the prefrontal cortex that the brain implements emotional and motivational processes. One unwitting consequence of the work my laboratory began on prefrontal asymmetries and affect is the view that the prefrontal cortex is the “center” or at least the primary region for all aspects of the emotional and/or motivational processes in question. It is essential that we remind ourselves that the prefrontal cortex is part of a larger and more complex circuit and that other components of this circuitry will undoubtedly be important for many of psychological phenomena of interest to the readers of this Special Issue. A related issue concerns the nature of the measure with which we are dealing. It has been easy for those who study EEG frontal asymmetry to ignore other components of the circuitry because the measure in question here does not reflect many of the other features of the circuit. In particular, scalp-recorded brain electrical signals reflect activity primarily from cortex and without more complex source localization methods which have not been used in any of the articles in this Special Issue, one cannot make inferences about subcortical signals.

2. Conceptual issues that underlie research on EEG asymmetries associated with emotion

2.1. Heterogeneity of prefrontal cortex

Many recent reviews have documented the important functional and anatomical divisions within the prefrontal cortex (e.g., Rolls, 1999). For the purposes of the present discussion, it is important to simply call attention to this fact and to indicate that the majority of the neuroscience literature indicates that the prefrontal sector most directly associated with emotion is the sector that is least likely to be reflected in scalp-recorded brain electrical signals—namely, orbital frontal cortex (e.g., Hornak et al., 2003). Both the lateral orbital sectors and the ventromedial sectors have been directly implicated in various aspects of emotion, with the orbital sectors in particular thought to play an important role in the assignment of affective value to stimuli (e.g., Rolls et al., 2003). It is true that there are major interconnections among the different sectors of the PFC and that the dorsolateral sector receives input from the orbital sector (Rolls, 1999). However, according to most investigators, the dorsolateral sector of the PFC is primarily associated with various cognitive processes, particularly with cognitive control (see Miller and Cohen, 2001 for review). It is the dorsolateral sector which is likely most directly reflected in the scalp signals from which metrics of functional prefrontal asymmetry are constructed.

Recent neurophysiological data from awake behaving rhesus macaques in whom single cell recordings were simultaneously acquired from multiple neurons in both dorsolateral and orbitofrontal sectors of PFC (Wallis and Miller, 2003) provide a new understanding of what these different regions of PFC may be doing and how they interact. These investigators recorded single cell activity as well as behavior during a reward preference task. The monkeys had to choose between pictures associated with different amounts of juice reward. Neuronal activity in both regions of PFC reflected the reward amount. However, neurons in the dorsolateral sector encoded both the reward amount and the monkey's forthcoming response while neurons in the orbital sector primarily encoded the reward amount alone. The authors propose that their data are consistent with a model where reward information enters the PFC via the orbital sector where it is then passed on to the dorsolateral sector and used to guide behavior. Unfortunately since neurophysiological studies of this kind are so difficult to perform and since there were only two animals tested, it was not possible for the authors to compare left- versus right-side recordings. However, one important conclusion to draw from this work is that tasks that include a response component will be more likely to show affect-related PFC activation asymmetry in the dorsolateral regions and it is activity in these regions that are most likely to be reflected in scalp-recorded brain electrical signals.

Recent studies have also identified a ventrolateral region of prefrontal cortex that shows robust asymmetries during response inhibition tasks. In response to cues that signal the requirement to inhibit a dominant response, activation of right inferior and middle frontal gyrus has been found (e.g., Garavan et al., 1999; Konishi et al., 1999). Moreover, patients with focal damage to the right inferior frontal gyrus show impairments on such tasks (Aron et al., 2003). Right ventromedial PFC also appears to play a specialized role in the inhibition of impulsive affective urges. Patients with damage specifically to this PFC sector on the right side, but not on the left side, have profound abnormalities in emotion-related decision making (such as on the Iowa Gambling task; Tranel et al., 2002; see also Clark et al., 2003), making more disadvantageous choices compared with their left-damaged counterparts. It appears that this sector of right prefrontal cortex may be particularly sensitive to punishment so that when it is damaged, patients no longer have the usual cues that signal threat and danger and so tend to act impulsively. It will be important in future research using EEG measures to utilize tasks that have been well-studied in imaging and lesion studies to determine if predictable changes in PFC electrical asymmetries occur.

2.2. PFC is part of a complex circuit involving other cortical and subcortical components

Emotion and motivation are instantiated in complex circuitry involving both cortical and subcortical components. Most major neuroscientists working on these topics have reached this conclusion (see Rolls, 1999; LeDoux, 1996; Damasio, 1994; Davidson et al., 2000c; Davidson et al., 2003). For example, we (Davidson et al., 2003) have described a circuit that primarily involves different sectors of the PFC, the amygdala, hippocampus, insula and anterior cingulate. Each of these structures plays a different, complementary role in specific features of emotion. Just as cognitive neuroscience has powerfully demonstrated the utility of differentiating among specific subcomponents of cognitive processes, so it is essential that we do the same with emotion. Toward the end of this section, we will explicitly consider what different sectors of the PFC might be doing in emotion and suggest different functions for the different sectors. Unfortunately though, little work at the human level has begun to parse emotion in a fashion that derives from and honors the distinctions that are made at the neural level. This will be an important task for future research.

With respect to the frontal EEG asymmetry literature, it is imperative that we be mindful of the fact that PFC, and particularly that sector of PFC likely contributing most to the brain electrical signals that are the subject of this Special Issue, represents only a small portion of the critical circuitry of emotion. Thus, for certain types of emotional processes, the presence of a particular pattern of functional prefrontal asymmetry may be necessary but not sufficient for the emotional state in question, or may simply be a contributory cause of the emotional state. For example, as Harmon-Jones (this issue) has demonstrated, certain types of anger under specific conditions may be associated with relative left prefrontal activation but this does not mean that the left prefrontal cortex is in any way a “center” for anger in the brain. We must ask what component of anger might be represented in the left prefrontal cortex and since left prefrontal activation occurs during other types of emotions, we must further ask what other brain regions must be recruited for anger to occur. Without additional measures that reflect other components of the circuitry, it is not possible to effectively address the question of what the PFC is uniquely doing in emotion.

When the patterns of anatomical connectivity are examined, it is apparent that one major target of prefrontal neurons from some PFC sectors, is the amygdala. Some researchers have suggested, based upon this anatomical arrangement, that one function of at least certain regions of PFC is to modulate or inhibit activity in the amygdala. Davidson (2000, 2002) has specifically suggested that regions of the left PFC in particular may play an important role in inhibiting the amygdala. Broadly consistent with this view are new data at the animal level. For example, Quirk et al. (2003) have shown that stimulation of medial PFC in rodents decreases the responsiveness of output neurons in the central nucleus of the amygdala. Caution must be exercised in generalizing from rodent to human PFC but nevertheless, these data raise the important suggestion that reciprocal relations between at least certain PFC regions and the amygdala may be important in understanding the functional significance of this emotion-related circuitry. Using a paradigm to study the voluntary regulation of emotion modeled after one we developed (Jackson et al., 2000), Ochsner et al. (2002) reported strong inverse relations between activation in the left ventrolateral PFC and the amygdala when subjects were requested to voluntarily downregulate their negative affect. These findings collectively imply that what the PFC is doing in emotion is clearly *not* mediating emotional responses but rather *moderating* patterns of activity in other parts of the circuit that control the primary emotional response.

2.3. Should measures of emotional experience be used to guide and test theory?

An issue that surfaces in several of the articles in this Special Issue and one that was noted by Cacioppo (this issue) in his commentary concerns the role of emotional experience. Most, though certainly not all of the extant research on frontal EEG asymmetry and emotion is based upon associations with self-report measures of emotional experience or of emotional traits, our own work included (e.g., Tomarken et al., 1992; Sutton and Davidson, 1997). While there are some important, notable exceptions to this, including some of our own work examining relations with hormonal and immune measures (e.g., Davidson et al., 1999; Kalin et al., 1998; Rosenkrantz et al., 2003), much of the literature is based upon associations with self-report. If we are to uncover what the PFC is doing in emotion, it will be important that we develop laboratory probes that do not rely solely upon self-report measures to provide information on aspects of affective processing that may not be directly reflected in conscious report. A recent example of this is a new study from our lab that investigated relations between baseline functional prefrontal asymmetry derived from brain electrical measures and startle responses during and following unpleasant pictures (Jackson et al., 2003). In this study we specifically hypothesized that functional prefrontal asymmetry would predict startle measures following the offset of a negative stimulus, rather than startle magnitude during the stimulus itself. This hypothesis was formulated based upon our suggestion that the left lateral prefrontal cortex may play an important role in the inhibition of the amygdala and thus in the downregulation of negative affect. On this view, the recovery following an unpleasant picture as reflected in the diminution of startle magnitude post-stimulus offset would reflect the decrease in negative affect following the negative stimulus and may be modulated by PFC inhibition of the amygdala. Our results strongly confirmed our hypothesis. Frontal EEG asymmetry did not predict startle magnitude during the unpleasant picture; it only predicted startle magnitude following the offset of the negative picture. It may well be the case that frontal EEG asymmetry measures are associated with self-report measures of mood, dispositional affect and/or behavioral inhibition and activation. However, these associations are unlikely to be particularly revealing about mechanism since such associations can arise for a multitude of reasons. Recovering slowly following the offset of an aversive stimulus may be associated with higher levels of dispositional negative affect and/or behavioral inhibition but such associations by themselves will provide little information to help mechanistically understand what role the PFC may be playing. Our study with startle measures during and following unpleasant stimuli is offered as an example of how we can begin to mechanistically dissect the stream of affective processing to help us better understand the role of the PFC in these processes. On the other hand, it is important that self-report measures be retained in our future studies because it is still of great interest to know how conscious mood is associated with prefrontal function and its correlates. Moreover, conscious mood may be a useful summary index that integrates and reflects a multitude of processes that are unlikely to be fully captured in any single process measure, and conscious mood may play an important regulatory function in behavior.

2.4. *Left prefrontal activity and anger—what are the implications?*

Harmon-Jones (this issue) reviews a growing corpus of literature that suggests that specific forms of anger, or anger elicited in particular contexts, is associated with left-sided prefrontal activation. He argues that these data are consistent with the approach–withdrawal framework rather than with a valence-based model for frontal EEG asymmetry. More than 20 years ago, I argued the same point (Reuter-Lorenz and Davidson, 1981) though at that time had little data to buttress our suggestion. We did publish the first data showing that anger elicited in infants when it was not accompanied by crying was associated with left-sided frontal EEG activation (Fox and Davidson, 1988). On the basis of the evidence from his lab, Harmon-Jones questions whether relatively greater left-sided frontal activity is a positive trait. There are several issues that are embedded here that should be disentangled. First is the distinction between baseline levels of asymmetry versus state-related changes. Most, though not all, of the evidence provided by Harmon-Jones and colleagues is based upon the latter type of measure, not the former. Secondly, it is important to ask just what the left PFC might be "doing" in anger-related affective processing. In light of the important data Harmon-Jones has gathered, it appears reasonable to suggest that one will find activation of the left PFC in anger-related situations where there are response options that enable the individual to overcome whatever obstacle is thwarting the goal. As such, in these situations it may indeed be indeed be the case that "relatively high left frontal brain activity is more psychologically and physically healthy than relatively less left frontal brain activity" (Harmon-Jones, this issue), despite suggestions to the contrary, though the requisite evidence to carefully evaluate this claim has not been gathered. The negative behaviors that frequently accompany anger may well be subserved by other brain regions that require other methods to detect. And then there is a growing literature on the peripheral biological correlates of individual differences in baseline functional prefrontal asymmetry where we have shown that individuals with more left prefrontal activity have lower levels of the stress hormone cortisol (Kalin et al., 1998), lower levels of cerebrospinal fluid measures of corticotropic releasing factor (CRF; Kalin et al., 2000), the central molecule that initiates the cascade of changes in the HPA system in response to stressful events, higher levels of natural killer activity both at baseline (Kang et al., 1991) and in response to challenge (Davidson et al., 1999), and higher antibody titers in response to influenza vaccine (Rosenkrantz et al., 2003). Collectively, these findings powerfully reveal that individuals with higher levels of left-sided prefrontal activity do indeed have a more positive profile of peripheral biological indicators. When these findings are considered in the context of other recent evidence from our lab showing that subjects with greater relative baseline left-sided prefrontal activity recover more quickly following a negative event (Jackson et al., 2003) and report higher levels of psychological well-being (Urry et al., in press), they indicate the left-sided prefrontal activity is associated with a nomological network that consists of effective coping with negative events and a resilient profile of peripheral neuroendocrine and immune function. If such individuals are also more prone to anger in certain situations, it may well be a form of anger that facilitates the rapid removal of obstacles that are thwarting goals. Of course, this perspective is still very much in need of additional confirmation and will be informed by studies that investigate both trait levels of prefrontal asymmetry as well as state variations in anger experience and expression and state variations in asymmetry. Moreover, the classification of a particular constellation of biological and/or psychological indicators as “positive” or “beneficial” is fraught with complexity. It is not my intention here to unpack these complicated issues, but only to suggest that the compelling new data on anger offered by Harmon-Jones (this issue) is not at all incompatible with the view that higher levels of left prefrontal activity may be associated with aspects of resilience.

2.5. What do we know and what must we still learn about what different sectors of the prefrontal cortex are “doing” in emotion?

Despite the current popularity of frontal EEG asymmetry measures, there is preciously little research that has systematically manipulated task parameters in a neurally-informed strategy to test specific hypotheses about the role of the left and right prefrontal cortex in different aspects of emotional processing. Harmon-Jones (this issue) and Nitschke et al. (this issue) are notable exceptions. As noted earlier, in light of the limitations of scalp-recorded brain electrical measures and what they reflect, it is likely that the frontal EEG asymmetry measures mostly reflect dorsolateral sectors of PFC. On the basis of a large body of both human and animal studies, we (Davidson et al., 2003) have proposed that greater left-sided dorsolateral activity may be associated with approach-related, goal-directed action planning. This would include instances of both pre-goal attainment positive affect as well as the approach component of anger when response options are available. This analysis implies that these effects will be particularly pronounced during periods of anticipation and planning. The temporal dynamics of shifting patterns of prefrontal asymmetry during pre versus post-goal periods is something that still must be systematically examined. We have been examining a number of tasks that explicitly manipulate reward and isolate periods in anticipation of reward (e.g., Sobotka et al., 1992; Skolnick and Davidson, 2002; Zinser et al., 1999; see also Miller and Tomarken, 2001). Though limited, the evidence accumulated to date indeed suggests that it is particularly during the period in anticipation of reward that the most pronounced left prefrontal activation is observed.

There is less consensus on what the right lateral sector of PFC might be doing in withdrawal-related emotion. On the basis of neuroimaging studies of spatial working memory, we have suggested that activation of right lateral PFC during withdrawal-related emotion may be associated with threat-related vigilance. In studies with rhesus monkeys conducted collaboratively with Kalin, we (Kalin et al., 2001) have reported that in response to a manipulation that elicits powerful increases in freezing behavior, there is also a parallel increase in behavioral signs of vigilance. Moreover, animals who display higher levels of these behaviors have greater right-sided baseline levels of lateral prefrontal activity (Kalin et al., 1998). This line of reasoning leads to a number of testable hypotheses concerning relations between right-sided PFC activity and the capacity to detect threat-related cues.

Because of the strategic location of PFC, with extensive anatomical connections to posterior cortical regions as well as subcortical regions, this sector of cortex is ideally located to recruit other processing regions to facilitate adaptive responding. This view of PFC borrows heavily from that formulated in the cognitive neuroscience literature on the role of PFC in cognitive control (e.g., Miller and Cohen, 2001).

What of other sectors of PFC that are not directly reflected in frontal EEG? First, we know that there is extensive intrinsic connectivity among the various subregions of PFC (Rolls, 1999). This pattern of anatomical connectivity can therefore provide the basis for orbital, ventromedial and ventrolateral sectors of PFC to modulate processing in the dorsolateral sector. There are also direct roles for these other sectors of PFC in emotion and in fact, it is precisely these sectors that are not directly reflected in scalp-recorded brain electrical activity that historically have been most closely associated with emotion. Based largely upon the work of Rolls in non-human primates and more recently in humans (Rolls, 1999; Rolls et al., 2003; see also work from our lab by Nitschke et al., 2004), the orbital sector of PFC can be thought of as cortex that computes affective value. It appears to track the hedonic response to a stimulus and not the stimulus properties itself. For example, OFC neurons will fire in response to food in a food-deprived animal. However, once the animal is fed to satiety, a completely different response in OFC is found to the identical food stimulus (Scott et al., 1995). In humans, similar effects have been reported. Unfortunately there has been very little attention paid to possible asymmetries in ventral and orbital sectors of PFC though there have been some suggestions of asymmetries in these regions OFC consistent with the general pattern observed in dorsolateral sectors but this needs to carefully studied (e.g., Kawasaki et al., 2001). And there is increasingly evidence, reviewed earlier, both from neuroimaging and lesion studies, of asymmetries in the ventrolateral sector of the PFC. It appears that right-sided ventrolateral PFC is particularly sensitive to cues for punishment and when damaged, patients display a profound insensitivity to such cues (e.g., Tranel et al., 2002). In the cognitive domain, this sector of PFC appears to be sensitive to stop cues that require the inhibition of behavior (Aron et al., 2003; Garavan et al., 1999; Konishi et al., 1999).

The ventromedial sector has been extensively studied by Damasio and colleagues (e.g., Damasio, 1994). They have suggested that ventromedial PFC provides a crucial substrate for affect-guided decision making. Patients with lesions in this area often have significant abnormalities in decision making. Based upon recent evidence in rodents, this sector of PFC may also play a very important role in modulation of the amygdale and extinction learning. Lesions in this region result in failures to exhibit normal patterns of extinction following the learning of a classically conditioned aversive association (Morgan et al., 2003). Whether there are functional asymmetries in this PFC sector and whether they behave in ways that are similar to those in the dorsolateral sector is something that critically needs study in future research.

Finally, I wish to end this section by raising the issue of the distal causes of individual differences in EEG measures of functional prefrontal asymmetry. Tomarken et al. (this issue) report the striking observation of relations between socioeconomic status (SES) and prefrontal asymmetry in adolescents. The lower the SES, the greater the relative right-sided prefrontal activity. Although there are clearly genetic influences on EEG measures of prefrontal asymmetry (Coan, 2003), we have suggested that environmental influences, particularly early in development, are likely to be present and to shape aspects of prefrontal function, including baseline measures of functional prefrontal asymmetry (Davidson et al., 2000a). At this stage, although the evidence for experience-dependent changes in prefrontal asymmetry in humans is strictly correlational and does not imply cause, the extant animal data that explicitly manipulates early environment finds both structural and functional asymmetric changes in prefrontal cortex (e.g., Lyons et al., 2002), thus clearly implying that important environmental influences on this circuitry are likely to exist in humans.

This very brief discussion is meant to underscore the importance of functional heterogeneity within the PFC and to call attention to the limitations of focusing either explicitly or in many cases, unwittingly, on just one sector of this massive expanse of cortex.

3. Empirical and methodological issues in the use of frontal EEG asymmetry measures in studies of emotional processes

3.1. Evidence of progress

The growing literature on methodological issues in the assessment of EEG asymmetry is leading to important advances that will improve the reliability and validity of these measures. The evidence presented in this Special Issue clearly establishes prefrontal EEG asymmetry measures as reflecting, at least in part, trait-like variations in brain function that appear to predict interesting and important features of affective style. As such, these measures have much to add to our current armamentarium of methods used to probe links between the brain and affect. Functional MRI (fMRI) is being used increasingly to study the neural basis of affect (see Davidson and Irwin, 1999; Murphy et al., 2003; Wager et al., 2003 for recent reviews). One important limitation of fMRI methods is that they cannot be used to make inferences about baseline levels of activity though perfusion MR methods could potentially be used for this purpose (Wang et al., 2003). An important direction for future research is the use of EEG asymmetry measures to predict individual differences in fMRI studies of localized neuronal activation patterns in response to affective challenges (see Shackman et al., 2003, from our lab for recent example). Another critical opportunity for future research is the use of source localization methods to more precisely describe the intracerebral sources of the scalp-recorded signals that we measure. Several recent studies from our lab illustrate the potential utility of these measures and underscore the differences in information yield when such source localization methods are utilized (e.g., Pizzagalli et al., 2002, 2003), although these methods have yet to be compared directly with functional neuroimaging data as I have suggested above. Also not yet evaluated is the differential reliability and validity of asymmetry metrics derived from direct surface recordings versus from source-localized intracerebral signals. And finally perfusion MRI can be used to obtain baseline data on localized cortical perfusion, and asymmetry can be computed from these measures and compared to EEG measures obtained from the same subjects.

3.2. *The problem of the reference electrode*

As several authors in this Special Issue have illustrated, the different reference electrode locations used in research on frontal EEG asymmetry continues to be a vexing problem. While some authors have demonstrated robust and consistent effects across different reference electrodes, this has not always been the case and it underscores the fact that EEG recordings reflect the potential difference between two locations and there is no electrically neutral location anywhere on the body. There still remains much methodological work to accomplish on this issue including the simultaneous assessment of brain electrical and hemodynamic or metabolic measures (see e.g., Goldman et al., 2002; Laufs et al., 2003). By using regional hemodynamic or metabolic measures as a gold standard against which to compare various EEG metrics, it may be possible to identify a set of procedures that consistently yields the most robust relations between brain electrical signals and more spatially precise measures of brain function. We have adopted this strategy and have begun to empirically dissect this complex issue and determine which EEG reference schemes and frequency bands most directly correlate with direct measures of regional glucose metabolism assessed with positron emission tomography (Oakes et al., 2004).

One issue of considerable importance to research on EEG measures of functional brain asymmetry is the use of the linked ears reference, a common choice in studies of frontal EEG asymmetry (see e.g., Minnix et al., this issue). As Allen et al. (this issue) correctly show, variations in electrode impedance cannot account for any detectable difference in signals across electrodes using modern high impedance amplifiers. This is true in all but one circumstance and that is when electrodes are linked *prior* to inputting the signal into the amplifier (Senulis and Davidson, 1989). Thus when a linked ears or mastoid montage is used, even slight variations in electrode impedance on each side can asymmetrically bias the signal. It is for this reason that we have suggested that a computer-averaged ears (or mastoids) reference be used if an investigator wishes to compute a linked ears or linked mastoid reference (see Davidson et al., 2000b).

3.3. *Frequency bands other than alpha*

It is striking that none of the articles in this Special Issue that focused on adult subjects included an analysis of frequency bands other than alpha. In several recent studies we have examined frequency bands other than alpha including theta, beta and gamma (Pizzagalli et al., 2001, 2002, 2003). In these studies, we also examined alpha power and in a number of cases, asymmetrical effects were found in bands other than alpha while effects in the alpha band were absent. Moreover, in our recent direct simultaneous comparison of EEG and PET measures of regional glucose metabolism (Oakes et al., 2004), we found that although alpha shows the predicted inverse relation with metabolism (see also Cook et al., 1998), the frequency band most consistently and strongly associated with glucose metabolism was gamma. Thus, although the frontal EEG asymmetry literature has traditionally focused on alpha power, it is important as we go forward to carefully examine other frequency bands as these may provide additional information not reflected in alpha power.

3.4. Bilateral variations in PFC are also important

Extant methods of analysis featured in the articles in this Special Issue emphasize, for the most part, asymmetrical variations in frontal brain activity. The computation of an asymmetry metric, while serving an important function, also masks the opportunity to examine bilateral variations in frontal brain activity. The sole exception in this group of articles is the Nitschke et al. (this issue) report; they illustrate the predictive value of bilateral variations in alpha power. It is important to underscore the fact that even if condition or group differences are found in asymmetry, such differences could be superimposed upon bilateral variations in activity and these bilateral variations in activity may be functionally significant (see e.g., Schmidt and Trainor, 2001). Future research in this area should include analysis methods that permit the systematic examination of bilateral variations in activation and assess the functional significance of such bilateral variations.

3.5. Importance of comparative research

Functional asymmetries are not the sole province of humans. Such asymmetries are found at many different levels of phylogeny (see Hugdahl and Davidson, 2003 for several reviews). And given the pervasive presence of affect at virtually all levels of phylogeny where behavior itself is observed, functional asymmetries associated with affective processes may be considerably more ubiquitous across the animal kingdom than asymmetries associated with language and communication. For example, there is a growing literature in rodents that is consistent with human data indicating a preferential role for regions of the right PFC in anxiety and withdrawal (see Berridge et al., 2003). In rhesus monkeys, we have recorded brain electrical activity from the scalp surface using procedures similar to those we use in humans and have found differences among animals in baseline levels of asymmetric prefrontal activity that are reliable over time and show systematic correlations with behavioral and biological measures that reflect anxiety and stressful responding (e.g., Kalin et al., 1998, 2000). Such animal models provide a foundation for research where lesions in particular regions of PFC can be made to establish the differential causal role of left and right prefrontal regions in specific types of affective behavior.

4. Summary and conclusions

This commentary provides some reflections on the current state of affairs in research on EEG frontal asymmetries associated with emotion. The first part addresses a series of conceptual issues and the second part some empirical and methodological issues. Of prime important for the future of EEG asymmetry research is that it make more meaningful contact with the growing corpus of literature on primate prefrontal function. One of the most lamentable characteristics of the current work on frontal EEG asymmetry is that it has evolved largely unconnected with the neuroscience literature on the structure and function of the PFC. Scalp-recorded measures of prefrontal activity likely reflect primarily dorsolateral PFC function, yet the PFC is anatomically and functionally heterogeneous. Careful consideration of this issue and developing hypotheses based upon findings from the neuroscience literature should aid future progress. Another critical issue is the fact that the PFC is embedded in a complex circuit involving other cortical and subcortical structures and these other structures likely play a very important role in many of the affective processes featured in the articles in this Special Section. However, because the EEG measures that are utilized in these studies do not directly reflect activity in other parts of the circuitry, these other neural components have, for the most part, been ignored by those investigators who study frontal EEG. Much of the research on frontal EEG asymmetry has examined the correlates of variations in asymmetry with self-report measures. While these reported associations have been interesting, they are typically not informative with regard to mechanism because the specific types of processes affected by prefrontal function are likely to themselves be opaque to self-report. Thus, while they influence self-report (such as variations in the time to recovery following a negative event), they are not themselves consciously accessible and thus such self-report measures will ultimately be uninformative if we hope to build neurally-inspired theory. The approach-withdrawal model of frontal asymmetry (see e.g., Davidson, 1992) receives considerable support from numerous studies in this Special Issue, most especially from Harmon-Jones, with his findings on anger. The provocative question of whether or not high levels of baseline left prefrontal activity, in light of the Harmon-Jones findings, still should be considered to be a positive trait, is addressed, with a tentative affirmation, despite the findings on anger. Finally, some discussion of what different sectors of the PFC might be doing in emotion is introduced.

In the second section of this essay, several methodological issues are considered including problems with the linked ears or mastoids reference, the importance of examining frequency bands other than alpha, using analytic methods that permit bilateral variations in frontal activity to be assessed, and some comments on the importance of comparative research to address some of the fundamental outstanding questions in this line of research.

The fact of this Special Issue is a testament to the enormous progress that has occurred in this area of research. It will be exciting to revisit this topic in 5 years since with the advent of new methods such as functional neuroimaging, particularly when they are combined with traditional psychophysiological measures (Davidson, 2003b), very rapid and novel progress can be expected.

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