Darwin and the Neural Bases of Emotion and Affective Style

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ABSTRACT: This article presents an overview of ways to think about the brain and emotion and consider the role of evolution and expression in shaping the neural circuitry of affective processing. Issues pertaining to whether there are separate unique neural modules hard-wired for emotion processing or whether affective processing uses more generalized circuitry are considered. Relations between affect and cognition—specifically, memory—are examined from the perspective of overlapping neural systems. The role of individual differences in neural function in affective style are discussed, and the concepts of affective chronometry, or the time course of emotional responding and emotion regulation, are introduced. Finally, the extent to which certain emotional traits can be viewed as trainable skills is considered, and the relevance of work on neural plasticity to the skill framework is addressed. Data from a variety of sources using different types of measures is brought to bear on these questions, including neuroimaging and psychophysiological measures, studies of individuals of different ages ranging from early childhood to old age, studies of nonhuman primates, and observations of patients with localized brain damage. Emotions are viewed as varying in both type and dimension. Honoring brain circuitry in parsing the domain of affects will result in distinctions and differentiations that are not currently incorporated in traditional classification schemes.

KEYWORDS: Darwin; emotion; affective processing; affective style; emotion regulation

Darwin's *Expression of Emotion in Man and Animals*[1] contained the seeds that have since blossomed into what now is generally called *affective neuroscience*. Darwin was extraordinarily prescient in his observations and predictions about the nervous system and emotion, though it has taken more than 100 years to witness the embryonic development of a neuroscience of emotion. The reasons for the long period of development are numerous and

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complex, but they are in part a function of the paucity of methods for interrogating the intact nervous system for much of the 20th century. The advent of neuroimaging has changed the landscape and has contributed, among other recent trends, to the rapid acceleration of knowledge in affective neuroscience. This essay will review some promising new developments in our understanding of the neural basis of emotion and individual differences in emotional reactivity and emotion regulation subsumed under the rubric of affective style. Throughout this review, suggestions made by Darwin in his classic 1872 monograph will be highlighted, and I will attempt to illustrate how they have come to be studied in contemporary affective neuroscience. I will mostly use examples from recent work in my laboratory but will also selectively refer to work of others where relevant.

Darwin's third principle is the "direct action of the excited nervous system on the body, independently of the will…" It is in this principle that Darwin declares his psychophysiological position and expresses his conjecture that much of the neural signaling about emotion from the brain to the body bypasses the will and is thus often nonconscious. Modern research in affective neuroscience has delineated circuitry that includes both cortical and subcortical territories implicated in different components of affective processing. Most investigators in this area now include at least the following brain regions in the circuitry that participates in most emotion: prefrontal cortex (PFC; multiple territories of the PFC are implicated and will be discussed below); amygdala; anterior cingulate; hippocampus; and insula. In several recent publications, I have discussed the functional contributions of each of these brain regions to affective processing.[2–4] In this essay, emphasis will be given to the prefrontal cortex and amygdala. An important challenge for modern research in affective neuroscience is anticipated by Darwin's intuition that most of our emotions are inextricably entwined with their expression. The dominant methods of affective neuroscience, at both the animal and human levels, most often precludes the natural full-blown expression of the emotions. Thus the data that we have are necessarily constrained and rarely include epochs of very intense emotion. Nevertheless, some consistent trends have emerged and will be highlighted below.

FUNCTIONAL NEUROANATOMY OF AFFECTIVE PROCESSING: PREFRONTAL CORTEX AND AMYGDALA

Prefrontal Cortex

Although the prefrontal cortex is often considered to be the province of higher cognitive control, it has also consistently been linked to various features of affective processing (see, e.g., ref. 5 for an early preview). Miller and

Cohen[6] have recently outlined a comprehensive theory of prefrontal function based upon nonhuman primate anatomical and neurophysiological studies, human neuroimaging findings, and computational modeling. The core feature of their model holds that the PFC maintains the representation of goals and the means to achieve them. Particularly in situations that are ambiguous, the PFC sends bias signals to other areas of the brain to facilitate the expression of task-appropriate responses in the face of competition with potentially stronger alternatives. In the affective domain, we often confront situations in which the arousal of emotion is inconsistent with other goals that have already been instantiated. For example, the availability of an immediate reward may provide a potent response alternative that may not be in the best service of the overall goals of the person. In such a case, the PFC is required to produce a bias signal to other brain regions that guide behavior toward the acquisition of a more adaptive goal, which in this case would entail delay of gratification. Affect-guided planning and anticipation that involves the experience of emotion associated with an anticipated outcome is the hallmark of adaptive, emotion-based decision making. Patients with lesions to certain zones of the PFC, particularly the ventromedial PFC, have been shown to exhibit profoundly impaired decision making.[7] Affect-guided anticipation is most often accomplished in situations that are heavily laden with competition from potentially stronger alternatives. In such cases in particular, we would expect PFC activation to occur. Certain disorders of emotional processing such as depression may be caused by abnormalities of affect-guided anticipation. For example, the failure to anticipate positive incentives and direct behavior toward the acquisition of appetitive goals are symptoms of depression that may arise from abnormalities in the circuitry that implements positive affect-guided anticipation. Our laboratory has contributed extensively to the literature on asymmetries in PFC function associated with approach- and withdrawal-related emotion and mood.[4,8] In this context, we suggest that left-sided PFC regions are particularly involved in approach-related, appetitive goals. The instantiation of such goals, particularly in the face of strong alternative responses, requires left-sided PFC activation; and hypoactivation in these circuits has been linked to depression. Right-sided PFC regions, alternatively, are hypothesized to be particularly important in behavioral inhibition and vigilant attention that often accompanies certain aversive emotional states and traits. Whether right-sided PFC activation is a core feature underlying withdrawal behavior in general, or behavioral inhibition and vigilant attention more specifically, is a question to which we still do not have an adequate answer. The prototype of the behavioral inhibition process, which we have hypothesized to be subserved by specific right PFC mechanisms, has recently been captured in several neuroimaging studies that involve variants of a go/no-go task, where a dominant response set is established to respond quickly, except for those trials in which a cue to inhibit the response is presented. Two recent studies using event-related functional

MRI (fMRI) have found a lateralized focus of activation in the right lateral PFC (inferior frontal sulcus) to cues that signaled response inhibition that were presented in the context of other stimuli toward which a strong approach set was established.[9,10] This is the same region of right lateral PFC that has been found to be activated in a number of neuroimaging studies in which withdrawal-related negative affect has been elicited.[4]

Depressed individuals with hypoactivation in certain regions of the PFC may be deficient in the instantiation of goal-directed behavior and in the overriding of more automatic responses that may involve the preservation of negative affect and dysfunctional attitudes. Such deficits would be expected to be unmasked in situations where decision making is ambiguous and where the maintenance of goal-directed behavior is required in the face of potentially strong alternative responses. As we will argue below, when the strong alternative responses involve affect, which they often do, the ventromedial PFC is particularly implicated.

Recent neuroimaging and electrophysiological studies suggest that the orbital and ventral frontal cortex in particular may be especially important for the representation of rewards and punishments, and different sectors within this cortex may emphasize reward versus punishment.[11–12] In particular, a left-sided medial region of the orbitofrontal cortex (OFC) appears particularly responsive to rewards, while a lateral right-sided region appears particularly responsive to punishments.[12] Kawasaki and colleagues[11] recorded from single units in the right ventral PFC of patients with implanted depth electrodes for presurgical planning. They found these neurons in healthy tissue to exhibit short-latency responses to aversive visual stimuli. Such studies provide important clues regarding the circuitry that might be most relevant to understanding differences among individuals in affective style. For example, there are individual differences in responsivity to rewards versus punishments that can be probed behaviorally using signal detection methods.[13,14] Most normal individuals exhibit systematic modification of response bias to monetary reward, but some do not. Those who do not showed elevated depressed mood. We would also predict that left medial OFC would be hyporesponsive to manipulations of reward in such individuals, while right lateral OFC to punishment would either be normal or perhaps accentuated.

AMYGDALA

Although a link between amygdala activity and negative affect has been a prevalent view in the literature, particularly when examined in response to exteroceptive aversive stimuli,[15] recent findings from invasive animal studies and human lesion and functional neuroimaging studies are converging on a broader view that regards the amygdala's role in negative affect as a special case of its more general role in directing attention to affectively salient stim-

uli and issuing a call for further processing of stimuli that have major significance for the individual. Extant evidence is consistent with the argument that the amygdala is critical for recruiting and coordinating cortical arousal and vigilant attention for optimizing sensory and perceptual processing of stimuli associated with underdetermined contingencies, such as novel, "surprising," or "ambiguous" stimuli (see also refs. 16–18). Most stimuli in this class may be conceptualized as having an aversive valence since we tend to have a negativity bias in the face of uncertainty.[19]

The role of the amygdala in the activation of cortex for further processing of salient stimuli may be most apparent in the visual system. Darwin commented in several places in *Expression* on the importance of the visual modality for both identifying prey and avoiding danger. A number of recent studies have found that when visual emotional stimuli are compared with visual nonemotional stimuli that are matched to basic visual characteristics, the visual cortex is more activated in response to the emotional compared with the nonemotional stimuli (see refs. 20,21). We and others have speculated that the increase in activation in visual cortex in response to emotional stimuli may be a function of back projections from the amygdala to primary visual cortex. Amaral and his colleagues[22] have identified pathways in the macaque brain that connect the basolateral region of the amygdala all the way down to V1 in primary visual cortex. This provides a mechanism whereby visual information processing can be modulated by affect-related signals from the amygdala.

Both structural and functional differences in the amygdala have been reported in disorders of emotion, particularly depression. Structurally, several recent studies reported an association between enlargement of amygdala volume and depression. This association has been found in depressed patients with bipolar disorder[23,24] as well as temporal lobe epilepsy (TLE).[25,26] In a recent study, Mervaala *et al*.[27] observed significant asymmetry in amygdalar volumes (right smaller than left) in patients with major depressive disorder (MDD) but not the controls. In TLE patients with dysthymia, left amygdala volume was positively correlated with depression severity, as assessed with the Beck Depression Inventory.[25] Although these findings depict a relation between increased amygdalar volume and depression, it is important to stress that (a) the causal relations between the two entities are still unknown, and (b) some inconsistencies among studies are present. Indeed, some studies reported either *decreased* bilateral volume in the amygdala core nuclei[28] or null findings.[29–31] Although the reasons are still unclear, it is interesting to note that two null findings were found in geriatric depression.[30,31]

Functionally, abnormal elevations of resting rCBF or glucose metabolism in the amygdala have been reported in depression during both wakefulness[32] and sleep.[33,34] In an FDG-PET study, Ho *et al*.[33] reported increased absolute cerebral glucose metabolic in several brain regions, particularly the amygdala (+44%), in 10 unmedicated men with unipolar depression during non-REM

sleep period. Further, in his recent review, Drevets[35] reports data from five consecutive studies in which increased rCBF or glucose metabolism has been consistently replicated in depressives with familial MDD or melancholic features. In a postmortem study, 5-HT2 receptor density was significantly increased in the amygdala of depressive patients committing suicide.[36] Abnormally increased amygdalar activation has also recently been reported in bipolar depression[37] and anxiety disorders, which often show a high degree of comorbidity with depression.[38–44] Further establishing a link between depression and amygdalar activation, two studies have reported a positive correlation between amygdalar activation and depression severity or dispositional negative affect in patients with MDD.[32,45] After pharmacologically induced remission from depression, amygdalar activation has been observed to decrease to normative values.[46] In familial pure depressive disease, however, increased (left) amygdalar activation persists during the remitted phases,[32] suggesting that at least in some subtypes of depression amygdalar dysfunction may be trait-like. Interestingly, remitted MDD patients showing symptom relapse as a consequence of serotonin depletion showed increased amygdalar activation *prior* to the depletion compared to those who will not relapse.[47] Finally, in one of the first fMRI studies using an activation paradigm, Yurgelun-Todd *et al*.[48] reported higher left amygdalar activation for bipolar patients than controls in response to fearful faces.

In light of the pivotal role of the amygdala in recruiting and coordinating vigilant behavior toward stimuli with underdetermined contingencies, hyperactivation of the amygdala in major depression may bias initial evaluation of and response to incoming information. Although still speculative, this mechanism may rely on norepinephrine, which (a) is oftentimes abnormally elevated in depression,[49] (b) is involved in amygdala-mediated emotional learning,[50] and (c) is affected by glucocorticoid secretion, which is often elevated in MDD.[51] Thus, these findings may explain cognitive biases towards aversive or emotionally arousing information observed in depression.

Increased amygdalar activation in depression may also represent a possible biological substrate for anxiety, which is often comorbid with depression. In this respect, elevated levels of glucocortocoid hormones—which characterize at least some subgroups of patients with depression—may be especially relevant, since elevated glucocorticoid hormones have been shown to be associated with increased corticotropin-releasing hormone (CRH) in the amygdala. Increased CRH availability may increase anxiety, fear, and expectation for adversity.[52]

In light of evidence suggesting a link between amygdalar activation on the one hand and memory consolidation and acquisition of long-term declarative knowledge about emotionally salient information on the other hand, the observations of dysfunctionally increased amygdalar activation in major depression are intriguing. As recently pointed out by Drevets *et al*.,[46] tonically *increased* amygdalar activation during depressive episodes may favor the emergence of

rumination based on increased availability of emotionally negative memories. Although still untested, it is possible that these aberrant processes may rely on dysfunctional interactions between the amygdala, the PFC, and the anterior cingulate cortex (ACC). Notably, structural abnormalities have been reported in territories of the PFC intimately connected with the ACC.[53,54] Recent functional imaging data implicate abnormalities in ACC function in depression.[21,55] ACC dysfunction, in particular, may lead to a decreased capability of monitoring potential conflict between memory-based ruminative processes and sensory information coming from the environment.

AFFECTIVE STYLE

Darwin admonished his readers to pay attention to individual differences. For example, early in *Expression* Darwin noted "…the insane ought to be studied, for they are liable to the strongest passions, and give uncontrollable vent to them" (p. 13).[1] He also underscored the importance of developmental differences in emotional reactivity for similar reasons. In this section, I will review one modern approach to the study of individual differences in emotional reactivity and emotion regulation, subsumed under the term *affective style*. This corpus of work includes the study of both normal individual variation as well as pathological extremes of such variation. The study of affective style has proceeded in individuals throughout the life span.

In several recent publications, I have suggested that the term affective style be used to denote a broad range of individual differences in different parameters of emotional reactivity. Davidson[56,57] has defined affective style as valence-specific features of emotional reactivity and affective responding. Specific parameters of affective style can be objectively measured including: (a) the threshold to respond; (b) the magnitude of the response; (c) the rise time to the peak of the response; (d) the recovery function of the response; (e) the duration of the response. The last three parameters all refer to different aspects of affective chronometry or the time course of emotional responding. We have proposed that time course variables are particularly germane to understanding individual differences that may reflect vulnerability to psychopathology since certain forms of mood and anxiety disorders may be specifically associated with either a failure to turn off a response sufficiently quickly and/or an abnormally early onset of the response that may then result in a bypassing of normal regulatory constraints. The specific parameters of affective style described above all jointly govern in a complex fashion the dispositional mood and other reportable characteristics that reflect affective style. In this section, data from my laboratory pertaining to relations between individual difference in both prefrontal and amygdala function and their relation to measures that reflect affective style will be summarized.

In both infants[58] and adults[59] there are large individual differences in baseline electrophysiological measures of prefrontal activation, and such individual variation is associated with differences in aspects of affective reactivity. In infants, Davidson and Fox[58] reported that 10-month babies who cried in response to maternal separation were more likely to have less left- and greater right-sided prefrontal activation during a preceding resting baseline compared with those infants who did not cry in response to this challenge. In adults, we first noted that the phasic influence of positive and negative emotion elicitors (e.g., film clips) on measures of prefrontal activation asymmetry appeared to be superimposed upon more tonic individual differences in the direction and absolute magnitude of asymmetry.[59]

During our initial explorations of this phenomenon, we needed to determine if baseline electrophysiological measures of prefrontal asymmetry were reliable and stable over time and thus could be used as a trait-like measure. Tomarken *et al.*[60] recorded baseline brain electrical activity from 90 normal subjects on two occasions separated by approximately three weeks. At each testing session, brain activity was recorded during eight 1-minute trials, four with eyes open and four with eyes closed, presented in counterbalanced order. The data were visually scored to remove artifact and then Fourier-transformed. Our focus was on power in the alpha band (8–13 Hz), though we extracted power in all frequency bands (see refs. 61 and 62 for methodological discussion). We computed coefficient alpha as a measure of internal consistency reliability from the data for each session. The coefficient alphas were quite high, with all values exceeding .85, indicating that the electrophysiological measures of asymmetric activation indeed showed excellent internal consistency reliability. The test-retest reliability was adequate, with intraclass correlations ranging from .65 to .75, depending upon the specific sites and methods of analysis. The major conclusion from this study was the demonstration that measures of activation asymmetry based upon power in the alpha band from prefrontal scalp electrodes showed both high internal consistency reliability and acceptable test-retest reliability to be considered a trait-like index. Similar findings have recently been obtained by Hagemann *et al.*[63]

On the basis of our prior data and theory, we reasoned that extreme left and extreme right frontally activated subjects would show systematic differences in dispositional positive and negative affect. We administered the trait version of the Positive and Negative Affect Scales (PANAS)[64] to examine this question and found that the left frontally activated subjects reported more positive and less negative affect than their right frontally activated counterparts.[60] More recently with Sutton[65] we showed that scores on a self-report measure designed to operationalize Gray's concepts of Behavioral Inhibition and Behavioral Activation (the BIS/BAS scales)[66] were even more strongly predicted by electrophysiological measures of prefrontal asymmetry than were scores on the PANAS scales. Subjects with greater left-sided prefrontal activation reported more relative BAS-to-BIS activity compared with subjects

exhibiting more right-sided prefrontal activation. Independently, Harmon-Jones and Allen[67] published findings that were consistent with Sutton and Davidson;[65] but see Hagemann *et al*.[68] and Davidson[69] for complications associated with attempts to replicate these basic findings.

We also hypothesized that our measures of prefrontal asymmetry would predict reactivity to experimental elicitors of emotion. The model that we have developed over the past several years (see refs. 56 and 70-72 for background) features individual differences in prefrontal activation asymmetry as a reflection of a diathesis that modulates reactivity to emotionally significant events. According to this model, individuals who differ in prefrontal asymmetry should respond differently to an elicitor of positive or negative emotion, even when baseline mood is partialled out. We[73,74] performed an experiment to examine this question. We presented short film clips designed to elicit positive or negative emotion. Brain electrical activity was recorded prior to the presentation of the film clips. Just after the clips were presented, subjects were asked to rate their emotional experience during the preceding film clip. In addition, subjects completed scales that were designed to reflect their mood at baseline. We found that individual differences in prefrontal asymmetry predicted the emotional response to the films even after measures of baseline mood were statistically removed. Those individuals with more left-sided prefrontal activation at baseline reported more positive affect to the positive film clips, and those with more right-sided prefrontal activation reported more negative affect to the negative film clips. These findings support the idea that individual differences in electrophysiological measures of prefrontal activation asymmetry mark some aspect of vulnerability to positive and negative emotion elicitors. The fact that such relations were obtained following the statistical removal of baseline mood indicates that any difference between left and right frontally activated subjects in baseline mood cannot account for the prediction of the film-elicited emotion effects that were observed.

The relation between individual differences in brain electrical measures of prefrontal activation asymmetry and depression is a topic that has received extensive treatment in several recent articles. There has been a failure to replicate[75] our initial findings of decreased left prefrontal activation in depression,[76–78] though there have also been several published independent replications or conceptual replications (e.g., refs. 79 and 80). Moreover, using positron emission tomography, Baxter and colleagues (e.g., ref. 81) have reported decreased activation in regions of left dorsolateral prefrontal cortex that were associated with depression severity (i.e., lower glucose metabolic rate predicted increased severity). Drevets and his colleagues[53] reported decreased activation in the subgenual prefrontal cortex in patients with depression that was more left sided, though the laterality of this finding is equivocal because of its proximity to the midline. Drevets and colleagues[53] also reported a highly significant reduction in gray matter volume in the left subgenual

PFC region. We have interpreted the decrease in left-sided prefrontal activation as a diathesis related to deficits in the approach system and in reward-related responding.[13,14] We also argued that this pattern of left prefrontal hypoactivation would be found only in certain subgroups of mood-disordered patients in light of the heterogeneity of the disorder (see ref. 69 for an extended discussion of both conceptual and methodological issues germane to this area). Most importantly, we have suggested that it is crucial to move beyond descriptive phenomenology and to examine with objective laboratory methods variations in reactivity to emotion elicitors in individuals with this hypothesized diathesis. We have proposed that individuals who display left prefrontal hypoactivation will show specific deficits in reactivity to reward, though the need to consider other components of the circuitry with which the prefrontal cortex is interconnected must be underscored in any effort to understand the neural bases of emotion and its disorders.

In addition to the studies described above using self-report and psychophysiological measures of emotion, we have also examined relations between individual differences in electrophysiological measures of prefrontal asymmetry and other biological indices that in turn have been related to differential reactivity to stressful events. Three recent examples from our laboratory include measures of immune function, cortisol, and corticotropin-releasing hormone. The latter two measures represent key molecules in the activation of a coordinated response to stressful events. Our strategy in each case was to examine relations between individual differences in measures of prefrontal activation asymmetry and these other biological indices. In two separate studies[82,83] we examined relations between the prefrontal activation indices and natural killer (NK) activity since declines in NK activity have been reported in response to stressful, negative events.[84] We predicted that subjects with greater right prefrontal activation would exhibit lower NK activity compared with their left-activated counterparts because the former type of subject has been found to report more dispositional negative affect, to show higher relative BIS activity, and to respond more intensely to negative emotional stimuli. In each of the two studies conducted with independent samples, we found that right frontally activated subjects indeed had lower levels of NK activity compared to their left frontally activated counterparts.[82,83] We also examined the magnitude of change in NK activity in response to stress and found that subjects with greater baseline levels of right prefrontal activation showed the largest-magnitude decline in NK activity compared with other subjects.[83] Very recently, we[85] have extended this work to include measures of *in vivo* immune function. In a sample of 52 subjects between the ages of 57 and 60 years, we measured prefrontal activation asymmetry according to our usual methods. In addition, we administered an influenza vaccine and measured antibody titers in response to the vaccine at several intervals following vaccination. We found that subjects with greater left-sided prefrontal activation at both baseline and in response to a negative affect challenge had

greater antibody titers in response to influenza vaccine, suggesting more robust immunity in response to vaccination.

In collaboration with Kalin, our laboratory has been studying similar individual differences in scalp-recorded measures of prefrontal activation asymmetry in rhesus monkeys.[86,87] Recently, we[88] acquired measures of brain electrical activity from a large sample of rhesus monkeys ($N = 50$). EEG measures were obtained during periods of manual restraint. A subsample of 15 of these monkeys was tested on two occasions four months apart. We found that the test-retest correlation for measures of prefrontal asymmetry was .62, suggesting similar stability of this metric in monkey and man. In the group of 50 animals, we also obtained measures of plasma cortisol during the early morning. We hypothesized that if individual differences in prefrontal asymmetry were associated with dispositional affective style, such differences should be correlated with cortisol, since individual differences in baseline cortisol have been related to various aspects of trait-related stressful behavior and psychopathology (see, e.g., ref. 89). We found that animals with right-sided prefrontal activation had higher levels of baseline cortisol than their left frontally activated counterparts (see FIG. 1). As can be seen from the figure, it is the left-activated animals that are particularly low compared with both middle- and right-activated subjects. Moreover, when blood samples were collected two years following our initial testing, animals classified as showing extreme right-sided prefrontal activation at age one year had significantly higher baseline cortisol levels when they were three years of age compared with animals who were classified at age one year as displaying extreme left-sided prefrontal activation. Similar findings were obtained with cerebrospinal fluid levels

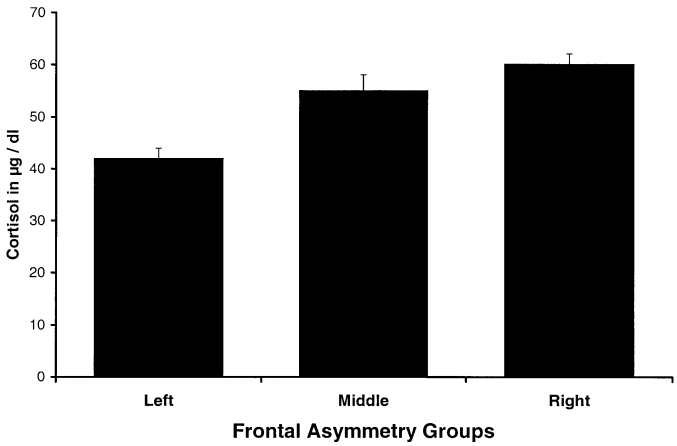

FIGURE 1. Basal morning plasma cortisol from one-year-old rhesus monkeys classified as left ($N = 12$), middle ($N = 16$), or right ($N = 11$) frontally activated based upon electrophysiological measurements. (Reprinted from Kalin *et al.*[88] with permission.)

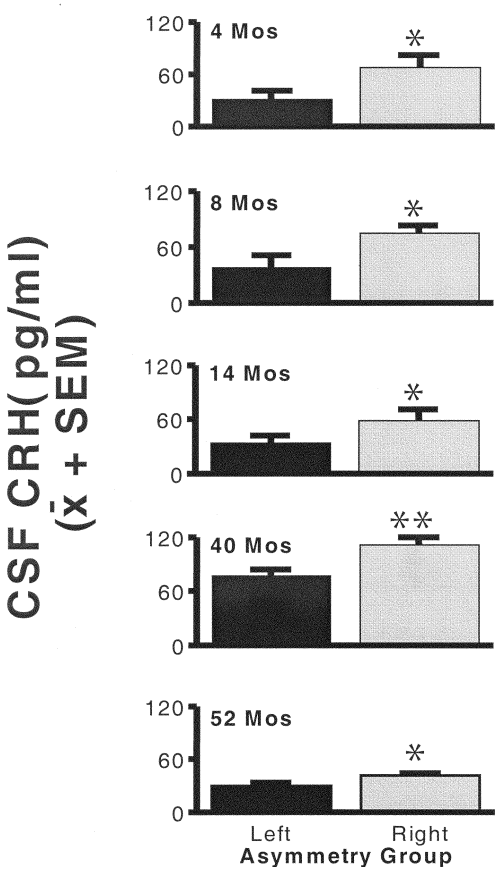

FIGURE 2. Differences between right ($N = 9$) and left prefrontally ($N = 10$) activated animals in cerebrospinal fluid measures of corticotropin-releasing hormone at five different ages. The original classification of the animals as extreme right or left activated was performed on the basis of brain electrical activity data collected when the animals were 13 months of age. (Reprinted from Kalin *et al.*[90] with permission.)

of CRH. Those animals with greater right-sided prefrontal activation showed higher levels of CRH (see FIG. 2).[90] These findings indicate that individual differences in prefrontal asymmetry are present in nonhuman primates and that such differences predict biological measures that are related to affective style.

As noted earlier, there are several regions of the PFC that play important roles in emotion. The OFC has been implicated as a primary region for decoding the affective value of stimuli.[91] Scalp-recorded brain electrical measures are not ideal for detecting activation in these more inferior regions of PFC. In a recent study, we[92] used fMRI to probe the OFC for individual dif-

ferences in a more subtle emotion, one that Darwin suggested was not associated with a specific expression. Darwin noted that "Although the emotion of love, for instance that of a mother for her infant, is one of the strongest of which the mind is capable, it can hardly be said to have any proper or peculiar means of expression…" (pp. 212–213).[1] To investigate individual differences in love between mother and infant, we brought primiparous mothers into the laboratory with their infants when the infants were 3–4 months of age. We photographed the infants and then used these photos in a subsequent scanning session during which the mothers were presented with pictures of their own infants and pictures of unrelated infants in a block design. We also had mothers rate their mood in response to seeing each type of photo. We found that the greater the increase in feelings of love, affection, and warmth that the mothers reported in response to seeing their own infants (compared with viewing unrelated infants), the greater the activation of the OFC. We used visual cortex as a control region to establish that the effects were indeed specific to OFC; and although visual cortex showed greater activation to pictures of own versus other infants, activation in this region was uncorrelated with feelings of love and other positive emotions reported by the mothers. These findings indicate that despite the lack of a unique expressive signal associated with love, sensitive measures of brain function do indeed reflect this emotion.

With the advent of neuroimaging, it has become possible to investigate the relation between individual differences in aspects of amygdala function and measures of affective style. We have used PET with flourodeoxyglucose (FDG) as a tracer to investigate relations between individual differences in glucose metabolism in the amygdala and dispositional negative affect. FDG-PET is well-suited to capture trait-like effects since the period of active uptake of tracer in the brain is approximately 30 minutes. It is inherently more reliable than O15 blood-flow measures because the FDG data reflect activity aggregated over a 30-minute period. We have used resting FDG-PET to examine individual differences in glucose metabolic rate in the amygdala and its relation to dispositional negative affect in depressed subjects.[45] We acquired a resting FDG PET scan as well as a structural MR scan for each subject. The structural MR scans are used for anatomical localization by coregistering the two image sets. Thus, for each subject, we used an automated algorithm to fit the MR scan to the PET image. Regions of interest (ROI's) were then drawn on each subject's MR scan to outline the amygdala in each hemisphere. These ROI's were drawn on coronal sections of subjects' MR images, and the ROI's were then automatically transferred to the coregistered PET images. Glucose metabolism in the left and right amygdala ROI's were then extracted. The interrater reliability for the extracted glucose metabolic rate is highly significant, with intraclass correlations between two independent raters $\geq .97$. We found that subjects with greater glucose metabolism in the right amygdala report greater dispositional negative affect on the PANAS scale. These findings indicate that individual differences in resting glucose

metabolism in the amygdala are present and that they predict dispositional negative affect among depressed subjects.

In a small sample of 12 normal subjects, we[93] have been able to examine the relation between the magnitude of MR signal change in the amygdala in response to aversive compared with neutral pictures and dispositional negative affect on the PANAS scale. We correlated the average value of the pixels with the maximum Student's *t* from the left and right amygdala with dispositional negative affect. There was a robust correlation such that increased signal intensity in the right amygdala was associated with higher levels of negative affect. A pixel in the fusiform gyrus that revealed robust activation by the aversive pictures was selected as a control region. We correlated the magnitude of activation in the pixel showing the maximal response in this region to the aversive pictures with dispositional negative affect and found no relation ($P > 0.5$). Moreover, the correlations in the amygdala and fusiform gyrus were found to be significantly different. The findings from the fMRI and PET studies of amygdala function indicate that individual differences in both tonic activation and phasic activation in response to aversive stimuli predict the intensity of dispositional negative affect.

EMOTION REGULATION: A KEY COMPONENT OF AFFECTIVE STYLE

One of the key components of affective style is the capacity to regulate negative emotion and specifically to decrease the duration of negative affect once it arises. We have suggested in several recent articles that the connections between the PFC and amygdala play an important role in this regulatory process.[3,4,56,57] In two recent studies, we[94,95] examined relations between individual differences in prefrontal activation asymmetry and the emotion-modulated startle. In these studies, we presented pictures from the *International Affective Picture System*[96] while acoustic startle probes were presented and the EMG-measured blink response from the orbicularis oculi muscle region was recorded (see ref. 97 for basic methods). Startle probes were presented during the slide exposure as well as at various latencies following the cessation of the pictures, on separate trials. We interpreted startle magnitude during picture exposure as providing an index related to the generation of the emotional response, while startle magnitude following the *cessation* of the pictures was taken to reflect the recovery from emotional challenge. Used in this way, startle probe methods can potentially provide new information on the time course of emotional responding. We expected that individual differences during actual picture presentation would be less pronounced than individual differences following picture presentation since an acute emotional stimulus is likely to pull for a normative response across subjects, while in-

dividuals are more likely to differ once the stimulus has terminated. Similarly, we predicted that individual differences in prefrontal asymmetry would account for more variance in predicting magnitude of recovery (i.e., startle magnitude poststimulus) than in predicting startle magnitude during the stimulus. Our findings in both studies were consistent with our predictions and indicated that subjects with greater right-sided prefrontal activation show a larger blink magnitude following the cessation of the negative stimuli, after the variance in blink magnitude *during* the negative stimulus was partialled out. Measures of prefrontal asymmetry did not reliably predict startle magnitude during picture presentation. The findings from this study are consistent with our hypothesis and indicate that individual differences in prefrontal asymmetry are associated with the time course of affective responding, particularly the recovery following emotional challenge. In a related study, we have found that subjects with greater baseline levels of left prefrontal activation are better able to voluntarily suppress negative affect.[98,99] Moreover, in an initial study using fMRI we have demonstrated that when subjects are instructed to voluntarily regulate their negative emotion, reliable changes in amygdala signal MR signal intensity are found.[100]

The findings from these studies indicate that individual differences in prefrontal activation may play an important role in emotion regulation. Individuals who report greater dispositional negative affect and who show increased reactivity to stressful events are more likely to be those individuals who have difficulty regulating negative affect and specifically in modulating the intensity of negative affect once it has been activated.

SUMMARY AND CONCLUSIONS

Darwin was a remarkable observer, and many of his observations presaged important research questions that are now central in affective neuroscience. One of Darwin's great contributions was the comparative study of emotion and his observations of expressive behavior and emotional processes in animals. This work provided an important foundation for the examination of the neural systems underlying emotion in nonhuman species. This corpus of evidence has been crucial in catalyzing the study of the neuroscience of emotion in humans using neuroimaging and related methods. Progress has been rapid over the past decade because of a remarkable convergence between findings at the animal and human levels. Although Darwin implicitly recognized the importance of individual differences in emotion by calling attention to possible sex differences, developmental differences, and differences between normal subjects and patients with psychiatric disorders, he did not systematically treat this issue. As this essay has documented, it is now possible to rigorously interrogate the brain circuitry underlying individual differences in emotional

reactivity with neuroimaging. Another topic not addressed by Darwin but that is now central to understanding emotion is the process of emotion regulation. Darwin implicitly acknowledged its importance by suggesting that emotions were less controllable for the "insane." Emotion regulation is likely ubiquitous and overlaps in time with the actual generation of emotion (see ref. 2 for review), making it difficult to isolate and distinguish from emotion per se. However, new paradigms have recently been developed that offer some promise in the study of both automatic and voluntary emotion regulation (see ref. 62), and they illustrate the importance of this construct for understanding individual differences in both normal and pathological emotion.

Darwin's powerful insights and extraordinary observations in *Expression* still stimulate and guide research on emotion, especially work on the neural substrates of emotion. Darwin recognized that emotions, unlike most other psychological processes, are instantiated in both the brain and the body. For him, both the heart and the brain were keys to understanding emotion; future research must be directed to the study of how the heart and brain interact during emotion. Darwin explained that "…when the heart is affected it reacts on the brain…so that under any excitement there will be much mutual action and reaction between these, the two most important organs of the body" (p. 69).[1]

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