The Neuroimaging of Emotion

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Running Head: NEUROIMAGING OF EMOTION

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Questions about the nature of emotion have existed since psychology emerged as a scientific discipline in the late nineteenth century (Darwin, 1898; Dewey, 1895; Irons, 1897; James, 1884). For a century, scientists were unable to measure emotions at their source, and so relied on measures of behavior, reported experience, and activity of the peripheral nervous system to address fundamental questions about what emotions are and how they function in the economy of the mind. While much has been learned that is of both scientific interest and practical value, questions about the nature of emotion remained fundamentally unresolved. The relatively recent introduction of neuroimaging techniques, particularly functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), provide a new perspective on the emotion in the intact human brain, and have the potential to identify which brain areas are consistently and specifically associated with particular types of emotional states. Fifteen years of neuroimaging research has investigated the neural underpinnings of emotions including responses to basic affective stimuli such as pictures or odors, the experience and regulation of the discrete emotional events that we refer to as disgust, anger, and desire, and the perception of emotion in others. These findings have the potential to shed new light on what emotions are and how they work.

We begin this chapter by sketching a hypothesized "neural reference space" for emotion (Barrett, Mesquita, Ochsner, & Gross, 2007; Edelman & Tononi, 2001), which refers to the set of brain structures thought to instantiate emotions and related affective states. We then examine how findings from neuroimaging studies map onto this space, and what they contribute to the understanding of the brain bases of affect and emotion. We take a meta-analytic approach, integrating across 165 individual studies to locate the regions most consistently activated across a range of emotion-related tasks. We refer to this set of regions

as the "observed neural reference space." Next, we bring meta-analytic evidence to bear on three unresolved issues in the emotion literature. First, we ask whether the experience and perception of emotion produce different patterns of brain activation. Second, we ask whether the experience of pleasant and unpleasant affect are instantiated by distinct circuitry in the human brain. Third, we address the methodological question of whether PET and fMRI are equally suitable for studying emotion in the human brain, particularly when imaging brainstem and midbrain areas. In addressing three questions, we also touch on other issues, such as the centrality of the amygdala in emotion, the representation and lateralization of affect in the brain, and the validity of fMRI as a means of studying emotional experience. Other recent meta-analyses have tackled the structure of emotion (Murphy, Nimmo-Smith, & Lawrence, 2003; Phan, Wager, Taylor, & Liberzon, 2002), so we do not address this question here.

The Hypothesized Neural Reference Space for Emotion-Related Phenomena

Animal and lesion studies guide and constrain current thinking about the neural systems that give rise to emotion. Animal models can provide exquisite neurophysiological detail that constrains theories about mental processes, and neuropsychology provides unique evidence on the brain components necessary for intact emotional processes in humans. While neuroimaging offers unique advantages in that it offers a probe of brain function in the intact human, interpretation of neuroimaging studies relies heavily on these complementary methods. Below, we provide a few pointers to the massive body of evidence on the affective brain that informs our interpretations of the body of neuroimaging studies to date. We begin in the oldest parts of the brain and work our way up to the cortical centers that so markedly differentiate humans from other species.

Brainstem

Brainstem nuclei form the oldest centers related to affective processing and generate autonomic output to regulate the heart, vasculature, and other visceral organs. Nuclei within these regions have generally bidirectional connections with other emotion-related structures, such as the medial prefrontal cortex (MPFC), insula, and amygdala (Amy) (Amaral, Price, Pitkanen, & Carmichael, 1992; Barbas, Saha, Rempel-Clower, & Ghashghaei, 2004; McDonald, 1998; Ongur, An, & Price, 1998; Ongur & Price, 2000). A particularly important structure is the midbrain periaqueductal gray (PAG), which is thought to coordinate coherent physiological and behavioral responses to threat (Bandler & Shipley, 1994; Holstege & Georgiadis, 2004; Van der Horst & Holstege, 1998). Stimulation of different longitudinal columns of PAG elicits distinct coordinated, organism-wide response 'modes' that mirror the natural affective reactions elicited by threat. For example, stimulation of lateral columns elicits 'defensive' behaviors such as facing and backing away from a perceived attacker, hissing, and attack when approached (Gregg & Siegel, 2001), autonomic responses including tachycardia, increased blood pressure and blood flow to the face, pupillary dilation, and piloerection (Lovick, 1992), and analgesia. Together, these effects are consistent with a defensive-aggressive emotional response. As PAG receives direct projections from numerous cortical regions, including ACC, MPFC, aINS, and medial temporal lobes (Shipley, Ennis, Rizvi, & Behbehani, 1991), the PAG might be thought of as an integrative emotional center, and it plays a central role in some conceptions of emotion (Panksepp, 1998).

In spite of their prevalence in animal models, brainstem nuclei are rarely discussed in neuroimaging studies, partly due to their small size and difficulty in localization. Many studies report activation in these subcortical areas, however, and we analyze the specificity

and reliability of these activations in this chapter. We find consistent activations around the human PAG, particularly in studies of negative emotional experience. These results underscore homologies between humans and other animals.

Diencephalon

The hypothalamus (Hy) and thalamus (Thal) comprise most of the diencephalon. Like the PAG, the Hy is a major player in animal models of emotion. It governs the pituitary and thereby the body's endocrine system, plays a major role in the regulation of motivated behavior and homeostatic processes (Sewards & Sewards, 2003; Valenstein, Cox, & Kakolewski, 1970), and interacts with the autonomic nervous system through large reciprocal connections with the PAG and other brainstem nuclei (Saper, Loewy, Swanson, & Cowan, 1976). The lateral Hy receives projections from diverse limbic structures and projects to the midbrain, middle hypothalamic zone, and medial Hy. The middle zone regulates autonomic functions and bottom-up forms of attention via connections to brainstem nuclei, including the PAG, reticular formation, parabrachial nucleus, ventral tegmental area, raphe nuclei, and spinal autonomic centers. And finally, the medial zone regulates endocrine function, such as the release of cortisol during stress. As we show here, activations in the human Hy and surrounding structures are reliable across studies and show a preference for positive emotional experience.

The Thal is perhaps best known for its role in sensory processing, but it contains over 30 distinct nuclei whose cortico-thalamic loops cover virtually the entire cortical mantle. The mediodorsal nucleus (MD) and the intralaminar nuclei are most closely associated with affective processes. Human thalamic activations are reliable in studies of emotion, and some parts show preference for emotional experience.

Subcortical Telencephalon

Overlying the brainstem and diencephalon are a group of subcortical areas that are typically identified as core limbic structures. These include Amy, HCMP, cholinergic basal forebrain nuclei (BF), and basal ganglia. The Amy is well-known for its role in emotion—particularly fear, though it also plays a prominent role in appetitive processes (Braesicke et al., 2005; Waraczynski, 2006). The basolateral complex plays a critical role in fear conditioning, the learning of associations between specific environmental cues and aversive outcomes (Anglada Figueroa & Quirk, 2005; Davis, 1992; Goosens & Maren, 2001; LeDoux, 2000; Nader, Majidishad, Amorapanth, & LeDoux, 2001). The central nucleus, at the dorsal end of the amygdala, is important for the physiological and behavioral expression of conditioned fear responses (Davis, 1992; Feldman, Conforti, & Saphier, 1990; Kalin, Shelton, & Davidson, 2004). However, the role of these structures in emotional experience (e.g., the *feeling* of fear) is less certain, as fear-like responses to naturally threatening stimuli do not always require the amygdala (Davis & Lee, 1998; Walker & Davis, 1997; Wallace & Rosen, 2001). As we show below, imaging studies suggest that activations observed in human amygdala are more likely to relate to visual cues that signal affective significance rather than negative experience.

The amygdala, like many gross anatomical structures in the 'affective brain,' plays roles in both positive and negative affective processes. It is critical for the evaluation of sensory cues associated with reward (Cador, Robbins, & Everitt, 1989; Everitt, Cador, & Robbins, 1989; Everitt et al., 1999) and the short-term updating of the reward-value of cues in context (Baxter & Murray, 2002; Schoenbaum, Chiba, & Gallagher, 1998; Schoenbaum, Setlow, Saddoris, & Gallagher, 2003). Recently, Paton et al. (2006) showed that separate

populations of amygdala neurons respond to stimuli that predict positive and negative future outcomes.

Taken together, all of this research suggests that the amygdala is important to the evaluation of sensory cues for relevance to the organism, and directs an organism to learn more about a stimulus so as to better determine its predictive value for well-being and survival (Davis & Whalen, 2001; Kim, Somerville, Johnstone, Alexander, & Whalen, 2003; Whalen, 1998). This is consistent with the idea that amygdala activations in human neuroimaging studies are related to the salience or potential information value of visual stimuli (Amaral, 2003; Liberzon, Phan, Decker, & Taylor, 2003; Whalen et al., 2004).

Interspersed with cell groups in the extended amygdala are a variety of cell groups spread throughout the basal forebrain (BF). Some, such as the bed nucleus of the stria terminalis (BNST), are likely to be important for fear and anxiety (Davis & Lee, 1998; Davis & Shi, 1999; Walker & Davis, 1997). Other nuclei serve as suppliers of acetylcholine to the cortex and play a key role in motivational modulation of attention (Sarter, Hasselmo, Bruno, & Givens, 2005) and sensory plasticity (Bear & Singer, 1986; Weinberger, 1995). These or other nuclei may be important for human reward and pleasure: Early stimulation studies in humans suggested that stimulation of the septal region in the BF can produce pleasurable responses (Heath, 1972; Heath, Cox, & Lustick, 1974), though these early observations may have actually been related to seeking or appetitive behavior related to stimulation of the ventral striatum rather than 'pleasure' per se. We show below that basal forebrain and septal regions are consistently activated in neuroimaging studies of emotion, and that different parts of this region are selective for positive and negative affect. Midline structures around the septal nuclei are activated preferentially by studies of positive

emotional experience, whereas more lateral areas around the BNST and extended amygdala are activated preferentially by studies of negative emotional experience.

The hippocampus, posterior to the amygdala, figures prominently in Gray's (Gray, 1978) affective/motivational theory of behavioral inhibition in anxiety. However, recent studies documenting the role of the hippocampus in long-term memory formation and consolidation (Squire & Zola-Morgan, 1991) have led researchers to suspect that its role in emotional behavior is memory-related. Consistent with this view, the hippocampus is particularly important for contextual fear conditioning in rodents (e.g., Maren, Aharonov, & Fanselow, 1997). In humans, hippocampal and medial temporal activations are reliable in emotion-related tasks but appear to be more related to perception of affective stimuli that emotional experience.

The basal ganglia are a set of subcortical structures that are critical for planning and initiating motivationally-relevant behaviors. Once thought to be primarily related to motor control, their functional role is likely to extend to the computation of affective value in a more general sense. The striatum (Str)—comprised of the Cau, putamen (Put), and NAC—and the globus pallidus (GP, not shown) comprise the major part of the basal ganglia. The ventral parts of the striatum (Str)—including NAC, ventral striatum (ventral caudate, Cau, and putamen, Put), and ventral pallidum (vGP)—play important roles in motivation, reward, and learning. Along with VTA and lateral Hy, they form a network of regions rich in dopamine and opioid receptors that might be considered the appetitive motivational 'backbone' of the brain (Berridge, 2004). Whereas this system was originally thought to mediate primary hedonic or 'reward' responses, there is now substantial evidence that dopamine signaling in this network—particularly in the mesolimbic pathway from VTA to

NAC—is more closely related to the generation of motivated behavior than to 'pleasure' per se (Berridge & Robinson, 1998; Salamone, Cousins, & Snyder, 1997). These areas are some of the most frequently activated structures in studies of human emotion, and different portions of these structures are preferentially activated by positive vs. negative emotional experience.

Paralimbic Cortex

The paralimbic 'belt' is a set of phylogentically older cortex with large, direct projections to subcortical and brainstem nuclei. These include the orbital frontal cortex (OFC), rostral medial frontal cortex, anterior insula (aINS), and anterior temporal cortex (TC). Damage to OFC is associated with inappropriate generation and regulation of affect, which may take the form of flattened affect, increased expression and reports of negative emotion, or inappropriate emotion given the social context, depending on the case (Beer, Heerey, Keltner, Scabini, & Knight, 2003; Berlin, Rolls, & Kischka, 2004; Hornak et al., 2003). Damage is also associated with reduced physiological output (e.g., heart-rate and skin-conductance (S. W. Anderson, Damasio, Tranel, & Damasio, 2000; Angrilli, Palomba, Cantagallo, Maietti, & Stegagno, 1999; Roberts et al., 2004).

The ventral areas of the medial wall have direct projections to the Hy and lower brainstem autonomic effectors (Saper, 1995). Subgenual cingulate (sgACC) and ventromedial prefrontal cortex (vmPFC) are related to visceromotor control in a number of animal studies (Vogt, Finch, & Olson, 1992), and sub-regions appear to play different and perhaps opposing roles in the generation and regulation or extinction of hypothalamic-pituitary-adrenal 'stress' responses (Sullivan & Gratton, 2002) and conditioned fear responses (Milad & Quirk, 2002). Rostral anterior cingulate (rACC) has also been

associated with diverse affect-related functions, including maternal bonding, pain, and emotion, and it may be further subdivided into more rostral affect-related regions and more posterior response-selection related regions (Devinsky, Morrell, & Vogt, 1995; Vogt, Nimchinsky, Vogt, & Hof, 1995). In human neuroimaging of emotion, distinct subregions of dorsal and ventral mPFC, rACC, and OFC are activated. Dorsomedial PFC and multiple regions within OFC are selective for studies of emotional experience, but ACC is not. Medial OFC and vmPFC are selective for positive emotion.

aINS, shown in Fig. 1, is connected with diverse subcortical 'limbic' regions and projects to brainstem autonomic centers. It has been associated with interoception of affect related body states, including perception of pain and itch (Craig, 2002), and with visceromotor control (Yasui, Breder, Saper, & Cechetto, 1991). The aINS can be divided based on cytoarchitecture and function into ventral and dorsal regions (Mesulam & Mufson, 1982). The evolutionarily older ventral portion, agranular insula (Ag) is a core paralimbic region and contains primary cortical regions for sensory-affective processing (taste and smell) and is particularly associated in human imaging studies with emotion (Wager & Feldman Barrett, 2004). The dorsal region, by contrast, is activated in a more diverse set of cognitive tasks and contains the insular/opercular junction commonly activated in tasks requiring the context-sensitive deployment of attention (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Wager, Reading, & Jonides, 2004) (In many cognitive studies operculo-insular activation is referred to as IFG). This distinction turns out to be important for our analyses, as the human studies we review show preference for positive emotional experience in the ventral aINS, near OFC and primary taste and smell cortices, and

preference for negative emotional experience in the dorsal aINS regions, which are most often activated by pain and tasks that elicit negative emotions.

The medial and lateral anterior TC are densely interconnected with OFC, and early studies of human TC stimulation produced particularly strong and vivid emotional experiences (Sem-Jacobsen, 1968). These experiences often took the form of re-living a period of the past (e.g., a scene from childhood) as though actually there, complete with emotive behavior appropriate for the situation. We find reliable activation of anterior TC in studies of emotional experience, with different portions preferentially activated by positive and negative emotions.

Above, we have summarized some of the broad roles thought to be played by the various structures that make up the affective brain. Next, we present the methods and results of our meta-analysis in more detail. Though the results are largely consistent with hypotheses based on animal and lesion data, they provide maps of the human affective brain that in many cases indicate that different regions within these broad structures may play different and even opposing roles.

The Meta-Analytic Approach

In spite of the growing literature on the neural bases of emotion, we still know very little about the precise functions of key brain regions in the affective brain that instantiate the emotional lives of humans. A major difficulty in human work is variability – studies of what scientists assume are the same phenomenon (e.g., the experience of fear) can produce widely varying results both across participants within a study and across studies. For the most part, this variability is treated as error, even though it may reflect real and important

differences in brain anatomy (at the individual participant level) or task requirements and therefore psychological process (at the level of the study). Single neuroimaging studies typically average signal across individuals to identify brain areas that show consistent activity across a group of participants. Similarly, with the use of meta-analytic techniques, we can average across studies to identify brain areas that show consistent activity across a group of studies. Meta-analyses not only allow us to identify consistent brain-process correspondences (i.e., the extent to which a brain area consistently shows increased activity with a psychological process), but they also allow us to identify the specificity of such correspondences. Of course, much of the detail and nuance of individual studies is lost in a meta-analytic approach, but its strength is that it allows us to view the affective brain painted in broad strokes, and provides us with a means to address whether ask the major psychological categories that scientists typically rely on – perception vs experience, positive vs. negative affect, or varieties of negative emotion (e.g., sadness vs. anger vs. fear) – produce reliable and specific differences in brain activity.

The Sample of Studies

We included findings from a total of 164 neuroimaging studies (58 PET and 106 fMRI) on unmedicated, healthy adults published between 1990 and 2005. These are summarized in Table 1 and described in detail in supplementary materials Table S1 online.[1] All studies were coded for whether they targeted "affect" (defined as a pleasant or unpleasant state arising from presentation of survival-related or social stimuli) or "emotion"

[1] In addition, there are certain methodological limitations to single neuroimaging studies that can be overcome with meta-analytic summaries. For example, current neuroimaging techniques are plagued by both low power and the presence of many false positives. Only 20% of the studies sampled corrected for multiple comparisons (i.e., tests of more than one brain region). Of these, many use inappropriate methods that do not provide adequate correction, yielding false positive results.

(defined as instances of categories typically labeled by the English words "anger," "sadness," "fear," "disgust," and "happiness").. We also coded other relevant study properties, such as whether a study involved perception or experience, whether positive or negative feelings were evoked (for studies of experience), and whether PET or fMRI, methods were used.[2], Papers were coded first by a team of four trained raters. Each paper was coded by two different coders. We included only activations (omitting deactivations because they are less consistently reported).

Multi-Level Analytic Strategy: Peak Density Analysis

Meta-analyses of neuroimaging studies do not usually compute average effect sizes as is done with behavioral data, but instead summarize the frequency with which studies report peak activation coordinates in a particular brain location (Fox, Parsons, & Lancaster, 1998; Laird et al., 2005; Wager, Phan, Liberzon, & Taylor, 2003; Wager, Reading et al., 2004)[3]. Each study reports one or more contrasts which map the difference in brain activity for two conditions (e.g., positive vs. neutral picture viewing). By convention, activated regions in each contrast are summarized as coordinates in a standardized, three-dimensional brain space divided in mm; x (left/right), y (back/front) and z (top/bottom) coordinates. In a meta-analysis, the brain is divided up into a set of three-dimensional cubic volumes (called voxels; each is 2 x 2 x 2 mm), and maps are constructed of the density of reported activation coordinates within a local volume (within 10 mm) around each voxel.

[2] Although emotions are the subset of affective responses that are elaborated with various sources of conceptual content (Barrett, Mesquita et al., 2007), we treated affect and emotion as separate categories in our analyses.

[3] Effect-size meta analysis have been performed, but are problematic in general due to inconsistencies in data analysis across studies that can influence effect sizes. In addition, the peak density method avoids the need to estimate effect sizes in regions for which effects are not reported.

Previous meta-analyses used activation coordinates as the unit of analysis. For example, if 12 studies with one contrast map each reported 18 peak coordinates within 10 mm of a voxel in frontal cortex, the density for that voxel would be $18/(10mm^3)$. That value would be compared to the distribution of values expected by chance in order to assess significance. Rather than treating individual peaks as the unit of analysis, our meta-analyses treat a contrast as a random effect with activation coordinates nested within contrast[4],. Thus, the density measure of interest is the number of *contrasts* (not the number of individual activation peaks) that produced activation near a voxel,. In the example above, there were 12 contrasts that reported activations near the frontal voxel of interest, which amounts to 12 nominally independent pieces of information, and our density count is 12/(10mm3). Studies might report multiple nearby peaks for the same contrast due to low spatial smoothness in the data, reporting conventions, low thresholds, or even voxel sizes used. Our method is insensitive to these types of variation across studies. As a result, a single study can no longer disproportionately contribute to the result by reporting many nearby peaks in an area.

For the present dataset, we included 437 contrasts, each associated with a set of reported coordinates. Each set of coordinates was transformed into a map of "active" voxels that were within 10 mm of a reported peak for that contrast. We then computed a summary density map of the proportion of contrasts activating near each voxel by taking a weighted average of contrast activation maps. The weight for each study was the square root of the sample size, multiplied by an adjustment weight for type of the analysis used for population

[4] For simplicity, we assume different contrasts reported by the same study are independent.

inference[5]. The values in this peak density map have a transparent interpretation: "density" refers to the number of contrasts or statistical parametric maps with a nearby (within 10 mm) peak, weighted by the quality of information provided by the study.

Statistical Inference and Thresholding

The density map is then compared to Monte Carlo simulations to identify voxels with activations that exceed the frequency expected by chance (i.e., a uniform distribution of activation coordinates across the brain's gray matter). Using a Monte Carlo simulation in which the observed number of activation coordinates from the 437 activation maps are placed at random locations throughout the brain—and repeating this process 5000 or more times—allows us to determine which locations in the brain show a greater-than-chance number of nearby activation coordinates, providing a stringent familywise error rate correction for search across the locations within the brain. Our approach was first to locate regions that are consistently activated across a significant number of these studies (the "observed neural reference space"), and then to analyze the likelihood of activating a region in relation to different categories of emotional phenomena.

The maps in Figs. 2-4 show voxels for which the density of reported peaks exceeded that expected by chance, corrected for search across the many voxels of the brain (i.e., family-wise error rate correction). The yellow color shows regions in which the peak density is high enough that the null-hypothesis chances of finding *a single significant voxel* anywhere in the gray matter of the brain is $p < .05$. The other colors use an 'extent-based' threshold,

[5] Larger studies are weighted more heavily. The square root transformation provides a measure closer to effect size. Studies that used "random effects" models appropriate for population inference were weighted 1.25 more heavily than those treating participants as a fixed effect. "Fixed-effects" models were commonly used in early neuroimaging studies but are not appropriate for generalizing to a population. They generally produce much higher effect sizes (e.g., Z-scores) for the same data.

in which the number of contiguous voxels above a primary threshold (e.g., $p < .001$) are counted and compared with the number of contiguous voxels expected by chance (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994). Colored regions show areas in which a *cluster of voxels this large* is unlikely to occur by chance anywhere in the brain. We use the Monte Carlo simulation to establish extent thresholds at $p < .001$ (orange in figures) and $p < .005$ (pink in figures). We report the significance of voxels at the highest primary threshold for which the significance criteria are met.

Visualization and Localization

The three-dimensional renderings and figures with brain slices presented in this chapter were reconstructed from a canonical MRI image (colin27.img, the single-subject template in SPM2; http://www.fil.ion.ucl.ac.uk/spm/software/spm2/). This brain was coregistered with the international standard Montreal Neurologic Institute (MNI) brain template (avg152T1.img) which is itself based on the average of 152 brains registered roughly to landmarks from the atlas of Talairach and Tourneaux (Talairach & Tournoux, 1988). To localize highly replicable regions, we overlaid significant voxels on the MNI average template and determined their locations using the atlases of Duvernoy (Duvernoy, 1995; Duvernoy & Bourgouin, 1999), Martin (1996), Haines (2000), and Ongur, Ferry and Price (2003); this method provided more accurate results than automated labeling systems. We use the single-subject brain only for visualization in figures because its anatomical detail makes brain landmarks more identifiable to readers. We do not report Brodmann areas because their boundaries cannot be identified with sufficient accuracy on this template brain, unless they are in regions shown in Ongur and Price, who provide labels registered to the MNI brain. While variation across labs and software packages in nominally similar

warping to 'Talairach space' produces inconsistencies among reported coordinates (Brett, Johnsrude, & Owen, 2002), the MNI template brain is the most popular template for electronic registration, so using it minimizes localization errors in the meta-analysis results.

The Observed Neural Reference Space for Emotion-Related Phenomena

Fig. 1 summarizes the regions that were consistently activated in our database of neuroimaging studies (Stereotactic coordinates for the most consistent activation foci are listed in Table S2). The right lateral surface of the brain (upper left panel), the left medial surface (upper right panel), the CB (purple shading), and the brainstem and prominent subcortical regions (lower right panel) are shown in 3-D rendering.

There was remarkable consistency between the hypothetical and observed neural reference spaces for emotion-related phenomena. As expected, we observed consistent activity in or closely associated with "limbic" areas. A striking feature of the map is the inclusion of diencephalic and brainstem regions that have been identified in animal models of affective behavior but are infrequently discussed in human neuroimaging studies. In the brainstem, PAG and VTA were consistently activated, whereas lower brainstem centers in the pons and medulla were not consistently activated (though some pontine activations were consistent in other analyses presented below). Consistently activated diencephalic regions included subthalamus, Hy, and much of the dorsal thalamus, though the maximal consistency in the thalamus was in the central medial zone, around the 'limbic' MD and CM nuclei. In the telencephalon, large significant regions of activation were observed in and around the amygdala extending into the basal forebrain, NAC, hippocampus, and ventral striatum and pallidum. In the paralimbic belt, consistent findings included vmPFC (10 m/r), multiple lateral OFC sites (42/12l and m; 13l), the aINS, and consistent findings in

the medial and lateral anterior TC (pHCMP and TP). Cingulate activations were largely limited to the rostral half of the ACC, corresponding to the so-called "affective" zone (Bush, Luu, & Posner, 2000). Strikingly, however, activations in the medial wall were clustered into at least three distinct groups, corresponding to pgACC, rACC, and sgACC.

The area of superior dmPFC above the cingulate sulcus (BA 9 extending back to BA 32) was consistently activated and distinct from ACC activation. The functional contributions of dmPFC have yet to be precisely determined, but recent research and theorizing suggests that these brain areas jointly contribute to making mental state attributions (for reviews, see (Adolphs, 2001; Blakemore, Winston, & Frith, 2004; Lane & McRae, 2004), such as when a person makes judgments about the psychological states of another person, or monitors, introspects, or makes inferences about his or her own moment-to-moment feelings (also see (Mitchell, Banaji, & Macrae, 2005b; Ochsner et al., 2004).

We also observed consistent activations in regions not traditionally considered part of the neural reference space for emotion, including those in the lateral frontal cortex, TC, OCC, and CB. These findings suggest that there are additional psychological processes that are involved in emotion-related phenomena that are perhaps overlooked in existing neuroscience models.

Although individual studies have reported lateral frontal activations in locations that span the expanse of cortex (see, e.g., Figs 4A and 5A), the only consistent activations across all studies lie in the bilateral inferior frontal gyrus (IFG), extending from the pars opercularis (Broca's area, BA 44) through pars triangularis (BA 45) and pars orbitalis on the inferior frontal convexity (BA 47/12 l). The activated region also extended into the frontal operculum and was contiguous with activation in OFC and aINS. Neuroimaging studies of

response inhibition, response selection, task switching, and working memory have commonly activated the area around BA 44/45 and the underlying operculum (Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Gabrieli, Poldrack, & Desmond, 1998; A. Martin & Chao, 2001; Poldrack et al., 1999; Wager, Jonides, Smith, & Nichols, 2005; Wagner, Maril, Bjork, & Schacter, 2001). Meta-analyses have suggested that the frontal operculo-insular border contiguous with the dorsal aINS, rather than the lateral surface, is the most consistently activated area across studies (Wager, Reading et al., 2004; Wager & Smith, 2003). A general role for BA 44/45 and the operculum might be context-based selection among competing stimulus-response mappings or sets (Thompson-Schill et al., 1997). In emotion-related phenomena, this region may be important for the information-selection processes critical for conceptual processing associated with meaning analysis (such as that associated with appraisal). In support of this notion, emotion- and pain-related activity in IFG and the operculum is modified by both manipulations of the meaning context in which affective stimuli are presented (Benedetti, Mayberg, Wager, Stohler, & Zubieta, 2005; Kong et al., 2006; Wager, Rilling et al., 2004) and voluntary regulation of emotional responses (Ochsner, Bunge, Gross, & Gabrieli, 2002).

Activation of STS/STG and inferior temporal and occipital 'association' cortices could be related to enhanced sensory integration, but their precise role in affective processing is unclear. Although the function of the posterior cingulate area remains unclear (Maddock, 1999), it may play a role in memory-guided representation of context important for conceptual processing in emotion (Maddock, 1999; Mantani, Okamoto, Shirao, Okada, & Yamawaki, 2005; Minoshima et al., 1997). V1 also showed consistent activation,

suggesting that early visual processing is enhanced when compared to neutral control conditions.

The consistent cerebellar activation we observed might be related to increased demands on motor planning during affective and emotional states, but there is accumulating evidence for a more direct cerebellar role in emotion-related phenomena. Electrical stimulation of deep cerebellar nuclei in humans, in particular the fastigial nucleus, has been shown to induce activity in mesolimbic affect-related areas (Heath, Dempesy, Fontana, & Myers, 1978) and, in some cases, it has elicited states of profound rage (Heath et al., 1974). Conversely, cerebellar damage often produces what might be considered a disorder of emotion regulation, characterized by fluctuations between flattened affect and inappropriate social behaviors (e.g., "trying to kiss the experiementer")(Schmahmann & Sherman, 1998) reminiscent of social and emotional deficits with OFC damage. The CB is connected with specific prefrontal regions in topographically mapped reciprocal circuits (Middleton & Strick, 1994, 2000) and with "limbic" regions, including the Hy (Haines & Dietrichs, 1984), OFC (BA 12), dmPFC (BA 9 and 32), portions of IFG (BA 46) and inferior frontal convexity (BA 46/12) (Middleton & Strick, 2001). Cerebellar efferents to these areas pass largely through DM in the thalamus, which we also find is consistently activated in human emotion. One hypothesis is that the CB might contribute to the processing of situational context (Schmahmann & Sherman, 1998) as part of a complex pattern-recognition system (Albus, 1971).

Comparing Experience and Perception

Studies of human affect and emotion (and their associated constrast maps) can be categorized as investigations of *experience* (involving the generation of feelings in response to

pictures, sounds, memories, imagery, or other stimuli based) or *perception* (involving the observation and judgment about the normative content in a stimulus, such as whether a picture of facial behavior is classified as an "expression" that depicts "fear," "anger," or "disgust"). The critical conceptual difference separating experience from perception is whether a contrast (comparing activity in an experimental vs. a control condition) captures activity related to the generation of subjective feelings. Of course, this distinction is often a matter of degree, because the passive viewing of some stimuli that are used in perception-based studies (such as photos from the International Affective Picture System) will evoke an affective response regardless of whether participants are asked to report it, and stimuli used in experience-based studies (such as memories of social situations or sounds) require the perception of emotional content. To perform this analysis, however, we distinguished contrasts where affective experiences were being generated from those where changes in the perceiver's affect was unlikely.

Studies of *experience* in our sample (see Table S1) typically involved the recall of personal experiences, the viewing of strongly evocative visual or auditory stimuli, or exposure to pleasant or unpleasant tastes or odors. Studies of *perception* involved judgments about visual stimuli such as facial expressions that were unlikely to produce a strong change in experience (though such stimuli can serve as primes that may influence subsequent behavior). Papers with ambiguous status were excluded from this analysis.

Meta-analysis density maps showing significant differences between experience and perception are shown in Fig. 2A and 3B. Some significant regions are shown on the same axial brain slices for direct comparison in Fig. 2C, with Experience vs. Perception in red and Perception vs. Experience in blue. The density maps identified brain locations where there

was a relative difference in peak activity between the experience and perception studies. Because the null hypothesis assumed that points from each condition were uniformly distributed throughout the brain, this analysis shows brain locations where differences in the *relative distribution* of peaks is large.[6]

The results show a striking dissociation. Contrasts for the *experience* of affect or emotion showed relatively greater activation for the medial subcortex (including Hy, VTA, PAG, dorsal pons, and surrounding reticular formation), the diencephalon (including the BF/ extended amygdala, Hy and Thal), areas of paralimbic cortex (OFC, aINS, vmPFC and TP), MTL, dmPFC, ventral IFG, and the deep regions of the CB surrounding the deep cerebellar nuclei. These findings are consistent with other work suggesting prominent roles for OFC (Kringelbach, 2005), aINS (Craig, Chen, Bandy, & Reiman, 2000), and DMPFC (Barrett et al., 2007) in the experience of affect and emotion. Moreover, they are consistent with stimulation studies in humans. Numerous case reports by Sem-Jacobsen (1968) and others show effects on experience of both positive and negative emotions with stimulation of the dorsal and orbital medial wall, and vivid emotional memories with anterior and medial temporal stimulation. Experience-related increases in subcortical and brainstem areas attest to the reliability of subcortical activation in neuroimaging studies, although they are less

[6] This analysis does not provide information about whether more studies of experience (or perception) activate an area in absolute terms. Information about the absolute frequencies of activation is provided by χ^2 (chi-square) analyses that test whether significantly more activation maps from experience studies vs. perception studies activate an area. These analyses are available from the first and second authors, and were not included here because of space limitations; the results agree in large part with the areas shown here. Also, these maps do not provide direct inferences about the likelihood of experience (or perception) given activation in a particular area (Poldrack, 2006). Density-based maps of relative distributions are very useful, however, because they control for the overall frequency of activation across conditions, and therefore allow for more subtle differences to emerge. An example of this occurs in our analysis of pleasant vs. unpleasant affective feelings.

frequently discussed than cortical activations. Interestingly, rdACC did not differentiate between experience and perception; it was activated by both types of studies.

Perception-related contrasts more consistently activated Amy, pHCMP, pgACC, dorsal IFG, inferior TC and OCC, and lateral CB. These findings are consistent with the idea that Amy activations in human neuroimaging studies are related to the salience or potential information value of visual stimuli (Liberzon et al., 2003), rather than playing some necessary role in emotional experience (A. K. Anderson & Phelps, 2002). Finding inferior temporal and occipital specialization for perception does not come as a surprise, given the strong relationship between these areas and visuospatial processing. Dorsal IFG and lateral CB specialization for perception may relate to pattern recognition and conceptual processing that is necessary for normal emotion perception. These regions are connected in topographically mapped loops (Middleton & Strick, 2001), suggesting they may be part of the same functional circuit. Of course, such conclusions about the precise function of these circuits are speculative, and they remain to be tested in focused individual studies. What is striking, however, is that different regions of the IFG seem to be differentially involved in experience and perception: The ventral and opercular parts for experience, and the more dorsal part for perception.

Comparing Pleasant and Unpleasant Experiences

Using only the 240 contrasts (in 95 studies) involving experience, we next examined whether pleasant and unpleasant experiences were implemented in separable distributed systems. A previous meta-analysis tackled the positive/negative distinction (Wager et al., 2003), but did not separate experience from perception, as we do here.

Reported activation peaks for unpleasant (blue) and pleasant (yellow) contrasts are shown in Fig. 3A and B, and meta-analysis density maps showing relative differences are shown in Fig. 3C and D, with Pleasant vs. Unpleasant in yellow and Unpleasant vs. Pleasant in blue. Overall, the results suggest dissociations based on valence that are in general agreement with hypothesized specializations based on animal and lesion studies. Pleasant experiences were associated with relatively greater activation in medial dopamine-rich areas (VTA, NAC, and portions of vStr), in Hy, vmPFC and right OFC. Unpleasant experiences were associated with more consistent activation in Amy, aINS, PAG, and left OFC and more posterior portions of vStr and vGP. The results provide a promising indication that different gross anatomical areas might be differentially sensitive to pleasant and unpleasant stimuli, although they do not imply that activation in any of these regions is uniquely associated with either category. In fact, chi-square tests revealed no region with greater absolute proportions of pleasant activations, primarily because unpleasant experiences elicit more robust responses that engage many parts of the brain. The relative specialization we report here is important, however, because studies of animal models have found that neurons and nuclear groups that are specialized according to valence are often contained within the same gross anatomical structure—for example, intermixed positive- and negative- expected value neurons within the amygdala (Paton et al., 2006), or rostrocaudal negative-positive gradients within the NAC (Reynolds & Berridge, 2002)—raising the question of whether neuroimaging truly provides the resolution to separate representations of positive and negative affect. Our results are in line with the idea that different brain regions have different relative concentrations of specialized neurons, and that

large-scale structure (aggregating across millions of neurons) in the affect system can be detected using neuroimaging.

An additional point that is worth noting is that while we did not compare left and right hemispheres using direct statistical contrasts, we do observe a pattern of lateralization in the OFC and basal forebrain (and a lack of lateralization in superior lateral cortex) that is different from that predicted by previous theories. Studies based on scalp electrical potentials (EEG; for a review see, e.g., (Davidson, 2000)) and lesion studies linking left-hemisphere damage to depression (Borod, 1992) suggest that the left lateral prefrontal cortex supports pleasant moods and reactions to pleasant stimuli, whereas the right lateral prefrontal cortex supports unpleasant moods processes. It is possible that lateralized EEG activity is predictive of mood or affective style, but the pattern of specific brain activation underlying those cortical potentials is more complex. Alternatively, arousal differences across studies might mask lateralized differences (Canli, Desmond, Zhao, Glover, & Gabrieli, 1998), or lateralization might be more closely related to approach-avoidance motivation than to affective valence per se, as suggested by our previous meta-analyses and recent work (Pizzagalli, Sherwood, Henriques, & Davidson, 2005; Wager et al., 2003). These caveats notwithstanding, the neuroimaging correlates of observed lateralization of affect in EEG studies remain to be elucidated.

The Search for Subcortical Circuits: Comparing PET and fMRI Studies

Most emotion-related research on rats and primates pinpoints midbrain and brainstem areas as important for emotional behavior, and thus far our meta-analyses suggest that these areas are particularly active during the experience of affect and emotion. Compared to PET imaging, fMRI is less well suited to the study of the basal telencephalon

and brainstem due to magnetic susceptibility artifacts[7]. The hypothesis, then, is that fMRI studies of emotion-related phenomena might under-estimate midbrain and brainstem contributions to affect and emotion. Alternatively, however, these issues might be counterbalanced by the greater spatio-temporal precision and potential to collect larger amounts of data with fMRI.

Using chi-square analysis, we compared density maps for contrasts from PET and fMRI studies to detemine whether one imaging method was more likely to activate particular brain regions in absolute rather than relative terms. The analysis tests the proportion of contrasts using each method that activated within 10 mm of each voxel, and thus controls for overall differences in the frequency of use of PET and fMRI. The map of regions with significant chi-square statistics, shown in Fig. 4, reveals no significant differences between PET and fMRI in the brainstem, basal forebrain, ventral striatum, or OFC. Thus, the benefits of fMRI in spatial resolution may compensate in part for increased artifacts, and thus that fMRI can be a useful tool for examining the subcortex. Superior cortical regions, as well as Amy and some other subcortical regions, appeared to be more consistent in fMRI studies (white in Fig. 4) —though we suspect that effects in Amy in particular may be related to the widespread use of a priori Amy regions of interest rather than inherently more reliable activation.

General Discussion

The meta-analyses reported in this chapter build on previously published meta-analyses of emotion (Murphy et al., 2003; Phan et al., 2002; Wager et al., 2003) in

[7] Typical blood-oxygen level dependent (BOLD) fMRI measures functional activity by being sensitive to local field inhomogeneities (Ogawa et al., 1992). A difficulty is that transitions from air sinus space to tissue around the base of the brain create local field inhomogeneities, resulting in both signal loss and distortion, which limits both sensitivity and localization.

important ways. First, whereas those analyses combined perception and experience of emotion and affect, we explicitly compared the two types of studies and found that they were distinguished by their relative concentration of peak activations: Brainstem, hypothalamic, and paralimbic selectivity for experience, and amygdalar complex and posterior cortex selectivity for perception. Second, we compared studies of pleasant and unpleasant experiences and found selectivity for pleasant experience in midline brainstem, hypothalamic, and ventromedial frontal regions, and selectivity for negative experience in distinct brainstem (PAG), insular, striatal, and orbital cortical regions. Third, we explicitly examined the suitability of fMRI as a method for interrogating brainstem and basal telencephalon and found that fMRI may be comparable to PET in its effectiveness as a tool for studying the brainstem and subcortex.

Of course, there is still much to be done. First, neuroimaging studies must continue to move away from referring to broad anatomical regions that in actuality perform different and often opposing functions. For example, the ACC encompasses around 15,000 2 x 2 x 2 voxels of brain tissue, but it is common for researchers to compare results from different studies at the gross structural level, trying to fit a single common interpretation to results that are in different areas with different anatomical projections and functional profiles. Using data across many studies to precisely demarcate regions of the brain, as we have done here, is an essential step towards building a more systematic method. Once a set of regions is identified for study, it becomes possible to examine their dynamics (e.g., via connectivity analyses and structural models) in a much more meaningful way.

Second, in interpreting findings from our meta-analyses, or from any single neuroimaging study for that matter, it is important to keep in mind that brain areas that

span even a few millimeters are most likely not consistently dedicated to any one process. Even individual neurons may participate in a number of functional circuits, and fMRI measures activity integrated over populations of neurons involved in different processes[8], including different types of affect (Paton et al., 2006). The seminal work of Sem-Jacobsen (Sem-Jacobsen, 1968) in humans and of Valenstein in rats (Valenstein, Cox, & Kakolewski, 1968) has shown, strikingly, that stimulation of brain sites very close together (no more than a few millimeters) can elicit vastly different emotional responses. In the words of Sem-Jacobsen (Sem-Jacobsen, 1976), "An electrode 0.5-1 cm from a positive point may give the opposite [emotional] response with about the same strength. There appears to be this dual arrangement in the ventromedial area of the frontal lobe, the central part of the temporal lobe, as well as other structures." (p. 516). In support of this notion, our summary of neuroimaging studies shows nearby regions with different functional specialization in the basal telencephalon, ventral basal ganglia, and inferior frontal cortex.

Furthermore, in early human electrical stimulation studies of emotion, while stimulation of the same site was often found to reproduce an emotional experience in the same session, elapsed time or variation of the behavioral contexts in which stimulation occured markedly affected the emotional response. Documentation of this phenomenon in animals led Valenstein to question the idea of fixed affective circuits (Valenstein et al., 1970). Thus, even with the relative precision of chronically implanted electrodes,

[8] Counting neurons and synapses is difficult, but to provide a general idea of neural connectivity, some estimates are around 13.7×10^9 neocortical neurons (Braendgaard, Evans, Howard, & Gundersen, 1990) and 164×10^{12} synapses (Tang, Nyengaard, De Groot, & Gundersen, 2001), yielding an average of nearly 12,000 synapses per neuron. Many cortical areas have around 70,000-100,000 neurons per mm2 of tissue, an area substantially smaller than a voxel in human neuroimaging studies.

Heraclitus' claim that "you can never step into the same river twice" (Plato, 360 BCE)may well apply to the emotional brain.

Due to these considerations, we believe that two kinds of paradigm shift are essential for advancing the neuroimaging of emotion. One is that researchers need to move from studying brain areas in isolation to identifying interconnected, distributed circuits. Functional connectivity analysis may provide more precise information about brain processing related to various affective states and events, and constrain inferences about regional activations based on patterns of connectivity. In this respect, neuroimaging plays a unique and complementary role to lesion studies in animals, because neuroimaging alone allows the simultaneous measurement of the entire brain and dynamic patterns of functional connectivity across diverse systems. Another is that researchers should move beyond mapping brain responses to individual psychological phenomena to making inferences about psychological states based on brain activity. Neuroimaging provides unique and valuable information about the organization of the human brain; what is at stake here is the ability to learn about the organization of the mind from brain data. Making psychological inferences from brain activity is an extremely difficult task, and functional inferences in neuroimaging studies have often been made in an *ad hoc* fashion. Valid psychological inference requires comparing activations across a number of psychological states; meta-analyses of the type we report here are one way to perform such comparisons. Formal inferences on psychological states using neuroimaging data can be performed using classifier systems, and this is a promising new direction.

Overall, the past 15 years have seen an explosion in the application of brain imaging methods to emotional phenomena. The emerging field of affective neuroscience has been

engaged in a search for answers to two interdependent questions, about the locations of brain regions that represent affective information and the psychological distinctions that define the conditions for their activation. As information is accumulated, specific mappings can be made between studies of normal human populations, studies of psychological and brain pathology, and animal models. Neuroimaging paves the way for synergy across these previously quite disparate fields by referring to the common 'language' of the brain. When data is aggregated across neuroimaging studies, there is a remarkable and somewhat underappreciated consistency with animal and human stimulation work. As such data is accumulated, more elaborated and refined mappings between brain activity and affective processes will yield yet greater synergy across the neurosciences.

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Table 1. Abbreviations

Localization prefixes/suffixes	
v	ventral
a	anterior
d	dorsal
r	rostral
s	superior
i	inferior
fr	frontal
lat.	lateral
m or med.	medial
BA	Brodmann's area
Brainstem	
Midbrain	
Midb	midbrain
PAG	periaqueductal gray
SC	superior colliculus
RN	red nucleus
VTA	ventral tegmental area
SN	substia nigra
Pons	
LC	locus coeruleus
Diencephalon	
Hy	hypothalamus
Thalamus	
Thal	thalamus
DM	dorsomedial nuc.
MGN	medial geniculate nuc.
CM	centromedian nuc.
STN	subthalamic nucleus
Subcortical telencephalon	
Amy	amygdala
HCMP	hippocampus
BF	basal forebrain (cholinergic)
septal	septal nuclei
Str	striatum (Cau/ Put)
Put	putamen
Cau	caudate
GP	globus pallidus
GPi	internal globus pallidus
NAC	nucleus accumbens
Paralimbic	
Ins	insula
Ag	agranular region of insula
vmPFC	ventromedial prefrontal cortex
OFC	orbitofrontal cortex
ACC	anterior cingulate cortex
rdACC	rostral dorsal anterior cingulate
pgACC	pregenual cingulate
sgACC	subgenual cingulate
TP	temporal pole
pHCMP	para-hippocampal cortex
MTL	medial temporal lobe
Other cortical regions	
Lateral frontal	
IFG	inferior frontal gyrus
frOP	frontal operculum
IFS	inferior frontal sulcus
Medial wall	
dmPFC	dorsomedial prefrontal cortex
PCC	posterior cingulate cortex
pre-SMA	pre-supplementary motor area
Temporal	
TC	temporal cortex
STS	sup. temporal sulcus
STG	sup. temporal gyrus
Occipital	
OCC	occipital cortex
V1	primary visual cortex
Cerebellum	
CB	cerebellum
quad.	quadrangular lobule

Note. Abbreviations for brain regions, organized by anatomical structure.

Table 2.

Summary of contrasts analyzed

Experience vs. Perception

	Experience	Perception	Mixed
PET	109	28	11
fMRI	131	129	29

Affective/Emotional Valence

	Negative	Positive	Mixed/ Nonspecific
PET	94	30	24
fMRI	187	65	37

Specific emotion

	Happiness	Anger	Disgust	Fear	Sadness	Mixed/Other
PET	17	10	4	11	23	9
fMRI	19	16	40	57	22	34

Correction for multiple comparisons

	Unknown	Corrected	Small-volume corrected	Uncorrected
PET	7	21	0	121
fMRI	8	73	28	186

Population inference

	No (infer on sample only)	Yes (infer on population)
PET	124	24
fMRI	74	215

Note. A summary of the 437 contrast maps from 165 studies used in the meta-analysis. Numbers reflect the number of contrasts in each category. Population inference refers to the number of contrasts that treated subject as a random effect, allowing valid population inference ("yes" in the table), as compared with contrasts that performed a 'fixed-effects' analysis and whose results cannot be generalized beyond the sample studied. Lower weights were given to 'fixed-effects' and smaller-sample studies in the meta-analysis.

Figure Captions

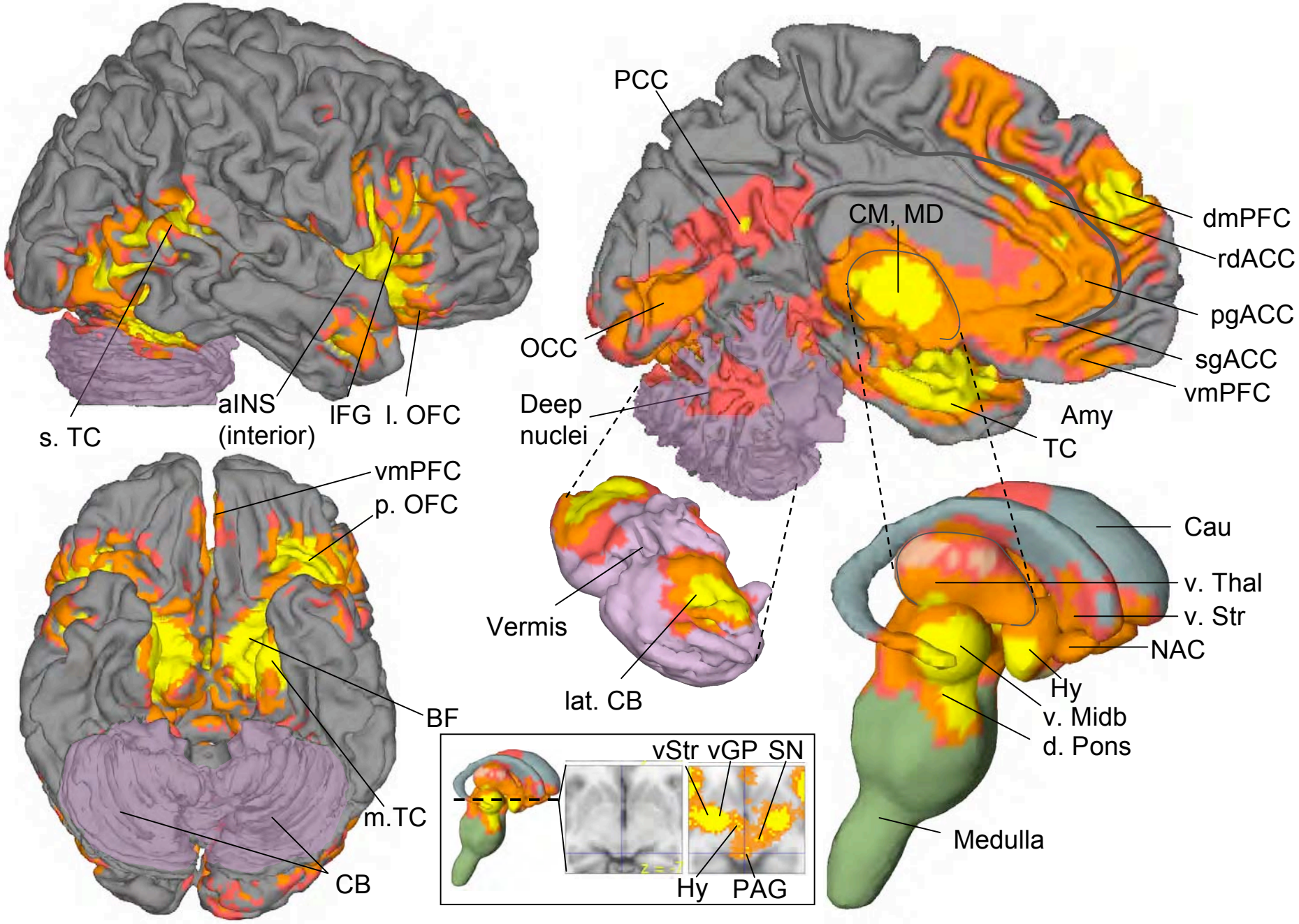
Figure 1. Consistently activated regions in human neuroimaging studies of affect and emotion, shown as colored regions. Details are provided in the text. Abbreviations are defined in the text and in Table 2.

Figure 2. Regions showing relatively more consistent activation for studies of Experience vs. Perception (A) and Perception vs. Experience (B). Some regions are shown on the same brain slices in (C) for direct comparison. Abbreviations are defined in the text and in Table 2.

Figure 3. A) Reported activation coordinates for contrasts of pleasant experience ('positive,' yellow circles) and unpleasant experience ('negative,' blue triangles) on the right lateral surface. B) Reported coordinates in the brainstem and diencephalon. C) Significant regions showing relative differences in frequency of activation for Positive vs. Negative (yellow) and Negative vs. Positive (blue) comparisons. D) The comparisons in (C) shown on brain slices to reveal subcortical locations. Abbreviations are defined in the text and in Table 2.

Figure 4. A) Reported activation coordinates for contrasts using PET (black circles) and fMRI (white triangles) on the right lateral surface. B) Meta-analysis results showing significant differences in absolute proportion of PET vs. fMRI studies (black) and fMRI vs. PET studies (white). The analysis used chi-square tests, controlling for the

frequency of use of each method. C) The comparisons in (C) shown on brain slices to reveal subcortical locations. Abbreviations are defined in the text and in Table 2.


s. TC
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(interior)
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l. OFC
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dmPFC
rdACC
pgACC
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vmPFC
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Amy
TC
vmPFC
p. OFC
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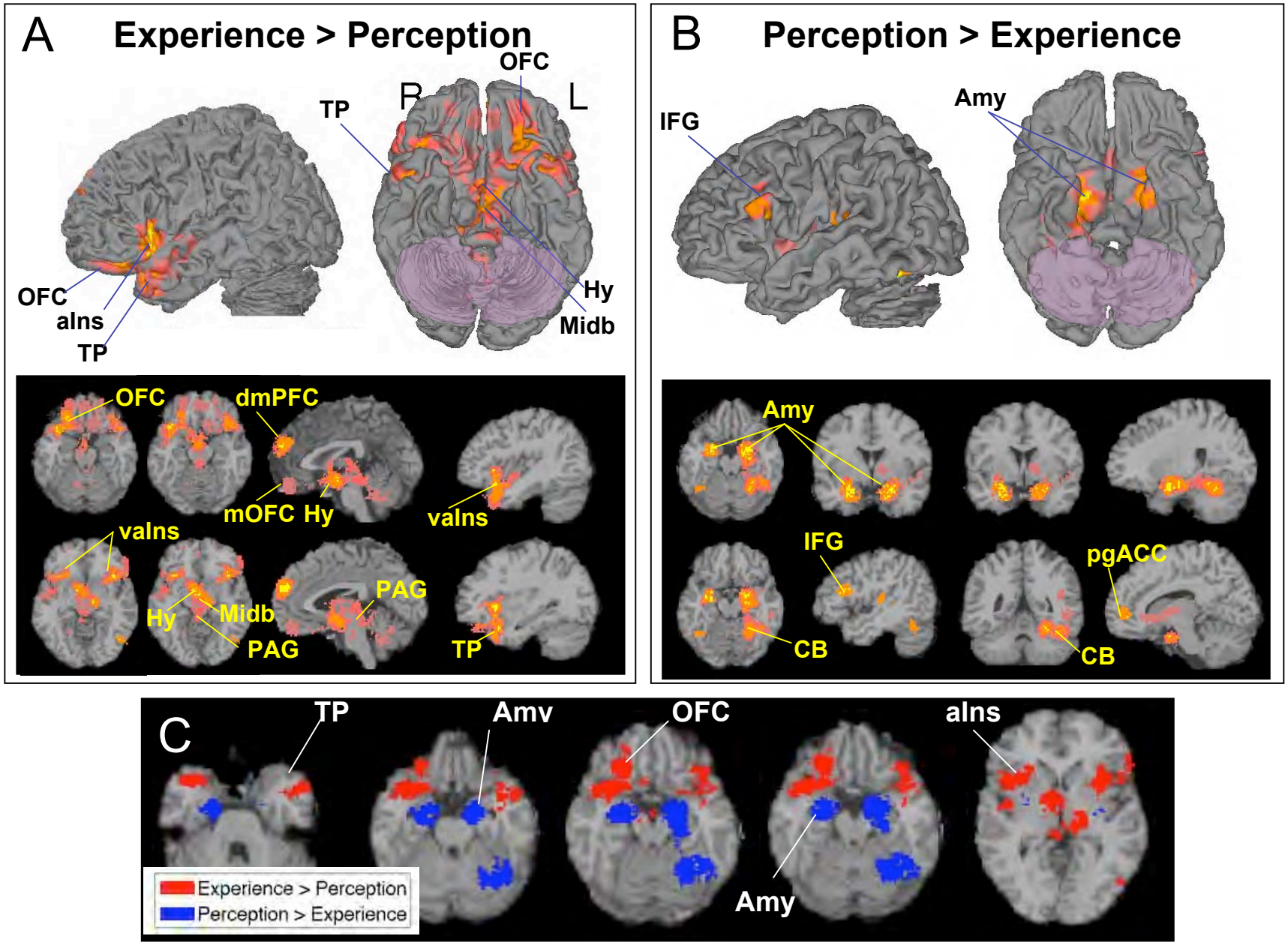
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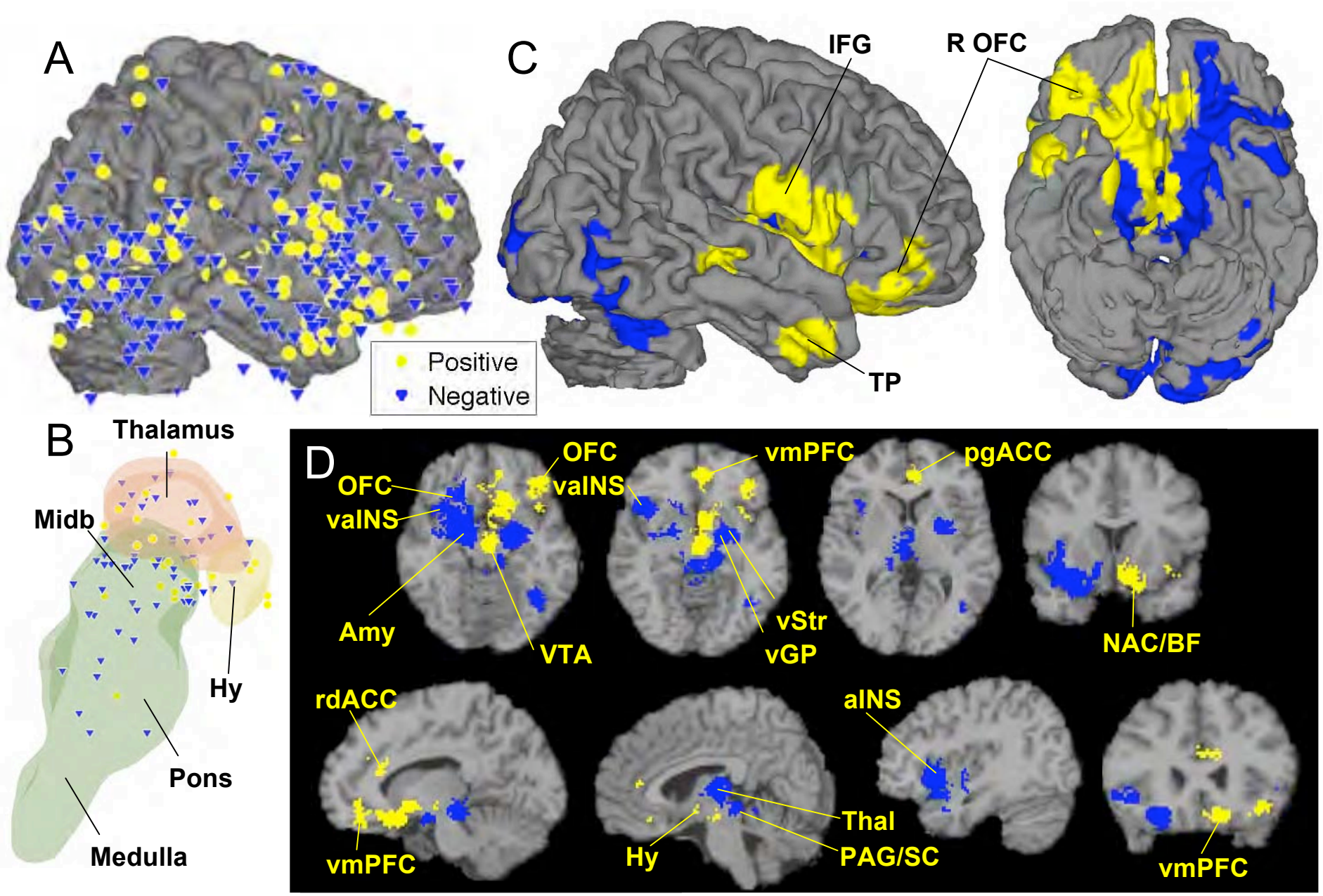
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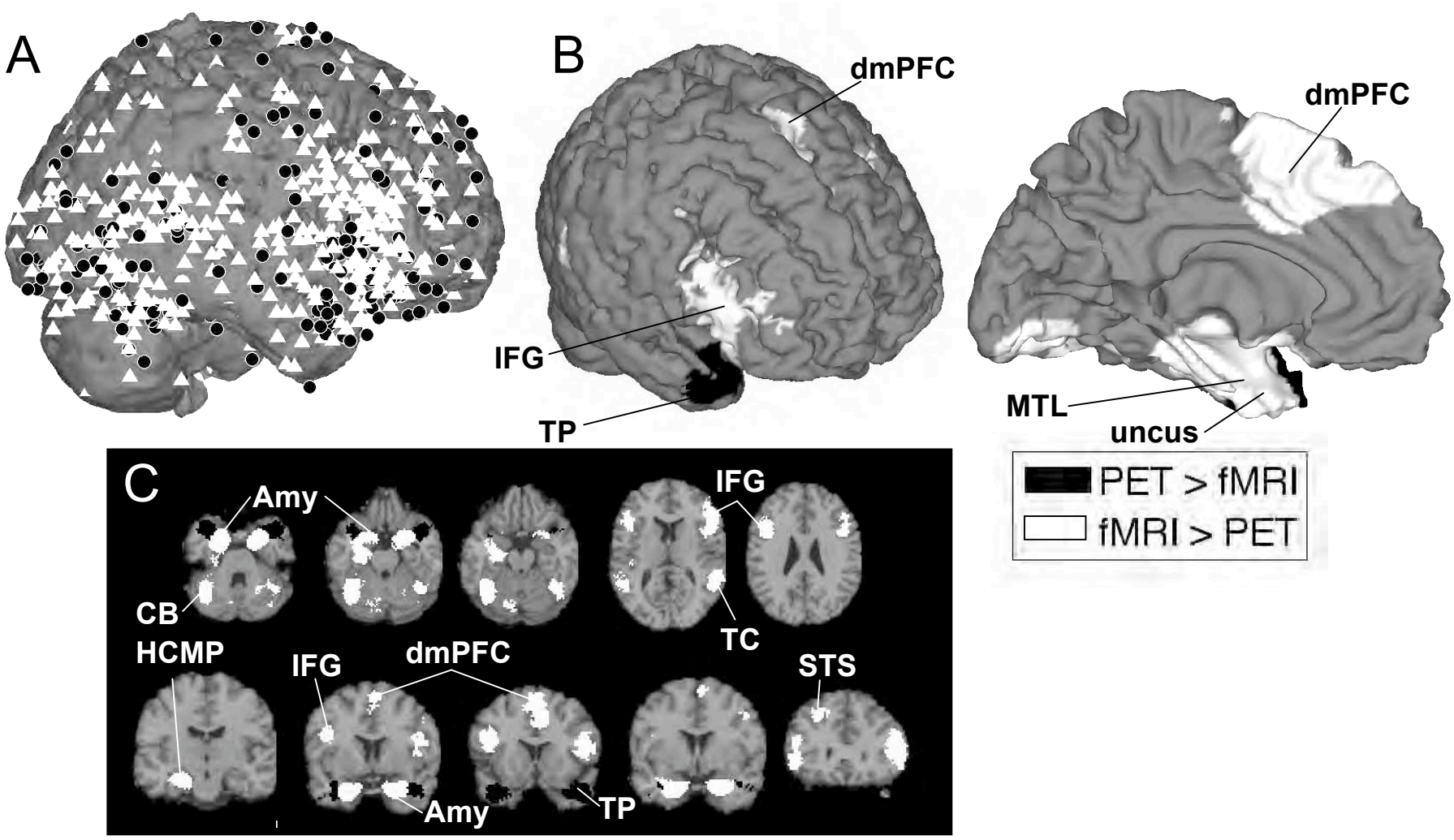
PAG/SC
aINS
vmPFC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dmPFC
TC
STS
Amy
TP

The Neuroimaging of Emotion

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Table 1. Studies included in the meta-analysis

Studies of emotional experience

						Emotion						Induction method				
1st author	Year	Imaging	Sex	N	Valence	Aff	Ang	Disg	Fear	Hap	Sad	Vis	Aud	T/Olf	Rec	Img
Schafer	2005	fMRI	X	40	Neg			o	o			o				
Grimm	2005	fMRI	X	29	Neg	o						o				
Hutcherson	2005	fMRI	F	28	Neg	o						o				
Cato	2004	fMRI	X	26	Neg	o									o	
Eugene	2003	fMRI	F	20	Neg						o	o				
Lang	1998	fMRI	X	20	Neg				o			o				
Levesque	2003	fMRI	F	20	Neg	o						o				
Stark	2003	fMRI	X	19	Neg			o	o			o				
Aron	2005	fMRI	X	17	Pos	o										o
Simpson	2000	fMRI	X	17	Neg	o						o				
Anderson	2003	fMRI	X	16	Neg	o								o		
Dolcos	2004	fMRI	F	16	Neg	o						o				
Gottfried	2002	fMRI	X	15	Pos	o								o		
Stark	2005	fMRI	X	15	Neg	o						o				
Canli	1998	fMRI	F	14	Pos	o						o				
Goel	2001	fMRI	X	14	Pos	o							o			
Fulbright	1998	fMRI	X	13	Neg	o								o		
Goldin	2005	fMRI	F	13	Pos	o					o	o				
Heinzel	2005	fMRI	X	13	X	o						o				
Markowitch	2003	fMRI	X	13	Pos						o				o	
Moll	2005	fMRI	X	13	Neg				o	o						o
Northoff	2004	fMRI	X	13	X	o						o				
Shirao	2005	fMRI	F	13	Neg	o									o	
Elliott	2000	fMRI	X	12	Pos	o				o		o				
Fitzgerald	2004	fMRI	X	12	Neg			o								o
Maratos	2001	fMRI	X	12	Pos					o	o	o				
Schienle	2006	fMRI	F	12	Neg			o	o			o				
Schienle	2002	fMRI	F	12	Neg			o				o				
DeAraujo	2003	fMRI	X	11	Pos	o								o		
Hariri	2003	fMRI	X	11	Neg							o				
Beauregard	2001	fMRI	M	10	Pos	o						o				
Canli	2000	fMRI	F	10	Neg	o						o				
Klein	2003	fMRI	F	10	Neg	o						o				
Lee	2004	fMRI	X	10	Pos						o	o				
Maddock	1997	fMRI	X	10	Neg	o							o			
Ruby	2004	fMRI	M	10	X		o									o
Wrase	2003	fMRI	F	10	Neg			o	o			o				
Yamasaki	2002	fMRI	X	10	Neg	o						o				
Kringelbach	2003	fMRI	M	9	Pos	o								o		
O'Doherty (b)	2001	fMRI	X	9	Neg						o	o				
Small	2003	fMRI	X	9	Neg					o				o		
Whalen	1998	fMRI	M	8	Neg		o		o			o				
Wright	2004	fMRI	X	8	Neg							o				
Beauregard	1998	fMRI	X	7	Neg						o	o				
Moll	2002	fMRI	X	7	Neg			o				o				
O'Doherty (a)	2001	fMRI	?	7	Neg	o								o		
Phana	2004	fMRI	X	7	Neg			o	o			o				
Bystritsky	2001	fMRI	X	6	Neg				o							o

Table 1 (con't).

Herpetz	2001	fMRI	F	6	Neg	o					o		o				
Nitschke	2004	fMRI	F	6	Pos	o	o						o				
Teasdale	1999	fMRI	X	6	Pos								o				
Francis	1999	fMRI	?	4	Pos	o									o		
Lorberbaum	1999	fMRI	F	4	Neg				o					o			
Damasio	2000	PET	X	25*	Pos		o		o	o	o					o	
George	1994	PET	X	21	Neg						o		o				
Kimbrell	1999	PET	X	16	Neg	o										o	
Paradiso	2003	PET	X	17	Neg	o		o		o			o				
Pietrini	2000	PET	X	15	Neg				o	o							o
Taylor	2000	PET	X	14	Neg	o							o				
Lane (a)	1997	PET	F	12	Pos	o							o				
Lane	1998	PET	F	12	X	o							o			o	
Partiot	1995	PET	?	12	Neg				o								o
Reiman	1997	PET	F	12	X				o				o			o	
Zald	1997	PET	F	12	Neg	o									o		
Aalto	2002	PET	F	11	Neg					o	o		o				
Aalto	2005	PET	F	11	Neg	o							o				
Gemar	1996	PET	M	11	Neg						o					o	
George	1995	PET	F	11	Neg						o					o	
Lane (c)	1997	PET	F	11	Pos	o							o			o	
Baker	1997	PET	M	10	Pos					o	o			o			
Beauregard	1997	PET	M	10	X	o							o				
Blood	2001	PET	X	10	Pos	o								o			
Blood	1999	PET	X	10	Pos	o								o			
Dolan	2000	PET	M	10	X	o							o				
George	1996	PET	M	10	Pos					o	o					o	
Lane (b)	1997	PET	M	10	X			o		o	o		o				
Liberzon	2000	PET	F	10	Neg	o							o				
Liberzon	2000	PET	F	10	Neg	o							o				
Liberzon	2003	PET	X	10	Neg				o				o				
Taylor	2003	PET	X	10	Neg	o							o				
Redoute	2000	PET	M	9	Pos	o							o				
Zald	1998	PET	F	9	Pos	o									o		
Dougherty	1999	PET	M	8	Neg		o										o
Liotti	2000	PET	F	8	Neg	o										o	
Mayberg	1999	PET	F	8	Neg											o	
Ottowitz	2004	PET	F	8	Neg						o						o
Paradiso	1997	PET	X	8	Pos	o							o				
Rauch	1999	PET	M	8	Pos	o										o	
Shin	2000	PET	M	8	Neg				o							o	
Taylor	1998	PET	F	8	Neg	o							o				
Kosslyn	1996	PET	M	7	Neg	o							o				
Pardo	1993	PET	X	7	Neg						o					o	
Fischer	1996	PET	X	6	Neg	o										o	
Isenberg	1999	PET	X	6	Neg		o		o	o	o		o				
Lane	1999	PET	M	6	X	o							o				

Table 1 (con't)

Studies of mixed or ambiguous perception / experience

						Emotion						Induction method				
Study	**Year**	**Imaging**	**Sex**	**N**	**Valence**	**Aff**	**Ang**	**Disg**	**Fear**	**Hap**	**Sad**	**Vis**	**Aud**	**T/Olf**	**Rec**	**Img**
Habel	2005	fMRI	M	26	Pos					o		o				
Kuchinke	2005	fMRI	X	20	Pos	o						o				
Crosson	1999	fMRI	X	17	X	o							o			
Wicker	2003	fMRI	M	14	Neg							o		o		
Hariri	2002	fMRI	X	12	Neg	o						o				
Zatorre	2000	fMRI	X	12	X									o		
Rolls	2003	fMRI	X	11	Neg	o								o		
Buchanan	2000	fMRI	M	10	X	o				o	o		o			
Tabert	2001	fMRI	F	9	Neg	o						o				
Paradiso	1999	PET	X	17	Pos						o	o				
Royet	2000	PET	M	12	X							o	o			
Royet	2001	PET	M	12	X	o								o		
Zatorre	2000	PET	X	12	X									o		
Frey	2000	PET	F	11	Neg	o							o			

Studies of emotional perception

						Emotion						Induction method				
Study	**Year**	**Imaging**	**Sex**	**N**	**Valence**	**Aff**	**Ang**	**Disg**	**Fear**	**Hap**	**Sad**	**Vis**	**Aud**	**T/Olf**	**Rec**	**Img**
Das	2005	fMRI	X	28	Neg				o			o				
Tessitore	2005	fMRI	X	27	X				o			o				
Liddell	2005	fMRI	X	25	Neg				o		o	o				
Fischer	2004	fMRI	X	24	Neg		o					o				
Williams_L	2004	fMRI	X	22	Neg				o			o				
KeslerWest	2001	fMRI	X	21	Neg					o	o	o				
Pessoa	2002	fMRI	X	21	Neg	o						o	o			
Fitzgerald	2005	fMRI	X	20	Pos		o	o	o	o	o	o				
Grobras	2005	fMRI	X	20	Neg		o					o				
Schroeder	2004	fMRI	X	20	Neg							o				
Hariri	2000	fMRI	X	16	X		o		o			o				
Somerville	2004	fMRI	X	16	Pos		o	o	o			o				
Fecteau	2005	fMRI	X	15	X								o			
Grandjean	2005	fMRI	X	15	Neg		o						o			
Reinders	2005	fMRI	X	15	Neg	o						o				
Gur	2002	fMRI	X	14	X			o	o	o		o				
Shin	2005	fMRI	M	13	Neg	o						o				
Williams_L	2005	fMRI	X	13	Neg		o	o	o			o				
Williams_M	2005	fMRI	X	13	X	o						o				
Dolan	2001	fMRI	X	12	Neg				o			o	o			
Iidaka	2001	fMRI	X	12	Neg							o				
Killgore	2004	fMRI	F	12	X		o			o		o				
Strange	2000	fMRI	X	12	Neg	o						o				
Vuilleumier	2001	fMRI	X	12	Neg						o	o				
Wang	2005	fMRI	X	12	Neg				o			o				
Adams	2003	fMRI	X	11	Neg							o				
Williams_L	2001	fMRI	M	11	Neg				o			o				
Breiter	1996	fMRI	M	10	Pos				o	o		o				
Gorno_tempini	2001	fMRI	X	10	Pos			o		o		o				
Hare	2005	fMRI	X	10	Pos							o				

Table 1 (con't)

McCullough	2005	fMRI	X	10	X	o						o				
Sato	2004	fMRI	X	10	Neg			o	o			o				
Wildgruber	2005	fMRI	X	10	X								o			
Critchley	2000	fMRI	X	9	X							o				
Lange	2003	fMRI	?	9	Neg	o						o				
Nomura	2004	fMRI	X	9	Neg	o						o				
Dolan	1996	fMRI	M	8	Pos					o		o				
Narumoto	2000	fMRI	X	8	X	o						o				
Phillips	2004	fMRI	M	8	Neg			o	o			o				
Phillipsb	1998	fMRI	X	8	Pos		o					o				
Whalen	2001	fMRI	X	8	Neg	o		o				o				
Phillips	1997	fMRI	X	7	Neg			o	o			o				
Phillipsa	1998	fMRI	M	6	Neg					o		o	o			
Sprengelmeyer	1998	fMRI	X	6	Neg			o	o			o				
Blair	1999	PET	M	13	Neg		o				o	o				
George	1996	PET	X	13	X								o			
Kilts	2003	PET	X	13	Pos		o		o			o				
George	1993	PET	F	9	X							o				
Pourtois	2005	PET	M	8	Neg	o						o				
Sergent	1994	PET	M	8	X	o						o				
Nakamura	1999	PET	M	7	X							o				
Imaizumi	1997	PET	M	6	X	o							o			
Morris	1999	PET	M	6	X	o							o			
Morris	1996	PET	X	5	Pos	o			o	o		o				
Morris	1998	PET	X	5	X	o			o			o				
						Emotion						**Induction method**				
						Aff	**Ang**	**Disg**	**Fear**	**Hap**	**Sad**	**Vis**	**Aud**	**T/Olf**	**Rec**	**Img**
Totals						**77**	**17**	**20**	**37**	**23**	**26**	**112**	**19**	**15**	**17**	**9**

*** Damasio 2000 had differing numbers of subjects for each emotion, ranging from 16 for the lowest and 25 for the highest.**