PERSPECTIVES

On the relationship between emotion and cognition

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Abstract | The current view of brain organization supports the notion that there is a considerable degree of functional specialization and that many regions can be conceptualized as either 'affective' or 'cognitive'. Popular examples are the amygdala in the domain of emotion and the lateral prefrontal cortex in the case of cognition. This prevalent view is problematic for a number of reasons. Here, I will argue that complex cognitive–emotional behaviours have their basis in dynamic coalitions of networks of brain areas, none of which should be conceptualized as specifically affective or cognitive. Central to cognitive–emotional interactions are brain areas with a high degree of connectivity, called hubs, which are critical for regulating the flow and integration of information between regions.

The relationship between cognition and emotion has fascinated Western philosophers for centuries. It is not surprising that much of that attraction has permeated brain science in general. Early reports, such as the now classic case of Phineas Gage, described how damage to specific parts of the brain caused changes (or lack thereof) in cognitive and emotional behaviours. Indeed, since at least Broca (1824–1880) the concept of functional localization has shaped our understanding of brain function. In attempting to localize affect in the brain, an appealing approach has been to separate the 'emotional brain' from the 'cognitive brain'.

In this Perspective I will make a case for the notion, based on current knowledge of brain function and connectivity, that parcelling the brain into cognitive and affective regions is inherently problematic, and ultimately untenable for at least three reasons: first, brain regions viewed as 'affective' are also involved in cognition; second, brain regions viewed as 'cognitive' are also involved in emotion; and critically, third, cognition and emotion are integrated in the brain. In the past two decades, several researchers have emphasized that emotion and cognition systems interact in important ways[1–7]. Here, I will argue that there are no

truly separate systems for emotion and cognition because complex cognitive–emotional behaviour emerges from the rich, dynamic interactions between brain networks. Indeed, I propose that emotion and cognition not only strongly interact in the brain, but that they are often integrated so that they jointly contribute to behaviour. Moreover, I propose that emotion and cognition are only minimally decomposable in the brain, and that the neural basis of emotion and cognition should be viewed as strongly non-modular.

Cognition and emotion

Cognition refers to processes such as memory, attention, language, problem solving and planning. Many cognitive processes are thought to involve sophisticated functions that might be uniquely human. Furthermore, they often involve so-called controlled processes, such as when the pursuit of a goal needs to be protected from interference. A prototypical example of a neural correlate of a cognitive process is the sustained firing of cells in dorsolateral prefrontal cortex (DLPFC) as a monkey maintains information in mind for brief periods of time[8,9]. With the advent of functional MRI (fMRI), a mounting literature documents how a variety of cognitive

processes are linked to specific parts of the brain. According to this literature, in the vast majority of cases, cognitive processes appear to engage cortical regions.

Whereas there is relative agreement about what constitutes cognition, the same cannot be said about emotion. Some investigators use definitions that incorporate the concepts of drive and motivation: "emotions are states elicited by rewards and punishers"[10]. Others favour the view that emotions are involved in the conscious (or unconscious) evaluation of events[11] (that is, appraisals). Some approaches focus on basic emotions[12] (for example, fear and anger), others on an extended set of emotions, including moral ones[6,13] (for example, pride and envy). Strong evidence also links emotions to the body[1,14]. For the purpose of this article, because of the inherent difficulty in providing clear definitions of both cognition and emotion, I will not further define these terms.

Brain structures linked to emotion are often subcortical, such as the amygdala, ventral striatum and hypothalamus (BOX 1). These structures are often considered evolutionarily conserved, or 'primitive'. They are also believed to operate fast and in an automatic fashion, so that certain trigger features (for example, the white of the eyes in a fearful expression[15]) are relatively unfiltered and always evoke responses that might be important for survival. Furthermore, the functioning of subcortical structures that mediate emotion is thought to be 'unaware'. In other words, an individual is not necessarily conscious of a stimulus that might have triggered brain responses in an affective brain region[16,17].

Affective brain regions in cognition

The hypothalamus was one of the first regions linked to emotion. It was perhaps not until the proposal by Papez[18] that a network theory for emotion was advanced. The so-called Papez circuit was further elaborated by MacLean[19], whose proposal became enshrined in the 'limbic system' concept. Unfortunately, although the term limbic system continues to be widely used today, it fails to provide a coherent description of the emotional brain (BOX 2). The original set of regions proposed by

MacLean includes many areas that are no longer viewed as critically linked to affect, such as the hippocampus (but see REF. 5). Conversely, many areas that were not originally included in the limbic system are believed to have important affective functions, for example the orbitofrontal cortex (OFC). Over the years, the set of regions that constitute the emotional brain has fluctuated considerably. What are the reasons for this state of affairs?

This Perspective shows that it has proven difficult to define the emotional brain because each one of the 'core' and 'extended' affective regions (BOX 1) is itself a complex area that is involved in numerous functions. Critically, these functions do not map cleanly onto 'affective functions' (see also REFS. 20,21). I will briefly illustrate this problem for the amygdala, a core 'affective' region, although the same could be done for other regions (such as the nucleus accumbens). For simplicity, in the remainder of this article, I will largely drop the quotes from 'affective' and 'cognitive'. Also, the terms 'affect' and 'emotion' will be used synonymously.

The amygdala in attention. Although more nuanced views of amygdala function have been suggested[22–24] (see also REF. 25), most proposals describe this structure in terms of affective functions. Indeed, the amygdala is often categorized as an affective region strongly linked to fear processing[26,27]. Evidence concerning fear conditioning in rats, deficits in the recognition of fearful expressions in patients with bilateral amygdala lesions and the robust responses evoked by fearful faces in neuroimaging studies, have popularized the view of the amygdala as a 'fear centre'. However, this structure is also involved in several functions that are closely linked to cognition, including attention and associative learning[28].

A central function of attention, a paradigmatic cognitive process, is to modulate sensory processing. For instance, attention to a stimulus increases neuronal firing rates (and fMRI responses) in sensory cortex and is believed to improve behavioural performance[29,30]. Such 'competitive advantage' also occurs during the viewing of emotion-laden visual stimuli[31,32]. The amygdala probably

underlies these effects. Indeed, recent studies have provided evidence that the amygdala mediates the processing advantage of emotional items[33]. Furthermore, in neuroimaging studies, amygdala activation is correlated with activation in the visual cortex[34,35] and this correlation is attenuated in patients with amygdala damage[36]. Thus, the amygdala might underlie a form of emotional modulation of information that in many ways parallels the attentional effects observed in the visual cortex.

For instance, during conditions of spatial competition during which target letters were shown superimposed on task-irrelevant photos of faces, affectively significant faces (owing to prior pairing with mild electrical stimulation) were more strongly encoded even though they were task-irrelevant[37]. In a second study, participants exhibited increased sensitivity to shock-paired relative to unpaired faces[38]: during a neutral/fearful discrimination task, they were more likely to report computer-morphed, graded faces as 'fearful' if they were shown in a colour that was previously paired with shock. Finally, in a third study, participants exhibited increased sensitivity for visual patches that were previously paired with shock[39]. Notably, increases in detection performance were paralleled by increases in visual activation across retinotopically organized cortex, including the primary visual area (V1). Overall, increasing the affective significance of a stimulus in a manner that is believed to be strongly amygdala-dependent[3,40] has effects that are similar to those of increased attention (see also REFS 41–43).

A widespread view is that the amygdala functions in a largely automatic fashion that is independent of top-down factors such as attention and task context[4,16] and thus, independent of conscious awareness. Consistent with this notion, amygdala responses are observed under conditions of inattention[44] and with minimal sensory input[15]. Recent studies have shown, however, that the amygdala functions in a manner that is closely tied to top-down factors[45–58]. For instance, amygdala responses are strongly dependent on attention, even for stimuli that are affectively significant (owing to previous pairing with mild shocks)[37]. Amygdala responses appear to be closely linked to perception, and are not simply predicted by the physical characteristics of the stimulus — for example, responses to a briefly presented, fearful face differ greatly depending on whether participants actually report perceiving a fearful face[49]. In general, controlling attention to,

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Box 1 | **The emotional brain: core and extended regions**

Medial view **Lateral view**
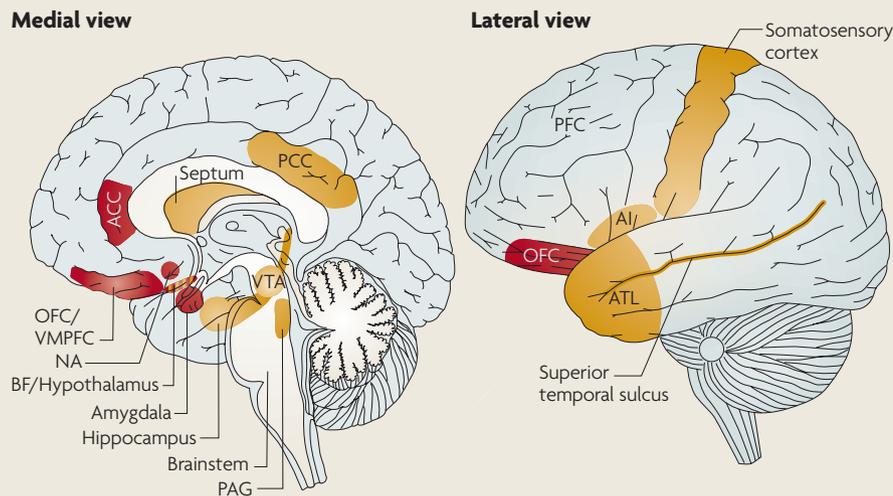
Summarizing the set of brain regions that comprise the emotional brain is plagued by possibly insurmountable conceptual difficulties. Nevertheless, some regions feature prominently in the discourse surrounding affective neuroscience. They are listed here based on an informal assessment of the frequency with which they appear in the literature; regions appearing with greater frequency will be labelled 'core', and less frequent ones as 'extended'. The core emotional regions (dark red areas in figure) include, subcortically, the amygdala, the nucleus accumbens (NA) and the hypothalamus, and cortically, the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC) (especially the rostral part) and the ventromedial prefrontal cortex (VMPFC). Extended regions (brown areas) include, subcortically, the brain stem, the ventral tegmental area (VTA) (and associated mesolimbic dopamine system), the hippocampus, the periaquaeductal grey (PAG), the septum and the basal forebrain (BF) (including the nucleus basalis of Meynert); and cortically, the anterior insula (AI), the prefrontal cortex (PFC), the anterior temporal lobe (ATL), the posterior cingulate cortex (PCC), superior temporal sulcus, and somatosensory cortex. Although one could attempt to link the core and extended regions to specific affective functions, such an attempt would be largely problematic because none of the regions is best viewed as 'purely affective'.

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and 'cognitively' changing the meaning of, emotionally evocative stimuli greatly affects amygdala responses[59].

Thus, converging evidence is starting to paint a dynamic and context-dependent picture of amygdala function which complements the notion that this structure becomes activated automatically in response to specific trigger features. These findings are consistent with early observations that electrical stimulation of the amygdala produced both attentional and affective responses[60]. More generally, they concur with the view that the "amygdala enables monitoring, updating and integrating sensory signals"[61] (see also REFS. 62,63).

Cognitive brain regions in emotion

The prefrontal and parietal cortices are thought to have a central role in cognition, for example in the control of attention[30,64–66]. The PFC, especially its lateral aspect, is critical for the maintenance and manipulation of information. It is also believed to detect conflict and perform 'cognitive control' operations that regulate the flow of information during non-routine, challenging situations[67]. However, since at least Nauta's synthesis of frontal lobe function[68], it has been suggested that the PFC has a central role in affect. Indeed, Nauta suggested that the frontal cortex could be considered "the major — although not the only — neocortical representative of the limbic system"[68].

It is now accepted that the PFC is not a homogeneous structure but can be subdivided into many regions based on functional specialization, cytoarchitecture and connectivity. Moreover, major PFC territories are involved in emotion — these include the anterior cingulate cortex (ACC), especially anterior and subgenual sites, the OFC, the ventromedial PFC (VMPFC) and the inferior portions of the inferior frontal gyrus abutting the anterior insula. Indeed, these sites feature prominently in several influential proposals[10,14,69]. Nevertheless, many current views of PFC function tend to focus on its cognitive aspects (see REF. 70 for a recent discussion). By minimizing the important insights of Nauta[68], Pribram[71,72] and others, they portray the PFC's core function as cognitive. For instance, an influential framework of PFC function mentions emotion only in a tangential manner[65]. Although several subregions of the PFC are currently acknowledged as important for emotion, a careful assessment of existing proposals suggests that they compartmentalize the PFC into separate affective and cognitive territories (see also REF. 73). It is particularly noteworthy that in what could be viewed as

a gradual retreat of cognitive functions into fewer and fewer PFC territories, lateral PFC (including DLPFC) still features prominently as purely cognitive. This cognitive outlook does not incorporate, however, the wealth of data demonstrating that cognitive and affective information are strongly integrated in the lateral PFC (see next section). In summary, many researchers who regard the PFC as heterogeneous suggest that emotion is confined to a set of PFC subterritories (for example, the OFC and the VMPFC) and that cognition is based in other areas (for example, in the LPFC, especially dorsally).

One notable exception concerns the work by Davidson and colleagues[5,69]. These authors propose that the left PFC is involved in approach-related, appetitive goals, especially when multiple alternative responses are possible. Additionally, hypoactivation in the left PFC is linked to depression. By contrast, the right PFC is proposed to be involved in situations that require behavioural inhibition and withdrawal, again, especially when alternative approach options are possible.

Integration of cognition and emotion

Functional studies. The LPFC is an example of a brain region in which cognition and emotion interact. Given that the LPFC

(especially the DLPFC) is commonly viewed as a purely cognitive area, this region provides a test for the hypothesis that cognition and emotion are strongly integrated in the brain.

An important dimension of cognition involves behavioural inhibition. Response inhibition (the processes required to cancel an intended action) is believed to involve control regions in the prefrontal cortex (for example, DLPFC, ACC and inferior frontal cortex)[74,75]. Goldstein and colleagues[76] investigated the interaction between the processing of emotional word stimuli and response inhibition. Response inhibition following negative words (for example, 'worthless') engaged the DLPFC even though this region was not recruited by negative valence or inhibitory task demands *per se,* revealing an explicit interaction between the two. Evidence for cognitive–emotional integration in the LPFC also comes from working-memory studies involving the maintenance and updating of information. For instance, when participants were asked to keep in mind neutral or emotional pictures[77], maintenance-related activity in the DLPFC was modulated by the valence of the picture, with pleasant pictures enhancing activity and unpleasant pictures decreasing activity relative to neutral pictures.

Box 2 | What is the limbic system?

The limbic system[18,19] probably deserves the distinction of being one of the most popular neural systems of the twentieth century[98]. Yet no generally accepted definition of the system exists — I contend that this is because the limbic system is frequently linked to the 'affective brain system'. Insofar as the latter has resisted agreed-upon characterizations, the limbic-system idea has also been problematic. In its original formulation it included the thalamus, the hypothalamus, the hippocampus and the cingulate cortex, in addition to other structures such as the amygdala and the septum. However, the term limbic is problematic in itself because historically it has been linked to diverse functions such as learning and memory, sensory processing, cognitive processing, motor functions and emotion[155].

A further source of confusion is that many authors, especially anatomists, use the term limbic on anatomical grounds. The limbus (or border) of the cerebral hemispheres comprises the cingulate gyrus (from the parolfactory area to the uncus of the parahippocampal gyrus[156]). Hence, regions along this 'belt' are typically designated as (anatomically) limbic, and include the anterior cingulate, the retrosplenial cortex, the hippocampal complex, the amygdaloid complex and other related basal forebrain structures (for example, the basal nucleus of Meynert). Readers should note that some of these regions (for example, the cingulate gyrus) are at times denoted as paralimbic[83] because their cytoarchitecture is more complex than that observed in other limbic regions, such as the amygdala. The increased cytoarchitectonic elaboration of regions such as the cingulate gyrus is shared with other medial regions, including territories of the temporal pole, the orbitofrontal cortex and the insula, which are at times denoted as paralimbic (or, to add to the confusion, simply limbic). It should also be noted that designations based on anatomical criteria do not necessarily imply a correspondence with the concept of the 'emotional' brain.

Thus, the limbic system does not appear to be a well-defined functional brain system. Early critics of the concept[89,157,158] have been joined more recently by LeDoux[92], who has suggested that the term be dropped. At the very least, researchers should not employ the term in a circular fashion, namely, to define the very system that they wish to study. Although current usage of term limbic system is of limited value, it might be premature to abandon the concept altogether. For instance, the idea of an anatomically based 'limbic lobe'[98] or of limbic regions based on anatomical criteria, could prove very helpful in understanding how cognition and emotion interact in the brain[93].

Interestingly, emotional pictures did not affect DLPFC responses during a second experimental condition during which participants were not required to keep information in mind, indicating that the modulation of sustained activity by emotional valence was particular to the experimental context requiring active maintenance. In another fMRI study[78], participants watched short videos intended to induce emotional states, after which they performed challenging working-memory tasks. Remarkably, bilateral LPFC activity reflected equally the emotional and working-memory task components, such that activity was not predictable given only information about either component in isolation. In addition, fMRI signals in the LPFC were predictive of task performance.

Taken together, functional studies of the LPFC provide evidence that cognition and emotion are integrated in this area (see also REFS. 5,79–82). BOX 3 summarizes additional evidence of the integration between cognition and motivation in the LPFC. As stated previously, other PFC territories, notably the OFC, VMPFC and ACC, are now considered to be strongly involved in affective function, and there is evidence for functional integration of cognition and emotion in these regions[1,14].

Structural connectivity.
Anatomy is often used to suggest a separation between cognition and emotion. In particular, lesion studies have been interpreted to show that specific areas support specific functions (for example, see REF. 27), a question that we will return to in a later section. Many of the brain structures deemed to be affective are subcortical, such as the hypothalamus, amygdala and nucleus accumbens. Interestingly, the cortical regions that are considered affective involve the more 'primitive' cortex. For instance, rather than the 6 (or more) differentiated layers in fully developed cortex, only 3 to 4 layers are observed in portions of the OFC[61,83] and ACC[83], which are often described as limbic or paralimbic on anatomical grounds (BOX 2).

In attempting to understand the relationship between emotion and cognition, however, it is important to consider other forms of anatomical information. Advances in our understanding of brain connectivity suggest that a given brain region is only a few synapses away from every other brain region[84,85]. Indeed, it appears that the brain is configured according to a small-world topology in which the path length between nodes is small — typically, cortical areas are connected directly or by just one or two

intermediate areas[86,87] — and nodes are highly clustered[88]. Thus, a careful consideration of brain connectivity is essential to understand potential cognitive–emotional interactions and integration.

Young and colleagues have quantitatively analysed brain connectivity[89,90]. They found that prefrontal areas were among those most distant from the sensory periphery, suggesting that they receive highly-processed and integrated sensory information. Such potential insulation of the PFC from the periphery is thought to be a key anatomical feature of this region and presumably confers the primate brain with a greater degree of flexibility[91]. Highly processed information would also be able to support the more abstract processing that is required for cognition. Interestingly, the analysis by Young

and colleagues revealed that the amygdala (and other regions, such as the hippocampus and entorhinal cortex) is equally removed from the sensory periphery — although in some species, direct sensory thalamic projections might be present[92]. In addition, the authors showed that the amygdala makes very widespread projections, connecting with all but 8 of the cortical areas they included in the analysis. They concluded that the amygdala "occupies a position at the very geometric centre of the topological map" (FIG. 1), suggesting that this structure is one of the most highly connected regions of the brain (see also REFS. 93,94). Overall, it appears that the amygdala, a core affective region, is at least as well situated to integrate and distribute information as certain PFC territories.

Box 3 | **Integration of cognition and motivation**
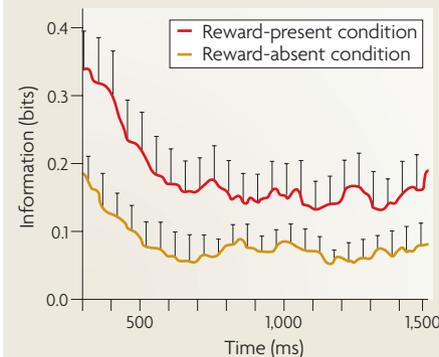
Motivation is commonly defined as what makes one work to obtain a reward or to avoid punishment. Emotion and motivation are closely linked as both depend on the relationship between the organism and its environment. In the case of emotion, the emphasis might be on the evaluative aspect of this relationship, whereas in the case of motivation it might be on how the organism acts in a given situation[159,160]. Although this article focuses on the relationship between emotion and cognition, a strong case can be made for the integration between motivation and cognition, too.

Cells in the lateral prefrontal cortex (LPFC) not only hold information concerning an object's shape and location, they are also modulated by reward magnitude. Watanabe[161,162] showed that in monkeys activity of dorsolateral prefrontal cortex (DLPFC) neurons reflects both working memory and reward expectancy. For instance, some neurons exhibited stronger sustained activity when an eye movement to the left (versus right) had to be generated at the end of the trial. At the same time, their firing rate was modulated by reward, being highest for a piece of raisin, intermediate for a piece of apple and lowest for a piece of sweet potato. Indeed, delay-related activity was modulated in a more quantitative fashion, such that a larger reward led to increased delay-related activity relative to a smaller reward[163]. Furthermore, neurons in the LPFC might represent the time-discounted value of an expected reward[164,165].

Additional studies suggest that motivational information not only modulates LPFC cell activity, but that cognition and motivation are integrated in the LPFC. For instance, during the delay period of a delayed-saccade task, some LPFC cells[166] increase their firing if the monkey is initially cued to make a saccade to the preferred direction (relative to the opposite direction); these cells also show increased firing during rewarded trials (relative to unrewarded trials) (see figure). However, spatial and reward information do not simply add during rewarded trials to the preferred direction. Instead, there is an increase of the amount of transmitted information with respect to target position, as quantified by information theory. In other words, the reward information appears to increase the discriminability of target positions, leading to an enhancement of performance (see also REF. 167).

Watanabe and colleagues have also described reinforcement-related neurons that exhibit activity changes only when reward is provided in the context of correct task performance; error-related neurons exhibit activity changes when an error is made and the reward is not given to the animal, again only in the task context. Thus, the activity of these neurons does not solely code motivational aspects, but rather codes the reward within the context in which a reward is given. These neurons appear to have a role in the animal's decision of whether or not the current behavioural strategy should be maintained[168,169]. Figure reproduced, with permission, from REF. 158 © (2002) American Physiological Society.
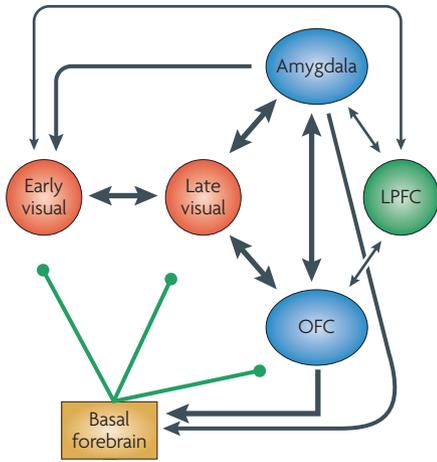
Figure 1 | Brain connectivity graph. Quantitative analysis of brain connectivity reveals several clusters of highly interconnected regions (represented by different colours). In this analysis by Young and collaborators[89], the amygdala (Amyg, centre of figure) was connected to all but 8 cortical areas. These connections involved multiple region clusters, suggesting that the amygdala is not only highly connected, but that its connectivity topology might be consistent with that of a connector hub that links multiple provincial hubs, each of which links regions within separate functional clusters. In this manner, the amygdala is hypothesized to be a strong candidate for integrating cognitive and emotional information. Figure labels represent different cortical areas with the exception of Hipp (hippocampus) and Amyg, which represent subcortical areas. Figure reproduced, with permission, from REF. 82 © (1994) Freund Publishing.

It is also instructive to consider the connectivity of the hypothalamus[95], as it has been long recognized for its importance in emotional behaviours[96,97]. In particular, through its descending connections that innervate brainstem motor systems, this structure is thought to have a key role in the implementation of goal-directed behaviours. Hypothalamic signals can also be conveyed to the cortex, mostly by way of the thalamus. Critically, prefrontal cortical territories project directly to the hypothalamus. Thus, the hypothalamus appears to be organized in such a way that it can generate both relatively reflexive behaviours and behaviours that are voluntarily triggered by inputs from the cerebral cortex[96]. Overall, this structure appears to be connected with all levels of the nervous system, including the neocortex[96], enabling important hypothalamic regulatory signals to have widespread effects on the brain. As stated by Swanson and colleagues[95]: "It is now clear that the hypothalamus provides a direct input to the entire cortical mantle, and that it may well represent the largest non-thalamic input to the cortex".

It is also important to consider the role of ascending systems. For instance, the basal nucleus of Maynert is a major part of the so-called magnocellular basal forebrain system[98]. The projections from this system reach all parts of the cortical mantle[98] and are involved in cortical arousal and attention mechanisms (see citations in REFS 98,99). In particular, basal forebrain corticopetal cholinergic projections appear to be crucial for diverse attentional functions, including sustained, selective and divided attention[99–101]. Of importance in the present context, the basal forebrain receives both cortical and amygdala inputs (for citations, see REF. 99). Recent anatomical evidence suggests the existence of specific topographically organized prefrontal–basal forebrain–prefrontal loops[102–104], so that specific prefrontal cortical targets of the basal forebrain connect back to sites from which the corticopetal fibres originate. Such loops provide a direct substrate

for cognitive–emotional integration, for example by allowing amygdala signals to be broadcast widely, including to fronto-parietal regions known to be important for the control of attention. More generally, the overall anatomical arrangement of the basal forebrain might involve multiple functional–anatomical macrosystems[105,106] with wide-ranging effects on brain computations and important clinical implications[100,105].

In summary, although anatomical information is often used to promote the idea that cognition and emotion are separated in the brain, the picture that emerges from connectivity data suggests a remarkable potential for integration of information. Regions that are often thought to be purely affective, such as the amygdala[93], the hypothalamus[96], the OFC/VMPFC[93] and the ACC, might function as important connectivity hubs.

Circuits for cognitive–emotional integration
Evaluating sensory information. One example of a brain function that requires cognitive–emotional integration is the evaluation of sensory information. Here, the interaction between cognition and emotion addresses the question: given the present sensory information and the organism's present internal state, how should it act? FIG. 2 illustrates these interactions in the case of visual processing; other modalities exhibit similar interactions (although important differences exist in the case of olfaction).

Visual processing engages the primary visual cortex (V1) and other 'early' visual areas (for example, the V2 and the middle temporal area). Although such processing is now recognized to be quite complex, more sophisticated processing occurs in 'late' areas (for example, along the inferior temporal cortex). Both the amygdala and the OFC receive highly processed visual input from these late visual areas[61,93]. Interestingly, these two structures have strong reciprocal connections with visual sensory areas. Amygdala connections, in particular, terminate at both late and early areas of visual cortex, including the V1 (REFS 107,108). Thus, both the amygdala and the OFC[109] are extremely well positioned to tune perceptual processing in sensory cortex based on stimulus evaluation (see previous discussion of emotional modulation). Visual inputs also reach the LPFC in a relatively direct manner. In particular, the ventrolateral PFC (Brodmann area (BA) 45/47) receives projections from V4, BA8 in the DLPFC receives inputs from V2 and BA46 receives some direct and indirect visual input via BA8 (see references in REF. 93).

Figure 2 | **Circuit for the processing of visual information.** The affective component of a visual item is reflected at multiple processing stages, from early visual areas (including V1) to prefrontal sites. Diffuse, modulatory effects exerted by the basal forebrain are shown in green. Crucially, cognitive and emotional contributions cannot be separated. For instance, visual cortical responses reflecting an item's significance will be a result of simultaneous top-down modulation from fronto-parietal attentional regions (see lateral prefrontal cortex (LPFC)–early visual connections) and emotional modulation from the amygdala (see amygdala–early visual connections). In this manner, the cognitive or affective origin of the modulation is lost and the item's impact on behaviour is both cognitive and emotional. Several connections are not shown to simplify the diagram. Line thickness indicates approximate connection strength. OFC, orbitofrontal cortex.

Overall, visual stimulation (or sensory stimulation, more generally) is rapidly conveyed to multiple regions that collectively are capable of evaluating the input. Thus, a series of neural computations involving several sites determines the significance of the stimulus. Note, however, that whereas it is natural to assume that information flows in a given direction (from the V1 to the late visual cortex to the amygdala to other frontal areas, and back), the parallel and reciprocal nature of the connectivity suggests that more distributed computational frameworks are better suited to describe this arrangement. In addition, the affective processing of a stimulus is not independent of cognitive factors such as attention. On the one hand, an item's affective significance appears to guide attention and enhance the processing of emotion-laden information[31,32]; on the other hand, goal-directed attention and task context influence the neural fate of affectively significant items[17,31]. Finally, the basal-forebrain system,

which is interconnected with the amygdala and the OFC, provides diffuse neuro-modulatory signals to both subcortical and cortical areas. This arrangement is able to enhance the processing of contextually significant information and thus, has both motivational and attentional consequences.

In summary, affective dimensions of a visual item are reflected at multiple processing stages, from early visual areas to prefrontal sites[52]. Critically, in most, if not all processing stages, cognitive and emotional contributions cannot be separated. For instance, visual cortical responses reflecting an item's significance will be a result of simultaneous top-down modulation from fronto-parietal attentional regions and emotional modulation from the amygdala. Consequently, the cognitive or affective origin of the modulation is lost.

Executive control. It is assumed that a cognitive control system exists. Control is required when behaviour calls for less reflexive actions, including circumstances that involve the overriding of prepotent responses[67]. The cognitive control system guides behaviour while maintaining and manipulating goal-related information. Traditionally, the LPFC, the ACC and the parietal cortex are viewed as central nodes in the control system[110–112]. LPFC circuits are especially adept at maintaining information for brief temporal intervals and manipulating information. The parietal cortex, in conjunction with the PFC, has an important role in the control of attention[113]. The function of the ACC is the subject of active research, but appears to include conflict detection[110,111] and/or error monitoring[114].

Although the LPFC, the parietal cortex and the ACC are believed to be central to cognitive control, I suggest a broader cognitive–affective control circuit (FIG. 3). Because an animal decides between possible goals or actions based on their value, control by necessity involves taking into account the costs and benefits of such goals and actions. The participation of the amygdala, the OFC and the nucleus accumbens in the proposed broader control circuit means that strategies for action dynamically incorporate value. In particular, the OFC and medial PFC are involved in computing outcome expectancies[115,116] — the OFC's role in anticipating future events extends to the amygdala, especially the basolateral complex, with which it has strong reciprocal connections[115]. Finally, dopamine neurons located in the ventral tegmental area and the substantia nigra (pars compacta)

project not only to the nucleus accumbens, but also to the frontal cortex[117,118], including the LPFC and frontal eye fields. Thus, the prediction and expectation of future rewards, including reward prediction errors, which might be an important function of the dopamine system, should feature prominently in the temporal unfolding of control.

The architecture of the proposed circuit (FIG. 3) suggests that cognitive and emotional contributions to executive control cannot be separated. For instance, I propose that LPFC signals involved in inhibitory processes reflect both cognitive variables (for example, probability that an inhibitory response will be required) and affective information (for example, whether negative or neutral stimuli are viewed before being required to inhibit a response). Thus, executive control effectively integrates cognition and emotion (and motivation (see also REF. 119).

It is important to note some oversimplifications in the descriptions above. First, the ACC appears to be involved in computing the benefits and costs of acting more generally, rather than only detecting conflict
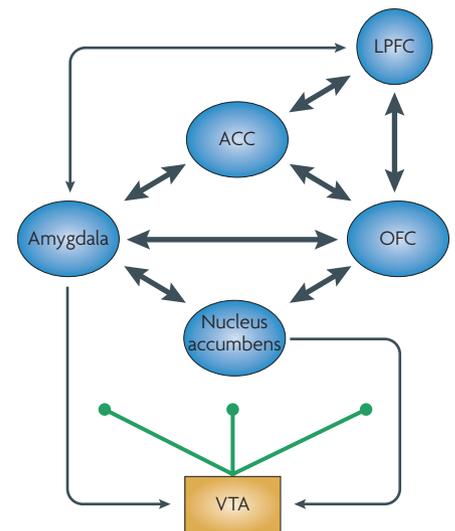

Figure 3 | **Circuit for executive control.** This extended control circuit contains traditional control areas, such as the anterior cingulate cortex (ACC) and the lateral prefrontal cortex (LPFC), in addition to other areas commonly linked to affect (amygdala) and motivation (nucleus accumbens). Diffuse, modulatory effects are shown in green and originate from dopamine-rich neurons from the ventral tegmental area (VTA). The circuit highlights the cognitive–affective nature of executive control, in contrast to more purely cognitive-control proposals. Several connections are not shown to simplify the diagram. Line thickness indicates approximate connection strength. OFC, orbitofrontal cortex.

and monitoring errors. For instance, ACC neurons encode the probability of reward[120], and at the same time, are critical for making decisions about effort costs[121–123]. Thus, the ACC has a role in evaluating whether the benefits are worth the cost of making an action[124]. Second, the LPFC has a role in maintaining and manipulating information, but can also integrate this content with both affective and motivational information (BOX 3). The LPFC might therefore act as a control hub in which multiple types of information converge and are integrated (see below). Critically, the convergence of both cognitive and affective/motivational information enables the LPFC to dynamically weigh multiple types of information in guiding action. Finally, the above discussion has been simplified by treating control as a somewhat monolithic process. In reality, control probably involves a range of processes that might vary from more 'reactive' to more 'effortful'[21] and that could have developmental trajectories[125].

A conceptual proposal

The previous section briefly outlined the circuits involved in the evaluation of sensory information and executive control. The description of these circuits is by necessity incomplete, for the reasons described below and in several discussions and proposals[89,126–133].

The simplest way to conceptualize the mapping between a brain area and behaviour is to assume a one-to-one mapping between an area and its function. For instance, the V1 is linked to visual perception (or a set of more basic visual functions, such as edge detection and stereopsis). Even though such an exercise becomes considerably less straightforward for more central areas (that is, farther from the sensory periphery), we can imagine extending it to many areas of the brain. The end product of such a strategy would be a list of area–function pairs. The brain areas might then be labelled as cognitive or affective based on their purported functions or how these functions are envisioned to ultimately shape behaviour. For instance, we could describe the amygdala as affective given its involvement in fear conditioning, and the ACC as cognitive given its role in monitoring conflict. As discussed, I believe that such dichotomization provides a poor description of the brain/mind, and I propose here that the one-area/ one-function viewpoint, although commonly used (or at the very least implicitly assumed), is problematic.

Structural connectivity. An alternative way to conceptualize the mapping between a brain area and behaviour is illustrated in FIG. 4. A given brain area, A, is involved in multiple neural computations, NC. Note that this initial mapping is itself many-to-many, so that a given area (for example, A1) is involved in the computation of several functions (for example, NC1 and NC3), and a given computation (for example, NC3) might be implemented by several areas (for example, A1, A2 and A3). These neural computations collectively underlie behaviour. One can describe the space of behaviours using affective and cognitive axes. Thus, any behaviour is by definition both cognitive and affective. Importantly, the axes are not orthogonal, such that a behaviour that is changed along the affective dimension compared to a different behaviour, will also be changed along the cognitive dimension. In other words, behaviour cannot be cleanly separated into cognitive or emotional categories.

An important aspect of the present proposal is that individual brain areas do not work in isolation, but instead are part of networks. Therefore, most neural computations should not be thought of as implemented by an individual area, but rather by the interaction of multiple areas. In addition, as pointed out by Mesulam[126], specific brain areas belong to several intersecting networks. Thus, the computations implemented by an area will depend on the particular network with which the area is affiliated at a particular time. For instance, areas A1 and A2 participate in the computation of NC3 when A1 and A2 are part of network N1 (FIG. 4). In another context, A2 might be affiliated with network N2, for example, whereas NC3 might be implemented in another manner. Thus, it is necessary to take into account the context in which neural computations are being carried out, because it depends on this context which brain areas will implement the computations.

To understand the impact of a region on behaviour, its connectivity pattern needs to be determined[134]. Recent advances in network theory[135,136] have shown that regions characterized by a high degree of connectivity (hubs[137]) are important in regulating the flow and integration of information between regions (area A2 in FIG. 4). However, whereas the number of connections of a region is important in determining whether it will function as a hub, the structural topology of a hub is also relevant. For instance, some regions are best characterized as 'provincial' hubs (they occupy a central position within a
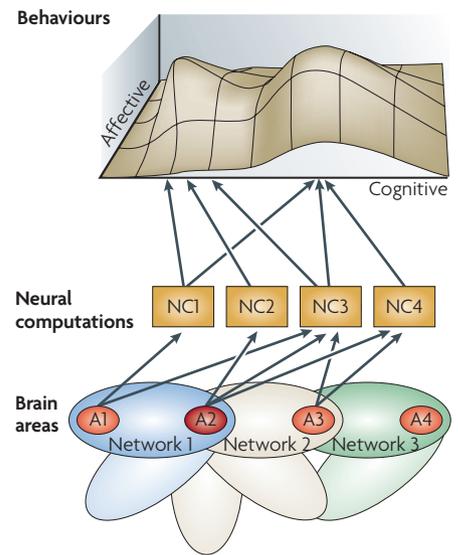

Behaviours

Affective — Cognitive

Neural computations NC1 NC2 NC3 NC4

Brain areas A1 A2 A3 A4 Network 1 Network 2 Network 3

Figure 4 | **Conceptual proposal for the relationship between anatomical sites, neural computations and behaviours.** Brain areas (for example, A2), which are connected to form networks (ellipses), are involved in multiple neural computations (for example, NC2, NC3 and NC4) and specific computations (for example, NC4) are carried out by several areas (for example, A2 and A3). Therefore, the structure–function mapping is both one-to-many and many-to-one; in other words, many-to-many. Multiple neural computations underlie behaviour. Each behaviour has both affective and cognitive components, indicated by the affective and cognitive axes. Note that the axes are not orthogonal, indicating that the dimensions are not independent from each other. Brain areas with a high degree of connectivity are called hubs and are critical for regulating the flow and integration of information between regions. The structural topology of the hubs is strongly linked to their function. For instance, connector hubs (such as A2) link separate region clusters (not shown) and are hypothesized to be crucial for the integration of cognition and emotion. See REF. 126 for a related scheme.

single functional cluster, for example, visual area V4[137]) or as 'connector' hubs (they link separate region clusters, for example, frontal eye fields[137]).

In the present context, connectivity information could be particularly important in understanding a region's role in emotion and cognition. Regions that are more peripheral (for example, non-hub regions with fewer connections) will often be described as either cognitive or emotional. This classification could be applied to provincial hubs, too. In both cases, regions whose function involves homeostatic processes and/or bodily representations will be viewed as emotional, whereas regions whose

function is less aligned with such processes will be viewed as cognitive. However, the existence of connector-hub regions that link distinct region clusters, effectively integrates emotional and cognitive regions, such that the distinction between the two is largely blurred (FIG. 4). At present, results from connectivity studies are incomplete because they include a limited number of prefrontal regions and, more critically, typically omit subcortical structures (but see FIG. 1). As larger databases become available for structural and network analysis, considerable progress is expected. Nevertheless, existing data offer some support to the present view. For instance, in a recent computational study, BA46 in the macaque LPFC was identified as a connector hub with an unusually large number of connections[137], which might explain why the LPFC is also important for the integration of emotion and cognition. I also propose that regions such as the amygdala function as cognitive–emotional connector hubs, consistent with the work of Young and colleagues[89] (FIG. 1). The ongoing discussion suggests that the impact of brain lesions will be strongly dependent on a region's structural embedding: lesions of more peripheral (non-hub) regions will produce relatively specific deficits, whereas lesions of regions that function as hubs will have a much greater impact on behaviour, an impact that will be strongly determined by the precise topology of the hub (for example, provincial versus connector). In particular, lesions of connector-hub regions will have widespread, and at times difficult to characterize, effects on cognitive and affective behaviours.

Functional connectivity. Whereas the above discussion has emphasized the role of structural connectivity, the importance of functional connectivity (for example, signal correlations between distant regions) needs to be highlighted as well[138,139]. In particular, the situation depicted in FIG. 4 should be viewed as a frame at a specific time, which captures the mapping at that time point. In general, the evolution of network affiliations through time will greatly influence structure–function mappings. In this context, large-scale integration mechanisms, possibly by phase synchronization across multiple frequency bands[140–142], are likely to have key roles in this process. Furthermore, multiple ascending neurotransmitter systems can affect ongoing computations and shift the neural computations implemented by brain areas[99]. Accordingly, the three-dimensional landscape of behaviours (FIG. 4) should be

viewed as dynamic, too. In some contexts, the two axes might be close to orthogonal, so that it would at times appear that cognition and affect are more or less independent.

An additional consideration in understanding structure–function mappings concerns the 'dynamics' implemented in specific regions. For instance, it is well documented that LPFC circuits can implement reverberating activity that can be sustained for several seconds. Such dynamics are not only important for extending the repertoire of LPFC computations but they are also likely to influence the precise form of functional connectivity that the LPFC will have with other regions. Consistent with this notion, Honey, Sporns and colleagues[143] have shown that simulated functional interactions depend on local dynamics. Therefore, the elucidation of the functional interactions that characterize cognitive–emotional couplings will require not only greater knowledge of structural connectivity properties, but also how local physiological properties impact both short- and long-range brain interactions.

The above considerations suggest that, in the vast majority of cases, the one-to-one mapping framework, and simple extensions thereof, describe the underlying structure very poorly. In fact, both degeneracy (many-to-one mappings, that is, multiple areas are capable of performing the same function) and pluripotentiality (one-to-many mappings) occur[131,132,144]. In particular, degeneracy has recently received much attention as understanding this issue is central to the interpretation of the impact of focal brain damage on brain function[130]. Having said that, it is important to note that lesions of specific brain regions, even highly connected ones, appear at times to lead to relatively specific behavioural deficits. For instance, lesions of the lateral/basolateral amygdala have been suggested to be necessary for the acquisition and expression of conditioned fear (see REF. 145 for an alternative view).

A simplification of the proposed scheme (FIG. 4) is that the x and y axes correspond directly to affective and cognitive dimensions. In all likelihood, several dimensions are involved, so that combinations of these dimensions would correspond more or less directly to the two dimensions that are used here. Clearly, part of the work required to advance our understanding of structure–function mapping involves refining the set of 'primitive' dimensions (see also REF. 146) that could characterize a rich set of behaviours.

We end this section by recasting our discussion in terms of 'decomposable' and 'nondecomposable' systems[147–149]. On the one hand, a decomposable system is one in which each subsystem operates according to its own intrinsic principles, independently of the others (that is, it is highly modular). On the other hand, a nondecomposable system is one in which the connectivity and inter-relatedness of the components is such that they are no longer clearly separable. I here advance the working hypothesis that emotion and cognition are only minimally decomposable[147]. In other words, the neural basis of emotion and cognition should be viewed as governed less by properties that are intrinsic to specific sites and more by interactions among multiple brain regions. In this context, note that relaxing the one-structure/one-function assumption described above by incorporating one, or a few, additional regions (for example, ACC–amygdala interactions[150]) is insufficient for mapping brain areas and functions properly because first, functional circuits include both multiple regions and neuromodulatory systems (FIGS 2 and 3); second, network affiliations are context-dependent and dynamic; and third, given the small-world topology of brain structural connectivity, hub regions, such as the amygdala and the hypothalamus, will have more important roles than regions that are not as highly connected.

Conclusions

Historically, emotion and cognition have been viewed as separate entities. One factor that could have contributed for this separation in the past century is methodological. For instance, data arising from single-unit or lesion studies usually allow the researcher to derive conclusions only concerning the specific areas being targeted. Research in the past two decades has shown that such view is deficient and that, if we are to understand how complex behaviours are carried out in the brain, an understanding of the interactions of the two is indispensable. Here, I have articulated the view that, in many cases, we must go beyond understanding interactions, some of which are suggested to be mutually antagonistic[7,70,151–153], to understanding how cognition and emotion are effectively integrated in the brain. As stated by Gray and colleagues[78], "at some point of processing, functional specialization is lost, and emotion and cognition conjointly and equally contribute to the control of thought and behaviour". This statement summarizes their findings concerning working memory performance following mood induction,

but I propose that it also aptly characterizes a vast array of situations. In other words, whereas many behaviours might be reasonably well characterized in terms of cognitive–emotional interactions such that emotion and cognition are partly separable, often true integration of emotion and cognition takes place, strongly blurring the distinction between the two. Furthermore, I propose that one fruitful way to refine our understanding of both interactions and integration will involve a more quantitative analysis of structural and functional brain connectivity, as briefly outlined in the previous section.

The viewpoint presented in this article suggests that behaviour is a product of the orchestration of many brain areas; the aggregate function of these brain areas leads to emotion and cognition. Many neurological disorders and mental illnesses are characterized by profound deficits in cognitive and emotional behaviours, including epilepsy, Alzheimer's disease, autism and schizophrenia. Outstanding questions concerning these and many other debilitating conditions centre on advancing our knowledge of how cognitive and emotional processes interact in both normal and abnormal circumstances. In the end, whereas there is some value to carving up the brain in terms of emotion and cognition, the understanding of complex, embodied behaviour necessitates comprehending the strong interactions between brain areas. To be certain, the idea of 'equipotentiality'[154] has clearly failed as a framework that explains how functions are represented in the brain. At the other extreme, the one-area/one-function viewpoint is equally deficient. Whereas equipotentiality was an easier target to refute, the latter framework has permeated brain science, albeit often in an implicit fashion. For instance, in a recent review Schultz[118] complained that "scholars have numerous and mutually exclusive views on dopamine function based on the fallacy that there should be only one major role for every brain system". Ultimately, to understand how emotion and cognition are mapped to the brain, a deeper understanding of the extent to which the underlying neural systems are decomposable is needed. In all likelihood, novel experimental and theoretical tools will be required to effectively attack this formidable problem.

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