Being a self: Considerations from functional imaging

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Abstract

Having a self is associated with important advantages for an organism. These advantages have been suggested to include mechanisms supporting elaborate capacities for planning, decision-making, and behavioral control. Acknowledging such functionality offers possibilities for obtaining traction on investigation of neural correlates of selfhood. A method that has potential for investigating some of the brain-based properties of self arising in behavioral contexts varying in requirements for such behavioral guidance and control is functional brain imaging. Data obtained with this method are beginning to converge on a set of brain areas that appear to play a significant role in permitting conscious access to representational content having reference to self as an embodied and independent experiencer and agent. These areas have been identified in a variety of imaging contexts ranging from passive state conditions in which they appear to manifest ongoing activity associated with spontaneous and typically 'self-related' cognition, to tasks targeting explicitly experienced properties of self, to demanding task conditions where activity within them is attenuated in apparent redirection of cognitive resources in the service of task guidance and control. In this paper, these data will be reviewed and a hypothesis presented regarding a significant role for these areas in enabling degrees of self-awareness and participating in the management of such behavioral control.

Keywords: Self; Self-awareness; Action; Resting state; Functional imaging

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1. Introduction

Efforts at understanding the self in a biological context typically emphasize the importance of acknowledging the self as embodied (experiences do not occur outside of one who experiences). However, in addition to 'grounding' the self in a body that provides the relatively invariant somatosensory background for experience, investigators from a variety of disciplines are now also beginning to 'ground' the self in action. In this view, useful understanding of the self is not even possible if separated from considerations of action (for a recent overview of this emerging perspective, see the series of papers in *Consciousness and Cognition, Vol. 12 (2003) pp. 487–782)*. It has been observed that nervous systems are only necessary for (i.e., are only present in) living creatures that move actively, providing such organisms with a capacity for intelligently strategizing their movements relative to their particular environments. With the potential for increasingly complex behaviors to be achieved along the phylogenetic scale have come increasing demands, as well as an increasing need to economize, on mechanisms (i.e.., a self) for their prediction and planning. This, it has been argued, has resulted in increasing cognitive capacities for the self's abstraction and conscious representation along the phylogenetic scale (Llinas, 2001).

A perspective derived from synthesis and interpretation of specific functional imaging data to be described in this paper is in agreement with such a 'grounding of the self in action' principle. It regards detailed empirical data on aspects of brain function as particularly useful in constraining some aspects of the discussion of self. In particular, it argues that there is a large amount of ongoing intrinsic activity within the brains of awake and alert adult human beings that includes coordinated interactions between brain regions involved in perception and action-planning and enables the production and experience of 'stimulus-independent' (self-related) thought. Significantly, several of these brain regions have frequently been observed to be engaged by tasks that target subjects' explicit consideration of various properties of themselves. It is also notable, however, that these same brain regions are commonly attenuated in their activity (to various degrees) in the context of other goal-directed tasks.

The perspective offered here endorses a systems view that presumes that there are varying levels of complexity in self-representation and self-awareness, whose elucidation will ultimately be significantly informed by considerations of species differences and findings from developmental psychology. It should be noted that, despite the importance of these comparative and developmental considerations, essentially all of the extant functional imaging data relevant to the current topic has been acquired on adult humans. Nonetheless, new insights into some of this imaging data are beginning to converge on a framework for a view of aspects of self that emphasizes, and may help to illuminate, some of its functional properties.

2. The self and neuroscience

2.1. Diverse perspectives

Investigations into questions of self are clearly controversial, however. In fact, some might wish to argue that it is too early or perhaps even inappropriate to undertake empirical investigations of self, perhaps particularly with a tool such as functional imaging. For example, within the tradi-

tional cognitive framework, it has been relatively easy to dismiss the self as epiphenomenal because of work showing that many, if not most, changes in behavior can be accounted for by externally caused automatic processes rather than conscious control (i.e., a 'will' or 'self').

However, such questioning of an 'efficacious' self presumes that there is a functional separation between perception and action (e.g., between 'seeing' and 'doing') that requires some kind of mediation. It has been suggested that aspects of the traditional framework of cognitive science, within which the self is generally modeled as a monitoring (or 'executive') function that mediates between perception (an input function) and action (an output function), are based more on folk-psychological assumptions than derived on the basis of empirical data (Jordan, 2003). As an alternative view, it has been argued that it may be more appropriate to regard the perception and action planning systems as inherently coupled, citing evidence for such a 'coupling' in instances of shared neural mechanisms, as in the existence of 'mirror neurons' (populations of cells identified in monkeys' premotor cortex that become active both when a monkey performs a given action and when he perceives a similar action being performed by an experimenter) (Di Pelligrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Rizzolatti et al., 1987). Such a conceptual reframing does not address whether or not the self exists as a causal mechanism, but rather permits conceptual emphasis to be shifted to what might be referred to as empirical regularities that individuals identify as self (Jordan, 2003). Jordan has elaborated a model in which such regularities may be characterized at the different levels of scale at which they are specified. These range from the level of particular effector systems (e.g., limbs and their movements), to more distal effects (e.g., particular tasks or goals), to even more distal (so-called 'virtual') effects (e.g., thoughts about goals, principles). Thus, one's sense of self may vary depending upon the task at hand at any particular moment, ranging from identification with more proximal effector systems as in the case of a novice musician at the moment of attempting to control his/her finger movements during a task performance to that of an expert musician whose more automated finger movements permit attention to and identification with the control of emotions or cognitions during performance of a piece. In this view, an individual's acknowledged self at any particular moment is regarded as that one that is prepotent in and constrained by the circumstances of a behavioral context. However, as also noted by Jordan, there are certain levels of event control that seem more 'appropriately' referred to by means of the term self, since they are more conventionally referred to as such. Such levels of event control include those events that may be performed with an other and require specifying, monitoring and producing one's events in relation to those anticipated from an other, i.e., the more commonly construed social conceptions of the self.

Considerations of self by neurophysiologists are relatively few. Llinas and co-workers, however, have, like Jordan, come to endorse the self as an abstraction arising from regularities in nature that have useful and important influences on intelligent organisms' (and particularly humans') behavior. In their view, the brain is largely a closed-system that is modulated by the senses (rather than 'driven' by sensory input), with perception and action-planning systems intrinsically coordinated (and, thus, inherently 'intentional'). In Llinas' formulation (Llinas, 2001), the brain is primarily a self-activating system, which derives from the intrinsic oscillatory capabilities of neurons organized within the thalamocortical system. This 'self-activation' is "geared toward the generation of intrinsic (sensorimotor) images" (Llinas, 2001) that can control prediction of events in the environment in addition to controlling responsivity to coordinated commands for motor execution (Llinas, 2001; Llinas & Pare, 1991).

Numerous other investigators are now exploring issues related to consciousness itself and asking the extent to which young children as well as nonhuman primates may have a sense of self, as well as self-reflective or metacognitive capacities, thoughts and representations. Significantly, investigators from research traditions as diverse as ethology and social psychology have converged on the notion that self-awareness fundamentally involves processes of discrimination and evaluation in the service of guiding and optimizing certain behaviors. Self-awareness at the level of consciousness of a body-image, for example, has been attributed to arboreal higher primates, and has been proposed to have arisen in order to enhance the planning and reduce the risk of clambering through the trees of such animals, who have a significantly larger body size than smaller monkeys and non-primates (Povinelli & Cant, 1995). At the human level, social psychologists have long noted the significance of self-awareness in influencing planning, decision-making, and behavioral control (Carver, 2003; Leary, 2004).

Thus, despite the obvious complexity of the concept and the diverse ways in which the term self has been used in folk-psychological discourse and scientific circles, serious empirical investigation with regard to aspects of self clearly have been and continue to be undertaken. What I have attempted to point out here as well is that there is some modicum of emerging consensus as well on the utility of investigations into self that are founded on an acknowledgement of the kinds of functionality that a sense of self may confer. In particular, self-awareness or access to representational content about the self may participate in the elaboration of control structures, which have been necessitated by the loosening of rigid stimulus-response bonds in higher animal species.

2.2. A functional imaging proposal

In the sections which follow, I will review a variety of functional imaging data that are beginning to converge on a set of brain areas that appear to play a significant role in permitting conscious access to representational content having reference to self from a first-person perspective. They consist of a set of higher-order association cortices in the frontal and parietal regions that have been identified in a variety of imaging contexts, ranging from connectivity analyses that underscore their status as a network to paradigms specifically targeting explicitly experienced properties of self. Importantly, activity in these areas has also been observed to vary between conditions that may be interpreted as differing in their degree of need for coordination of working memory and action planning resources in the service of behavioral control.

To appreciate the significance of such functional imaging data and their potential relevance to such issues, however, it will be important to present a variety of material. First, some background regarding the nature of functional imaging signals themselves will be presented. This will facilitate an understanding of so-called 'activations' and 'deactivations' as well as the proposed 'physiologic baseline' and its relationship to what has been called the resting state (i.e., that awake and alert mental state associated with a relaxed and passive behavioral state). These concepts allow us to consider some of the inherent background activity that has traditionally gone unrecognized in the use of functional brain imaging. Finally, functional imaging data illustrating relationships between this background activity and the activity of a unique set of prefrontal and parietal brain regions will be described. A hypothesis regarding a significant role for these areas in enabling self-awareness will also be presented.

3. A functional imaging approach to self

3.1. The functional imaging experiment

From a participant's perspective, a functional imaging experiment confronts him/her with particular demands, notably the experimenter's instructions. After providing some time for the subject to become accustomed to the scanner environment, investigators expose the subject to specific experimental stimulation.

3.2. Functional imaging signals

The functional imaging signal fundamentally involves a *change* in local blood flow within the brain of the subject (Raichle, 1998). This is accompanied by an increase in the metabolism of glucose that parallels in magnitude and spatial extent the change in blood flow (e.g., see Hand & Greenberg in Woolsey et al., 1996). The change in the local consumption of oxygen is much smaller in magnitude than either the increase in blood flow or glucose utilization (Fox & Raichle, 1986; Fox, Raichle, Mintun, & Dence, 1988). This results in an increase in the local blood oxygen content, creating the blood oxygen level dependent (BOLD) signal of fMRI (Kwong et al., 1992; Ogawa, Lee, Kay, & Tank, 1990). It has been shown that a spatially localized increase in the fMRI signal, directly and monotonically reflects an increase in neural activity (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001), and that the time course of this signal, which is based on the vascular response to the neural activity, is a temporally delayed and spatially dispersed reflection of the underlying neural activity, beginning about 2 s after the latter's onset and reaching a plateau in about 7 s (see also Boynton, Engel, Glover, & Heeger, 1996).

Historically, initial interest in and interpretation of functional brain imaging studies focused on the correlates of these imaging signal increases (so-called activations). However, researchers have now become increasingly aware of the fact that signal decreases (so-called deactivations) also occur (Shulman et al., 1997). While focal decreases in imaging signal intensity have been noted for some time, their interpretation has been challenging and has resulted in differing opinions as to their origin and significance (Shmuel et al., 2002; Smith, Singh, & Greenlee, 2000; Tootell et al., 1998). Interestingly, some of these focal decreases appear between or within perceptual systems, such that decreases in activity may appear in auditory or somatosensory cortices when engaging in a task involving visual perception, for example (e.g., Ghatan, Hsieh, Petersson, Stone-Elander, & Ingvar, 1998; Haxby et al., 1994; Kawashima, O'Sullivan, & Roland, 1995), or within portions of the somatosensory cortices or visual cortices while other portions of these same systems exhibit increases in activity during tasks that target them (e.g., Drevets et al., 1995; Shmuel et al., 2001, 2002; Tootell, Tsao, & Vanduffel, 2003). It has been suggested that such decreases reflect the limiting or suppression of information processing in sensory areas that are not needed for current task performance (e.g., see Drevets et al., 1995), thus facilitating the processing of information expected to carry behavioral significance by promoting its 'signal-to-noise.'

In addition to such signal decreases within sensory cortices, however, there is also a unique set of areas in higher-order association cortices that exhibit decreases in activity in averaged data obtained relative to a passive behavioral condition (in the functional imaging field referred to as the 'resting state' condition) across a wide variety of goal-directed tasks, such as various language
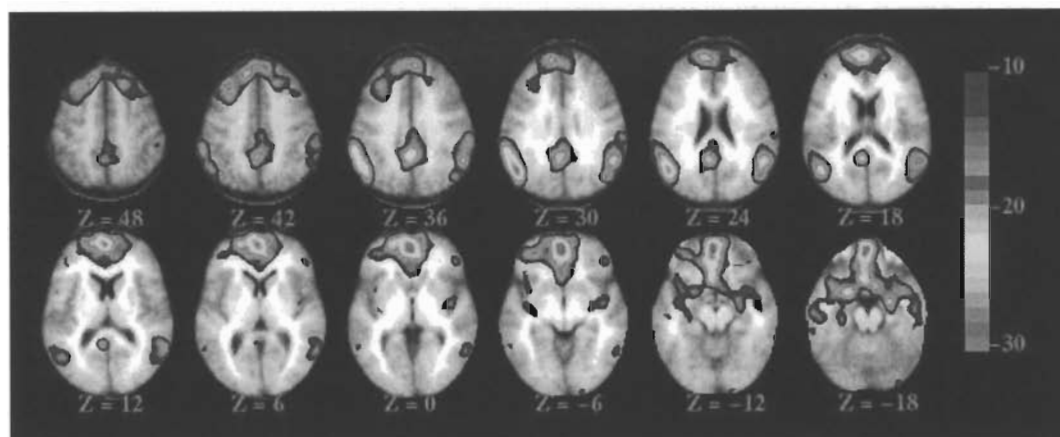
Fig. 1. Transverse images of PET data averaged across 9 cognitive tasks ($n = 134$) demonstrating the pattern of the commonly observed (task-induced) decreases.

tasks and visuospatial tasks (Shulman et al., 1997) (Fig. 1). This set of higher-order brain areas is of particular note in the context of this paper. Data supporting the suggestion that signal decreases in these higher-order areas have a functionality analogous to those in perceptual systems, but at the higher level of intrinsic coordination of perceptual and action-planning systems will be detailed below. What is important to note at the moment, however, are some of the physiological characteristics of these various imaging signal decreases.

In particular, such signal decreases are not likely to be directly or simply attributable to local inhibitory processes (i.e., related to the activity of GABA-ergic neurons). This is because such local inhibitory processing, requiring energy, is likely to be associated with signal *increases* in the same way as excitatory processing (related to the activity of glutamatergic neurons) (Ackerman, Finch, Babb, & Engel, 1984; Lauritzen, 2001; Lauritzen & Gold, 2003), though the details of the neurovascular coupling involved in local inhibitory processing are currently less well understood. Also, and more importantly, recent neurophysiological observations (Gold & Lauritzen, 2002; Shmuel et al., 2003; Shmuel, Augath, Rounis, Logothetis, & Smirnakis, 2003) indicate that these signal decreases are the result of actual decreases in neuronal activity, particularly in local field potentials (neuronal activity in axon terminals and dendrites), which reflect the input to as well as local processing within neuronal ensembles. In other words, these signal decreases appear to reflect effects of long-range input (arising from other regions of the brain) rather than simply local neuronal processing.

Thus, imaging signal changes and the underlying neural activity appears to consist of actual increases (activations) and decreases (deactivations), reflecting aspects of the information processing landscape as it organizes and reorganizes to address particular environmental (task) demands.

3.3. The physiological baseline

In the average adult human, the brain represents about 2% of the total body weight, but accounts for about 20% of the oxygen consumed and, thus, calories (energy) consumed by the body

(Clark & Sokoloff, 1999). In relation to this very high rate of baseline metabolism, regional imaging signals are remarkably small, in metabolic terms often less than 5% of the ongoing metabolism of the brain in that particular area. These are modest modulations in ongoing or baseline activity and do not appreciably effect the overall metabolic rate of the brain (Sokoloff, Mangold, Wechsler, Kennedy, & Kety, 1955; Fox, Burton, & Raichle, 1987; Fox, Fox, Raichle, & Burde, 1985; Fox, Miezin, Allman, Van Essen, & Raichle, 1987). (For further details regarding this physiological 'baseline' and how it has been characterized within a functional imaging framework, see Section 5.)

Importantly, not only does this physiological baseline account for the majority of the brain's metabolic requirements, but there are several lines of evidence that suggest that functionally significant signaling processes are inherent within it. These include measurements of brain energy metabolism using magnetic resonance spectroscopy (Hyder, Rothman, & Shulman, 2002; Shulman, Hyder, & Rothman, 2001; Sibson et al., 1998) that have indicated that up to 75–80% of the entire energy consumption of the brain is devoted to glutamate cycling and, hence, signaling processes, as well as neurophysiological studies that have noted 'spontaneous' electrical activity that does not bear any obvious relationship to specific sensory or motor tasks (Arieli, Sterkin, Grinvald, & Aertsent, 1996; McCormick, 1999; Sanchez-Vives & McCormick, 2000; Shu, Hasenstaub, & McCormick, 2003; Tsodyks, Kenet, Grinvald, & Arieli, 1999), and is thought to not simply represent 'noise' (e.g., see Ferster, 1996; Kenet, Bibitchkov, Tsodyks, Grinvald, & Arieli, 2003; McCormick, 1999). In effect, such activity has been suggested to not simply represent random (and thus 'meaningless') firing of neurons, but to have a relationship to significant operations and functions of the neural system.

This spontaneous spiking activity is relatively low in frequency as compared with vigorous bursts of activity seen during experimental task performance, which may bear a relationship to the manner of representing or coding information and offer differential economies of energy use as well (Attwell & Laughlin, 2001; Laughlin & Sejnowski, 2003). That is, the effective connectivity of the brain that supports information processing is highly dynamic (Laughlin & Sejnowski, 2003), apparently changing on both slow time scales (that may support a type of coding of information for more sustained and long-term use and require less local energy consumption) as well as fast time scales (that may support a type of coding for more transient computational needs and require momentarily greater local energy consumption).

Such a view of neural processing dynamics would be consistent with the notion that has been offered that in the physiologic reservoir of baseline activity, where oxidative metabolism[1] is the primary source of energy (Gusnard & Raichle, 2001), there has developed a very efficient strategy for managing large amounts of information on a sustained or long-term basis. This would complement the situation for functional imaging activations, where glycolysis[2] assumes a more important role as a source of energy (Fox et al., 1988), and may have the potential for supporting more rapidly varying and time-limited information processing for immediate purposes, such as those

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[1] Oxidative metabolism is an energy-producing metabolic process in which glucose is reduced to carbon dioxide and water yielding a large amount of energy (per pathway 'cycle') but relatively slowly. Oxidative metabolism requires oxygen.

[2] Glycolysis is the first step in the metabolism of glucose and requires no oxygen. It yields smaller amounts of energy than oxidative metabolism (per pathway 'cycle'), but does so rapidly, making it available when energy requirements increase suddenly (e.g., as with a sudden increase in neuronal activity).

involved in functional imaging experimental task performance. (For further discussion of these issues, see Gusnard & Raichle, 2001.)

How might this so-called baseline neuronal activity be viewed? It has been suggested to constitute, at least in part, actual information processing (Gusnard & Raichle, 2001; Shu et al., 2003; Tononi & Edelman, 1998). Here functional brain imaging with both PET and fMRI provide a potentially unique perspective. This emanates directly from the observation of imaging signal decreases, in particular, in the previously mentioned set of higher-order association cortices during the performance of a wide variety of goal-directed tasks.

This set of decreases is seen in medial prefrontal and parietal cortices as well as lateral parietal cortices bilaterally (Mazoyer et al., 2001; Shulman et al., 1997) (Fig. 1). Current evidence indicates that these specific imaging decreases do not simply correspond to functional imaging 'activations' in the resting state condition as has been suggested (Mazoyer et al., 2001) but do, in fact, arise from the physiologic baseline (for a more detailed defense of this assertion see Raichle et al., 2001). This suggests that they might more appropriately be referred to as areas that, in the resting state condition, are functionally active rather than 'activated.' This would be consistent with functionality that is spontaneous and virtually continuous, being attenuated only under certain behavioral conditions when such functionality is either less salient or might actually interfere with the implementation of other more salient processing demands.

Two recent observations using novel approaches to the study of the resting state condition (i.e., lying in the scanner, awake, eyes closed, with cognition unconstrained by experimental stimulation or specific behavioral instructions from the investigator except to rest quietly) also provide new information on how activity in these higher-order brain regions may, in fact, relate to resting state cognition.

Using an fMRI imaging strategy that has been employed in several laboratories (Biswal, Yetkin, Haughton, & Hyde, 1995; Coren, 1969; Lowe, Mock, & Sorenson, 1998; Xiong, Parsons, Gao, & Fox, 1999), investigators at Stanford (Greicius, Krasnow, Reiss, & Menon, 2003) explored the interregional temporal correlations of spontaneous BOLD signal fluctuations in the resting state condition in 14 subjects using regions-of-interest in medial parietal cortex as well as ventral anterior cingulate cortex—regions that are among those regularly exhibiting the commonly-observed decreases in the aforementioned association cortices. What emerged was evidence for significant correlations in the spontaneous and 'experimentally unconstrained' activity among a group of areas virtually identical with those that have been identified with the commonly observed decreases (Fig. 2). Prior to this published study, the evidence for a network of interrelated areas exhibiting coordinated activity in the resting state condition had been indirect, being based on repeated demonstrations of this set of regional decreases in the comparison of some investigator-specified task condition to a resting state condition. This paper was the first to provide direct evidence of coordinated activity in the same network of areas *in* the 'resting state.'

The second study (Laufs et al., 2003) used a novel approach to analyzing fMRI data acquired in the resting state condition, employing an analysis driven by variations in simultaneously acquired EEG frequency bands. Changes in the power within these bands were correlated with magnitude variations in regional BOLD signals from the brains of normal subjects engaged for 20 min in the resting state condition. The authors observed that areas in dorsolateral parietal and prefrontal cortices (areas thought to be important in the support of directed visual attention) varied inversely with α power (8–12 Hz), whereas a significant number of the areas associated with the commonly
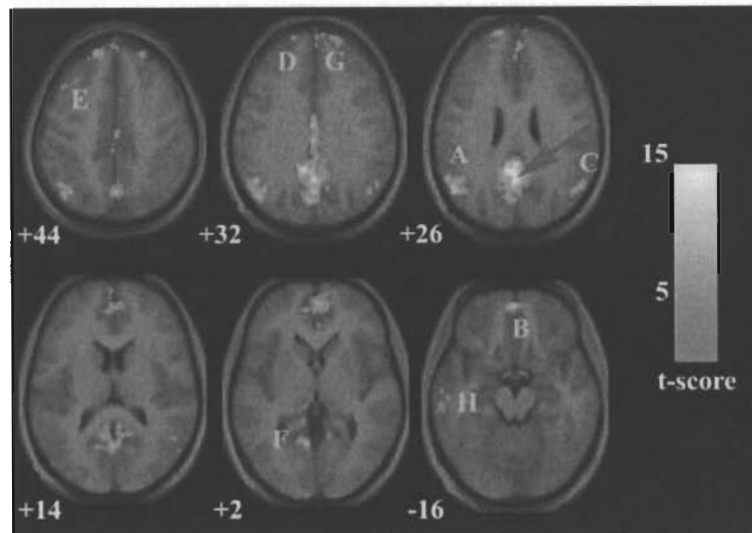
Fig. 2. Map of the resting-state neural connectivity for the posterior cingulate corex (PCC) (arrow indicates the PCC peak used for the analysis). The labels A–H designate the significant clusters in order of descending t-score (reprinted with permission from the (Greicius et al., 2003)). Note correspondence of this map with the pattern of the common decreases (Fig. 1).

observed decreases in higher order association cortices varied directly with power in a β band (17–23 Hz range)—an EEG band thought to be associated with cognitive processing. The authors concluded that the resting state condition appears to be characterized by temporal fluctuations in functional activity ranging from "inattention" to "spontaneous cognition" and that these functional states are associated with changes in organized neural activity in the aforementioned brain systems.

This study also makes an additional point. While the time-scale of the fluctuations used in resting-state connectivity analyses (<0.1 Hz), such as that performed in the study by Greicius and co-workers, is far removed from the neuronal time-scale, this study (Laufs et al., 2003) as well as recent data from simultaneous recording of local field potentials and functional brain imaging in monkeys (Leopold, Murayama, & Logothetis, 2003) support the notion that the low-frequency and inter-regionally coherent fluctuations identifiable in fMRI data have relationships to neurophysiologically meaningful brain activity.

Thus, there is now a variety of data that support the notion that a set of brain regions involving specific frontal and parietal association cortices (Figs. 1 and 2) constitutes a coordinated network of activity in the resting state condition. Some of the dorsal prefrontal and parietal brain regions in this network include areas that have undergone particularly remarkable expansion between the monkey and human (Ongur, Ferry, & Price, 2003; Orban, Van Essen, & Vanduffel, 2004; Van Essen, 2005).

3.4. Self-awareness and task performance

A significant amount of PET and fMRI data have also emerged from functional imaging studies specifically targeting various explicitly experienced properties of the self, which implicate these

same brain regions. Such studies usually involve the presentation of visual or auditory stimuli (typically words or pictures) and require that the subjects perform some task. These tasks have ranged from asking subjects to make explicit evaluative judgments about themselves, for example, to having them explicitly take an interpersonal or spatial perspective, or endorse the experience of themselves versus another as being the cause of an action. In all of these studies (noted below), subjects made explicit reference (typically via a graded or yes/no categorical judgment response, for example) to some aspect of their own mental or somatic states, to some aspect of themselves (or their construal of some aspect of an 'other's' self) in a relational context, or to some conceptual knowledge of themselves (or an 'other's' self).

In a recent article, Newen and Vogeley (Newen & Vogeley, 2003) extensively discuss the results of several of these, what might initially be viewed as rather disparate, functional imaging studies in the context of an effort at operationalizing the concept of a first-person perspective. They also note the convergence of the results of these studies on several of the aforementioned association cortices, and articulate a hypothesis that these brain regions may together be viewed as a "neural signature for human self-consciousness that is recruited independent from the degree of representational complexity to be performed."

In these studies, for example, mental state considerations, whether explicitly reflecting on aspects of one's own mental state (or attributing mental states to others), have generally been shown to engage the dorsal anterior paracingulate and dorsal medial prefrontal regions (Frith & Frith, 2003; Gusnard, Akbudak, Shulman, & Raichle, 2001; Lane, Fink, Chau, & Dolan, 1997; Shallice, 2001). Other imaging studies targeting retrieval of personal or episodic memories involving verbal and nonverbal material (Cabeza & Nyberg, 2000; Cabeza et al., 2004) have included this same prefrontal region.

Episodic memory retrieval tasks as well as tasks involving explicit spatial perspective-taking have also been shown to engage portions of the medial parietal region comprising posterior cingulate, precuneus and retrosplenial cortex (Maguire, 2001; Shannon & Buckner, 2004; Vogeley & Fink, 2003). This medial parietal region has also been implicated in numerous tasks involving orienting oneself in large-scale space (Maguire, 2001). In a summary of work considering a variety of empirical data, including functional imaging data, Vogeley and Fink (Vogeley & Fink, 2003) have suggested that tasks involving taking a first-person perspective in space, in action as well as social interaction tend to implicate these medial prefrontal and parietal regions, along with a lateral parietal region, particularly on the right side.

There is a long history of neuropsychological lesion data indicating that this right lateral parietal region plays some important role in attending to aspects of one's personal space (Behrmann, 1999; Farrell & Robertson, 2000) as well as one's extensions (e.g., by means of tool-use) into that space (Ackroyd, Riddoch, Humphreys, Nightingale, & Townsend, 2002; Maravita, Spence, & Driver, 2003). In the functional imaging literature, this lateral parietal region has also been implicated in attention to the experience of movement and in attributions of agency (Farrer et al., 2003; Farrer & Frith, 2002; Jackson & Decety, 2004).

Accessing semantic information or making semantic judgments about persons, including oneself, have also been shown to engage portions of the medial prefrontal region (Craik et al., 1999; Kelley et al., 2002; Kjaer, Nowak, & Lou, 2002; Mitchell, Heatherton, & Macrae, 2002) as well as the medial parietal (Kelley et al., 2002; Kjaer et al., 2002) and lateral parietal regions in both hemispheres (Lou et al., 2004; Mitchell et al., 2002). Interestingly, in a recent paper (Lou et al.,

2004) involving PET and transcranial magnetic stimulation (TMS), the authors reported selective disruption of accessing semantic knowledge about oneself when TMS was applied to the medial parietal area.

A question that immediately arises, however, is what is the nature of the processing occurring in these areas? While it is the case that tasks requiring subjects to partake in various explicit self (or agent)-referential behaviors employing semantic memory, episodic memory, spatial as well as social (theory-of- mind) perspective-taking have been shown to engage these brain regions, there are other tasks in the literature that have been reported to engage them as well that do not specifically target such phenomena and range from simple conditioning and other learning paradigms to complex tasks involving memory, judgment and/or problem-solving. How might one reconcile this?

Once again, clues may arise from consideration of functionality that has been associated with having a self or self-awareness. As previously noted, self-awareness or access to representational content about the self at different levels of complexity appears to participate in the elaboration of control structures that have arisen with the loosening of the rigid stimulus–response bonds that dominate the behavior of lower animal species. Kinsbourne has suggested that self-awareness requires the ability to escape from ambient stimulus control so that attention may be disengaged from the salient stimulus field and shifted 'internally' to the processing of representations about the self, its attributes and experiences (Kinsbourne, 2005). Such an ability is also required for numerous tasks that require accessing internal representations having salience in the phenomenal present, such as episodic memory retrieval as well as judgment, learning and problem-solving tasks that necessitate disengagement from a salient external stimulus or thought (such as an incorrect assessment or solution) in order to permit their replacement in awareness with task-appropriate internal representations. More complex and elaborate forms of self-awareness as found in adult humans are also likely to go along with greater working memory capacities, permitting a larger number of, at times, unrelated or conflicting representations to be in mind or differentially suppressed as one of them controls behavior (Kinsbourne, 2005).

There have been few functional imaging attempts to identify neural correlates of explicitly identified 'stimulus-independent' cognition. One study that did specifically target 'stimulus-independent thought', however, correlated such thought with activity in the medial prefrontal region (McGuire, Paulesu, Frackowiak, & Frith, 1996). Another study that investigated both episodic memory retrieval and what was called a 'random episodic memory' condition (involving uncensored spontaneous thinking as might occur during analytic therapy using free association) found that the areas that the two conditions had in common were the medial prefrontal and the precuneus/retrosplenial regions (Andreasen et al., 1995). These data suggest that 'stimulus-independent' or 'spontaneous' internal representations that are consciously accessible to the subject are at least enabled by activity in some of the aforementioned higher order brain regions (Figs. 1 and 2).

Other sources support the view that these cortical areas "enable" self-awareness. Several PET studies, for example, have contrasted altered states of awareness with the normal waking state. Levels of awareness or consciousness were investigated by varying levels of anesthesia in one imaging study by means of the general anesthetic, propofol (Fiset et al., 1999). In that PET study performed on five volunteers, consciousness was experimentally varied from the completely awake alert state to unconsciousness. In addition to the global depression of cerebral blood flow that is well-known to occur with anesthesia, regional decreases in blood flow were also observed that, in the cortex, were most prominent in medial parietal and prefrontal areas.

Another group used PET to assess brain metabolism in patients during and after recovery from a vegetative state (defined as impaired awareness in the setting of normal arousal) and found that the areas that resumed normal metabolism after patients' recovery of consciousness largely consisted of medial parietal and lateral parietal areas (Laureys, Lemaire, Maquet, Phillips, & Franck, 1999)—areas again significantly overlapping some of those engaged by the commonly observed decreases and demonstrating functional connectivity in the normal resting state. This group has also performed functional connectivity analyses on imaging data from such patients and reported an altered correlation in activity between these medial parietal cortices and dorsal medial and lateral prefrontal cortices compared to normal controls, which normalized after patients' recovery (Laureys et al., 2000).

PET studies of normal adult subjects during various stages of sleep have also shown that medial parietal and medial prefrontal cortices along with portions of dorsolateral prefrontal cortex exhibit attenuated activity in sleep conditions relative to the awake state (Maquet, 2000).

These brain regions are frequently engaged together when they are attenuated in their activity in the context of a wide variety of goal-directed tasks (Mazoyer et al., 2001; Shulman et al., 1997), though the degree of attenuation of activity among the various regions may differ somewhat depending upon the task. Importantly, it has been observed that the magnitudes of the decreases in activity in these brain regions may vary with task difficulty (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003). Greicius and Menon in following up on their previous work have also observed that the magnitude of the decreases appears to depend upon the degree to which tasks engage subjects (Greicius & Menon, 2004). These findings have led to the suggestion that the magnitude of these regional signal decreases may be related to the amount of working memory and attentional resources that the subject has actually allocated in the service of the task and shifted away from 'internal' cognitive processing.

In their use of independent components analysis, Greicius and Menon specifically noted that the integrity of this particular network of areas was still discernable in the context of their passive perceptual tasks (repeated presentations of visual and auditory stimuli), where deactivations were infrequently observed. But, perhaps most significantly, they also observed that the greater a subject's 'deactivations' in that network, the greater that subject's activation in other locations to the visual and auditory stimuli presented during the experimental tasks. Such a finding is consistent not only with the notion that these areas are associated with a reallocation of working memory and attentional resources between ambient stimulus-data and 'stimulus-independent' data in the context of a task, but also with the notion that some of these higher-order areas actually play a role in the biasing and ability to successfully coordinate perceptual and action-planning systems in the service of strategic task processing.

Lesion data suggest that the coordination of processes involved in multi-tasking, such as task learning, remembering task contingencies, following a plan and remembering one's actions, is significantly impaired by lesions in posterior cingulate and medial and polar aspects of (particularly dorsal) prefrontal cortex (Burgess, Veitch, De Lacy Costello, & Shallice, 2000). Investigators using functional brain imaging have also endorsed a role for these respective areas in the controlled coordination of multiple demanding cognitive operations, such as retrieval success in demanding memory tasks (associated with the parietal regions Shannon & Buckner, 2004) and the strategic coordination of multiple cognitive operations (associated with anterior prefrontal regions Ramnani & Owen, 2004).

In our laboratory, we have also observed that learning tasks may have an impact on the magnitudes of the signal decreases in this network. Consistent with the findings of McKiernan et al. (McKiernan et al., 2003) and Greicius and Menon (Greicius & Menon, 2004), decreases tended to be greatest in magnitude when the tasks were novel and most difficult. There was a return of activity towards the baseline as the tasks became more automated and less demanding, particularly in the parietal regions. Interestingly, the tasks significantly differed with regard to the evolution of the signal decreases in the medial prefrontal region over time. This finding may be related to differences in specific task details. In this case, one task involving verb generation to a presented noun was performed with eyes open (Simpson, Snyder, Gusnard, & Raichle, 2001), while the other consisting of a challenging mental arithmetic task was performed with eyes closed (unpublished data). Though both tasks were clearly challenging, the task performed with eyes closed resulted in greater and more immediate prefrontal decreases, possibly related to greater and more immediate ease at disengaging from one potent source of ambient stimulus control.

4. Summary and concluding comments

There is now a variety of data supporting the notion that specific frontal and parietal association cortices (Figs. 1 and 2) constitute a network of coordinated activity. In relatively passive state conditions, such as resting with eyes closed (Laufs et al., 2003), visual fixation (Greicius et al., 2003), and passive perception (Greicius & Menon, 2004), this network is identifiable as coherent in its activity using various imaging methods. In such passive states, it has been argued that these areas are particularly important for supporting ongoing cognitive processes (Gusnard & Raichle, 2001). These areas have been suggested to participate significantly in the support of spontaneous semantic (McKiernan et al., 2003) and mnemonic (Andreasen et al., 1995; Greicius & Menon, 2004) processes, as well as 'stimulus-independent thought,' more generally (McGuire et al., 1996). Activity in some of these areas individually as well as together have also been observed to correlate with alterations in states of awareness (Fiset et al., 1999; Laureys et al., 1999; Maquet, 2000). It is particularly significant that this network, and particularly the dorsal medial prefrontal and parietal regions within it, is implicated in tasks instructing subjects to make explicit reference to some aspect of themselves. On the basis of such data, it is here suggested that activity in these areas is particularly important for enabling aspects of self-awareness and may account for many of the empirical regularities that individuals identify as self.

Depending upon task demands (McKiernan et al., 2003) and the degree to which subjects may become engaged in task performance (Greicius & Menon, 2004), these areas tend to decrease in activity, which may correspond to some disabling of self-awareness or ability to consciously access and monitor representational content about one's self. Such disabling could be responsible for the experience associated with immersion in activities executed without self-consciousness.

Obviously, the flexibility and degree of reallocation of working memory and attentional resources associated with such experiences of greater or lesser self- awareness is also likely to vary and to depend on various factors, including the extent to which the subject is able to disengage from stimulus control, whether that be control by stimuli such as salient visual cues (e.g., facial expressions, or stimulus features in a non-automated task) or subjective stimulation (e.g., the emotional arousal associated with some affective state, or feedback associated with positioning

of the body in performance of a non-automated task). The 'relevant' and specific sense of self identified (on the basis of the aforementioned 'empirical regularities') in such settings may also contribute to the biasing or cueing required for redirecting the flow of cognitive resources in the service of a task (i.e., for the self-regulation).

Finally, it is interesting to note that significant portions of this network have also been implicated in depression (e.g., Drevets, 2001; Mayberg et al., 1999) and Alzheimer's disease (e.g., Lustig et al., 2003). These states are associated with excessive self-focus and gradual dissolution of capacities for self-awareness, respectively. Such findings add further to the notion that it is intact functioning of these brain areas along with their coordinated activity that is important for enabling routine self-awareness.

In conclusion, additional work clearly needs to be done in order to refine many details of this proposal. While this unique set of prefrontal and parietal brain areas may enable spontaneous cognition and self-awareness, it is not likely that these areas alone are sufficient for such cognition. Which additional areas are engaged and how they are temporally coordinated in the accessing of any particular self-related content is likely to depend on the motivation for self-reflection as well as the level of 'event control' (Jordan, 2003) an individual is attending to at any particular moment. Further investigation of such details should pose exciting challenges. As no one self appears to exist (Metzinger, 2003), it is also likely that such work will not be concluded any time soon.

5. Technical note

For purposes of clarity, it is useful to define more precisely what we mean by a physiological baseline and how it is to be distinguished from activations and deactivations. It should be noted that this definition has arisen in the context of a functional imaging framework, but that converging evidence using other methodologies suggests that its conceptual foundations rest on aspects of brain function of broader relevance.

Fundamental to this notion of a physiological baseline is the observation that, in normal adult humans lying quietly in a PET scanner awake and alert with eyes closed (Raichle et al., 2001), there is a close match between local blood flow and oxygen utilization averaged over time (data obtained with PET usually over $\sim$30 min; Mintun, Raichle, Martin, & Herscovitch, 1984), a relationship which is often expressed in terms of the ratio of oxygen consumption to oxygen delivery. This ratio ($\sim$0.40 in the adult human) has come to be known as the oxygen extraction fraction (OEF) and is characterized by its spatial uniformity across the brain despite marked regional differences in both blood flow and oxygen consumption between gray matter and white matter as well as among gray matter areas.

By contrast, activations are characterized by a local fall in the average resting OEF which results from a local increase in blood flow that is not accompanied by a commensurate increase in oxygen consumption (Fox & Raichle, 1986; Fox et al., 1988), leading to increased local blood oxygen content and the fMRI BOLD signal (Ogawa et al., 1990).

It follows that a physiological baseline can be defined as the *average* OEF obtained across individuals or within an individual across time while such individuals rest quietly awake and alert with eyes closed. It is, thus, constituted by an absence of activation in terms of an average OEF. (For more details regarding derivation of the concept of the physiologic baseline, please see Raichle et al., 2001).

The uniformity of the OEF in averaged data obtained at rest in the normal brain suggests that equilibrium exists between the local metabolic requirements necessary to sustain an *ongoing* level of neural activity and the blood flow in that region. We have suggested (Gusnard & Raichle, 2001; Raichle et al., 2001) that this equilibrium state identifies a baseline level of neuronal activity.

Consequently, areas with a reduction in this equilibrium OEF are regarded as *activated* (i.e., neural activity is increased above the baseline level), while those areas not differing from the brain mean OEF are considered to be at *baseline*. In this scheme, increases in the OEF (i.e., decreases in the BOLD signal) define areas of *deactivation* (i.e., where neural activity is decreased below the baseline level). Importantly, obvious decreases in the OEF from the brain mean, which would indicate areas of activation, are *not* present in averaged data from subjects resting quietly awake and alert with eyes closed (Raichle, 1998).

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