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Essential Functions of the Human Self Model Are Implemented in the Prefrontal Cortex

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The human self model comprises essential features such as the experiences of ownership, of body-centered spatial perspectivity, and of a long-term unity of beliefs and attitudes. In the pathophysiology of schizophrenia, it is suggested that clinical subsyndromes like cognitive disorganization and derealization syndromes reflect disorders of this self model. These features are neurobiologically instantiated as an episodically active complex neural activation pattern and can be mapped to the brain, given adequate operationalizations of self model features. In its unique capability of integrating external and internal data, the prefrontal cortex (PFC) appears to be an essential component of the neuronal implementation of the self model. With close connections to other unimodal association cortices and to the limbic system, the PFC provides an internally represented world model and internal milieu data of the organism, both serving world orientation. In the pathophysiology of schizophrenia, it is the dysfunction of the PFC that is suggested to be the neural correlate for the different clinical schizophrenic subsyndromes. The pathophysiological study of psychiatric disorders may contribute to the theoretical debate on the neuronal basis of the self model.

Key Words: prefrontal cortex; self model; schizophrenia; association cortex; neuropsychology; philosophy of mind.

1. INTRODUCTION

The emerging field of consciousness research integrates psychological, neuroscientific, and philosophical considerations around the relationship of mind and brain. One of the focuses of the recent debate is the concept of the human self as a matter of empirical neuroscience. If empirical indicators for different domains of the human self model can be found, then an operationalization and a mapping to neuronal structures become possible. ''Classical'' features of the self dealt with in the philosophical as well as psychological tradition may be then viewed as implemented in the brain in specific neuronal network architectures.

Psychiatric diseases are of special interest in this respect, as they may present with different pathological conditions of the self model. In schizophrenia, the clinical symptomatology can be reconstructed as a disturbance of the self model or the ''self-monitoring'' capacity based on theoretical accounts worked out by Frith (1993, 1995, 1996). This article focuses on schizophrenia, although there are other psychiatric disorders, such as personality or identity disorders, which also may well affect the

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self model. Among these, schizophrenia is the most extensively empirically studied psychiatric disorder with regard to its underlying neuropathology.

In searching for the neural correlate of the self-model and the clinical subsyndromes of schizophrenia, the prefrontal cortex (PFC) can be shown to be central to the generation of schizophrenic subsyndromes. Further evidence for the integrative functions of the PFC comes from neuropsychological and functional imaging studies in healthy individuals. Recently, Damasio (1994) analyzed the historical case of Phineas Gage, presenting with a discrepancy between characterological decline and preserved cognitive functions. The brain reconstruction revealed a corresponding lesion of the ventromedial portions of the PFC, providing a prominent example of how brain research of the PFC may contribute to philosophical and neuroscientific considerations dealing with different concepts of the self model.

2. KEY CONCEPTS

2.1. Consciousness

Consciousness is viewed here as the integrated internal representation of the outer world and our organism based on actual experiences, perceptions, and memories providing reflected responses to the needs of our environment.

In such a functional third-person view, consciousness as a fundamental tool for our orientation in the world relies upon the integrative, supramodal, sensory-independent, holistic representation of the world. This world model refers to different coordinate systems, object- and viewer-centered perspectives in space representation, and physical and subjective time-scales in time representation. These frames are in turn based on data of the different sensory systems. Having invoked these internal representations, consciousness serves as a reliable and robust presentation platform providing ''availability to thought'' (Putnam, 1994) for integration of actual perception, memory, or mental imagery in order to generate valid and useful reactions to the environment.

From a first-person phenomenal perspective, consciousness appears as a purely subjective experience, which only I am able to experience for myself by introspection. Comparing my own behavior with the behavioral patterns of other human beings, I am able to assign consciousness to other human beings by analogy and even to the vast majority of neuropsychiatric patients. Any human being can experience an extraordinary range of conscious states with different individual contents. Consciousness may not vary only in content, but also in degree. In clinical medicine, consciousness is graded ranging from wakefulness to coma, which distinction is useful for the evaluation of the prognosis and the choice of adequate treatments.

2.2. The Self Model

The human self model is a theoretical construct comprising essential features accessible by introspection. Among these are, first, the experience of ownership or agency, second, the experience of perspectivity with conscious states being centered spatially around my body, and third, the experience of unity forming a long-term coherent whole of beliefs and attitudes.

The experience of ownership is reflected by the use of a pronominal syntax in

language and the experiential quality of agency that I am performing my movements for myself and having my own perceptions, memories, and thoughts. The experience of perspectivity refers to the incorporation of my memory, perceptions, and thoughts in my own body and thus to the experience of a literally spatial, body-centered perspective. The step-wise acquisition of the construct of space including the experience of perspectivity in developmental psychology was studied extensively by Piaget and Inhelder (1948). Basis of the unity experience is the long-term coherent whole of beliefs and attitudes, which is consistent with preexisting autobiographical contexts through lifetime. In the short-term range (10 s to 1-s range), there seems to be only one conscious state at a time. If two different contents are competing, these competing stimuli are not simultaneously represented, but a contraintuitive or implausible unified conscious state appears or one of the competing stimuli dominates (Baars, 1997, pp. 54, 89). The experience of unity of our conscious experience stands for ''the idea of a single person, a single subject of experience and action'' (Nagel, 1971). This long-term stability is also put forward by Baars (1997, p. 142); it allows the self to act as ''observer, agent, and guardian of the continuity of experience'' (Baars, 1997, p. 161).

These basic properties are reintegrated in the self model as an episodically active complex neural activation pattern, possibly based on an innate and ''hard-wired'' model of the spatial properties of the system (Metzinger, 1993, 1995; Damasio, 1994; Melzack, Israel, Lacroix, & Schultz, 1997). The resulting self model is a continuous source of internally generated input, which is activated whenever conscious experiences including the features of ownership, perspectivity, and unity over time occur. The model creates a spatial model of one's own body, which is independent of external input and which becomes the center of the experiential space. As the nervous system is not able to detect the activation of the self model as such, it remains unconscious.

> The phenomenal self . . . endows our conscious space with . . . centredness and perspectivalness . . . based on internal input: the part of the body image activated by proprioceptive input. . . . The part of this neural activation pattern which is independent of external input produces a continuous representational basis for the body model of the self and in this way anchors it in the brain. Whenever there is phenomenal consciousness at all, there also exists this unspecific, internal source of input. . . . The representational correlate—the self-model—is a functional module, episodically activated by the system in order to regulate its interaction with the environment. . . . Since the processuality of the objective process of self-modelling is not represented on the level of content . . . , the representational model of the system also possesses the aspect of presence in every individual psychological moment and the typical form of holism which cannot be transcended on the level of experience. (Metzinger, 1995, pp. 452–454)

It is important to state clearly that consciousness and self model are quite different from each other in nature, although not completely independent. They may be interpreted as quasi-orthogonal concepts, which can vary independently from each other only to some degree, as conscious states are necessary prerequisites for the self model. In contrast, conscious states are not sufficient for the self model, as, for instance, demonstrated in meditative states. Consciousness is presenting the world model constituted by the supramodal, sensory-independent, holistic representation of the world. The self model as continously activated endogeneous activation of proprioceptive

input is integrated in a complex internal representation matrix in the brain. After this conceptual framework, the operationalization of self model features is a necessary step to discuss its neuroanatomical implementation.

3. SCHIZOPHRENIA

3.1. Schizophrenia as Clinical Disorder of the Self Model

The self model as summarized above allows the reconstruction of different psychopathological symptoms. Psychopathology revealed that mainly three different groups of symptoms define schizophrenic subsyndromes (Liddle, 1987; Johnstone, 1991), which include psychomotor poverty (poverty of speech, flattening of affect, retardation of action), disorganization (incoherent speech, incongruity of affect), and reality distortion (hallucinations, delusions). A disturbance of the experience of ownership correlates with the symptoms of thought insertion or thought broadcasting experiences, the loss of the experience of being the agent of one's own actions, and the experience of hallucinations, which are no longer being experienced as self-induced internal perceptions (Vogeley & Curio, 1998). A disturbance of the experience of perspectivity, as a disturbance in the single, coherent, and temporally stable model of reality, centered around a single phenomenal subject, would result in depersonalization and derealization syndromes. A disturbance of the unity experience of being a coherent person could result in the experience of no longer being one single person identical over time as depersonalization or in ego-dystonic symptoms.

Frith has suggested a self-monitoring disturbance as underlying the pathophysiological principle of schizophrenia (Frith, Friston, Liddle, & Frackowiack, 1991; Frith, 1993, 1996). This monitoring capacity is for instance used for the differentiation between self- and world-generated perception as the decisive criterion between imagination and (normal) perception. To distinguish reliably between self- and world-induced perception, the process of induction of the perception must be accessible. If this monitoring capacity is disturbed, self-induced perception may appear as world-induced and hallucinatory experience may result. In pure sensory deficit conditions, for instance, I am also unable to monitor my own speech, but I am still aware of it is a sensory deficit. The fact that hallucinations comprise affective as well as cognitive components is the basis for their frightening, threatening, shaming, etc. character and underscores their ''significance'' for the hallucinating person. The preserved pragmatic function (in its strict linguistic sense) of verbal hallucinations was shown by Leudar, McNally, and Glinski (1997), demonstrating that hallucinated voices are known to the patient, that they are referring in their content to an actual situation, and that they are often directed to the patient. Another clinical example is the phenomenon of thought insertion of which schizophrenic patients may complain. In this case, the patient is not able either to recognize or to monitor the self- or non-self-induced character of his own thoughts. They are just present, and he cannot be sure whether or not these thoughts are his own.

3.2. Neuropsychology of Schizophrenia

For the essential features of ownership, perspectivity, and unity no especially designed neuropsychological paradigms exist so far, but already established neuropsy-

chological paradigms can be utilized as empirical indicators for these features, at least for ownership and unity experiences. As a basic prerequisite for the integration of external world data and internal milieu data working memory provides the necessary platform to present data ''on-line'' for a certain period of time and to allow the comparison of actual perceptions and memory contents (Goldman-Rakic, 1987, 1997).

There have been a number of working memory studies on schizophrenics demonstrating marked deficits in patients (for review Goldman-Rakic, 1994), mainly on spatial as well as verbal working memory tasks. Among classical paradigms are so-called delayed response tasks, in which a certain response is expected from the test person after a time delay. Strous, Cowan, Ritter, and Javitt (1995) were able to demonstrate an impairment in their ability to match two tones after a delay between them of 300 ms without any impairment when presenting the two tones without delay. ''Visuospatial scratchpad'' functions were assessed by Fleming, Goldberg, Binks, Randolph, Gold, and Weinberger (1997) in schizophrenic patients. Via a spatial delayed response task the authors were able to show specific memory impairment on spatial tasks involving the prefrontal lobe.

Working memory capacities and feedback processes are also necessary in the Wisconsin Card Sorting Test (WCST). Test persons are asked to sort graphic stimuli according to color, form, and number of the symbols shown, but the rules change during the test. The essential feature of the WCST is that the rules are not given explicitly, but must be inferred by the results; the sorting ''guesses'' obtain how fast and how reliably the rules are sorted out (Milner, 1963). This strategy task involves activity of the prefrontal lobes. Schizophrenic patients show significantly lower relative blood flow in prefrontal regions during this task than do healthy volunteers. Analyses of samples from two combined studies showed the patients to have significantly lower relative flow in prefrontal regions both at rest and during activation and higher flow in the left striatum during activation, suggestive of a defect in the frontostriatal interrelationship in schizophrenia (Rubin, Holm, Madsen, Friberg, Videbech, Andersen, Bendsen, Stromso, Larsen, Lassen, & Hemmingsen, 1994).

For the judgment about the ownership or agency of the own perceptions or thoughts as self-model feature, some candidate paradigms have been applied to schizophrenia. A well-established deficit in schizophrenics is for instance, disturbance in the generation of saccadic eye movement as a kind of willed action. In a PET study, Nakashima, Momose, Sano, Katayama, Nakajama, Niwa, and Matsushita (1994) demonstrated in volitional saccades a complete lack of activation of the dorsolateral prefrontal cortex (DLPFC), which was activated in normal controls, suggesting functional hypofrontality. Corroborating a metabolic decrease in the frontal lobes in schizophrenics, Andreasen, O'Leary, Flaum, Nopoulos, Watkins, Boles Ponto, and Hichwa (1997) examined 17 neuroleptic-naive patients at an early stage of illness. Electrophysiologically, the initial MRP components (RP and and NS′) were found to be reduced in schizophrenics, indicating an impairment of the voluntary preparatory process in schizophrenia (Singh, Knight, Rosenlicht, Kotun, Beckley, & Woods, 1992). They were shown to have a decreased metabolic rate in the prefrontal regions bilaterally, which may form the neural basis of schizophrenia, leading to a deficit in volition. Schizophrenic patients with a passivity syndrome may, in contrast to other subsyndro-

matic groups of schizophrenics, develop problems with representing their own intentions to act as Frith and Done (1989) demonstrated in a motor error correction task presented to schizophrenics. Patients with experiences of alien control of their thoughts and actions were significantly less likely to make error corrections in the absence of visual feedback. Mlakar, Jensterle, and Frith (1994) showed a deficit of schizophrenics in keeping track of their performance and remembering their recent actions when drawing a picture. Although still able to perform actions, the patients are no longer aware of the ownership of their own actions appearing as a defect in ''central monitoring.''

The experience of unity as a coherent model over time is established by autobiographical memory, which contains the contexts of our memories and our lifetime history. Activation of autobiographical memory has been shown to activate fields in a prefronto-thalamo-cerebellar network (Andreasen, O'Leary, Cizadlo, Arndt, Rezai, Boles Ponto, Watkins, & Hichwa, 1996; Fink, Markowitsch, Reinkemeier, Bruckbauer, Kessler, & Heiss, 1996). Schizophrenic patients showed considerable difficulties in coordinating and monitoring the process of retrieving, receiving, processing, and expressing information, leading to the idea of ''cognitive dysmetria'' (Andreasen et al., 1996). This cognitive dysmetria, which literally addresses measurement defects in the processing of ideas, hypotheses, etc., is suggested as an important underlying cognitive dysfunction that could explain diverse schizophrenic symptoms. An important class in this respect of paradigms is theory of mind (TOM) studies, in which an assignment of opinions, attitudes, etc. to someone else (''X knows, believes, etc., that *p*'') is expected. This appears to be relevant for the self model as it is likely that this capacity is built upon our own autobiographical experience, which is projected to another person's mind. ''The reference to a self may be the basis of a model of the alter ego, of other people's mind, or models of the self and alter-ego may coevolve'' (Delacour, 1995).

This capability of ''mindreading'' is an important component in social interaction and communication and can be tested in TOM paradigms, originally designed in primates and further developed in developmental psychology of humans (Baron-Cohen, 1995). Employed mostly in autism research, TOM studies have also been performed on schizophrenic patients. Frith and Corcoran (1996) studied schizophrenic patients in comparison to normal healthy controls. They found an exclusive TOM deficit in patients with a paranoid delusional syndrome, whereas patients with negative features or incoherence showed TOM deficits as well as memory deficits. This supports the hypothesis that specifically the positive symptom of paranoid delusions reflects TOM deficits, whereas TOM tasks could be performed relatively well by patients presenting only with passivity features. Doody, Götz, Johnstone, Frith, Cunningham, and Owens (1998) found a specific deficit in schizophrenic patients in a cartoon-based TOM paradigm in a second-order TOM design (e.g., ''Where does Mary think that John has gone to buy an ice cream?''). These modeling capacities are also presentable and testable in texts as short stories. Corcoran, Mercer, and Frith (1995) developed a TOM design in which the intention of a person had to be inferred, which was given in the story only implicitly by indirect speech. In particular, schizophrenics with negative symptoms performed worse than normal persons. TOM paradigms are of considerable importance as they allow the modeling of another person's

propositional attitudes on the basis of one's own past, which can be used as heuristic pool. Whether a capacity of experiencing agency or a central executive is a prerequisite of the ability to model other minds is still a matter of debate and cannot be resolved yet (Baron-Cohen, 1995, p. 128).

3.3. Neurobiological Basis of Schizophrenia

The hypothesis of the central role of the dysfunctionality of hetermodal association cortices in the pathophysiology of schizophrenia was recently put forward by Pearlson, Petty, Ross, and Tien (1996). A central idea in the organic etiology of schizophrenia is the concept of dysconnectivity in the DLPFC or interconnections between DLPFC and other areas of the heteromodal association cortex (HMASC) (Liddle, 1995). As the DLPFC has a key role in working memory and presentation of information on-line, the breakdown of this function then probably induces a breakdown of cortical area communication (Hoffmann & McGlashan, 1993). Brain-imaging studies indicate that the underlying neuropathology entails disordered functional connectivity within the neural networks in heteromodal association cortices putatively corresponding to the supervisory mental processes, which would be consistent with Kraepelin's own speculation about the essential nature of the condition (Liddle, 1995). One possibility is an altered connectivity between heteromodal association cortex and other cortical areas (Weinberger, Berman, Suddath, & Torrey, 1992) or subcortical structures (Silbersweig, Stern, Crith, Cahill, Holmes, Grootonk, Seaward, McKenna, Chua, Schorr, Jones, & Frackowiak, 1995). A disruption at any site of the network could lead to virtually any variant of a ''frontal lobe syndrome'' (Berman and Weinberger 1990). In accordance with recent research, a heuristically useful reconciliation should be centered on the functional neuroanatomical concept of prefrontal-temporolimbic cortical connectivity embedded in a developmental ''dysconnection'' of temporolimbic-prefrontal cortices (Weinberger and Lipska 1995).

On the neuronal network level, it is still a matter of debate whether a cortical hyperconnectivity (e.g., David 1994) or hypoconnectivity is more plausible (e.g., Hoffmann & McGlashan, 1994) in explaining the schizophrenic symptomatology. However, the concept of a microdysconnectivity is of course not the only explanatory model for the neurobiology of schizophrenia, but it appears plausible on the basis of evidence that has been obtained up to now in neuropathological research on schizophrenic brains. Yet there are no consistent data on the cortical synaptic density that could be used convincingly in favor of hyper- or hypoconnectivity, respectively (Glantz & Lewis, 1997; Gabriel, Haroutunian, Powchik, Honer, Davidson, Davies, & Davis, 1997). In the prefrontal area, a neuronal network disturbance was shown by a decreased interneuronal density in layer II and, to a lesser extent, in layer I in schizophrenic subjects compared with control subjects (Benes, McSparren, Bird, SanGiovanni, & Vincent, 1991). The neuronal density was significantly lower in layer VI of the prefrontal cortex, layer V of the cingulate, and layer III of the motor cortex (Benes, Davidson, & Bird, 1986).

This framework has led to the hypothesis of considerable changes in the prefrontal lobe of schizophrenics and could be verified in our own studies with a variety of different neuroanatomic methods. In our own postmortem sample of 25 schizophrenic

brains compared to 25 control brains, a significant bilateral volume decrease of the prefrontal region in male schizophrenics was found. The gyrification index (GI), determined as the ratio between the total length of the contour defining the cortical surface in coronal serial sections and the length of the contour segments not buried in the sulci, provides an estimate of the degree of cortical folding (Zilles, Armstrong, Schleicher, & Kretschmann, 1988) and can also be used for quantitative analysis of gyrification during ontogeny (Armstrong, Schleicher, Omran, Curtis, & Zilles, 1995). In our sample, we found a significant hypergyria in the right prefrontal region of male schizophrenics and a nonsignificant hypogyria in female schizophrenics (Vogeley, Schneider-Axmann, Tepest, Pfeiffer, Bayer, Bogerts, Honer, & Falkai, submitted for publication, -a).

As gyrification occurs after neuronal migration, a close relationship between these two processes was postulated (Richman, Stewart, Hutchinson, & Caviness, 1975). Therefore, we started to study cytoarchitectonic features of Brodmann's area (BA) 10 quantitatively by measuring the laminar distribution of cell body volume ratios (gray level index, GLI) over the whole cortex according to Schleicher and Zilles (1990). A significant reduction of mean GLI in schizophrenics was found. Studying cytoarchitectonic features in BA 9, Selemon, Rajkowska, and Goldman-Rakic (1995) demonstrated an overall increase in neuronal density with reduced cortical thickness. Recently, Rajkowska, Selemon, and Goldman-Rakic (1998) found in the same sample and region a reduction of the mean neuron somal size, reaching statistical significance only in lamina III. The neuronal density of extra large neurons was reduced by 40%; the neuronal density of small- and medium-sized neurons was increased by 70 to 140%, so that the density increase of small neurons seems to compensate for the reduction of extra large neurons. Taken together, these data are suggestive of a relative ''hyperinnervation'' of neurons in the prefrontal cortex of schizophrenics as shown by the increase in neuropil volume per cell body volume (Vogeley, Kawasaki, Jung, Tepest, Schleicher, Zilles, & Falkai, submitted for publication, -b).

4. NEUROPSYCHOLOGY OF THE PREFRONTAL CORTEX

The DLPFC spans most of the lateral surface of the frontal lobes. Microscopically, the human PFC can be divided into structurally distinct cytoarchitectonic areas corresponding to Brodmann areas 9, 10, and 46 (Fig. 1). Different cytoarchitectonic areas are postulated to correspond to different functional roles: ''The function creates its organs'' (Brodmann, 1909, p. 285). Functionally, the DLPFC belongs to the HMASC, which in addition comprises the inferior parietal lobule (Brodmann areas 39 and 40) and parts of the superior temporal gyrus (Broadmann area 22).

Different neuropsychological capacities are implemented in the PFC, although this activation is by no means strictly limited to the PFC. For instance, autobiographical memory does involve hippocampal formation, and verbal tasks in working memory conditions also activate temporal cortex areas. Of course, the following list of neuropsychological paradigms that can be assigned to the PFC is incomplete and is oriented along the essential features of the self model. Other potentially relevant paradigms activating the PFC include semantic tasks (Kapur, Rose, Liddle, Zipursky, Brown, Stuss, Houle, & Tulving, 1994; Vandenberghe, Price, Wise, Josephs, & Frackowiak,

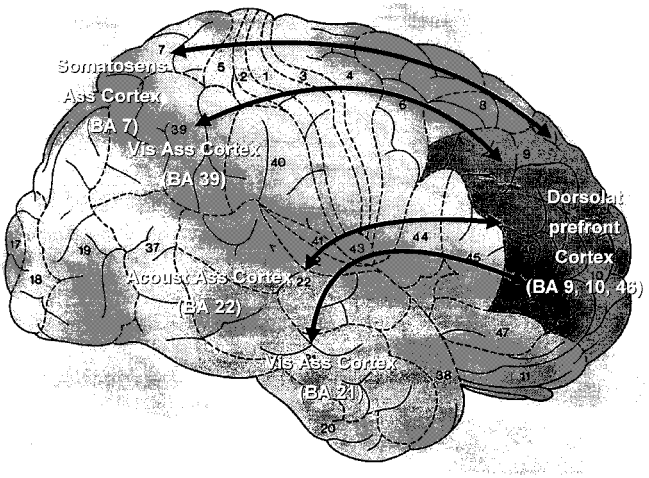

FIG. 1. Lateral surface of the right hemisphere. The extent of the dorsolateral prefrontal cortex is marked. Numbers correspond to Brodmann areas (modified according to Nieuwenhyus, Voogd, and van Huijzen, 1988).

1996) and attentional tasks (Posner & Petersen, 1990; Kapur et al., 1994; Posner, 1994). Evidence for a cingulo-fronto-parietal network was shown by anatomical tracing methods in the monkey brain (Morecraft, Geula, & Mesulam, 1993) as well as in humans (Rees, Frackowiak, & Frith, 1997).

4.1. World Modeling

The DLPFC receives afferents from virtually all neocortical areas that contain the various cortical projection sites and their corresponding unimodal association cortex areas of the different sensory modalities such as somatosensory (parietal lobe), visual (occipital lobe), auditory, gustatory, and olfactory modalities (temporal lobe). This was reviewed in rhesus monkeys by Jones and Powell (1970) and subsequently corroborated by a number of other groups (for review, see Fuster, 1989). The PFC thus works as a ''convergence zone'' according to Damasio (1994, 1996). Interestingly, the frontal lobe does not contain any primary sensory area itself. This feature of integrating information from different sensory modalities is obviously a necessary step for the internal world modeling important for our orientation in the world, which is the necessary counterpart of the self model aiming at advantageous behavior of the organism responding to its environment.

After functional segregation of different aspects of a given stimulus in a given modality (or many modalities), reintegration must take place to generate a unified representational matrix. For instance, in the visual system information processing is implemented in the striate cortex and is worked up further in the so-called what- (inferotemporal cortex) and where-streams (parietal cortex) providing object coding and spatial coding of complex visual stimuli (Tanaka, 1992; Zeki, Watson, Lueck, Friston, Kennard, & Frackouiak, 1991; Van Essen, Anderson, & Felleman, 1992; Courtney, Ungerleider, Keil, & Haxby, 1996). The reintegration of what-and where-

streams in the primate DLPFC has been demonstrated recently by Rao, Rainer, and Miller (1997) in an electrophysiological single-cell recording study. Half of the recorded cell population in the DLPFC showed activity that correlated simultaneously with both spatial and object coding.

4.2. Body Image

A central issue of the self model is the experience of perspectivity in a spatial sense centered around my own body as worked up in its genetic aspects by Piaget and Inhelder (1948). This feature depends on an internal representation of the organism's body, fermed body schema, body image, or corporeal awareness, and is realized in the brain by a source of continuously generated input about internal milieu data, at least partly genetically determined (Melzack, 1997). Whenever experiences of perspectivity occur, this continual source of interoceptive and proprioceptive input is activated in parallel, presenting a spatial model of one's own body independent of external input and which becomes the center of the experiential space. As Damasio worked out in his ''somatic marker hypothesis,'' this body image involves activation of the right parietal region and of the PFC, especially in its ventromedial parts, which ''establishes a simple linkage ... between the disposition for a certain aspect of a situation ..., and the disposition for the type of emotion that in past experience has been associated with the situation'' (Damasio, 1996, p. 1415). This is anatomically reflected in the strong relationship to diverse constituents of the limbic system, especially paralimbic cortical regions, such as the cingulate, parahippocampal gyri, and orbitofrontal cortex. Data about the internal milieu of the organism become available to the PFC on the basis of prefrontal-temporolimbic cortical connectivity (reviewed by Mesulam, 1985; Fuster, 1989; Cummings, 1993; Van Hoesen, Morecraft, & Semendeferi, 1996).

This linkage then serves judging situations on the basis of former emotional reactions to similar situations in order to ''constrain the decision-making space by making that space manageable for logic-based, cost–benefit analyses'' (Damasio, 1996, p. 1415). This ''body in the brain'' was recently reviewed by Berlucchi and Aglioti (1997) as ''a mental construct that comprises the sensory impressions, perceptions and ideas about the dynamic organization of one's own body and its relations to that of other bodies.'' Teleologically, this serves survival of the whole organism by continuously representing the functional states of the body image, which is represented in the somatosensory region of the right parietal cortex (Damasio, 1994). The rapid and repetitive reinstantiation of the body image is based on a prefronto-parietal network, which is unconscious, inasmuch as it is continuously reconstituted in its process (Damasio, 1994, 1996; Metzinger, 1995). Cheil and Beer (1997) suggested more broadly viewing adaptive behavior as the interaction of the nervous system, the body, and its environment.

4.3. Working Memory

One of the leading concepts in understanding the functions of the DLPFC is the concept of working memory, which means having data on-line (Goldman-Rakic, 1987, 1994, 1997). Working memory is responsible for the temporary storage of relevant contextual information from the recent past, about the general plan, or re-

garding aspects of an object or event that is not part of what is actually perceived. The main feature of working memory is its ''ever-changing content'' (Spitzer, 1997), comparable to the metaphor of a scratchpad or the Freudian ''Wunderblock'' (Freud, 1925); this does apply to the sensory cortices as well. The working memory can be considered as part of a central executive system opposite to slave systems like the so-called visuospatial sketchpad. This view is based on the original contribution of Baddeley (1986), presenting a dual-track model of working memory. Central to this model is a so-called central executive system, comprising different functions as ''attention controller, organizer of learning and retrieval planner'' (Baddeley & Della Sala, 1996). This central executive is assumed to use slave systems, which serve processing of visuospatial (visuospatial sketchpad) and language-based information (''phonological loop'' or ''articulatory loop'').

The availability of data and the temporal bridging are probably a necessary step in constituting the subjective experience of unity of our conscious experience and may be identified with brain activity in the DLPFC (Goldman-Rakic, 1997). In the same sense, Fuster (1989) emphasized the cross-temporal integration by the DLPFC as the ability to respond to stored, ''quasi-delayed'' information and not only to direct immediate stimulation. This is a basic prerequisite for consciousness. Supporting this temporal bridging or cross-temporal contingency concept, well-known neuropsychological test designs use so-called delayed response tasks, in which a reaction on a cue is expected after a delay (Fuster, 1991). Lesions in the PFC correlate with poor scores on delayed response tasks as shown in primates (Goldman-Rakic 1987) and in frontally lesioned humans (Verin, Partiot, Pillon, Malapani, Agid, & Dubois, 1993).

4.4. Autobiographical Memory

The unity experience relies basically on the availability of our individual personal history as the long-term memory platform. Working memory and autobiographical memory work on different time-scales. Encoding and retrieval of narrative, episodical, or autobiographical memory provide the context of former experiences, attitudes, opinions, and so forth, which are the basis for a certain style of decisionmaking over time. This of course is by no means sufficient for the unity experience, but may serve as an empirical indicator. Autobiographical memory puts functionally more weight on the contextual environment of an actual perception instead of the semantic content. Combined functional imaging and neuropsychological studies clearly demonstrate the central role of the PFC in encoding and retrieval of old episodical memory in addition to the involvement in constituting the working memory platform.

Preferentially, the left PFC is engaged in the encoding of autobiographical memory, whereas the right PFC seems to be engaged in the retrieval of autobiographical memory (Tulving, Kapur, Craik, Moscovitch, & Houle, 1994; Markowitsch, 1995; Fletcher et al. 1997). In more detail, it can be shown that the right PFC seems to be more engaged in the retrieval success than in retrieval effort as reviewed by Fletcher, Frith, and Rugg (1997). This is corroborated by empirical evidence for deficits in the recall of autobiographical memory after lesions of the left DLPFC as summarized by Markowitsch (1995). Activation of the right DLPFC could also be demonstrated by Fink et al. (1996) in the recall of old episodical memory with specific personal

qualities in contrast to impersonal qualities in their operationalized paradigm. In the ''impersonal'' condition subjects were studied during presentation of sentences describing autobiographical contents of another person's, biography, in the ''personal'' condition of their own autobiography. However, psychopathology conditions have not been studied so far by this sort of paradigm family examining autobiographical memory.

4.5. Social Inferring or Theory of Mind

Of eminent relevance to the self model is the ability to mindread, which needs a self model serving as source for projection to model a TOM of someone else or alternatively coevolves with the self model (Delacour, 1995). The development of the capacity of modeling another's mind could well be an evolutionary innovation in humans. It has been proposed that on an evolutionary time-scale only recently has explicit representational knowledge become available, although implicit knowledge of beliefs and intentions has existed for hundreds of millions of years. This evolutionary change can be correlated to the growth of the association cortex, especially the prefrontal cortex (Povinelli & Preuss, 1995). Coined by Premack and Woodruff (1978) in studies with primates, TOM studies were further developed in human developmental psychology. According to Baron-Cohen (1995, p. 31), the positive capacity of mindreading comprises four different modules, which are the intentional detector, the eye-direction detector, the shared-attention mechanism, and the theory of mind mechanism (TOMM). The first three are necessary for the constitution of the TOMM. Formally, the function of mindreading of TOM can be described as a representation of epistemic mental states comprising an agent, an attitude, and a proposition, e.g., ''Peter believes that it is raining'' (Wimmer & Perner, 1983; Baron-Cohen, Leslie, & Frith, 1986; Pratt & Bryant, 1990). This allows the representation of mental states of an agent even if the proposition is not true, e.g., ''Peter believes that it is raining'' may be true, although ''It is raining'' may be false (Leslie & Thaiss, 1992; Leslie & Roth, 1993).

In a TOM paradigm, a subject must model the knowledge, attitudes, or beliefs of another person. Presented by a cartoon or by telling a history, the behavior of another person must be modeled prospectively by the test person. In performing imaging studies, Baron-Cohen, Ring, Moriarty, Schmitz, Costa, and Ell (1994) found a rCBF increase in the orbitofrontal cortex on the right side in comparison to the left side in a HMPAO-SPECT study. In a PET study, Goel, Grafman, Sadato, and Hallett (1995) presented a picture sequence with objects from everyday life. Test persons had to decide whether Christopher Columbus would have been able to infer their function. A differential activation was found in the PFC on the left side.

4.6. Willed Action

A last group of experiments includes studies of self-paced movements that exemplify willed action. Introspectively, all features of the self model comprising ownership, perspectivity, and the experience of unity also apply to willed action, as a consciously performed movement is always *my own* movement, is always performed from a certain perspective in a spatial sense centered around my own body, and is incorporated in my own autobiographical history. Teleologically, intentional acts as

part of adaptive behavior are the ultimate goal, with its ''output'' of our world and self modeling serving our survival.

In studies on willed action in humans, activation of the PFC can be demonstrated consistently. Kawashima, Itoh, Ono, Satoh, Furumoto, Gotoh, Koyama, Yoshioka, Takahashi, Takahashi, Yanagisawa, and Fukuda (1996) showed PFC activation corresponding to self-paced proximal and distal arm movements. Such voluntary processes are prepared by a so-called Bereitschaftspotential or movement-related potential (MRP). Unilateral PFC lesions preferentially reduced the readiness potential and negative shift components of the MRP, indicating that the PFC is involved in a neural network beginning at least 1000 ms prior to movement (Singh & Knight, 1990).

5. NEURONAL IMPLEMENTATION OF THE SELF MODEL

A major principle in brain architecture is that of functional segregation, for instance, in sensory specific, unimodal cortical systems, which in turn include the functional principle of reintegration happening in the HMASC areas, reflected in the debate on modularism and holism (Vogeley, 1995). Microscopically, all vertebrate nervous systems consist of uniform building blocks, modular neuronal networks (Szentágothai, 1983, 1985; McConnell, 1988; Leise, 1990) (see Fig. 2). The location of a neuronal network, its position in the nervous system, and its position in specific functional systems define its functional role. Reciprocal thalamocortical projections, intralaminar thalamic nuclei, and the reticular formation of the brain stem are basic arousal constituents (Castro-Alamancos & Connors, 1996; Munk, Roelfsema, König, Engel, and Singer 1996), whereas different contents of consciousness are released by activation of different cortical regions addressed by subcortical brain structures: ''content requires cortex'' (Newman, 1997).

However, the modular organization of the brain is by no means static. On a long time-scale, plasticity phenomena are well known in repetitive action and in pathological conditions like deafferentiation (e.g., Mazziotta & Phelps 1984; Friston, Frith, Passingham, Liddle, & Frackowiak, 1992; Weiller, Chollet, Friston, Wise, & Frackowiak, 1992). On a short time-scale, rhythmic oscillation phenomena with a frequency of 40–60 Hz are well known (Eckhorn, Bauer, Jordan, Brosch, Kruse, Munk, & Reitboeck, 1988; Engel, König, Kreiter, & Singer, 1991), generating coherence and coding of external stimuli (Barinaga, 1990; Singer, 1991). Neurophysiological studies show coactivation of cortical areas, and electrophysiological studies revealed interarea synchronization leading to computational advantages of these implementations (Bressler, 1995). Thus, the self is not any sort of central knowledge and control station, but corresponds to a biological state, which becomes continuously reactualized and attributed to conscious contents of our perceptions.

Based on these brain architectural principles and the above described evidence, the PFC appears as the most important component in the neuronal implementation of the self model. Many, if not all, of the different symptoms of dysfunction of the PFC may be the result of a disturbance of cross-temporal contingencies (Fuster, 1991; Hoffmann & McGlashan, 1993), which seems to be a central pathogenetic mechanism. Cross-temporal contingencies are responsible for keeping contents on-line in working memory. That the temporal order of subjective events is not a naive reflec-

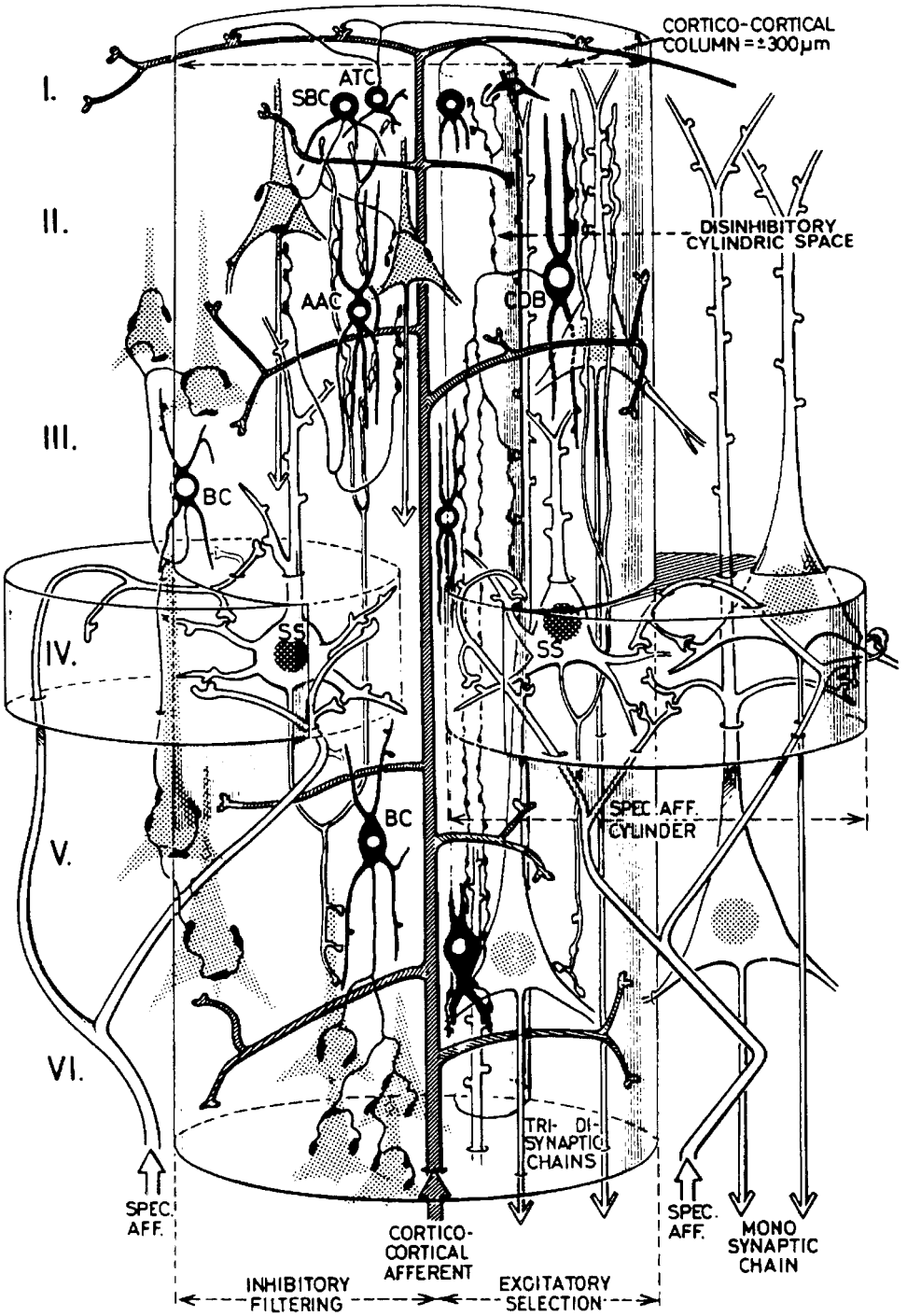

FIG. 2. Typical neocortical module grouped around central thalamic afferences, which feed intramodular processing with interneurons and efferences via pyramidal cells (according to Szentágothai, 1983).

tion of the outer world, but a product of the brain's interpretational processes, was also emphasized by Dannett and Kinsbourne (1992). Deficits in the experience of ownership could well be due to a complex dysconnection syndrome between the prefrontal and other association cortex areas. Particular sequences of an action or the internal visualization of a former memory as a mental image usually involves awareness of its induction or source. This source is usually recognized as me; for instance, I have intended a certain movement that is now happening, I have evoked a certain memory now present as a mental image. If this sequence is no longer adequately presented on an inner time-table, this awareness of induction is lost systematically (and not only occasionally as, for instance, in meditative states). This may then lead to the loss of experience of ownership or to the experience of alien control. Similarly, disturbances in the prefronto-parietal network as a putative source of continuously generated input about internal milieu data may result in the loss of experience of body-centered perspectivity. Evidence comes from the work by Damasio (1994, 1996), who assigns central judgement functions to the ventromedial parts of the PFC. If this continuous reactualization of current experiences and proprioceptive information is disturbed, the result would be the loss of experiential perspectivity. Loss of the sense of unity on a long time-scale may already occur in disturbances of the above-mentioned mechanisms providing the continously feeding of body image and the experience of ownership. The unity experience over time basically needs the incorporation of autobiographical memory with activation of the temporal lobe. If autobiographical memories are not adequately integrated into the current contents of consciousness, a disruption takes place, which disturbs the experience of a coherent whole over time and may lead to depersonalization syndromes.

In summary, the PFC, especially its dorsal parts, is a constitutive component of a complex neural network architecture comprising various sites to generate experiences of ownership, perspectivity, and unity on the phenomenal level. It does so by integrating mulitmodal perceptions and proprioceptive body image information. Behavioral adaptation to challenging new situations is provided by monitoring ongoing elaborated programs and previously established automatic programs. The function of the PFC may thus be defined as an ''active, transformational process in which sensory data are synthesized into the simplest possible representation for the purpose of maximizing behavioral efficiency'' (Shobris, 1996).

A global workspace theory taking these various aspects of a large-scale neuronal network into theoretical account was worked out by Baars (1997). Consciousness may be seen metaphorically as a ''working theater.'' A central aspect of consciousness is that it provides access to central nervous system functions, while being a central nervous system function itself at the same time. A central part of this metaphorical device is the ''stage,'' which is the platform for actual and potential conscious contents or experiences. The stage is partly illuminated by a ''bright spot,'' the attentional searchlight. This spot is directed by some ''agents behind the stage,'' which correspond to unconscious processes. The ''theater play'' as stream of consciousness is presented to the ''audience,'' which is again unconscious and corresponds to different executive functions such as motor actions, interpretation systems, or motivational systems. This is the framework. ''Paying attention ... becoming conscious of some material ... is the universal solvent of the mind'' (Baars, 1997, p. 304). Obviously, the PFC plays a cardinal role in this ''theater.''

Future research must concentrate on two different areas in this field. First, future research must focus on psychopathology in correlation to brain sites, networks, or mechanisms. As inaugurated and repetitively put forward, for instance, by Christopher Frith, we are in need of an extensive neuropsychological reconstruction of psychopathology to reintegrate psychopathological symptoms into neuroscience. The best way to do this is to reconstruct their symptoms as neuropsychological symptoms. In a first step, we can utilize the already well-established neuropsychological syndromes and experimental paradigms, which means that we must search for symptoms in neuropsychology that are similar to those in psychopathology. In a second step, these similarities may be used as heuristic tools to look for new experimental paradigms. Therefore, future research in ''neuropsychological psychopathology'' should focus in addition on the development of new functional paradigms that can be operationalized for functional imaging studies. This is especially important because there are as yet no adequate paradigms available that explicitly test the features of ownership, perspectivity, or unity. A possible strategy could be to develop paradigms that attempt to establish self-assignment capacities according to for instance, false-belief designs from the TOM paradigm family. Up to now, there has apparently been no neuropsychological paradigm established that is able to differentiate between self-assignment and assignment to others. Second, future schizophrenia research must continue to focus on the neurobiological changes in the brains of schizophrenics in order to further elucidate the dysconnectivity hypothesis. Studies of changes in the neuronal network including studies on neuronal cytoarchitecture, synaptic density, and myelination are necessary and must be extended to other heteromodal association cortex areas. This includes the morphological, immunohistochemical, and molecular characterization of changes in the macro- and microconnectivity of different brain regions.

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