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Review

Conscious brain, metacognition and schizophrenia



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ABSTRACT

Recent findings indicate that the binding and synchronization of distributed neural activities are crucial for cognitive processes and consciousness. In addition, there is increasing evidence that disrupted feature binding is related to experiences of disintegration of consciousness in schizophrenia. These data suggest that the disrupted binding and disintegration of consciousness could be typically related to schizophrenia in terms of Bleuler's concept of "splitting". In this context, deficits in metacognitive capacity in schizophrenia may be conceptualized as a spectrum from more discrete to more synthetic activities, related to specific levels of neural binding and neurocognitive deficits. This review summarizes the recent research on metacognition and its relationship to deficits of conscious awareness that may be found in schizophrenia patients. Deficits in synthetic metacognition are likely linked to the integration of information during specific processes of neural binding. Those in turn may be related to a range of mental activities including reasoning style, learning potential and insight.

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1. Introduction

In 1881, Eugen Bleuler began developing his view that the core problem among individuals with psychosis is determined by disruptions of thought-linkages and deficits in the coordination of different psychological functions. These anomalies were thought to lead to a "loosening of associations" related to the process of splitting. Bleuler defined the term splitting as a process of formation of complex mental structures linked to incompatible experiences producing numerous divisions in mental processes (Bleuler, 1918/1906). In his work: "Dementia praecox or the group of the schizophrenias", Bleuler (1911), introduced the term "schizophrenia" to describe the illness that replaced Kraepelin's dementia praecox (Bleuler, 1911/1955, 1918/1906; Jung, 1909). Bleuler thought that: "...the 'splitting' of the different psychic functions is one of its most important characteristics" (Bleuler, 1911/1955, p.8). According to Bleuler (1911/1955) some psychic complexes creating aggregates of thoughts, feelings and affects may dominate personality structure, while other complexes may be "split off" and operate as fragments connected with the others in an "illogical" way.

In historical context Bleuler's definition of "split mind" as a characteristic feature of disturbed cognition in schizophrenia is related to

Descartes' proposal the binding multidimensional information from various sensory modalities that enables conscious experience (Bob, 2015; Barrera-Mera and Barrera-Calva, 1998). The so-called "binding problem" leads to the unresolved question where and how the information is integrated into the whole and how this information is specifically linked to previous experience in the spatio-temporal memory. An important question for further research of the integration of distributed brain activities is whether the essential integrative role can be attributed to a specific structure in the brain or whether this ability is inherent to the cognitive network as a whole. In addition it is not known how spatial convergency is provided for the synthesis of processed information that emerges and for example, there are only a few neural connections between specific visual areas that correlate with color and motion (Bartels and Zeki, 2006; LaRock, 2006; Zeki, 1994, 2003). For example, visual consciousness requires activity in many areas of the brain and the components of the high-level visual representations, closely linked to focused attention, need to access these structures, form a perceptual object and bind together various features of an object (Zeki and Bartels, 1999; Cavanagh, 2011).

A key evidence for the binding problem reported studies of primate extrastriate visual cortex which have shown that different neurons within the visual system participate on processing of different features of a seen object (Desimone et al., 1985; Schein and Desimone, 1990; Ghose and Tso, 1997). For example, Desimone et al. (1985) have found that neurons in visual area (V4) and inferior temporal cortex (IT) are sensitive to many kinds of information relevant to object

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recognition. They also found that special contribution of V4 neurons to visual processing may lie in specific spatial and spectral interactions and that many different stimulus qualities are processed in parallel mode of processing. Similar results reported Ghose and Tso (1997), who also found that V4 contains modular assemblies of cells related to particular aspects of processed object-based representations. There is also evidence in research of moving objects that other neurons in the middle temporal area and the medial superior temporal area encode various aspects related to the motion of the stimulus (Treue and Andersen, 1996; O'Keefe and Movshon, 1998).

Significant contribution to this discussion about mechanisms of large scale integration reported Crick and Koch (1992, 2003) in their studies of the visual consciousness. They proposed that the problem of binding may not be resolved only as a simple consequence of synchronization among large groups of neurons. As a basis for that opinion they emphasize the binding problem of distributed information representing a seen object by groups of synchronized excited neurons that are located at different parts of the brain. This problem has emerged in connection to findings that features of an object such as color, shape, texture, size, brightness, etc. produce activity in separate areas of the visual cortex (Crick and Koch, 1992; Felleman and Van Essen, 1991; Singer, 1993, 2001). In context of these findings the hypothetical center for brain information convergency that enables perceptual consciousness and conscious experience was termed "Cartesian theatre" (Crick and Koch, 1992; Dennett, 1991). Recent neuroscience, however, has not located a distinct place in which distributed information in the brain comes together. Additionally, there is evidence that neocortical processing is distributed during all sensory and motor functions (Singer, 1993, 2001).

The predominant view in neuroscience of consciousness is that neuronal synchronization is a phenomenon that is necessary for the large scale integration of distributed neuronal activities. There is increasing experimental evidence that coherent neuronal assemblies in the brain are functionally linked by phase synchronization among simultaneously recorded EEG signals and that this time-dependent synchrony between various discrete neuronal assemblies represents neural substrate for mental representations such as perception, cognitive functions and memory (Varela et al., 2001; Lachaux et al., 1999). These functions are related to distributed macroscopic patterns of neuronal activity which involve multiple neuronal subsystems bound into a coherent whole (Braitenberg, 1978; Van Putten and Stam, 2001). According to recent data, a mechanism that enables binding of distributed macroscopic patterns of neuronal activity, represented by neural assemblies, into the coherent whole is still unresolved and represents a fundamental problem in neuroscience [i.e., the binding problem: how the brain codes and integrates distributed neural activities during processes connected to perception, cognition and memory] (Woolf and Hameroff, 2001; Lee et al., 2003a; Arp, 2005; Fidelman, 2005; Velik, 2010). The theory of feature binding originates with distributed coding and states that neurons involved in the processing of a single object will tend to synchronize their firing, while simultaneously desynchronizing their firing from the remaining neurons not involved in the processing of the object (von der Malsburg and Schneider, 1986). An essential feature of neuronal assembly coding is that individual neurons or subsystems can participate at different times in an almost unlimited number of different assemblies (Sannita, 2000; Varela et al., 2001). The same neurons can participate in different perceptual events and different combinations of these neurons can represent different perceptual objects. Synchronization of these different perceptual objects is related to the integration of perceptions into a coherent whole (Singer and Gray, 1995). As a candidate mechanism for the integration or binding of distributed brain activities is the so-called gamma activity—high frequency oscillations according to some studies varying from 20 to 100 Hz. This activity occurs synchronously across brain regions and underlies the integration of diverse brain activities (Singer and Gray, 1995; Wang and Buzsaki, 1996; Buzsaki, 2006; Bob and Mashour, 2011).

In this context, majority of recent studies on neural correlate of consciousness have focused on EEG analysis and observed functionally relevant periods of synchronization mainly in gamma frequency band in various species and brain structures during attention, perception, motor and memory tasks (Singer, 2001; Lee et al., 2003a; Jensen et al., 2007). Together these findings suggest that a candidate mechanism for the integration or binding of distributed brain activities is the gamma activity which enables to different neuronal circuits to enter into synchrony with the perceptual information. This integrative process enables to these simultaneously active neuronal clusters oscillate together during transient periods of synchronized firing and this coherent whole enables to connect various memories and associations involved in the process and generate a coherent process of perception, cognitive processing, memory and consciousness (Buzsaki, 2006). Several recent findings suggest that the higher and the lower frequencies may play a specific role in binding and connectivity with specific manifestation in cognition and its disturbances. These results agree with the findings that disconnection and disturbed binding as a correlate of mental disintegration in schizophrenia may be related to decreased or increased synchrony (Lee et al., 2003a; Tononi and Edelman, 2000; Uhlhaas and Singer, 2006). Decreased or increased synchrony associated with schizophrenia symptoms likely reflects process of functional segregation of sets of neurons that occurs in different cortical areas and causes segregation or increased information flow across specialized brain areas of the brain (Sporns et al., 2000, 2002).

Through this mechanism gamma activity occurs synchronously across brain regions and underlies the integration of diverse brain activities (Singer and Gray, 1995). Crucial result of these studies is a direct link between visual perception and gamma synchrony in the cat visual cortex reported by Eckhorn et al. (1988). Following this finding, functional significance of synchronous gamma activity in selective attention, perceptual processing and recognition was repeatedly demonstrated in animal and human studies (Meador et al., 2005; Rodriguez et al., 2004; Jensen et al., 2007). Together these data strongly suggest that complex cognitive functions are organized at a global level that enables to integrate primitive functions organized in localized brain regions (Bressler and Kelso, 2001; Bob, 2011). In this context, current predominant hypothesis relies on the assumption of the global mode of functioning that is based on large-scale information processing that requires mechanisms of functional integration of multiple disparate neural assemblies (Varela et al., 2001; Fries et al., 2001; Jensen et al., 2007).

Although the majority of research on feature binding has focused on synchronous gamma activity, there is evidence that synchronous activities in other frequency bands may also participate in functional integration of distributed neural activities into the coherent whole (Bressler et al., 1993; Lee et al., 2003a). Following these findings Dennett (1991) proposed "a multiple drafts" theory of consciousness model that does not define consciousness as a unitary process but rather a distributed one. Instead of a single central place i.e. "Cartesian theatre," there are various events of content-fixation that occur in various places at various times in the brain (Dennett, 1991, p. 365).

On the other hand there are possible limitations and controversial points whether neural synchrony mediates visual feature grouping or just represents its neural correlate that in principle does not explain the process of feature binding or "binding problem" (Palanca and DeAngelis, 2005; Bob, 2011; Ray and Maunsell, 2015; Bosman et al., 2014; Merker, 2013). Nevertheless the evidence for this view linking consciousness and gamma activity was reported by a whole series of experimental results in cognitive neuroscience and psychology (LaRock, 2006; Varela and Thompson, 2003; von der Malsburg, 1996, 1999; van der Velde and de Kamps, 2006; Zeki, 2003).

Recent findings indicate that these characteristic mental deficits related to conscious integration in schizophrenia are typically linked to abnormalities in brain development and neurocognitive deficits in information processing, verbal memory and executive functioning (Braff et al., 2007; Green et al., 2013; Hori et al., 2012; Light and Braff, 2005;

Toulopoulou et al., 2007). In this review, we propose that these cognitive deficits typical for schizophrenia may be related to specific deficits of information integration in the process of neural binding. Such deficits in neural binding may be linked to the disintegration of conscious experience and mental life as well as metacognitive disturbances in schizophrenia.

2. Disturbed neural synchrony and schizophrenia

In this context, accumulating evidence from electrophysiological, physiological and anatomical studies indicates that abnormalities in the synchronized electromagnetic field reflecting activities of neuronal assemblies may play a central role in the pathophysiology of schizophrenia (Bob, 2012; Uhlhaas and Singer, 2010; Uhlhaas et al., 2008; Woo et al., 2010). These studies show that schizophrenia involves abnormalities in brain oscillatory activity as measured by EEG synchrony. Specifically, there are abnormalities in gamma band activity of EEG electromagnetic spectrum and likely these abnormalities are related to cognitive deficits and other symptoms of schizophrenia (Bob et al., 2008, 2010; Lee et al., 2003a, 2010; Uhlhaas and Singer, 2010; Uhlhaas et al., 2006; Woo et al., 2010). For example, Uhlhaas et al. (2006) have found that increased phase synchrony correlates with the positive symptoms of delusions and hallucinations. Similarly, Lee et al. (2003b) in an auditory oddball paradigm experiment reported changes in frontal and left hemisphere gamma synchrony. They found that positive symptoms related to Reality Distortion are associated with increased right synchrony, Psychomotor Poverty is related to decreased left hemisphere synchrony and disorganization symptoms show a widespread enhancement with a delay in frontal Gamma synchrony (Lee et al., 2010). Other study examining relationship between disturbed long-range synchrony of gamma oscillations and clinical symptoms has been reported by Mulert et al. (2011), who found positive correlation between auditory hallucinations symptom scores and phase synchronization between the primary auditory cortices. Also another study documenting positive correlations between the phase synchronization of beta and gamma oscillations and hallucination symptoms in schizophrenia patients has been reported by (Spencer et al., 2004). These deficits in neural oscillations likely may represent the functional correlate of dysconnectivity in cortical networks underlying the associative splitting and characteristic fragmentations of mind and behavior.

In context of understanding schizophrenia as associative splitting and disturbed contextual awareness, Uhlhaas et al. (2006) found that deficits in Gestalt perception in schizophrenia patients are associated with reduced phase synchrony in the beta-band (20–30 Hz) but not in the gamma-band (40–70 Hz) suggesting that the coordination deficit of neural activities are related to specific cognitive dysfunctions associated with Gestalt and contextual associations.

Linking disturbances of integrative mental functions has been also reported in studies focused on deficits in self-monitoring. For example, Ford et al. (2008), who reported relationship between gamma synchrony and corollary discharges in schizophrenic patients. They found that gamma band neural synchrony that preceded pressing of the button was decreased in the patients, which is consistent with findings that deficits in self-monitoring and willed actions could result from a dysfunction of the corollary discharge system reflecting communication between the frontal and temporal lobes related to the breakdown of self-monitoring, self-agency self-awareness and insight (Feinberg, 1978; Fishman, 2008; Ford et al., 2001, 2007; Ford and Mathalon, 2005; Frith, 1987; Taylor, 2011; Friston and Frith, 1995). These deficits in schizophrenia are typically related to impaired information processing that may increase the modularity of brain functions (Ford et al., 2008) which may cause that for example, inner speech is misidentified as external voices (Ford et al., 2001, 2007; Poulet and Hedwig, 2007).

These disturbed interactions between brain structures produce patterns of temporal disorganization with decreased functional connectivity

that may underlie specific perceptual and cognitive states and cause disintegration of information across specialized brain areas of the brain in schizophrenic patients (Crossley et al., 2009; Kuhn and Gallinat, 2013; Parnau et al., 2013; Sporns et al., 2000, 2002; Uhlhaas and Singer, 2010). This disintegration of consciousness probably produces defective self-monitoring and self-experiencing (Feinberg, 1978; Ford and Mathalon, 2005; Ford et al., 2001) and this lack of information integration likely reflects the process of functional segregation of sets of neurons localized in different cortical areas and may represent an underlying mechanism of process of dissociation, disturbance of conscious experience and self leading to lack of contextual awareness, self-monitoring and insight (Bob and Mashour, 2011).

In this context, interesting data related to contextual awareness have been reported by Farina et al. (2014), who studied relationships between memories of attachment and EEG connectivity using coherence analysis. They found that after administration of the adult attachment interview in patients with dissociation these patients did not show increased EEG connectivity displayed by healthy controls. These data suggest specific disintegrative effect of retrieval of traumatic attachment memories and disturbed contextual awareness in dissociative patients. This result is in agreement with data reported by Lee et al. (2014), indicating that functional connectivity in resting state in patients with PTSD is decreased compared to controls and these levels of functional connectivity in the patients were significantly correlated with PTSD symptom severity. These data also suggest that decreased connectivity reflects contextual disturbances related to traumatic and stressful memories.

On the other hand, similar findings on EEG connectivity associated with contextual awareness were studied by Bowden et al. (2005) during an experience of insight. They found a sudden burst of high-frequency gamma-band in scalp EEG reflecting neural activity immediately before insight solutions. They concluded that solvers abruptly change the focus of their solving efforts just before insight, allowing information linking various problem elements to manifest into consciousness (Bowden et al., 2005). Characteristic changes in gamma oscillations during increased levels of awareness during the experience of insight reported also Sheth et al. (2009), who recorded multivariate electroencephalogram signals in healthy participants while they solved verbal puzzles. They found gamma band increased in right fronto-central and frontal electrode regions when the solution was correct, and when participants used successful (vs. unsuccessful) utilization of the external hint. They proposed that increased awareness and insight typically reflect transformative thoughts characterized by efficient recovery of information from memory and focused attention to a problem (Sheth et al., 2009). Some data also indicate, that for example artists as compared to non-artists also show significantly higher phase synchrony in EEG in the high frequency beta and gamma bands due to their ability of binding various details of the complex artworks to create internal representations (Bhattacharya and Petsche, 2002). Also other studies indicate that increased gamma oscillations are closely associated with contextual awareness, insight, emergence of new perspectives and creative solutions (Dietrich and Kanso, 2010; Jung-Beeman et al., 2004; Sandkuhler and Bhattacharya, 2008) and conscious awareness related to attentional focus in general (Baars, 2002; Tononi, 2004; Tononi and Edelman, 1998; Uhlhaas and Singer, 2010).

Taken together accumulating evidence from experimental and clinical studies shows that the process of dynamic binding and information integration that enable consciousness and awareness are related to transient and precise synchronization of neuronal activities which is significantly disturbed in schizophrenia (Lee et al., 2003a; Tononi and Edelman, 2000). These disturbed interactions produce patterns of temporal disorganization in neural synchronization which is related to decreased functional connectivity underlying specific perceptual and cognitive states, and cause disintegration of information across specialized brain areas in schizophrenic patients (Sporns et al., 2000, 2002; Bob and Mashour, 2011).

These disturbances in neural coordination may represent the functional correlate of dysconnectivity and binding deficits in cortical networks. These findings provide novel concepts which connect neuroscience descriptions with processes of conscious disintegration and phenomenological levels describing typical subjective experiences related to schizophrenia including perceptual anomalies, delusions and subjective experiences related to intentionality and meaning of life that as specific subjective qualities of individual experience cannot be reduced on description of brain processes (Hoffman et al., 2008; Mishara and Fusar-Poli, 2013; Uhlhaas and Mishara, 2007).

In this context, recent findings show crucially new concept how we can understand schizophrenia without reductionist viewpoints usually represented by a postulate that psychological processes including self-reference and conscious experience per se represent just epiphenomena of neurophysiological processes (Bob, 2015; Vahey and Whelan, 2015).

These current findings have intriguing and important implications for therapy that in the future may be focused on meaningful connections and relationships between mind and brain that via psychotherapeutic influences may enable to integrate brain functions.

3. Stress, trauma and mental disintegration

According to recent findings typical neurocognitive deficits in schizophrenia, mainly secondary verbal memory, immediate memory, executive functioning and vigilance are closely linked to dysfunctional behavior and impaired psychosocial functioning (Lin et al., 2011; Lipkovich et al., 2009). For example, attention and working memory are closely associated with social and functional competence and neurocognitive deficits have also been detected prior to onset of illness (Bowie et al., 2008; Carrión et al., 2011; Kurtz, 2011; Lin et al., 2011; Lipkovich et al., 2009). Such deficits may also influence how individuals with schizophrenia can learn new skills as well as accurately detect and respond to environmental demands (Corrigan and Green, 1993; Green, 1996).

In this context, Walker and Diforio (1997) suggest that trauma, stigma, poverty, isolation, and attachment patterns play a significant role in the development of the neurocognitive abnormalities of schizophrenia. They proposed “a neural diathesis-stress model” which integrates the psychosocial and biological research on stress in schizophrenia. The model is based on evidence that stress worsens symptoms and that the diathesis is associated with a heightened response to stressors. The authors indicate that one possible neural mechanism is the augmenting effect of the HPA axis on dopamine synthesis and receptors that in turn may lead to abnormal dopamine receptor functioning. In close relationship with the documented hippocampal damage in schizophrenia these abnormalities could significantly contribute to hypersensitivity to stress in schizophrenic patients.

In relation to this work, Read et al. (2001) developed “a traumagenic neurodevelopmental model”. The model is based on basic principles of the diathesis-stress model of schizophrenia and proposes that a genetic deficit creates a predisposing vulnerability in the form of oversensitivity to stress related to early aversive life events such as child abuse or parental neglect which, according to recent evidence may contribute to the development of schizophrenia (Bob and Mashour, 2011; Fan et al., 2008; Gil et al., 2009; Lysaker and LaRocco, 2009; Lysaker et al., 2007; Roy, 2005; Sar et al., 2010; Scheller-Gilkey et al., 2004; Vogel et al., 2009). For example, Lysaker and LaRocco (2008) studied the prevalence of significant traumas in schizophrenia patients and reported that two thirds of these chronic schizophrenia patients exhibited clinically significant trauma symptoms including intrusive experiences, defensive avoidance, dissociative experiences and other symptoms of mental disintegration. Also another recent study indicates that hallucinating schizophrenia patients had higher percentages of dissociative experiences in comparison to other schizophrenia patients (Perona-Garcelan et al., 2008).

Together these findings suggest that “mental disintegration” as a decreased ability to integrate cognitive and emotional information that enables to form integrated self in the sense of Bleuler’s concept of splitting may be an important aspect in the pathogenesis of schizophrenia. Recent findings indicate that psychological splitting in schizophrenia is likely specifically presented on a neural level as disrupted organization in neural communication that may complementarily reflect inter-related processes between mind and brain underlying disturbances of mental integration that likely present a neural representation of the splitting in schizophrenia (Bob and Mashour, 2011). As recent data suggest, splitting as a process of mental disintegration is also closely linked to deficits of the mind’s metacognitive abilities, which means disturbed ability to think about thinking and create connections between mental events and integrate them into larger complex representations (Bob and Mashour, 2011; Lysaker et al., 2013a).

As suggested by Moskowitz (2008), when Bleuler proposed disturbances of associations as the core feature of schizophrenia, he did not refer merely to confusion due to the intrusion of unrelated ideas and to the loss of fundamental ability of “associational synthesis” (p. 44) which reduced the understanding of oneself as an embodied agent to a set of fragments which no longer served as a guide for goal directed activity. Bleuler assumed that this lack of synthesis had an organic origin but could also serve as a proximate cause of dysfunction. Bleuler presented detailed accounts of schizophrenia patients who are not able to function socially or vocationally and due to the loss of the ability to synthesize associations into larger images of oneself and others which then results in metacognitive dysfunction.

4. Conscious awareness and metacognition

Conscious experience of the self and others requires reflection of what is happening in the moment within one’s own body and in the world around which is called metacognition (Dimaggio and Lysaker, 2015). Metacognition as a psychological process represents a spectrum of mental activities that involves thinking about thinking, ranging from more discrete acts in which people recognize specific thoughts and feelings to more synthetic acts in which context of intentions, thoughts, feelings, and connections between events, are integrated into larger complex representations (Dimaggio et al., 2009; Lysaker et al., 2013c; Dimaggio and Lysaker, 2015).

Metacognition describes a range of mental activities ranging from discrete to synthetic. (Pinkham et al., 2013; Lysaker et al., 2013c). Synthetic forms of metacognition act in a different manner than do specific beliefs or singular judgments that also affect life. Synthesized understandings lend meaning to events, and thus, supply reasons why to carry out a certain act and to decide what is best done to resolve dilemmas given the unique psychology of oneself and the others in one’s life (Dimaggio et al., 2009; Lysaker et al., 2013c; Dimaggio and Lysaker, 2015).

Metacognition is related to the construct of mentalizing and both are characterized by an ability to think about oneself and others, though the latter considers disruptions of these processes happen in the context of disturbed attachment (Dimaggio and Lysaker, 2015). Both discrete and synthetic metacognitive activities allow persons to form evolving and flexible representations for themselves and others and thus are a cornerstone of the ability to regulate affect and behavior (Dimaggio et al., 2009; Lysaker et al., 2013c).

Deficits have been found in abilities to detect very specific mental activities such as behaviors, emotions and memories (Bacon et al., 2011; Fournier et al., 2002; van ’t Wout et al., 2007). Looking at larger psychological phenomena persons with schizophrenia experience trait like deficits in metacognition in both earlier and later forms of illness (Lysaker et al., 2012; Vohs et al., 2014). They may, for instance, experience stable difficulties considering thoughts as subjective in nature, recognizing the complex internal states of others, understanding how events can be seen from different perspectives, and using metacognitive

knowledge to manage distress. Multiple studies have linked metacognitive deficits with negative symptoms (Hamm et al., 2012; Lysaker et al., 2005; McLeod et al., 2014; Nicolò et al., 2012; Rabin et al., 2014) as well as intrinsic motivation (Tas et al., 2012; Vohs and Lysaker, 2014). Metacognition has also been linked with functional competence (Lysaker et al., 2011c), subjective sense of recovery (Kukla et al., 2013), stigma resistance (Nabors et al., 2014), therapeutic alliance (Davis et al., 2011), vocational function (Lysaker et al., 2010a) and interpersonal relationships (Lysaker et al., 2010b, 2011b).

5. Metacognition, brain connectivity and plasticity

In addition, current findings show that metacognition as an ability to create a “cognitive wholeness” through various association pathways, as already suggested by Bleuler, on neural level likely corresponds to the ability of the brain to integrate information mainly linked to EEG synchrony in gamma band and other frequencies of which neurobiological substratum is unknown (Bob, 2011; Lee et al., 2003a; Peled, 1999; Tononi and Edelman, 2000). From this point of view recent research suggests that brain disintegration corresponds to psychological disintegration (Crick, 1994; Baars, 2002; Bob, 2015). In this context, building metacognitive abilities through specific forms of learning during psychotherapy likely also influences the brain integrative processes. These findings indicate that learning and memory processes including a wide variety of environmental factors may influence development of synaptic connections through new gene expression and that psychotherapy as a special learning process may specifically influence and modify brain functions, metabolism in specific brain structures and also genetic processes (Gabbard, 2000, 2007; Kandel, 1998, 1999).

In this sense, according to recent findings there is evidence that consciousness may integrate brain functions (Baars, 2002; Kanwisher, 2001; Varela et al., 2001) and might be a gateway to brain integration that enables access between otherwise separated neuronal functions (Baars, 2002). In addition, current empirical data suggest that various metacognitive practices related to meditation techniques with many culturally different forms likely have very similar neurophysiological correlates that could be related to increased brain synchrony and integration (Fell et al., 2010; Travis and Shear, 2010). Other recent data also suggest that meditation, similarly like hypnosis functions through attentional mechanisms that may influence brain processing of incoming sensory stimuli and regulate underlying brain dynamics, such as an interplay between cortical and subcortical structures and hemispheric interactions (Bob, 2008; Crawford, 1994; Edmonston and Moscovitz, 1990; Rainville et al., 2002; Tang et al., 2007; Travis and Shear, 2010).

This influence of consciousness on brain integration may significantly change during various states of consciousness, in hypnosis (Baars, 2002), or during specific experiences such as psychotherapy or meditation (Fell et al., 2010; Travis and Shear, 2010). In this context, recent data indicate that meditation may significantly increase conscious awareness and focus attentional functions characterized by increased beta and gamma activity, reflecting increased brain synchrony and integration (Fell et al., 2010; Tang et al., 2007; Travis and Shear, 2010), and also may influence brain plasticity and morphology as for example gray matter or white matter density (Hölzel et al., 2011; Jang et al., 2011). Typical and intriguing examples how metacognitive abilities may influence brain structures show data about “metacognitive” meditation technique “mindfulness” (Chiesa and Serretti, 2010; Davidson et al., 2003; Hölzel et al., 2007; Ives-Deliperi et al., 2011; Sheridan, 2003). Using this meditation technique direct intriguing influences on cortical thickness and other brain structural changes have been reported (Grant et al., 2013; Hölzel et al., 2011; Lazar et al., 2005; Luders et al., 2012; Tang et al., 2010, 2012; Fox et al., 2014). As recent meta-analysis indicates (Fox et al., 2014) numerous studies have found that the gray and white matter may be shaped by meditation. This research shows that at least eight brain regions may be significantly altered by meditation, mainly regions of frontopolar cortex (Brodmann area 10) related to

meta-awareness and also exteroceptive and interoceptive body awareness related to sensory cortices and insula and may influence memory consolidation and reconsolidation related hippocampal activities and morphology. Other findings show that meditation may influence emotional and self-regulatory processes mainly related to structures of anterior and mid cingulate and orbitofrontal cortex, and also intra- and interhemispheric communication via superior longitudinal fasciculus and corpus callosum.

Taken together these data are in agreement with recent evidence indicating that neural correlates of various mental states related to perception, cognitive functions, and memory are based on various levels of information connectivity and integration (Baars, 2002; Kanwisher, 2001; Varela et al., 2001). In this context, the influence of consciousness on neural integration likely explains the brain changes during various states of dissociated consciousness, in hypnosis (Baars, 2002; Bob, 2003; Li and Spiegel, 1992; Nelson and Bower, 1990; Rainville et al., 2002), or during meditation (Fell et al., 2010; Travis and Shear, 2010).

These changes may occur as a consequence of changes in attentional functions that, according to several data in the case of meditation, are characterized by increased beta and gamma activities reflecting increased brain synchrony (Fell et al., 2010; Moss, 2002; Tang et al., 2007; Travis and Shear, 2010; Travis et al., 2004; Stuckey et al., 2005). Based on these findings metacognition, as a most prominent aspect of meditation increasing self-reflective attentional functions, most likely may be described as a highly integrated state of consciousness (Jankowski and Holas, 2014) related to high neuronal connectivity and integration (Fell et al., 2010; Travis and Shear, 2010). This increased connectivity may appear on various levels of neural functions and allows dynamically connected information processing that most likely have a crucial role in integrative processes related to meditation and psychotherapy.

6. Conclusion

In this close relationship between brain functions and metacognition, it is likely that it may have clinical implications that are important to consider. If indeed brain neurocognitive functions through various levels of neural binding interact with metacognition, then in therapeutic interventions persons need to learn how to function in various metacognitive frameworks. In this context, recent development of integrative forms of psychotherapy shows novel perspectives how in practice of psychotherapy it is possible to help to form more complex and integrated representations of the self and use this knowledge to respond to psychological problems (Hasson-Ohayon, 2012; Lysaker et al., 2011a, 2013b; Salvatore et al., 2012).

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