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Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Neural signs and mechanisms of consciousness: Is there a potential convergence of theories of consciousness in sight?

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ARTICLE INFO

Keywords:

Consciousness
Theories
Unified theory
Temporo-spatial dynamic
Spontaneous activity

ABSTRACT

Various theories for the neural basis of consciousness have been proposed, suggesting a diversity of neural signs and mechanisms. We ask to what extent this diversity is real, or whether many theories share the same basic ideas with a potential for convergence towards a more unified theory of the neural basis of consciousness. For that purpose, we review and compare the various neural signs, measures, and mechanisms proposed in the different theories. We demonstrate that different theories focus on neural signs and measures of distinct aspects of neural activity including stimulus-related, prestimulus, and resting state activity as well as on distinct features of consciousness. Therefore, the various mechanisms proposed in the different theories may, in part, complement each other. Together, we provide insight into the shared basis and convergences (and, in part, discrepancies) of the different theories of consciousness. We conclude that the different theories concern distinct aspects of both neural activity and consciousness which, as we suppose, may be integrated and nested within the brain's overall temporo-spatial dynamics.

1. Introduction

1.1. Neuroscience of consciousness - quest for a unifying framework with a unified theory

Consciousness is a core feature of our mental life. Various highly promising neuroscientific theories have been proposed to explain the neural substrates of consciousness. While marking major progress in the neuroscience of consciousness in the last 20 years, this has also led to a considerable controversy and divergence about which neuronal measures and what kind of underlying mechanisms can account for consciousness (Boly et al., 2017; Koch et al., 2016; Storm et al., 2017). This has recently prompted the need to decide which theory is 'right' and which ones are 'wrong' (Reardon, 2019).

Alternative to such dichotomous approach of 'right' and 'wrong' theories, one may also search for a unifying framework that reconciles the different seemingly contradictory theories on a deeper level. Following other disciplines like physics and biology, we here pursue

such approach of reconciliation. Specifically, we aim to provide a first step towards the development of such deeper unifying framework that carries the potential to integrate and reconcile the different theories including the potential for the development of a unified theory of consciousness.

However, the development of such unifying framework with a unified theory of consciousness is hindered by a rather dazzling diversity in the current field of the neuroscience of consciousness. Among others, such diversity concerns different theories, explananda, experimental paradigms, and the kinds or levels of neural activity. Let us briefly illustrate this diversity (Table 1).

1.2. Diversity I – different theories and their explananda

While being well aware about the arbitrariness of any selection, some of the most prominent and widely discussed neuroscientific theories of consciousness include Recurrent Processing Theory (RPT) (Lamme, 2006) (Lamme, 2010), Synchrony Theory (ST) (Engel and

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Table 1
Overview of the different measures, features, and mechanisms of consciousness in different theories.

	Temporo-spatial Theory of Consciousness (TTC)	Embodied theory (ET)	Predictive Coding Theory (PCT)	Integrated Information Theory (IIT)	Synchrony Theory (ST)	Recurrent Processing Theory (RPT)	Global Neuronal Workspace Theory (GNWT)	Higher-Order Thought Theory (HOT)
Main Explanandum	Phenomenal and subjective features of consciousness: Form, level/state, and content of consciousness	Emotion & Self-Consciousness Content and State of consciousness	Content of consciousness in perception and cognition	Phenomenal Consciousness, Content of consciousness	Phenomenal Consciousness, Content of consciousness	Phenomenal Consciousness, Content of consciousness	Access Consciousness: Content and State of consciousness	Phenomenal and access Consciousness; Content of consciousness
Main Techniques to Measure Neural Activity	fMRI, EEG, MEG, ECoG, Computational modelling	EEG, fMRI, Brain-Body (e.g. heart rate), Synchrony, Pupil Size	EEG, MEG, fMRI, Computational modelling	EEG, ECoG, MEG, fMRI, TMS-EEG Computational modelling	Animal physiology, EEG, MEG	Animal physiology, EEG, fMRI	fMRI, EEG, MEG, ECoG, Computational modelling	Psychophysics, fMRI
Primary Subjects	Humans, Healthy, neurologic, and psychiatric subjects	Human	Human	Human, Neurological Patients	Rat, Cat, Monkey, Human	Monkey, Human	Human, Neurological Patients	Human
Major Modality	All sensory modalities and all domains (cognitive, affective, etc.)	Emotion, Vision	All sensory modalities and the various forms of cognition	All sensory modalities with a strong focus on the visual modality	Vision	Vision	Vision, Audition, Language	Vision
Fields/Disciplines of Origin and ideas	Neuroscience, Physics of dynamic systems, Psychiatry, Philosophy	Affective/Emotional and Visceral Neuroscience	Computational and Cognitive Science	Theoretical Neuroscience, Physics, Mathematics	Neuroscience	Visual Neuroscience	Cognitive Psychology, Language	Philosophy, Cognitive Neuroscience
Major Paradigms to Manipulate Consciousness	Spatiotemporal manipulation of sensory and cognitive tasks, Psychiatric Disorders, Disorders of Consciousness	Manipulation of the spontaneous fluctuations of Visceral States in relation to cognitive/emotional tasks	Prediction paradigms with the measurement of empirical prior and prediction error	Transcranial magnetic stimulation, Anesthesia, Sleep, Disorders of Consciousness	Anesthesia, Binocular Rivalry, Pharmacological	Masking, Rivalry, Anesthesia, Change Blindness, Inattentional Blindness, TMS, Pharma	Masking, Attentional Blink, Inattentional Blindness, TMS	Masking & others combined with Metacognition Reality Monitoring
Type of Activity	Spontaneous activity, Resting state, Pre- and Post-Stimulus activity and their Interaction	Pre-Stimulus, Post-Stimulus, State	Pre- to Post-Stimulus Interaction	Post-Stimulus, State	Post-Stimulus, Pre-Stimulus	Post-Stimulus (Pre-Stimulus)	Post-Stimulus	Post-Stimulus
Neural Signatures of Consciousness	Measures of Temporo-spatial dynamics: PLE, LZC, ACW, Entropy, SD, TTV, Entrainment with phase coherence	Heartbeat evoked potential, Intertrial phase coherence, other neuro-visceral measures	Neural correlates of prediction error	Phi, PCI, LZC	Neural Synchrony	Contextual Modulation, Feedback, VAN	Late EEG, MEG (P3b), WSMI, Decoding, others, Dorsolateral prefrontal cortex	Dorsolateral prefrontal cortex
Timing of Consciousness	Over long time scales extending from milliseconds to minutes and even hours, relationship of faster and slower frequencies	Temporal scales of brain-body modulation over milliseconds to minutes	Timing of anticipation and stimulus	Early after stimulus onset within 100-300ms	Early after stimulus onset within 100-200ms	Early (~200 ms in humans)	Late (>300 ms in humans)	
Mechanism of Consciousness	Temporo-spatial dynamics and its mechanisms; Integration of pre- and post-stimulus activity	Brain-Body Coupling: neural monitoring of visceral functions	Predictive Coding, Error Minimization	Integration of information	Assembly Formation, Binding and grouping	Recurrent processing	Global Ignition, Access	Higher Order Thought, Representation Reality Monitoring
Associated Cognitive Functions	No particular cognitive as specific for consciousness	Emotion and self, interoceptive awareness	Attention, Task Relevance, Perceptual Organization	No specific cognitive function	Perceptual Binding and Grouping	Perceptual Organization	Attention, Working Memory	Metacognition
Neural 'Locus' of Consciousness	Global-to-local brain activity and its temporo-spatial alignment to body and environment	Brain-Body coupling	Top-down modulation with neuro-anatomical hierarchy of predictive error minimization	Occipito-Parietal Cortex	Sensory Cortex, Thalamo-Cortical connection	Visual (sensory) Cortex	Prefrontal Cortex	Prefrontal Cortex

The Table shows different theories of consciousness (upper row) and how they determines different neuronal and phenomenal features of consciousness (most left column). The different colours indicate the main focus of the respective theories on different forms of neural activity including spontaneous activity (yellow), prestimulus (orange), early (red), and late stimulus-related activity (pink). Since spontaneous activity is still present as background activity and thereby shapes early and late stimulus-related activity, its colour is extended throughout.

Singer, 2001) (Llinás et al., 1998), Integrated Information Theory (IIT) (Tononi et al., 2016), Global Neuronal Workspace Theory (GNWT) (Dehaene et al., 2011; Mashour et al., 2020) (Naccache, 2018), Temporo-spatial Theory of Consciousness (TTC) (Northoff and Huang, 2017; Northoff, 2013, 2014, 2018), Predictive Coding Theory (PCT) (Hohwy, 2013), Higher-Order Thought theory (HOT) (Brown et al., 2019), Operational Space-time theory (OST) (Fingelkurts et al., 2010), Entropy theory of consciousness (Carhart-Harris, 2018a,b, Carhart-Harris et al. 2014), social-perceptual attention theory of consciousness (Graziano and Kastner, 2011), and Embodied Theory (ET) (Park and Tallon-Baudry, 2014). Several other theories (including primarily non-neuronal theories like quantum theories) have been suggested but are not discussed here as that would be beyond the scope of this paper. To more or lesser extent, one can say that roughly each of these theories claims to explain consciousness in a different way.

Diversity is also manifest in the fact that different theories target distinct explananda on the side of consciousness. For instance, phenomenal features such as the ‘experience of content’, e.g., the ‘what it is like’ (Nagel, 1974) or phenomenal (P-) consciousness (Block, 2005) are the explanandum in RPT, IIT, ST, and TTC, while theories like GNWT and HOT seem to target more cognitive aspects like the ‘awareness of content’, or access (A-) consciousness, linked to functions like top-down attention (see Nani et al., 2019; Graziano and Kastner, 2011), working memory, access or meta-cognition (Cleeremans et al., 2020). Yet other theories are somewhat less specific about what aspect of consciousness is targeted, or focus more on general mechanisms of perception, such as PCT, or on the coupling of perceptual states with action, the body (Seth et al., 2011), emotions (Damasio, 1999), or the self (Metzinger, 2009). Since they focus on different aspects of consciousness as their explanandum, the different theories of consciousness may not necessarily be incompatible with each other.

1.3. Diversity II – different techniques, activities, subjects, and paradigms

Proposed neural correlates of consciousness are investigated by different techniques like single cell recordings or other invasive techniques, mostly performed in animals, or imaging techniques such as fMRI, EEG, MEG, or intracranial recordings mostly in humans. In addition, neural activity can be manipulated by lesions, cooling, pharmacological interventions (anesthesia and others), TMS, TDCS or even genetic manipulation. These different techniques create sets of rather diverse data. We focus on the systemic molar level of neural activity featured by regions and networks. In contrast, we neglect the cellular level of consciousness as it would be beyond our scope (Sanchez-Vives et al., 2017, Sanchez-Vives et al., 2020, Goldman et al., 2019).

One also needs to consider whether the focus is more on stimulus-related/task-evoked activity or, alternatively, on resting state (Raichle et al., 2001) or spontaneous activity. Yet another important issue concerns the subjects. Consciousness and its potentially underlying mechanisms and measures can be investigated in both human or non-human subjects, the latter raising questions about the presence of consciousness in these animals. Moreover, one also needs to consider whether studies are conducted in healthy subjects or in pathological groups. Most prominent in the field are studies of neuropsychological disorders like blindsight or neglect, but psychiatric disorders like schizophrenia or depression may also provide an entrance point to study consciousness, especially its organisation and structure (Northoff, 2013, 2015)

Even more diversity comes with the different experimental paradigms that are used to test the different theories. For instance, the focus on the more cognitive features of consciousness like access or awareness requires report paradigms while phenomenal features are probably better investigated using no-report paradigms (Tsuchiya et al., 2015).

Moreover, paradigms like masking or rivalry naturally focus on manipulating more perceptual aspects of consciousness while more cognitive paradigms like the attentional blink or change blindness target functions like visual attention and memory (Kim and Blake, 2005). Yet others emphasize that affect and emotion provide the main experimental paradigm for studying consciousness (Damasio, 2010, 1999; Panksepp, 1998; Solms, 2019). Whether the distinct experimental paradigms target similar features of consciousness (like qualia or other phenomenal features) or distinct aspects (like phenomenal vs cognitive vs affective features) remains unclear at this point.

1.4. Diversity III – stimulus-related, pre-stimulus, and spontaneous activity

The diversity is further amplified by the focus on different forms of neural activity. Many theories take stimulus-related activity and its various measures (see below) as the neural correlate of consciousness. Yet other theories, such as TTC and PCT, focus more on pre-stimulus activity or even resting state activity (TTC) as they may strongly impact stimulus-related activity and its association with consciousness. Finally, given that consciousness is already present even in the resting state regardless of stimulation, spontaneous activity, and how this interacts with incoming information, should be taken into account

To find convergence in this wide range of theories, explananda, neural signals and associated mechanisms will not be easy. We group our overview along the lines of stimulus-related (first part), pre-stimulus (second part), and spontaneous activity (third part), trying to find commonalities in neural signals and relationships between proposed mechanisms. In the final part of our paper, we will discuss whether convergence between the different neural measures and their respective theories is possible, and if so, where and how. The main point of our paper is to demonstrate that the different neuroscientific theories of consciousness target distinct aspects of neural activity, i.e., spontaneous, prestimulus, or stimulus-related activity, and subsequently rely on different neuronal measures targeting distinct aspect of consciousness. This is demonstrated in Table 1 that provides a roadmap for the whole paper by showing an overview focusing on the main theories discussed here while several others, i.e., related ones, will be discussed in the text (but are not listed in the table) (see Table 1).

2. First part: Stimulus-related activity – neural signs and mechanisms

We first consider all activation that is evoked after the presentation of a stimulus. It is generally assumed that some aspect of this activity must reflect the neural mechanisms that generate the conscious percept of the shown stimulus: the Neural Correlate of Consciousness or NCC. Stimulus-related or task-evoked activity is usually characterized in spatial and temporal terms; spatially, it may be elicited in specific regions while temporally it may occur in early and later time intervals. We will consider both aspects separately.

2.1. Stimulus-related activity: posterior vs frontal signals

Different theories assume different regions as crucial for consciousness, i.e., prefrontal vs posterior regions (Boly et al., 2017; Odegaard et al., 2017; Overgaard, 2018; Storm et al., 2017), primary sensory regions (Hurme et al., 2017), or the whole brain (Huang et al., 2016a,b; Zhang et al., 2018). Which regions are deemed relevant is, in part, dependent on the explanandum (Fig. 1).

a ‘Posterior’ theories: IIT and RPT

Especially the proponents of RPT, as well as those of IIT claim that posterior regions in the brain, such as sensory cortex itself (Lamme, 2006) or occipito-temporo-parietal or otherwise posterior ‘hot zones’ (Boly et al., 2017) (Koch et al., 2016) are by themselves sufficient to

mediate the phenomenal or experiential features of consciousness, not only during awake, but also in dream states (Boly et al., 2017; Hurme et al., 2017; Förster et al., 2020; Koivisto and Revonsuo, 2010; Storm et al., 2017). No involvement of anterior regions as those in prefrontal cortex is required as these may be more related to subsequent cognitive processing of the contents rather than the experience of the contents, e.g., consciousness itself (but see (Knotts et al., 2018; Naccache, 2018; Odegaard et al., 2017) for different views).

RPT has been developed mainly to explain some empirical observations on the transition from unconscious to conscious vision (Lamme, 2000). In experiments where visibility of stimuli was manipulated with techniques such as masking or TMS, it was noted that feedforward activation of the visual hierarchy (information spreading from V1 to V2, V4, IT etc) was not sufficient for conscious experience, while recurrent processing (signals going in the reverse direction, e.g. from IT to V1) are necessary (Fahrenfort et al., 2007; Lamme et al., 1998a, 2001; Ro, 2010; Wokke et al., 2013). Other key findings were the absence of recurrent signals in anesthesia (Lamme et al., 1998b), or other instances of spontaneous lapses of conscious vision (Lamme et al., 2000).

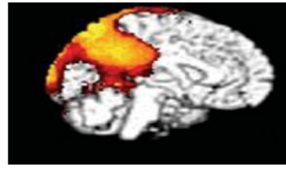
The key mechanism supported by recurrent processing is that of perceptual organization or the ‘binding’ of features (color, shape, motion, faceness, etc) in distant parts of the visual field (each neuron having a restricted receptive field) (Lamme, 1995; Zipser et al., 1996). In this sense, RPT is very similar to ST, the latter being more specific about the way in which perceptual grouping or binding is achieved, namely by synchronous coupling of the spike train activity of the neurons involved, primarily in the gamma range frequency (Engel et al., 2001; Engel and Singer, 2001). According to RPT (and somewhat less explicitly in ST), all perceptual organization required for conscious vision is achieved by visual cortex, frontal cortex having only modulatory influence, if any at all. Perceptual organization and binding are considered sufficient for conscious experience, as they explain the key feature of conscious percepts; their unity or ‘wholeness’.

IIT even takes this ‘unity’ as axiomatic (amongst other aspects of conscious experience), and from that builds the notion that the key explanandum of consciousness is ‘integrated information’ (Tononi, 2008; Tononi et al., 2016). An intuitive example that is often given is that in a photo camera, all pixels on the CCD chip independently register the light at each location in the visual scene. Cutting the chip in two halves would not give different information than is present on the chip as a whole. Hence the information is not ‘integrated’ and not conscious (Tononi, 2012). In the brain, however, cutting –say– the visual cortex in half would induce large changes in the type and amount of information that is present (given all lateral connections), because there, information is integrated.

The amount of integrated information can be calculated (in theory), resulting in a measure called ‘Phi’, that scales both with the amount of information in the system and the extent of integration. IIT predicts low levels of Phi in brain parts such as the cerebellum (where information content is high, but connectivity does not support a high level of integration), or in states such as epilepsy (where integration is high, but the overly strong synchrony between neurons renders them useless to convey unique information) (Tononi, 2012).

Higher degrees of Phi are supposed to reflect higher levels of integration and consequently higher likelihood of the respective object becoming phenomenally conscious. The visual cortex, and the combination of visual, other sensory and parietal cortices in particular (the so called ‘posterior hot zone’) are considered prone to possess high Phi, and hence should suffice to generate a conscious sensory experience without any involvement of prefrontal regions (Boly et al., 2017; Koch et al., 2016) (although their inclusion does result in even higher levels of Phi).

b ‘Frontal’ theories: GNWT and HOT

GNWT: Prefrontal cortex**IIT: Posterior cortex**

Consciousness

Fig. 1. Stimulus-induced activity and its spatial neural correlates of consciousness.

The figure shows the presumed localization of consciousness in theories focusing on stimulus-induced activity.

Upper left is the dorsolateral prefrontal cortex that is favored by the Global Neuronal Workspace Theory (GNWT) and the Higher-order Thought theory (HOT).

Upper right is the posterior cortex that is presumed to be the localization of consciousness in Integrated Information Theory (IIT) and Recurrent Processing Theory (RPT).

The GNWT, in contrast, postulates that the dorsolateral prefrontal cortex (DLPFC) takes on a central role in mediating the contents of consciousness, or at least conscious “access” to the contents. The DLPFC is a core region of the Global Neuronal Workspace, together with other regions like inferior parietal cortex, mid-temporal cortex, precuneus, and anterior cingulate (as well as the respective thalamo-cortical connections; Aru et al., 2019, Sanchez-Vives et al., 2020) (Dehaene et al., 2017, 2014; Dehaene and Changeux, 2011; Dehaene, 2014).

The global workspace is the region where sensory information is made globally ‘accessible’ to other cognitive functions, such as working memory, cognitive manipulation, decision processing, language (as in N400) or report. Only when such access occurs, sensory content is elevated to conscious perception (Naccache, 2018). A key role is also played by attention as one of the mechanisms that puts sensory information into the global workspace. The frontoparietal network is known to play a major role in top-down attention as well as working memory. This is the basis for the assumption by the advocates of posterior theories that the frontal cortex is in charge of higher-order cognitive functions as in intelligent computing which have to be distinguished from consciousness in terms of phenomenal experience though (Koch 2019).

In HOT, it is postulated that sensory information itself is a ‘first order’ representation, not sufficient to give rise to conscious experience. A ‘second order’ re-representation or ‘higher order thought’ is required to elevate first order representations to consciousness. Different versions of HOT exist, each proposing different mechanisms for generating the higher order thought.

Key differences between these versions are whether the first order sensory content is either re-represented as a ‘thought’ or in another format, or whether there is any re-representation at all. In the latter case, a mechanism like perceptual reality monitoring ‘pointing’ to the first order representation may suffice (Brown et al., 2019). Either way, in most versions of HOT, the mechanisms that do the ‘elevation’ from first order to conscious representation typically are thought to reside in prefrontal cortex (if any localization of these mechanisms is given at all). Although not identical, related to higher order thought is the function of metacognition (Lau and Rosenthal, 2011). In metacognitive tasks, subjects are asked how certain they were of a perceptual decision. Finally, it shall be mentioned that, in addition to prefrontal and posterior regions, thalamo-cortical connections and subcortical regions have also been considered key to consciousness. Having been considered early on as central for integration (Edelman and Tononi, 2000; Tononi and Edelman, 1998), thalamo-cortical connections are considered key to integrating the two central dimensions of consciousness, namely state and content (Aru et al., 2019, Sanchez-Vives et al., 2020, Northoff, 2017). That is further supported by demonstrating that deep

brain stimulation in thalamus induced partial reversal in a subject suffering from unresponsive wakefulness state (UWS) (Schiff et al., 2007).

Concerning even more subcortical regions, recent studies in both humans and monkeys demonstrated that neural activity in the subcortical acetylcholinergic nucleus basalis Meynert, strongly mediates global brain activity on the cortical level and the associated level of arousal (Liu et al., 2018; Turchi et al. 2018; see also Tanabe et al., 2020 as well as Parvizi and Damasio, 2003). The findings suggest that the state or level of consciousness may be closely related to subcortical activity (nucleus basalis Meynert, thalamus) while the content may be decided on the cortical level (Bachmann and Hudetz, 2014). Albeit preliminary, these findings suggest that consciousness featured by both content and state/level (Aru et al., 2019) arises from subcortical-cortical interaction whose exact mechanisms remain yet unclear.

2.2. Stimulus-related activity: early vs late signals

a feedforward vs recurrent processing of visual input

When a visual stimulus is presented, information about that stimulus speeds through the brain at an amazing pace. Within 150–200 milliseconds almost all parts of the brain are activated by this stimulus in a ‘feedforward sweep’ of information processing where all parts of the visual brain extract a wide range of features from the image, ranging from simple ones like shape, color or motion to more complex ones like whether a face is present or not (Lamme and Roelfsema, 2000). But also higher, more cognitive areas extract information like whether a response has to be given or withheld or what the relevance of the stimulus is for certain tasks (van Gaal et al., 2012). Even divergent theories like RPT and GNWT more or less agree that such early stimulus-related activity, as measured for instance by the N100 is not related to consciousness. The feedforward sweep is generally accepted to be an unconscious process (Crick and Koch, 2003; Dehaene et al., 2006; Lamme, 2006).

Following the feedforward sweep, horizontal connections between cells with distant receptive fields, and feedback connections between higher and lower level areas enable what is called ‘recurrent’ or ‘re-entrant’ processing (Lamme et al., 1998a). In monkeys, the temporal sequence of events has been recorded in quite some detail. For an oriented texture defined square, the earliest responses in V1 can be recorded at 40 ms, in V4 at 52 ms. The edge of the figure is detected by inhibitory interactions between neighbouring cells via horizontal connections at 60 ms in V1, 67 ms in V4.

Then, feedback connections from V4 to V1 generate a modulation of V1 activity at 95 ms that is reflecting the figure-ground organization of

the scene. Finally, the task relevance of the stimulus is reflected in a further increase of the response at 159 ms in V4, and 204 ms in V1. So while feedforward (V1 to V4) activation extract basic features (orientation) and their mutual inhibition, while feedback (V4 to V1) signals reflect perceptual organization and attention or task relevance (Poort et al., 2012) (Lamme et al., 1999).

In humans these latencies are longer, but the order of events is similar. Following early ERP components like the N100, signals related to perceptual organization are recorded at latencies ranging between 150–200 ms like N2 being related to attention (Lamme, 2010). ERP components that signal attention like N2, task relevance, access or report like P3 are typically in the 200–300 ms range. While the early signals are typically localized in occipital regions, the later P300 or P3b components tend to originate from more central or frontal regions.

An alternative explanation for these delayed signals would incur subcortical pathways, that reach higher level areas before the feedforward sweep does. These would then in turn retrogradely activate earlier areas. Such subcortical connections have been shown to provide input to parietal, temporal and frontal cortex. Some of these may be sufficiently fast to ‘catch up’ with the feedforward sweep. Various specific inputs from subcortical to cortical regions need to be considered.

Input from the superior colliculus and pulvinar towards parietal cortex, such as motion areas MT and MST, is able to sustain direction selective responses even without input from V1 (Azzopardi et al., 2003). Pulvinar input to the posterior parietal cortex plays an important role in guiding hand movements (Mayer et al., 2019). The frontal eye field is known to have extremely short visual response latencies (Pouget et al., 2005), most likely mediated by subcortical pathways. Other subcortical inputs come from regions like the brainstem, basal forebrain, pons, or locus coeruleus, providing more widespread cholinergic (Ballinger et al., 2016) or noradrenergic (Samuels and Szabadi, 2008) input, that are important for a variety of cognitive functions such as arousal, memory, attention and more. The latencies of such projections are not precisely known. Either way, the notion of recurrent interactions is likely to be more complex than just involving cortical interactions; at some point in time both cortical and subcortical information will get integrated in a brain-wide mesh of recurrent interaction.

b Early versus late recurrent signals: RPT vs GNWT

At what time point during post-stimulus activity consciousness starts may again depend upon the explanandum. RPT, seeing perceptual organization as central to consciousness, identifies a time point around 100–200 ms, (earlier in monkey than human brains) as the neural onset of conscious perception. This is very similar to what others have coined the ‘visual awareness negativity’ (VAN), and attention-related signals like N2 that also peak at around 200 ms (if not earlier) (Eklund and Wiens, 2018; Koivisto and Revonsuo, 2010; Förster et al., 2020). This is the moment where recurrent or feedback processing sets in and starts to mediate perceptual organization. GNWT, with its focus on access rather than phenomenal consciousness points at the later activity (P300 and, more specifically the P3b) as being the key signature of ‘global ignition’, the becoming available of sensory information for other parts of the brains, and hence consciousness (Dehaene and Changeux, 2011; Sergent et al., 2005).

2.3. Stimulus-related activity beyond amplitude: from synchrony to complexity

a Synchrony theories: ST, TTC

Aside from stimulus induced activity having a particular spatial and temporal distribution, it may also have other characteristics that may be relevant to consciousness. A long-held idea is that the extent to which activity between different (sets of) neurons is synchronous or not is of particular value (Engel et al., 2001; Singer, 2001, 1998). Predating

any talk of consciousness is the hypothesis that synchronous neural activity is the ‘label’ by which neurons encode that they belong to an ‘assembly’ or group of neurons representing the different features of a single object (Singer, 1999). This ‘synchrony = perceptual binding’ hypothesis was supported by numerous experiments, but also refuted by other ones (Lamme and Spekreijse, 1998; see also Ray and Maunsell, 2010; Hermes et al., 2015; Pitts et al., 2014). Given the negative findings, synchrony may well account for perceptual binding but not necessarily for consciousness as it may occur in an unconscious way (Ray and Maunsell, 2010; Hermes et al., 2015; Pitts et al., 2014)

Much focus is on the role of high frequency synchrony, as reflected in gamma band oscillations in EEG or local field potentials, but other frequencies play various roles as well (Buzsáki and Draguhn, 2004). Some put particular emphasis on oscillations that are mediated by thalamocortical loops (Llinás et al., 1998). Indeed, gamma band synchrony is strongly suppressed during anesthesia (Alkire et al., 2008). Also, it was found that conscious recognition of Moony scenes is reflected in gamma band synchrony (Engel et al., 2001), and that dichoptic masking has a strong effect on oscillations in the gamma, beta and alpha ranges (Fahrenfort et al., 2012).

Taken in a more extended way beyond specific frequencies like gamma, binding and synchronization of neuronal activity across different time scales and regions also figure prominently in other theories like operational space-time theory (OST) (Fingelkurts et al., 2010) and the temporo-spatial theory of consciousness (TTC) (Northoff et al., 2019; Northoff and Huang, 2017). These theories clearly share similarities with theories like RPT and IIT, in that they too see a key role for processes like perceptual binding and organization, or for the integration of information in consciousness by emphasizing their dynamic temporo-spatial underpinnings.

b Complexity theories: IIT

A somewhat related aspect of stimulus induced activity is the ‘complexity’ of the signal that is evoked and the information it contains. One such measure of information is the ‘perturbational complexity index’ (PCI), that has been applied in various TMS-EEG studies probing the impact of a magnetic pulse delivered to the cortex on neuronal activity (D’Andola et al., 2018; Casali et al., 2013a). PCI aims to measure the degree to which TMS pulses induce a spatiotemporally complex response, measured by a Lempel Zev Complexity (LZC) analysis of the evoked activation.

LZC measures the number of units that are needed to explain a time series of signals. If a high number of units is needed the LZC is high, indicating irregularity and thus a more complex signal; if, in contrast, the number of units is low, the LZC will be low, reflecting regularity and thus a less complex signal.

Following IIT, low values in PCI are supposed to index the loss of either integration or differentiation of neuronal activity which is suggested to be the core feature of consciousness by IIT. PCI has been shown to almost linearly scale with the level of arousal and consciousness in a wide range of states ranging from deep sleep to vegetative state, minimally conscious state or locked in syndrome, and during sedation and anesthesia (with various drugs like midazolam, xenon, and propofol) (Bodart et al., 2018, 2017; D’Andola et al., 2018; Casali et al., 2013a; Massimini et al., 2007, 2005). These results support the core role of integrated information in consciousness, as proposed by IIT.

c Trial-to-trial variability: TTV

Beyond its amplitude and complexity, a third aspect of stimulus induced activation is the extent to which this activation is stable and reproducible or not. Trial-to-trial variability (TTV) is a way to measure this. When TTV is reduced after stimulus onset (‘TTV quenching’ (Churchland et al., 2010)), variability in the amplitude of responses to

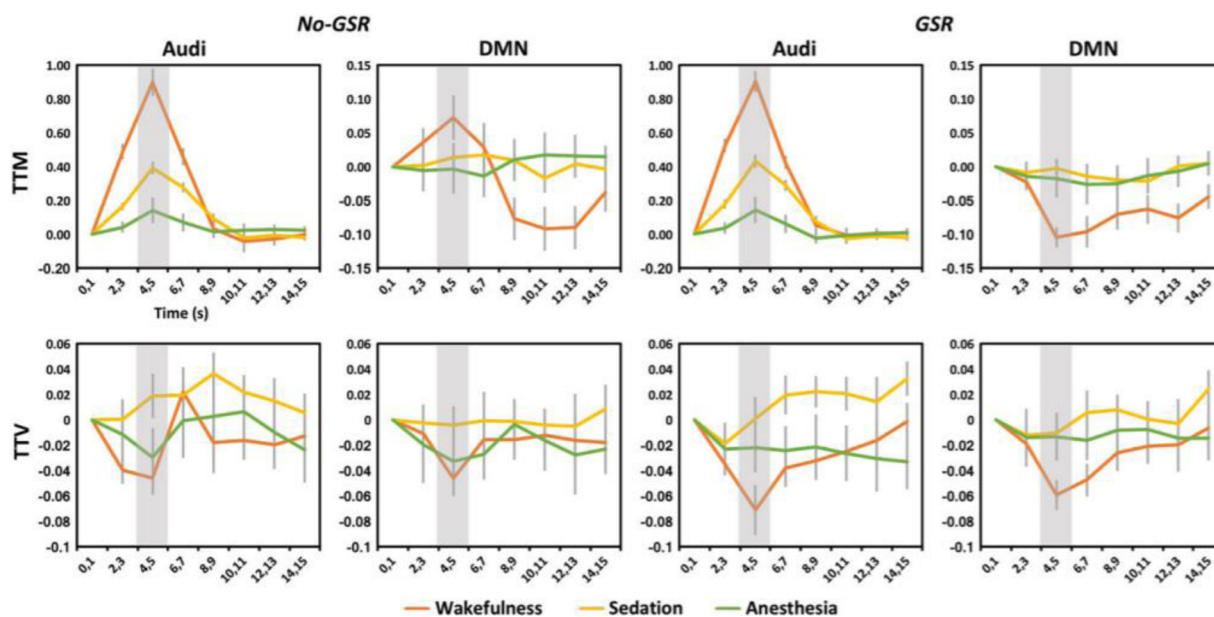


Fig. 2a. Amplitude and trial-to-trial variability of stimulus-induced activity during the presence (wakefulness) and partial (sedation) and total (anesthesia) absence of consciousness (Huang et al., 2018).

The figure shows fMRI-based the trial-to-trial magnitude (TTM) (upper row) and trial-to-trial variability (TTV) (lower row) in auditory cortex (audi) and default-mode network (DMN) during wakefulness, sedation, and anesthesia. Task consisted in auditory presentation of self- and non-self-related stimuli (own name vs other name). TTM and TTV are calculated without global signal regression (No GSR; left) and with global signal regression (GSR; right).

The figure shows increases in TTM in especially auditory cortex in wakefulness while less increase or no increase is observed in sedation and anesthesia. The TTV is decreased in both regions during wakefulness in especially GSR whereas TTV no longer decreases or even increases during sedation and anesthesia. Together, these data show that TTM and TTV differ from each other during different states and in different regions.

one and the same stimuli is reduced, indicating that the brain responds in a more similar and thus stable way to these stimuli than when TTV is high (Schurger et al., 2015). Recent studies associate TTV with consciousness in both EEG/MEG and fMRI: the more TTV is reduced across different trials, the more likely the respective content will be conscious (Arazi et al., 2017; Baria et al., 2017; Huang et al., 2018; Wolff et al., 2019) (Fig. 2a).

TTV quenching may signal the suppression of noise, or of the ongoing dynamic that is carried over from the pre-stimulus period to post-stimulus activity (Huang et al., 2018; Wolff et al., 2019). The observation of stronger TTV quenching in conscious versus unconscious contents suggests that such suppression of the brain's intrinsic noise by the external stimulus is central for associating the latter's contents with consciousness, which is one of the key tenets of TTC (see below). One of the mechanisms of TTV quenching may be that a conscious stimulus evokes more synchronous or recurrent activation, that stabilizes the neural signals.

3. Second part: Pre-stimulus activity – neural signs and mechanisms

3.1. Pre-stimulus activity determines content and arousal

Various studies describe the impact of pre-stimulus activity levels on the contents and the level or state, i.e., arousal of consciousness in both fMRI, EEG/MEG or single unit activity. Concerning the contents, fMRI studies showed that if the level of pre-stimulus activity in the fusiform face area (FFA) is high, subjects will perceive the stimulus as face whereas low pre-stimulus activity in FFA will bias subjects towards perceiving the same stimulus as vase (Hesselmann et al., 2008; Sadaghiani et al., 2010).

The pre-stimulus power and phase synchrony of alpha oscillations (8–13 Hz) in the EEG strongly impacts whether one perceives a visual stimulus or not (Benwell et al., 2017; Dijk et al., 2008; Romei et al., 2010; Wolff et al., 2019). Other frequencies in the pre-stimulus period

like slow cortical potentials (0.1–1 Hz) and delta, theta, and beta power, but also pre-stimulus functional connectivity impact subsequent stimulus-related activity and its association with consciousness (Baria et al., 2017; Benwell et al., 2017; Podvalny et al., 2019; Sadaghiani et al., 2015, 2010).

Single cell recordings in monkeys showed that the level and amount of synchrony of spontaneous V1 activity determined whether subsequent stimulus processing would engage recurrent processing, and hence conscious perception and report of the stimulus (Super et al., 2003). Also, a high degree of synchronization in the pre-stimulus state is associated with higher degrees of post-stimulus desynchronization, which enhances awareness of the respective stimulus or content (van der Togt et al., 2006). Together, these data suggest that consciousness is not only dependent upon the stimulus-related activity itself but also on the pre-stimulus level of activity. This effect seems to arise primarily by how the latter (pre-stimulus activity) shapes the former (stimulus induced activity).

In addition to predicting specific contents of consciousness, another role for pre-stimulus activity may be that it reflects the level of arousal, i.e., conscious state (Laureys, 2005; Northoff, 2013). It has been argued that pure processing of the content is by itself not sufficient for consciousness, one also requires a certain level or arousal to be associated with that content (Bachmann and Hudetz, 2014; Northoff and Huang, 2017; Aru et al., 2019). In that case, one would expect that pre-stimulus activity serves a dual role, that is, mediating both content and its associated level or arousal. A recent MEG study tested such dual role, indeed demonstrating that pre-stimulus activity reflected both category-specific content of consciousness (as pre-stimulus activity levels predicted the subsequent contents) and a more general process related to arousal (as indexed by pupil size) (Podvalny et al., 2019).

3.2. Pre- to post-stimulus interaction and trial-to-trial variability (TTV)

The traditional way of conceiving pre-stimulus – stimulus interaction is in terms of a purely additive interaction where the activity

elicited by the stimulus is simply superimposed upon the ongoing pre-stimulus activity level (Fox et al., 2006; Arieli et al., 1996). However, recent data using both fMRI (He, 2013; Huang et al., 2017) and EEG/MEG (Baria et al., 2017; Wolff et al., 2019) show that the pre-stimulus activity level impacts subsequent stimulus-related activity in a non-linear way as pre-stimulus activity shape post-stimulus activity level (ERP) and trial-to-trial variability (TTV), in different ways.

High degrees of pre-stimulus variance (Arazi et al., 2017; Huang et al., 2018; Schurger et al., 2015), strong slow frequencies (Baria et al., 2017), or high synchronization (Super et al., 2003; van der Togt et al., 2006) make it possible for the stimulus to induce larger changes, such as variance suppression with TTV reduction, shifts to faster frequencies, or desynchronization during the post-stimulus interval, which all make consciousness of the stimulus more likely. If, in contrast, pre-stimulus dynamics exhibits low variance, stronger faster frequencies, and low synchronization, the external stimulus can no longer induce much change which decreases the chance of consciousness.

Accordingly, it is the degree of change during post-stimulus activity relative to the intrinsic ongoing dynamics of the pre-stimulus interval, as measured by the TTV, which seems to be central for associating consciousness to external stimuli. Taken in such sense, consciousness can neither be associated exclusively with either post-stimulus activity or pre-stimulus activity. Instead, pre- and post-stimulus activity must interact in a certain way, with supposedly strong TTV quenching, i.e. stimulus-related suppression of the ongoing pre-stimulus variability, to associate consciousness to contents.

3.3. A theory based on pre- and post-stimulus interaction: TTC

These findings on the importance of pre-stimulus activity for consciousness are one of the starting points for the Temporo-Spatial Theory of Consciousness (TTC) (Northoff, 2013; Northoff et al., 2019; Northoff and Huang, 2017) to look beyond stimulus-related activity. Specifically, the TTC focuses on how the impact of the external stimulus on the brain during stimulus-related activity depends upon the brain's pre-stimulus variability (Huang et al., 2018; Wolff et al., 2019).

This can be compared to the situation of a surfer riding on the ocean's waves. The ocean's waves can be characterized by power, high or low, speed/frequency, i.e., slow or fast, and their phase angles, i.e., sharp or smooth. The surfer staying afloat (conscious, in this metaphor) depends both on the activity of the surfer (stimulus-related activity), as on the waves of the ocean (pre-stimulus or ongoing activity). Specifically, the surfer (= stimulus-related activity) needs to adapt and integrate her/himself to the power, the speed/frequency, and the phase angle of the waves. Only if the two interact in a meaningful way, the surfer becomes 'part of the waves' and stays erect.

In the same way, an external stimulus has to interact with ongoing activity such that the two get integrated into the current stream of consciousness. The external stimulus needs to be integrated within the power, the frequency/speed, and the phase angles of the ongoing spontaneous activity as measured in the pre-stimulus period. If the external stimulus is not integrated at all, it will not become conscious. This may occur, for instance, when a specific external stimulus "arrives" at the "wrong" point in time, like low power, too slow speed, and low excitable phase angle (like the peak rather than the trough; Huang et al., 2017) – the external stimulus may be processed but remains unconscious ('reception without perception'; Hudetz et al., 2015).

Yet another scenario is that there are no waves in the spontaneous activity at all anymore in which case any external stimulus independent of its timing may remain unconscious as due to lack of temporo-spatial dynamic. A final scenario would be that the waves of the spontaneous activity may still be there but organized and structured in an abnormal way with changes in power, speed/frequency, and/or phase angles – that leads to abnormal form or organization of consciousness as in psychiatric disorders (Northoff, 2013, 2015, 2018) (Fig. 2b).

The TTC highlights the central role of the pre-stimulus activity's

spatiotemporal dynamic (as well as that of spontaneous activity, see below) for the neural processing of stimuli including their association with consciousness. In the same way as ocean waves give a boost and acceleration to the surfer, the pre-stimulus activity's waves can expand the stimulus beyond itself (Buzsáki and Draguhn, 2004), that is, to points in time and space beyond the ones at which it actually occurs, i.e., "going beyond" (Buzsáki 2006).

The TTC takes such "going beyond" in a literal way when speaking of 'temporo-spatial expansion': the more the pre-stimulus waves can expand the stimulus' actual points in time and space of the outer world beyond themselves, the more likely the stimulus and its contents will expand in time and space in a virtual way, i.e., longer duration and more extension, and the more likely the respective content will become conscious. Unlike in the GNWT, such expansion is not primarily cognitive, as by accessing cognitive function related to the global neuronal workspace. Instead, the stimulus' virtual expansion is primarily dynamic as driven by how the temporo-spatial dynamic of the brain's spontaneous activity, i.e., pre-stimulus, relates to the stimulus including its own temporo-spatial dynamic.

4. Third part: Spontaneous activity – neural signs and mechanisms

4.1. Spatiotemporal dynamics – how can we measure it?

The brain's spontaneous activity exhibits an elaborate temporal and spatial structure mainly on the cortical level which, in part, is driven by the subcortical level of thalamo-cortical connection (Aru et al., 2019, Sanchez-Vives 2020). Ultimately one would assume that cortical and subcortical levels form one coherent structure with different temporal and spatial scales nesting within each other, i.e., temporo-spatial nestedness. However, due to the lack of integrated subcortical-cortical data (see Wang et al., 2019 for an exception), we here focus mainly on the cortical organisation of the spontaneous activity.

Spatially, the spontaneous activity is reflected in various networks organized in a small-world way (Bullmore and Sporns, 2009; Raichle, 2015). The spontaneous activity's temporal dynamics shows an oscillatory pattern, ranging from ultrafast frequencies (40–180 Hz) to infraslow ones (0.01–0.1 Hz) (Buzsáki and Draguhn, 2004). The power in these frequency ranges is strongest in the slowest and weakest in the faster frequencies. The relationship of these frequencies, not just their absolute power, is central for consciousness to occur, as it will be highlighted in this and especially the next section.

The spontaneous activity's spatiotemporal structure is not static but dynamic as it constantly changes its configurations showing strong synchrony as emphasized in the operational space-time theory of consciousness (OST) (Fingelkurts et al., 2010). Hudetz et al. (Hudetz et al., 2015) therefore speak of a 'dynamic repertoire' that describes the range or number of different configurations the spontaneous activity's spatiotemporal structure can take on. The relation between different frequencies of neuronal activity can be described as being scale-free or scale-invariant due to the fact that the relationship between the power of the frequencies is the same regardless of what range of frequencies one looks at (Chialvo, 2010; He, 2013; Hiltunen et al., 2014; Huang et al., 2016a,b; Linkenkaer-Hansen et al., 2001). This scale invariance or self-similarity can be measured in the frequency domain and expressed by

$$P \propto 1/f^\beta$$

P stands for power, which is proportional to the inverse of the frequency (f) raised to the power β (He, 2014). Here β is referred to as the power-law exponent (PLE), which indicates the degree of self-similarity. A value of 0 for this parameter would indicate no structure being present, as in a white-noise signal while any higher value is possible only by the presence of some structure in the time course of the signal, as in pink noise. Scale-free activity in the time domain, that is, the scale-free fluctuations of oscillations, can be measured by detrended

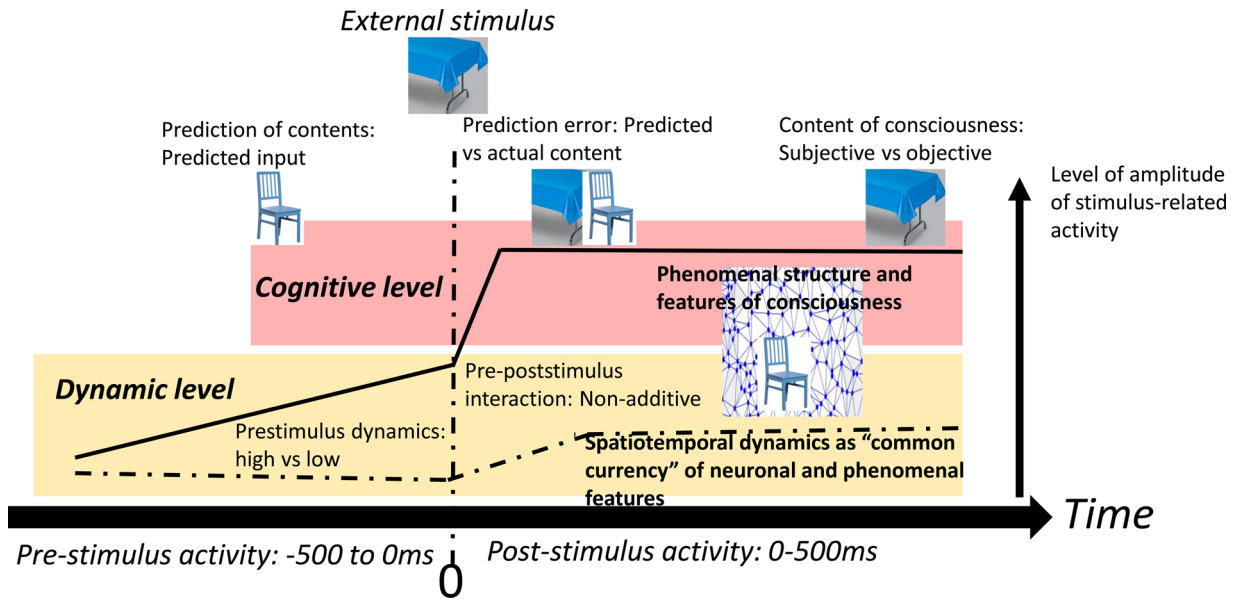


Fig. 2b. Pre-poststimulus interaction – Dynamic (lower level) and cognitive (upper level) characterization. The figure shows two levels of the interaction of prestimulus and post-stimulus activity.

Upper level: The cognitive level operates more at the surface and can be characterized by prediction of specific contents (like a chair) in the prestimulus period (upper left). That predicted content is compared with the actual content (a table in our example) resulting in the prediction error. The prediction error, in turn, determines the content of consciousness, i.e., its subjective (chair) or objective (table) nature (upper right).

Lower level: The dynamic level operates on a deeper level and shaped by the continuously ongoing activity as manifest in prestimulus activity. The continuous and the dotted line stand for two different levels of prestimulus activity dynamics, high and low. Prestimulus activity is determined by its spatiotemporal dynamics which interacts in a non-additive (rather than additive) way with the external stimulus. The spatiotemporal dynamics provides a certain structure, a spatiotemporal structure, that is manifest in the structure and organisation of phenomenal consciousness within which the content (chair) is integrated and embedded. The spatiotemporal structure provides the shared feature or “common currency” (Northoff et al., 2019) of neuronal and phenomenal features.

Lowest level: The arrow depicts the time, prestimulus period is about –500 to 0 ms while the post-stimulus is about 0–500 ms.

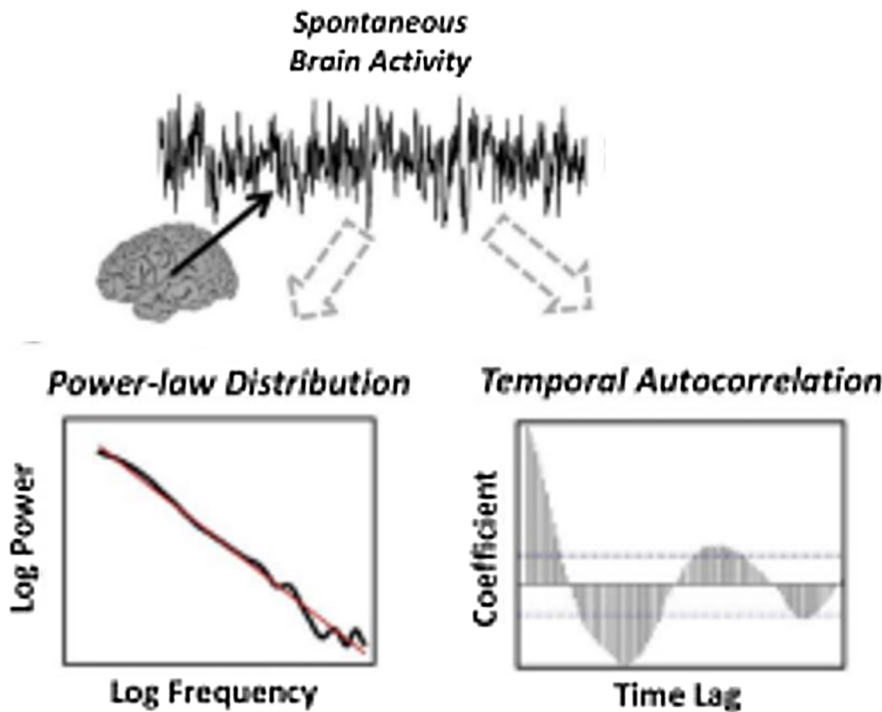


Fig. 3a. Spontaneous activity (upper) and its scale-free nature (lower left) and temporal autocorrelation (lower right).

The figure shows a power spectrum (upper part) and its scale-free nature (lower left) and autocorrelation structure (lower right).

The upper part shows raw data with an processed signal. That signal is further processed in terms of its power spectrum which then can be plotted on a graph (lower left) with frequency range on the x-axis and power on the y-axis with both being in presented in logarithmic way (log). We see the typical power law distribution with strong power in slower frequencies and weaker power in faster frequencies. On the lower right, one can see the temporal autocorrelation with the time lag on the x-axis and the degree of correlation on the y-axis (see Huang et al., 2016a).

fluctuation analysis (DFA) (Linkenkaer-Hansen et al., 2001). Both PLE and DFA have been associated with distinct facets of consciousness like multisensory perception (Ferri et al., 2019), learning of chemistry formulae (Bongers et al., 2019), meditation (Irrmischer et al., 2018), and self (Kolvoort et al., 2020; Huang et al., 2016a,b, Wolff et al., 2019).

Moreover, we will see that both reduced and extended levels of consciousness go along with opposite changes in scale-free activity (PLE, DFA) (Fig. 3a).

Yet another measure is entropy, such as Shannon entropy, which describes the degree of order or disorder in a time series: the more

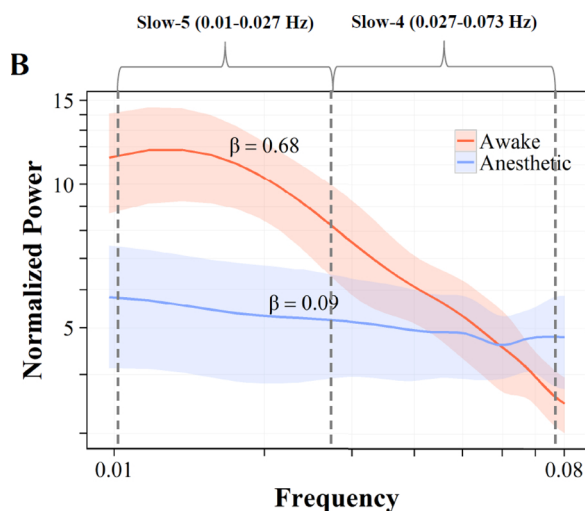


Fig. 3b. Loss of scale-freeness of spontaneous activity in anesthesia. The figure shows a power spectrum from fMRI resting state data in awake state (red line) and anesthetic state (blue line) (Zhang et al., 2018). X-axis = frequency, Y-axis = Normalized power. The data show the complete loss of the scale-free shape of the power spectrum in the anesthetic state which is due to the complete loss of the strong power in the slow frequencies. Instead of being steep following a power-law distribution, the power spectrum is completely flat and no longer follows a power-law distribution, i.e., it is no longer scale-free (see Zhang et al., 2018).

uniform the probability distribution of the time series, the higher the degree of entropy and thus the larger the spatiotemporal repertoire (Bravi et al., 2011). If, in contrast, the probability of one particular value is much higher than the others, one will measure low entropy – the spontaneous activity exhibits then a high degree of order with a rather limited spatiotemporal repertoire. Higher degrees of entropy may lead to extended consciousness as it is suggested in the entropy theory of consciousness (Carhart-Harris et al., 2014; Carhart-Harris, 2018a,b).

Finally, another measure of the spontaneous activity's spatiotemporal repertoire is complexity. Roughly, complexity, as indexed by Lempel-Zev complexity (LZC), describes the number of unique patterns in the time series: the higher the number of unique patterns one requires to account for the whole time series, the higher the LZC, and thus the higher the complexity with a larger spatiotemporal repertoire (Bravi et al., 2011; Wolff et al., 2019). The LZC is at the core of what is calculated as PCI as index of consciousness in the IIT; the PCI is the normalized version of the LZC applied to the EEG changes evoked by TMS (D'Andola et al., 2018; Casali et al., 2013a). These various measures have been probed mainly in states where consciousness is either lost (as in sleep, anesthesia, or coma) or expanded (drug-induced); the results will be described in the next section.

4.2. Spatiotemporal dynamics in reduced and extended consciousness

Various resting state studies mainly investigated the static and more recently dynamic functional connectivity between different regions as well as within and between networks (like default-mode network, visual and auditory networks, somatosensory-motor network, executive control network, dorsal and ventral attention network, salience network) (Demertzi et al., 2019; Huang et al., 2018, 2020; Qin et al., 2015; Owen, 2019). However, despite extensive insights, there are no functional connectivity patterns and neural networks that are specific for consciousness. For instance, the default-mode network (DMN) is more or less preserved during unconscious states (Fransson, 2006; Raichle, 2015). These findings raise the need for alternative measures (see above) of the spontaneous activity's spatiotemporal dynamics during altered states of consciousness.

The most recent studies by Demertzi et al. (2019) and Huang et al. (2020) observed changing network patterns like between default-mode network and dorsal attention network (DAT) to be highly predictive of the level of consciousness. Moreover, as Demertzi et al. (2019) demonstrate, we can observe transitory 'unconscious spatial patterns' in conscious healthy subjects (but less often than in unconscious subjects) while 'conscious spatial patterns' also occur in anesthetic, unresponsive wakefulness, and sleep states (but less often than in fully awake states). The difference between presence and absence of consciousness comes ultimately down to relative (rather than absolute) differences in spatial dynamics, that is, frequency of particular spatial patterns.

Going beyond spatial dynamics and its decrease during the loss of consciousness, measures of temporal dynamics also suggest reduced dynamics during the absence of consciousness. For instance, entropy and complexity of the brain's spontaneous activity are reduced in states where the contents of consciousness become sparse (Bodart et al., 2017; Casali et al., 2013b; Lewis et al., 2012; Rosanova et al., 2012)). If the contents and consciousness are lost completely, entropy and complexity (LZC or its perturbational variant PCI (D'Andola et al., 2018; Casali et al., 2013a)) of the spontaneous activity break down (Barttfeld et al., 2015; Bodart et al., 2017; Chennu et al., 2014; Gosseries et al., 2011; Hudetz et al., 2015; Sarasso et al., 2015; Sitt et al., 2014; Tagliazucchi and Laufs, 2014).

Loss of consciousness also goes along with reduced dynamics, i.e., decreased range in the power spectrum as measured by scale-free activity. During early sleep stages (N1 and N2), sedation, and loss of consciousness (anesthesia, N3 sleep), power in the faster frequencies is reduced while power in the slow frequencies (0.01 to 0.1 Hz) is preserved or abnormally increased as demonstrated in both fMRI and EEG/MEG (Fingelkurts et al., 2012; Lewis et al., 2012; Sitt et al., 2014). Reflecting the relative power increase in slower frequencies, studies reported increased PLE (or increased DFA) during sleep (N1, N2, and N3 stages), sedation, MCS, and mild non-surgical anesthesia (Huang et al., 2018; Meisel et al., 2017; Tagliazucchi and Laufs, 2014; Zhang et al., 2018) (Fig. 3b).

Interestingly, investigations in drug-induced psychosis demonstrated opposite findings in the various dynamic measures, that is, increased (rather than decreased) degrees of entropy and/or complexity in the spontaneous activity during the usage of different psychedelic drugs like ketamine, LSD, psilocybin, and 'ayahuasca' (Atasoy et al., 2017; Schartner et al., 2017; Tagliazucchi and Laufs, 2014; Viol et al., 2017). Importantly, the degree of entropy correlates with the intensity of psychedelic experience: the higher the degree of entropy, i.e., disorder, the more intense the psychedelic experience, characterized by an increased number and 'richness' of contents (Atasoy et al., 2017; Carhart-Harris, 2018; Schartner et al., 2017).

In addition to entropy and complexity, recent studies (fMRI and E/MEG) on drug-induced psychosis (using ketamine, psilocybin, LSD, and/or 'ayahuasca') also demonstrated increased power in the faster frequencies (Atasoy et al., 2017; Carhart-Harris et al., 2016; Carhart-Harris, 2018; Schartner et al., 2017; Viol et al., 2017). In contrast, power in the slower frequencies was preserved in these states. The relative power balance was thus shifted toward the faster frequencies, which results in a lower PLE.

Interestingly, sleep deprivation shares a commonality of increased arousal with drug-induced psychosis, which, behaviorally, manifests as increased vigilance and sensitivity to stimuli. Similar to drug-induced states, sleep deprived subjects also show lower PLE values (on EEG) (Meisel et al., 2017). Together, these studies suggest that the increased power in the faster frequencies is a neural correlate of the behavioral state itself, i.e. extended consciousness, rather than being related to the underlying cause, i.e. drug or sleep deprivation.

Finally, another interesting clinical condition is epilepsy. One can experience abnormal contents in medial temporal epilepsy and/or experience clouding of consciousness with reduced or complete loss of state/level (Blumenfeld, 2011; Lambert and Bartolomei, 2020). All that

happens in the brain's spontaneous activity, where abnormal spatio-temporal dynamics from subcortical over posterior to anterior cortical regions has been observed during seizure progression (Blumenfeld, 2011; Foley et al., 2014; Lambert and Bartolomei, 2020). Hence, epilepsy can be conceived an interesting test case for how the spontaneous activity can yield or, more correctly, lose its own conscious content (as presumably based on one's own internally-oriented cognition as distinguished from externally-oriented cognition) while, at the same time, mediating the level/state of consciousness (see also Aru et al., 2019 and Northoff, 2017 for linking state/level and content of consciousness).

4.3. Brain-heart dynamics - embodied approaches

In addition to its spatiotemporal dynamic, the brain's spontaneous activity can also be characterized by the continuous interoceptive input from the own body (see also (Seth and Tsakiris, 2018)). The interoceptive processing and thus the body is the focus of those who claim that embodiment (Noe, 2004) including the brain-body relation are crucial for consciousness (Azzalini et al., 2019; Park et al., 2018; Park and Blanke, 2019; Park and Tallon-Baudry, 2014; Tallon-Baudry et al., 2018). They observe that neuro-cardiac measures like the heartbeat evoked potential (HEP) and inter-trial coherence (ITC), that signal the synchronization of neural activity with the cardiac input, are related to different forms of consciousness.

Specifically, the degrees of HEP and ITC in visual cortex are related to conscious visual perception (Park et al., 2018; Tallon-Baudry et al., 2018). While the degrees of the same measures in ventromedial prefrontal cortex, insula, and somatosensory cortex correlates with the subjectively measured extents of emotional awareness (see also (Critchley and Garfinkel, 2017)) and bodily awareness (Azzalini et al., 2019; Park and Blanke, 2019). Neuro-cardiac coupling, i.e., HEP and ITC, in ventromedial prefrontal cortex is related to self-consciousness; the stronger the HEP and ITC, the higher the degrees of self-consciousness (Babo-Rebelo et al., 2016a).

In addition to cortical regions, subcortical regions may also be central here in. fMRI studies focusing on functional connectivity in relation to heart beat variability identified a subcortical network including various mid brain and brain stem regions – that was described as “central autonomous network” (CAN) (Rabellino et al., 2017; Thome et al., 2017). Hence, the impact of the heart and, more generally, the interoceptive (and proprioceptive) input streams from the body to the brain (and ultimately consciousness) may, in part, be mediated by subcortical regions in brain stem, midbrain, and thalamus (see also Aru et al., 2019).

Together, these data strongly suggest that the subcortical-cortical brain-body connection is central for consciousness. It should be noted, however, that the embodied approaches rely experimentally mostly on paradigms (and scales) that allow comparing first- and third-person perspective (rather than conscious vs unconscious). These theories therefore are more about the potential neural correlates that yield the first person perspective – which may in turn be the core of consciousness to which phenomenal experience is added (Park and Tallon-Baudry, 2014; Seth et al., 2011).

5. Fourth part: Convergence between the different measures and their theories

We summarize our findings in Table 1. Note that this table can hardly do justice to the full complexity of the different theories, their proposed mechanisms, associated neural signals or bodies of work. It is primarily intended as a shorthand overview. We now turn to the question to what extent the different theories and their associated measures of neural signals converge towards a commonly held view or belief on what the neural origin of conscious experience (or the conscious state) may be. We clearly see such convergence, in all stages – stimulus induced, pre-stimulus, and ongoing activity.

6. From brain to consciousness – architecture and neuroanatomy

a From independent, isolated, and segregated to inter-dependent, distributed, and integrated neural activity

Theories like RPT, GNWT, IIT, ST, TTC, and PCT all agree on that a feedforward pass through the brain may enable fairly intelligent visually (or other sensory) guided behavior, up to the execution of high level cognitive functions (van Gaal et al., 2012). However, it is generally assumed that this ‘feedforward sweep’ is unconscious (Crick and Koch, 2003) (Lamme, 2018), primarily because the cortical modules do not share information other than in a feedforward, reflex-arc-like fashion (Lamme, 2010). Hence, the agreement consists in that consciousness requires an operational architecture that goes beyond simple feedforward loops.

There is disagreement though what exactly such operational architecture consists in and the nature of the required interaction. The proposals range from a global neuronal workspace architecture (GNWT) over an integrated architecture (IIT), predictive hierarchies (PCT), operational space-time (OST) (Fingelkurts and Fingelkurts 2010), and recurrent processing architecture (RPT) to temporo-spatial nestedness (TTC). Future imaging and probably modelling studies are required to decide which of these or, alternatively, some other form of operational architecture is necessary to provide the predisposition or capacity for consciousness (Northoff, 2013, 2014a and b).

One core proposal shared by RPT and others is that these kinds of interactions are made possible by the recurrent processing architecture of the cerebral cortex (fueled eventually by subcortical-cortical bottom-up modulation as from brain stem, mid brain, and thalamus; Aru et al. 2019): such recurrent organisation is constituted by horizontal connections with a cortical area, and feedback connections from higher level areas back to lower ones.

Independent of its exact nature, there is somewhat agreement on the role of such operational architecture. RPT, GNWT, IIT, ST, TTC, OST, and PCT either explicitly or implicitly agree that key to understanding consciousness is the transition from independent, i.e., segregated and isolated, to mutually interdependent, i.e., integrated and distributed, neural activity (which may eventually span across both cortical and subcortical regions). Integrated distributed activity is supposed to lead to stable, synchronous and integrated subcortical-cortical assemblies, integrated cores, or stable attractors which, following the TTC, reflects the dynamic and henceforth temporo-spatial basis of consciousness.

Most interestingly, various of the neuronal measures mentioned above in the different theories do, to some extent, reflect such integrated, distributed and ultimately dynamic temporo-spatial processing including feedback modulation: VAN, synchrony, late and sustained ERP components, TTV, complexity measures (PCI, LZC), and scale-free activity with nestedness. Despite their differences, all these measures gauge the extent to which neurons share their information with other neurons/regions' information: such ‘sharing’ is described in terms of integration (IIT), cognitive access (GNWT), prediction (PCT), or temporo-spatial dynamics (TTC)

Taken together, we can see convergence between the different theories of consciousness towards a more inter-dependent, integrated, and distributed neural basis of consciousness. While that may look evident if not almost trivial nowadays, we have to consider it in the perspective of time. 50 years ago, consciousness was basically not present in neuroscience as it was conceived a subject of philosophy (rather than science). 30 years ago consciousness started to enter neuroscience where, initially, it was still considered a matter of (feedforward) convergence of low level towards high level processing, towards some ‘pinnacle’ of processing where consciousness would reside (Toates, 2006) as it, to some extent, re-surfaces in the HOT with its assumption of some specialized function called ‘higher-order thought’ (Brown et al., 2019; Lau and Rosenthal, 2011). (Fig. 4a).

The last 20–30 years of research undermined this assumption by

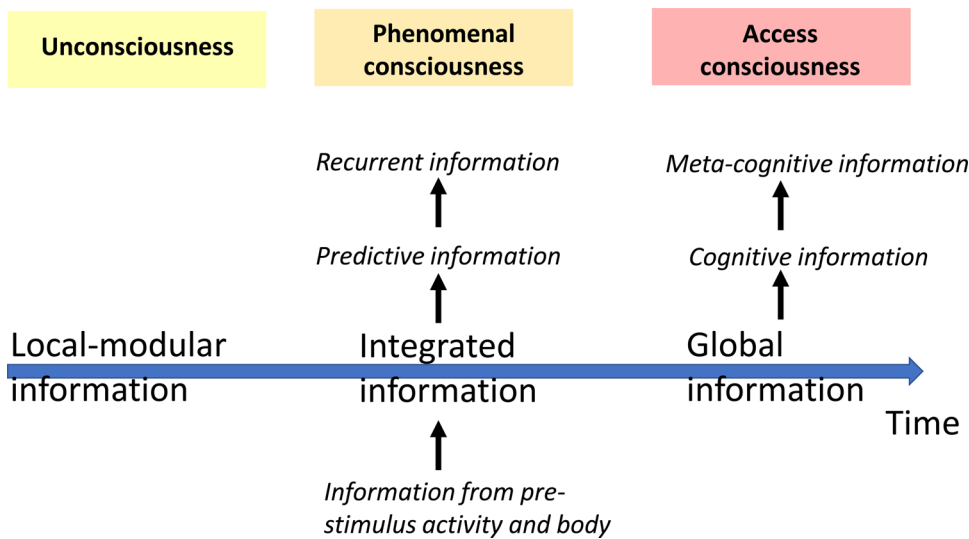


Fig. 4a. Relationship between local, intermediate, and global processing with regard to consciousness.

The figure shows the relationship of different forms of consciousness (unconscious, phenomenal consciousness, reflective consciousness (upper level) to different stages of information processing (lower level). Purely local-modular processing remains unconscious. Integrated information including predictive and recurrent information can yield phenomenal consciousness (Integrated Information Theory/IIT; Recurrent Processing theory/RPT). While global information with cognitive and meta-cognitive information yields access consciousness as postulated in Global Neuronal Workspace Theory (GNWT) and Higher-order Thought theory (HOT).

showing a different neural basis and model of consciousness to hold. The old hierarchical models have been replaced by more integrated, distributed, and inter-dependent models of consciousness – this is the current state. The future may be to unravel the subcortical-cortical basis and neuronal mechanisms of these integrated, distributed and inter-dependent features in the brain’s neural architecture. Here, the TTC is most explicit in proposing a dynamic layered architecture with tempo-spatial nestedness spanning across all levels and scales of the brain’s spontaneous activity including its alignment to body and environment (Northoff and Huang, 2017; Northoff, 2018). Whether that could provide the so far missing unifying architectural framework remains to be seen in the next 10–20 years.

b Can posterior and frontal theories be reconciled?

One main difference between theories lies in which regions in the brain are mandatory to mediate the integrated, distributed, and inter-dependent interaction required for consciousness to occur. A major divide is between theories that consider integration of neural activity in sensory regions as sufficient for (sensory) consciousness (like RPT, IIT, ST), and those that see a preferred role for regions like the prefrontal cortex in integrating information to a sufficient extent (GNWT).

PCT is somewhat unspecific or in-between in this respect; some version see predictions as coming from within sensory cortex itself (Bastos et al., 2012), some versions require frontal or prefrontal involvement (Dürschmid et al., 2019), others lean towards interoception as being a source (Seth et al., 2011). ET seems related to the latter version, as it sees a specific role for the integration of sensory information with bodily states which is mediated by both sensory posterior regions (Park et al., 2014) and prefrontal regions like ventromedial prefrontal cortex (Babo-Rebelo et al., 2016b, 2019).

Can we reconcile the seemingly opposing views about the posterior vs prefrontal regions? Since they target different explananda, e.g. perceptual vs cognitive, both suggestions may not be incompatible. Posterior regions may mediate the phenomenal or experiential aspects of sensory contents for which no cognitive involvement including access and reporting is yet required. Neural activity may then spread from posterior to anterior regions like the DLPFC that allow for additional cognitive processing of the sensory contents like their accessing, reporting, knowing, and meta-cognition of that very same sensory content (see Baars et al., 2013).

Recent developments using so called ‘no report’ paradigms indeed suggest to dissociate consciousness of sensory contents from their subsequent cognitive processing which, neuro-anatomically, should dissociate posterior and frontal regions (Boly et al., 2017; Tsuchiya

et al., 2015). Such dissociation also seems to occur on a temporal basis as the posterior vs frontal divide coincides with the early vs late dichotomy (e.g. VAN vs P3b); this suggests that different conscious contents as well as distinct levels or aspects of consciousness are processed in different parts of the brain at different points in time.

Yet another most recent line to reconcile or better go beyond the dichotomy of frontal and posterior approaches to consciousness consists in global brain activity (GBA). The relevance of GBA for consciousness is supported by studies in healthy subjects. These demonstrate that GBA is related to more global effects in visual perception like the global precedence effect (i.e., unspecific global features are perceived faster than more specific local features) (Liu and Luo, 2019; Romei et al., 2011, 2012). What is often coined as prefrontal-visual cortical top-down modulation may converge with GBA that, prior to the arrival of the stimulus, already sets the neuronal context for the subsequent processing and perception of visual stimuli, that is, what features of the stimulus are perceived, i.e., local or global, in which way, i.e., conscious or unconscious.

GBA can be measured by the global signal (GS) in fMRI which, despite much controversy (Power et al., 2017; Murphy and Fox, 2017), exhibits a succinct electrophysiological basis (Scholvinck et al., 2010; Liu et al., 2018; Zhang et al., 2020). GBA is important for the level of consciousness as suggested by various studies (Huang et al., 2016a,b, Tanabe et al., 2020). A recent fMRI study investigated GBA, i.e., GS in different states like sleep, UWS/MCS, and anesthesia. They observed that the degree of reduction of GS is related to the level of consciousness across the different states – GS may be an index of the level of consciousness.

At the same time, the observed different topographical distributions of GS in the different states (like more prefrontal and more posterior topographies) in the three forms of consciousness (Tanabe et al., 2020). The authors assume that the distinct GS topography in the different states may reflect differences in their phenomenology of consciousness including its contents. GBA as measured by GS in fMRI may then not only reconcile different localizations like prefrontal vs posterior but also the different dimensions of consciousness, i.e., level and content.

c Consciousness – distinct aspects and multilayered

Of course, such convergence may seem a refusal to ‘bite the bullet’ with respect to where exactly the transition from unconscious to conscious processing occurs. This will strongly depend on what one considers the major explanandum of this transition. In fact, there seems to be relatively little disagreement on what the different parts of the brain must contribute to the content of consciousness.

Recurrent or integrated information processes in the sensory parts of the brain contribute to the transition from fragmented to perceptual organization. While cognitive operations carried by more frontal parts provide top-down attention, access, working memory and report with respect to those sensory contents processed in the posterior parts. Which of the two are the key ingredient of consciousness is to some extent even a metaphysical issue (Lamme, 2010), and it is probably best to qualify it as a stalemate between different concepts of what consciousness really is about (Lamme, 2018).

One way to resolve this puzzle is to distinguish between different contents of consciousness, i.e., sensory and cognitive (and affective, etc.) all being associated with phenomenal experience. One may then assume that the different contents processed in different regions may nevertheless be mediated by one and the same neuronal mechanism (operating in all regions) yielding their phenomenal consciousness. The nature of such content- and region-unspecific neuronal mechanism remains unclear, yet.

One proposal put forward by the TTC (Northoff and Huang, 2017) is that dynamic mechanisms like non-additive pre-post-stimulus interaction with temporo-spatial expansion (see above) may operate in all regions in a content-unspecific way (as distinguished from cognitive mechanisms that are more or less region- and content-specific). Yet another candidate mechanism could be the above described global brain activity that could provide yet another way how phenomenal consciousness can be associated with different contents in a region- and content-unspecific way. Moreover, those very same contents may undergo different levels of processing and different functions like sensory, cognitive, affective, which modulates these contents allowing us to access them in different ways (Baars et al., 2013 in his version of the GNWT). One and the same content like an originally purely sensory content may then be processed in posterior regions in such way as to become phenomenally conscious. At the same time, the same sensory content may be relayed to and become available for the prefrontal cortex that, on the basis of its cognitive operations, may allow us to access and report that content.

Taken together, rather than being a homogenous entity, consciousness may be conceived as a highly heterogenous multifaceted neuronal process with different levels or layers of neuronal activity nesting within each other (Northoff and Huang, 2017; Northoff, 2017). The concept of layers is used throughout this paper to indicate nestedness: in the same way the different Russian dolls nest within each other, that is, the smaller one is nested or contained within the next larger one, consciousness and the brain's neural activity are supposed to be characterized by different layers that contain and nest within each other. In short, we reserve the term layer for designating nestedness (Fig. 4b,4c,4d).

Nestedness in such sense applies to both phenomenal and neuronal levels, i.e., consciousness and brain. That carries the consequence that the nested organisation of the brain's neural activity may be related to and ultimately surface in a more or less analogous nested organisation of the contents of consciousness: they include global and local components, content-unspecific and -specific components, and different temporal and spatial scales – this multifaceted nature of the contents of consciousness may be described as gestalt by figure (local activity) and background/ground (global activity) (see above and also gestalt theory). Temporo-spatial nestedness may consequently provide a “common currency” of brain and consciousness, i.e., neuronal and phenomenal levels (Northoff et al., 2019) as it is postulated in the temporo-spatial theory of consciousness (TTC) (Northoff and Huang, 2017).

7. Stimulus-related activity – function and dynamics

a Stimulus-related activity – function for consciousness

The exact function like a particular cognitive process that is mediated by integrated distributed interaction remains subject to dispute. The

various theories differ widely in what they see as the key functional role or cognitive process of such interactions. RPT posits that perceptual organization – mediated by recurrent visual interactions – elevates unconscious to conscious vision (Lamme, 2015), and a somewhat similar role is suggested by theories that see synchrony or binding as crucial, like ST (Engel and Singer, 2001). IIT claims a more general role for the ‘integration of information’, yet when looking at the axioms from which IIT departs, this integration is also strongly rooted in phenomenal aspects like perceptual unity and organization (Tononi, 2008). However, IIT denies being a functionalist theory (Doerig et al., 2019).

How can we specify the cognitive processes? The recurrent processing that is signaled by late events like P3b is claimed to mediate a function called ‘access’, or the making available of (sensory) information to other senses, motor output, working memory or report. Only when this happens, consciousness (including phenomenal experience (Naccache, 2018; Overgaard, 2018)) is claimed to arise by for instance the GNWT (Dehaene et al., 2006).

With some imagination, this can be seen as an extension of perceptual organization or integration, in the sense that what is now added to the organized sensory percept are aspects of value, purpose, behavioral context, memory, and language. One can conceive of the organized percept of a face at some point getting valued as pretty, as belonging to someone you know, while uttering her name. These are all aspects that make the experience undeniably richer. Whether these additions are key to becoming conscious of that face as such brings us back to the stalemate signaled earlier, that is, which component of consciousness is considered key.

Of a different nature are the functions that PCT claims as crucial. Some versions of PCT are somewhat reminiscent of GNWT, in the sense that the predictions that constitute the ‘prior’ are often related to top-down attention, task relevance or other more cognitive aspect of consciousness (Friston, 2010; Seth et al., 2011). There are other versions of PCT, however, where these predictions are more of a perceptual nature, operating in the domain of perceptual organization (Bastos et al., 2012). Then, PCT is more akin (in the functional sense) to RPT, ST, or IIT. PCT is however often unclear about where exactly consciousness arises in the interaction between (feedback) prediction, (feedforward) error, and the resulting update.

Finally, PCT seems functionally related to ET, as some versions of PCT (Seth et al., 2011) specifically see the body, heart, etc. as constituting priors upon which sensory inputs ride. But ET also has its own functional claims, in particular about how the neural monitoring of visceral and/or proprioceptive inputs by the brain constitute the self, and the ego-perspective of consciousness (Tallon-Baudry et al., 2018, Blanke 2015).

b Stimulus-related activity – reconciling function and dynamics

Despite their differences in determining the exact function for consciousness, IIT, GNWT, RPT, ET, and PCT converge in that specific cognitive or bodily functions are crucial for consciousness. Such functional perspective is complemented by the more dynamic view of TTC. Rather than assuming specific cognitive or bodily function, the TTC takes a more general stance by pointing out the need for considering the underlying temporo-spatial dynamic of these functions. Cognitive or bodily function is here complemented by a dynamic mechanism that, unlike the former two, operate across different regions and contents, i.e., region- and content-unspecific.

The TTC assumes that the temporo-spatial dynamics of the prestimulus period must be such that it allows embedding or enveloping the actual stimulus or input in a wider temporo-spatial framework: the latter must extend beyond the stimulus' or input's actual points in time and space which allows to expand the stimulus or input beyond its own purely physical space-time features. Temporo-spatial expansion is understood in a virtual way as “going beyond” (Buszaki 2006) the physical features of the stimuli, i.e., their specific points in time and space, by

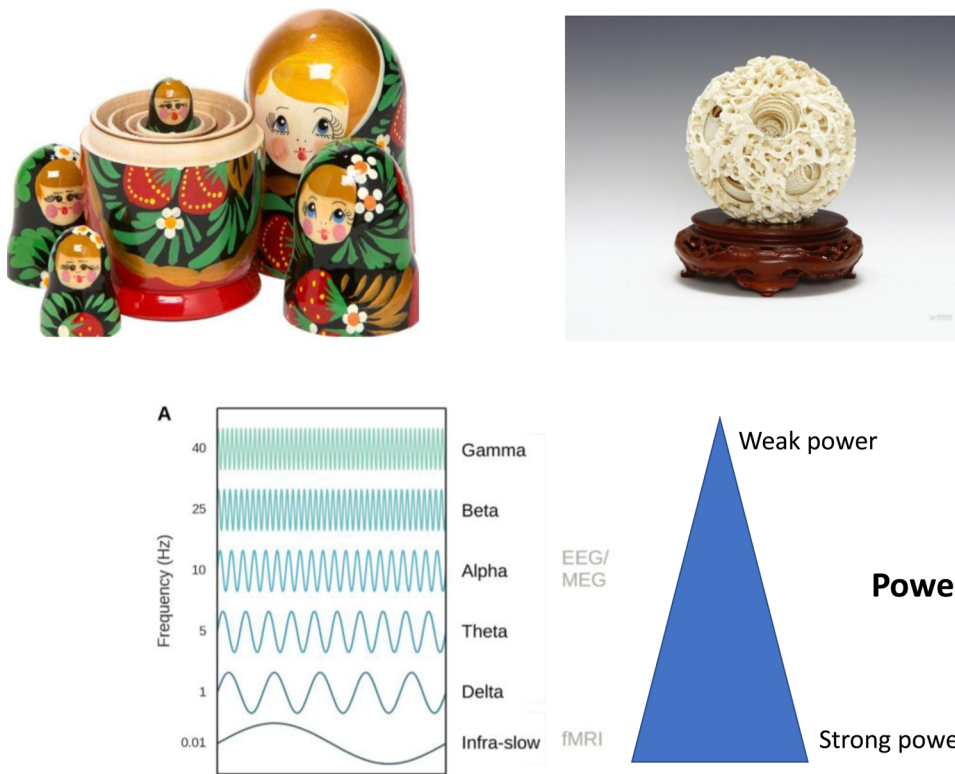


Fig. 4b. Examples of nestedness showing Russian dolls (upper left), Chinese crystal ball (upper right), and the brain's power spectrum (lower middle).

The figure shows three examples of nestedness. Upper left: the Russian dolls with smaller dolls being nested within the next larger one. Upper right: the same holds for the Chinese crystal ball where different sizes of the same shape are nested and intricately contained and integrated within each other. Lower left and right: the power spectrum with its different frequencies (lower left) that show different degrees of power (lower right) is yet another example of nestedness where the strongly powered slower frequencies contain or nest the weakly powered faster frequencies.

extending or expanding the latter to others in both past and future in a virtual way (Northoff and Huang, 2017; Huang et al., 2017).

Such temporo-spatial expansion, so the TTC, requires non-additive or non-linear interaction of pre- and post-stimulus activity (Huang et al., 2017). In contrast, simple superposition of prestimulus activity levels and stimulus-related effects with their merely additive interaction would not be sufficient for such virtual temporo-spatial expansion of the stimulus which therefore would remain unconscious. The function mediating consciousness is here no longer primarily cognitive or bodily but dynamic that, unlike the former two, operates across different regions and contents, i.e., region- and content-unspecific.

In sum, the different theories diverge in the nature of the exact function associated with integrated, distributed, and interdependent processing. The function may be sensory (perceptual organisation/

RPT)), cognitive (access/GNWT, prediction/PCT), bodily (prediction/PCT, neural monitoring of bodily input/ET), or dynamic (temporo-spatial expansion/TTC). An interesting proposal, as put forward in Spatiotemporal Neuroscience (Northoff et al., 2020), is that temporo-spatial dynamic processes also shape sensory, bodily, and cognitive functions including their respective contents – that may make possible for the dynamic level to associate consciousness with specific contents and functions.

8. Spontaneous activity and stimulus-related activity – Integration and nestedness

a Stimulus-related, pre-stimulus, and spontaneous activity - Integration

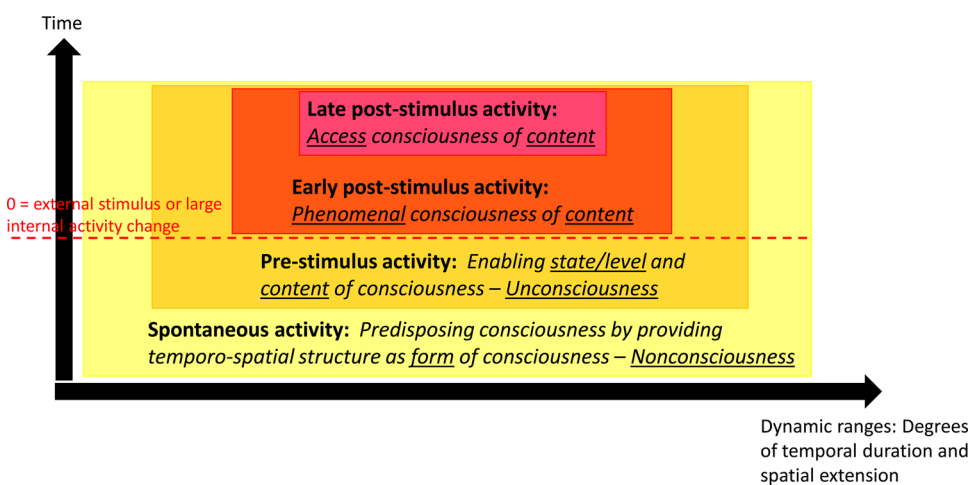


Fig. 4c. Temporo-spatial nestedness of the different aspects of neural activity and their relation to consciousness.

The figure shows how different forms of neural activity are contained and nested within each other in temporo-spatial dynamical terms. The spontaneous activity shows the largest spatial extension and strongest slow frequencies. Both are reduced with less spatial extension and less slow frequencies in the prestimulus activity. Both spatial extension and range of slow frequencies are further reduced in early stimulus-induced activity and even more so in late stimulus-induced activity. Due to these temporo-spatial differences, the different forms of neural activity are associated with different dimensions of consciousness including form (spontaneous activity), state/level (prestimulus activity) and content (pre-

and post-stimulus).

Finally, prestimulus period itself remains unconscious, early stimulus-induced activity is related to phenomenal consciousness while late stimulus-induced activity is featured by access consciousness. The different dimensions (form, state/level, content) and types or forms (unconscious, phenomenal consciousness, access consciousness) are thus characterized in temporo-spatial dynamical terms.

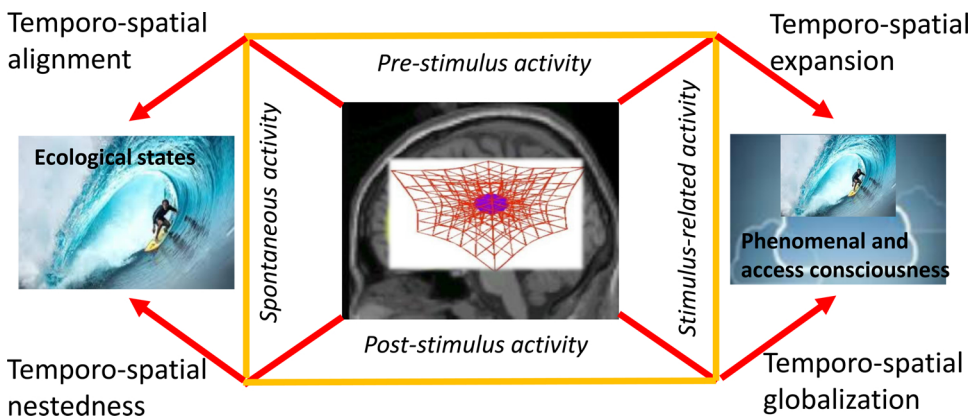


Fig. 4d. Different dynamic temporo-spatial mechanisms of consciousness in the Temporo-spatial theory of consciousness (TTC).

The figure shows the four temporo-spatial mechanisms as postulated in the temporo-spatial theory of consciousness (TTC) and how they are related to different forms of neural activity (Northoff and Huang, 2017).

There is temporo-spatial alignment to the environment that is mediated by the spontaneous activity and its synchronization to its ecological context (left part). That is also reflected in the spontaneous activity's temporo-spatial nestedness featuring its scale-free nature which is symbolized by the spatial grid laid over the brain. Temporo-spatial expansion is associated with pre- and stimulus-induced activity while temporo-spatial globalization is mediated by the late post-stimulus activity (right part) – both lead to phenomenal and access consciousness.

Our review showed that measures of all three, stimulus-related, pre-stimulus, and resting state activity are related to consciousness. This raises the question for the interaction of the three types of neural activity. Two recent studies using fMRI and MEG demonstrated that the spontaneous activity's dynamics (e.g., its power law exponent, delta/alpha power, and oscillatory/fractal components) correlate with the degree of non-additivity during pre-post-stimulus interaction (Aru et al., 2019; Huang et al., 2017; Wainio-Theberge et al., 2020; Wolff et al., 2020).

Yet other studies showed that the spontaneous activity's shaping of stimulus-related activity, as mediated by its degree of scale-freeness, i.e., power law exponent (PLE), is related to distinct aspects of consciousness including multisensory perception (Ferri et al., 2015, 2017), self-consciousness (Huang et al., 2016a,b, Wolff et al., 2019; Kolvoort et al., 2020; Scalabrini et al., 2017), animate social interaction through touch (Scalabrini et al., 2019), and even complex cognitive functions as learning of chemistry formulae (Bongers et al., 2019). Together, albeit preliminary, these data suggest that the divide of stimulus-related, pre-stimulus, and spontaneous activity may be artificial and more due to operational constraints than truly reflecting the brain's neural processing and functioning by themselves (i.e., independent of our measurement) (Northoff, 2014a, and b, 2018).

To obtain a more comprehensive integrated view, one may want to link the different measures of stimulus-related, pre-stimulus, and spontaneous activity with each other. This is, for instance, suggested in the TTC that associates different temporo-spatial mechanisms and distinct aspects of consciousness with the different forms of neural activity including their interaction, i.e., rest-stimulus interaction (Northoff et al., 2010a, b; Northoff and Huang, 2017; Northoff, 2018) (Fig. 4c and 4d).

Specifically, one may want to investigate whether the neural measures of stimulus-related activity like P3b, N2/VAN, PCI, and TTV are shaped by the spontaneous activity and its dynamics as measured by PLE/DFA, ACW, LZC, Entropy, and others. Given the supposed scale-invariant or scale-free nature of consciousness, as postulated by the TTC (Northoff and Huang, 2017; Northoff, 2018) and others (Tagliazucchi et al., 2013, 2016, Zhang et al., 2018), one may hypothesize that increased scale-invariant integration and temporo-spatial nestedness of the three forms of neural activity (including their different spatial and temporal scales) will make more likely consciousness. That remains to be tested though.

b Dimensions of consciousness – state/level, content, and form

Yet another related issue concerns the distinction of different

dimensions of consciousness, namely state/level, content, and, more recently, form (Bachmann and Hudetz, 2014, 2017, Northoff, 2013, 2014a and b, 2015, 2017, 2018). While the contents of consciousness are probed in stimulus-related activity on the cortical level, the state/level may be more related to pre-stimulus and resting state activity as well as subcortical regions, i.e., thalamo-cortical and/or nucleus basalis meynert (Podvalny et al., 2019; Aru et al., 2019; Liu et al., 2018; Sanchez-Vives et al., 2020).

A novel third dimensions, the form of consciousness, refers to its structure or organisation on the phenomenal level like its complex gestalt with figure and background/ground (see above) (Northoff, 2013, 2014a and b, 2018, Northoff and Heiss, 2015). Neuronally, the form of consciousness on the phenomenal level may be related on the neuronal level to the spontaneous activity's architecture like its temporo-spatial nestedness across cortical and subcortical regions (Northoff and Huang, 2017, Northoff, 2013) (see also Fig. 4c).

The distinction of form from both content and state/level is further supported by the fact that alterations in the form of consciousness can be observed in psychiatric disorders (Northoff, 2013, 2015). In contrast, alterations in state/level are related to the disorders of consciousness like sleep, UWS, and anesthesia while altered contents can be observed in regional lesions as in neurological disorders. Finally, the three dimensions may be related to the three kinds of neural activity discussed here. The form is mediated by the spontaneous activity's temporo-spatial structure (see part III), the content may be related to post-stimulus activity (and pre-stimulus) (see part I in our paper), and the state/level may be mediated by especially the pre-stimulus activity levels (Sadaghiani et al., 2009, 2010, 2015, Podvalny et al. 2019).

c Neural correlates of consciousness – preNCC, proper NCC, and NCCcon

The data suggest that stimulus-related, pre-stimulus, and resting state activity take on different roles for consciousness. Measures of stimulus-related activity like VAN, P3b, PCI, TTV, and synchrony are presumed to be sufficient neural correlates of either the phenomenal aspects of consciousness (NCC proper (Koch et al., 2016), or its cognitive aspects (by some called the consequences of consciousness: NCCcon (Aru et al., 2012)). This distinguishes them from measures of pre-stimulus activity like pre-stimulus activity amplitude, synchrony, variability, or power spectrum that are supposed to enable consciousness (neural prerequisites of consciousness: preNCC (Aru et al., 2012 which used NCCpre as original transcription).

The conceptual distinction of preNCC, proper NCC, and NCC con (Aru et al., 2012; de Graaf et al., 2012) hints upon a deeper issue. They

all refer to the sufficient neural correlates, that is, those neuronal features that are present when consciousness is present. We can now see that those neuronal features that are supposedly sufficient for consciousness concern distinct time points of stimulus-related activity including prior time points in prestimulus (preNCC), at stimulus onset and early on (proper NCC), and later (NCCcon) (see Baria et al., 2017). Their exact relationship remains unclear, though.

PCT provides a potential proposal of their relationship by linking the different time points of the empirical prior in pre-stimulus activity, i.e., preNCC, to later ones during stimulus-related activity as prediction error, i.e., NCC proper. The exact temporal dynamical underpinnings of empirical prior and prediction error may unclear though. More generally, it may be hypothesized that temporo-spatial dynamics may provide the glue or connection between pre- and post-stimulus activity and subsequently between preNCC, NCC proper, and NCCcon.

d Neural predispositions of consciousness (NPC) – necessary conditions or capacity

The NCC leave more or less open the role of the spontaneous activity as measured in resting state. Various studies in both healthy and neurologic/psychiatric subjects demonstrate involvement of the spontaneous activity in consciousness (see above). Its exact role remains unclear, though. Spontaneous activity by itself, i.e., independent of specific stimuli or tasks as processed in stimulus-related or task-related activity, is not sufficient for the contents of consciousness. Becoming conscious of specific contents requires additional stimulus-related activity or, at least, neuronal changes in the resting state analogous to the former amounting to ‘virtual’ stimulus-related activity; Northoff and Gomez-Pilar, 2020; Zhang et al., 2018, 2020).

Together, these and other findings (see above in part III) led to the assumption that the spontaneous activity provides the necessary albeit not sufficient neural conditions of consciousness. The spontaneous activity provides the neural capacity or neural predisposition of consciousness (NPC) (Northoff, 2014a, 2016, 2017, 2018, Northoff and Huang, 2017; Northoff and Heiss, 2015) (Fig. 5a). Such neural

predisposition or capacity makes possible consciousness while not realizing its actual manifestation: in the absence of such neural predisposition, consciousness will become altogether impossible while its presence does not automatically guarantee the manifestation of actual consciousness (as additional neuronal mechanisms, i.e., NCC, are required for that) (see Fig. 5a).

How can we describe the NPC in more empirical detail? For instance, different levels of sedation ranging from light to deep sedated anesthesia (as well as N1-N3 sleep stages and MCS) lead to a shift in the spontaneous activity’s power spectrum towards the slow frequencies (Zhang et al., 2018; Huang et al., 2018; Tanabe et al., 2020; Sanchez-Vives et al., 2017, 2020). What unites these different cases with the fully awake state is that the basic shape of the power spectrum, that is, its scale-free nature is still preserved – even if actually absent, consciousness still remains possible in these cases as the NPC are preserved. In contrast, in more extreme cases like surgical anesthesia and coma, the basic shape of the power spectrum with the steep decline in power from slow to fast frequencies is no longer present (Zhang et al., 2018; Huang et al., 2018). Instead, the power spectrum now exhibits a completely flat curve with equally low power values for both slow and fast frequencies (Zhang et al., 2018; Huang et al., 2018). Since, as long as the drug is administered, these subjects lost their capacity for consciousness, together with a loss of the basic scale-free shape of the power spectrum, one may consider the scale-free nature of the power spectrum, i.e., its shape, the NPC. Even if the NCC were present, consciousness will remain absent here as the NPC are not longer present – consciousness becomes altogether impossible. Accordingly, the NPC describe some sort of default-activity, the brain’s baseline, which, being indispensable or necessary for consciousness, has been associated with the brain’s scale-freeness (Northoff and Heiss, 2015; Zhang et al., 2018; Huang et al., 2018) and slow frequencies (Sanchez-Vives et al., 2017).

e Temporo-spatial dynamics – phenomenal features and “common currency”

How can we relate and ultimately provide a unifying framework for

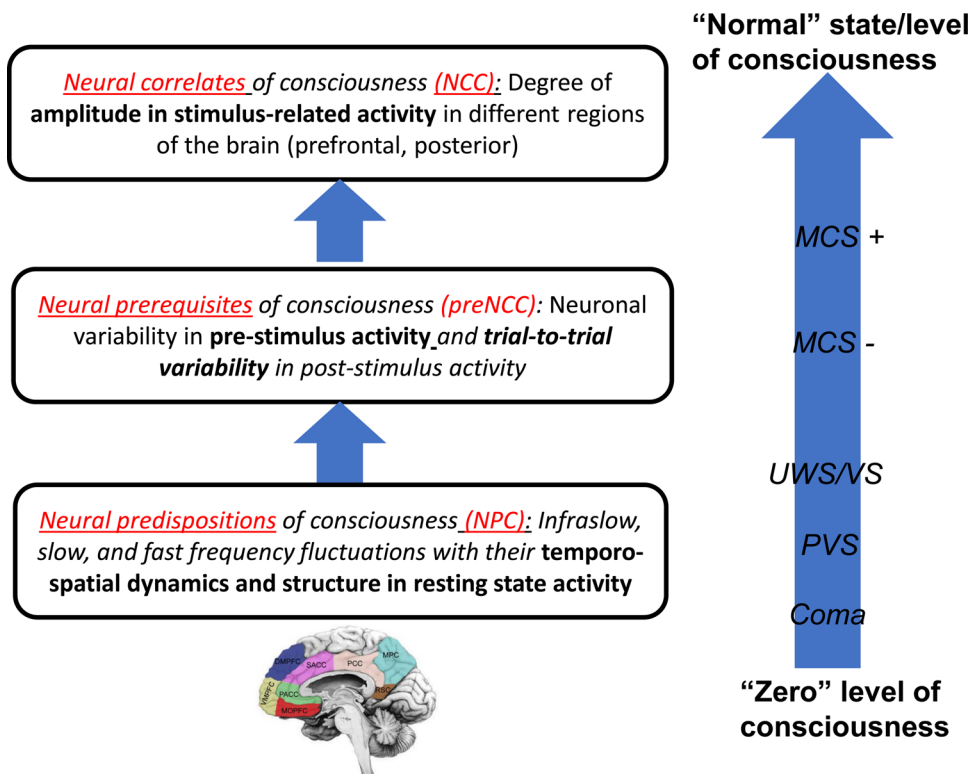


Fig. 5a. Different neural conditions of consciousness.

The figure shows the three different kinds of conditions of consciousness (see also Northoff and Heiss, 2015) and how they are related to different states/levels of consciousness and its different clinical conditions (arrow on the right).

From bottom to top:

The neural predisposition of consciousness (NPC) refer to the necessary non-sufficient neural conditions of consciousness that are constituted by the resting state activity and its temporo-spatial dynamics including the scale-freeness of slow and fast frequencies. Loss of the NPC leads to coma, persistent vegetative state (PVS) and unresponsive wakefulness state (UWS)/vegetative state (VS).

The neural prerequisites of consciousness (preNCC) describe the enabling neural conditions related to prestimulus activity and its impact on trial-to-trial variability in post-stimulus activity. Loss of the preNCC leads to the minus and plus forms of minimally conscious state (MCS -, MCS +).

Finally, there are the neural correlates of consciousness (NCC) that refer to the sufficient neural conditions of consciousness which are supposed to be mediated by stimulus-related activity in different regions. Presence of the NCC leads to the “normal” conscious state.

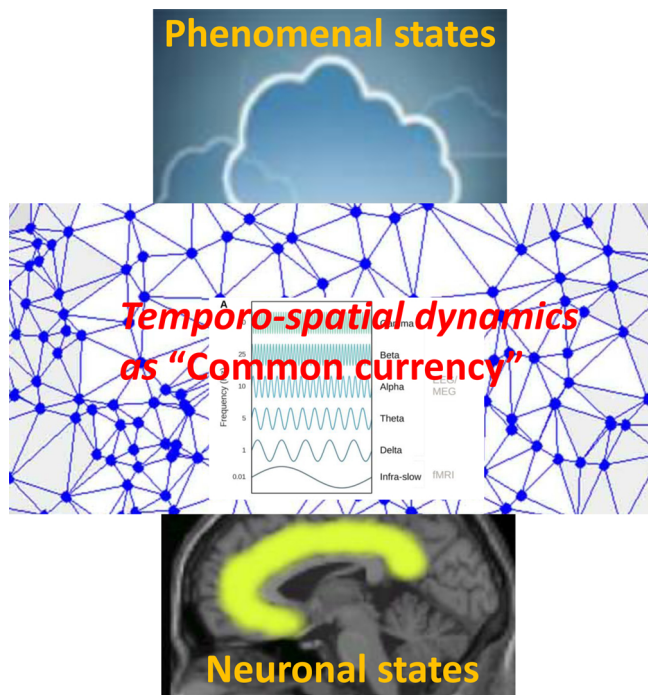


Fig. 5b. Temporo-spatial dynamics as “common currency” of neuronal and phenomenal states.

The figure shows a novel approach to the question of the relationship of neuronal and phenomenal states, i.e., brain and consciousness.

Traditionally, a causal relationship between neuronal and phenomenal features is assumed as both are presumed to be different. Instead of presuming both states to be principally different, the “common currency” approach (Northoff et al., 2019) assumes some basic similarity between neuronal and phenomenal states which makes possible the former’s transformation into the latter. Neuronal and phenomenal states are now no longer conceived as principally different as such basic similarity allows the former’ transformation into the latter. Such basic similarity is described as “common currency” as it, for instance, compares a shared currency between two business people from different countries with different currencies. In the case of neuronal and phenomenal states, that “common currency” is supposed to consist in temporo-spatial organisation and structure (as reflected by the grid in the middle) which can be tracked in the brain’s neuronal activity and in the temporal and spatial structure and shaping of our consciousness (like a stream of consciousness).

the different neural conditions and theories of consciousness including NCC, preNCC, proper NCC, and NCCcon? Theories focusing on stimulus-related activity (RPT, ST, GNWT, HOT) may target specifically the NCC (or NCCcon). While theories like PCT and TTC, that highlight the role of prestimulus activity may rather address the neural prerequisites of consciousness or preNCC. Providing a more comprehensive framework, one may assume that the different NCC’s are nested within each other, i.e., NCCcon within NCCproper that by itself is nested in temporo-spatial terms within preNCC.

Moreover, looking beyond the sufficient neural conditions of NCC, we may also need to search for the necessary non-sufficient neural conditions, the neural predispositions of consciousness (NPC). Theories focusing on the spontaneous activity including its temporo-spatial dynamics, like ET and TTC may tackle predominantly the predisposition or capacity for consciousness, i.e., NPC. That does not only promise a more extensive account of consciousness including the spontaneous activity but may also carry high clinical relevance: loss of the NCC may lead to unconscious while the basic capacity for consciousness, i.e., NPC, is still preserved which, in contrast, may no longer be the case if NPC is lost (Northoff and Heiss, 2015). Following the assumption of nestedness, NPC may provide the larger and overarching temporo-spatial frame for the nesting of the spatiotemporally more restricted

preNCC, proper NCC, and NCCcon.

Describing the necessary but not sufficient neural conditions of consciousness, the NPC touch upon the key question, namely whether any of the above described neural signs and measures are specifically related to the phenomenal features of consciousness, i.e., the what it is like (Nagel, 1974; Northoff, 2013, 2014a, 2018).

IIT and other theories like RPT claim that their supposed NCC can account for the phenomenal feel. The TTC takes a different stance. It postulates that the NCC with all its three forms need to be complemented by the NPC: without that what is necessary or indispensable (even if insufficient by itself), i.e., NPC, for something else, i.e., consciousness, we will not understand how the latter can be characterized by phenomenal features. According to the TTC, any theory of consciousness that does not consider NPC remains essentially incomplete (Northoff, 2013, 2014, 2018 for the more philosophical implications).

What exactly does the NPC need to provide to make possible the phenomenal features of consciousness? This, so the TTC (and also the OST; Fingelkurts et al., 2010), is the temporo-spatial dynamics of the brain’s spontaneous activity: the temporo-spatial dynamics provides the kind of organisation or structure that is manifest in the phenomenal experience as signified by a corresponding organisation or structure, i.e., form. If, in contrast, the spontaneous activity’s temporo-spatial dynamics no longer provides that organisation or structure in its neuronal activity, as in disorders of consciousness, or, an altered one, as in psychiatric disorders, the phenomenal features and consecutively consciousness will be either lost (disorders of consciousness) or abnormally altered (psychiatric disorders) (Northoff, 2013, 2014a, 2015, Northoff, 2018, 2020) (see Fig. 5b).

In sum, temporo-spatial dynamics may be manifest in both neuronal and phenomenal activity in more or less corresponding ways (the details of which remain unclear as to now). One can therefore say that temporo-spatial dynamics provides a shared feature, a “common currency”, of neuronal and phenomenal/mental states (Northoff et al., 2019, 2020). The brain’s inside or “deep interior” as the philosopher Thomas Nagel, i.e., its spontaneous activity’s temporo-spatial structure, may provide a template, i.e., a form, that, as “common currency”, allows for assigning phenomenal features to external stimuli from the outside of the brain, i.e., body and world. What Buszaki recently described as “inside-out” approach (Buszaki 2019, see also Pennartz et al., 2019 and Wolff et al., 2020 as well as Northoff et al., 2010a, b, Northoff 2012, and Northoff, 2014a; and b for earlier versions of such inside-out approach) is here extended to the case of consciousness, i.e., its phenomenal features for which the brain’s inside may be indispensable.

Acknowledgment

This project/research has received funding to GN from the European Union’s Horizon 2020 Framework Programme for Research and Innovation under the Specific Grant Agreement No. 785907 (Human Brain Project SGA2). We are grateful to Michele Farisco and Kathinka Evers for helpful comments and suggestions on earlier versions. Moreover, GN is grateful for financial support from CIHR, PSI, Hangzhou Normal University and the 7th Zhejiang University Hospital of Mental Health.

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