



Review article

How do the brain's time and space mediate consciousness and its different dimensions? Temporo-spatial theory of consciousness (TTC)

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ABSTRACT

Time and space are the basic building blocks of nature. As a unique existent in nature, our brain exists in time and takes up space. The brain's activity itself also constitutes and spreads in its own (intrinsic) time and space that is crucial for consciousness. Consciousness is a complex phenomenon including different dimensions: level/state, content/form, phenomenal aspects, and cognitive features. We propose a Temporo-spatial Theory of Consciousness (TTC) focusing primarily on the temporal and spatial features of the brain activity. We postulate four different neuronal mechanisms accounting for the different dimensions of consciousness: (i) "temporo-spatial nestedness" of the spontaneous activity accounts for the level/state of consciousness as neural predisposition of consciousness (NPC); (ii) "temporo-spatial alignment" of the pre-stimulus activity accounts for the content/form of consciousness as neural prerequisite of consciousness (preNCC); (iii) "temporo-spatial expansion" of early stimulus-induced activity accounts for phenomenal consciousness as neural correlates of consciousness (NCC); (iv) "temporo-spatial globalization" of late stimulus-induced activity accounts for the cognitive features of consciousness as neural consequence of consciousness (NCCcon).

1. Introduction

1.1. General background

Consciousness is a complex phenomenon that includes different dimensions. The initial characterization of consciousness by contents (Crick and Koch, 2003; Koch, 2004) has been complemented by the level or state of consciousness (Bachmann and Hudetz, 2014; Koch et al., 2016; Laureys, 2005). Recently, additional dimensions have been suggested. One such dimension is the distinction between phenomenal/experiential and cognitive aspects of consciousness (Cerullo et al., 2015; Northoff, 2014). Another dimension was introduced with the form (or structure) of consciousness (Northoff, 2013, 2014). The form of consciousness pertains to the grouping and ultimately the

organization of different contents, which, neuronally, is supposedly associated with the spontaneous activity and its spatiotemporal structure. The exact neuronal mechanisms underlying the different dimensions of consciousness, e.g. level/state, content/form, phenomenal/experiential, cognitive/reporting, including their relationships remain an open question.

Many studies in especially healthy subjects sought to associate consciousness with stimulus-induced or task-evoked brain activity. Specifically, the stimulus-induced or task-evoked activity refers to those neural activity changes that are related to and sufficient for the contents of consciousness (Koch et al., 2016) therefore speak of content-neural correlates of consciousness (NCC). Temporally, content-NCC is associated with event-related potentials such as the N100 and P300 (Bachmann and Hudetz, 2014; Dehaene and Changeux, 2011; Koch

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Consciousness Dimensions	Level/State	Content/Form	Phenomenology /Experience	Cognitive Processing /Reporting
Experimental testing	Task-free/resting-state paradigms	Pre-stimulus paradigms	Post-stimulus no-report paradigms	Post-stimulus report paradigms
Types of brain's neural activity	Spontaneous activity	Pre-stimulus activity	Early stimulus-induced activity	Late stimulus-induced activity
Temporo-spatial features	Infra-slow fluctuations Temporal correlations Cross-frequency coupling Small-worldness Dynamic repertoire	Non-linear interaction between pre- and post-stimulus-evoked activity Phase-preference	P50 and N100 Posterior cortical hot zones Sensory areas Cortical midline regions	Gamma activity P3b wave Prefrontal-parietal recruitment loops
Neuronal mechanisms	Temporo-spatial nestedness	Temporo-spatial alignment	Temporo-spatial expansion	Temporo-spatial globalization
Terminology	Neural predisposition of consciousness (NPC)	Neural prerequisite of consciousness (preNCC)	Neural correlates of consciousness (NCC)	Neural consequence of consciousness (NCCcon)

Fig. 1. Four Temporo-Spatial Mechanisms Account for Four Dimensions of Consciousness.

et al., 2016). Spatially, stimulus-induced or task-evoked activity in higher-order brain regions like prefrontal cortex and posterior cortical “hot zones” may be the NCC for mediating conscious content (Dehaene et al., 2014; Dehaene and Changeux, 2011; Koch et al., 2016).

More recently, different components of stimulus-induced activity have been identified including the distinction between early and late stimulus-induced activity, as well as the interaction between pre-and post-stimulus activity. Early stimulus-induced activity, as tested for in so-called no-report paradigms may be related to the phenomenal features of consciousness (e.g. experience), while late stimulus-induced activity is supposedly more related to its cognitive components (e.g. reporting and awareness of contents) (Koch et al., 2016; Lamme, 2010; Northoff, 2014; Tononi et al., 2016; Tsuchiya et al., 2015). While on the other end, prior to stimulus onset, several studies demonstrated that the level of pre-stimulus spontaneous activity impacts both stimulus-induced activity and the respectively associated content of consciousness (Boly et al., 2007; Hesselmann et al., 2008; Mathewson et al., 2009; Ploner et al., 2010; Qin et al., 2016; Sadaghiani et al., 2015, 2010, 2009; Schölvinck et al., 2012; van Dijk et al., 2008; Yu et al., 2015). The relevance of pre-stimulus activity level suggests a central role of the brain’s spontaneous activity for consciousness. This is also supported by other studies in subjects with altered state of consciousness, such as unresponsive wakefulness state (UWRS), sleep, and anesthesia; these subjects showed major changes in the brain’s spontaneous activity (Bayne et al., 2016).

Why and how are these different forms of neural activity (i.e. spontaneous, pre-stimulus, early, and late stimulus-induced activity) related to consciousness and its different dimensions? To date, this has not yet been thoroughly examined. We here suppose that these different forms of neural activity reflect different ways of how the brain constructs its own inner time and space, i.e. its intrinsic time and space (see below for definition). This amounts to what we describe as “Temporo-spatial Theory of Consciousness (TTC)”.

1.2. Aim and overview

Time and space are the central and most basic building blocks of nature. Time and space can be constructed in different ways. While the different ways of constructing time and space have been extensively investigated in physics, their relevance for the brain’s neural activity and, even more importantly, consciousness remains largely unknown though. Current neuroscientific views focus mainly on information, behavioral, affective, or cognitive features of brain and consciousness, e.g. Information Integration Theory/IIT (Tononi et al., 2016), or

cognitive, e.g. Global Neuronal Workspace Theory/GNWS (Dehaene et al., 2014; Dehaene and Changeux, 2011), or Predictive Coding (Friston, 2010; Hohwy, 2016; Seth and Friston, 2016). While these views presuppose and implicitly touch upon the brain’s own time and space, they do not consider time and space themselves – central dimensions of the brain’s neural activity – in an explicit way, that is, how the brain itself constructs time and space in its neural activity.

Given that (i) time and space are most basic features of nature and (ii) that the brain itself is part of nature, we here consider the brain and its neural activity in explicitly temporal and spatial terms. In other words, we conceive the brain’s different forms of neural activity (spontaneous, pre-stimulus, early and late stimulus-induced activity) in primarily temporo-spatial terms rather than informational, behavioral, cognitive or affective terms. This, as we postulate, is central for understanding how the brain can generate consciousness with its different dimensions. In this sense, consciousness can be understood as a temporo-spatial phenomenon of the brain’s neural activity.

The main and overarching aim of this review is to provide a unified hypothesis that directly links and thus integrates the different forms of neural activity with the different dimensions of consciousness. Such integrative coherent framework is suggested to consist in temporal and spatial features of the brain’s neural activity (across its different kinds). Based on various lines of empirical evidence, here we postulate the four dimensions of consciousness (level/state, content/form, phenomenal/experience, cognitive/reporting) are mediated by four corresponding temporo-spatial neuronal mechanisms: (i) the neuronal mechanism of “temporo-spatial nestedness” accounts for the level or state of consciousness; (ii) the neuronal mechanism of “temporo-spatial alignment” accounts for selecting the content and constituting the form of consciousness; (iii) the neuronal mechanism of “temporo-spatial expansion” accounts for the phenomenal dimension of consciousness, e.g. experience with qualia; (iv) the neuronal mechanism of “temporo-spatial globalization” accounts for the cognitive dimension of consciousness, e.g. the reporting of its contents (see a summary in Fig. 1). The TTC is primarily a neuroscientific theory of brain and consciousness, which may carry major philosophical implications in terms of a novel view of consciousness, and a paradigm shift from mind-body problem to world-brain problem (Northoff, 2016, 2017).

1.3. Definition of the brain’s time and space

What do we mean by the terms “time” and “space”? One would argue that the brain’s neural activity is by default temporal and spatial. This makes any account of consciousness and its different dimensions in

temporo-spatial terms rather self-evident if not trivial or banal. We therefore need to clarify what exactly we mean by the concepts of “time” and “space” in TTC.

The TTC refers to time and space of the brain; that is, how the brain constructs its own time and space in its neural activity. One may thus speak of “time and space” of the brain, or the “intrinsic” time and space of its neural activity. The construction of such “intrinsic” time and space of the brain itself needs to be distinguished from our perception and cognition of time and space including their neural correlates – the latter presupposes the former. The focus in this paper is not on the neural correlates of our perception and cognition of time and space but rather on how the brain itself constitutes its own “intrinsic” time and space (see Appendix 2 in Northoff, 2014 for more details).

The brain’s “intrinsic” time concerns the “duration” of neuronal activity embedded in specific frequency ranges. These frequency ranges are distinguished from higher frequency ranges like ultrasound (Nagel, 1974), or lower frequency ranges of other nature phenomena such as seismic earth waves (He et al., 2010). As for the brain’s “intrinsic” space, we speak of the “extension” of neural activity across different regions and networks in the brain. Briefly, the brain’s “intrinsic” time and space or its “operational time and space” (Fingelkurts et al., 2013), can be characterized by “temporal duration” and “spatial extension” of its neural activity.

Let us describe the notions of “temporal duration” and “spatial extension” of the brain’s neural activity in more empirical detail. Firstly, the “temporal duration” is related with the temporal ranges or circle durations of neural oscillations and/or fluctuations. This includes different frequencies ranging from infraslow (0.0001–0.1 Hz) over slow (0.1–1 Hz), delta (1–4 Hz), and theta (5–8 Hz) to faster frequencies like alpha (8–12 Hz), beta (13–30 Hz), and broadband gamma (30–240 Hz) (Buzsáki, 2006; Buzsáki et al., 2013; Buzsáki and Draguhn, 2004). These different frequencies show different functions and, most likely, associated with different underlying neurophysiological mechanisms that give rise to a wide range of behavioral and functional opportunities (Buzsáki, 2006).

Secondly, the “temporal duration” of the brain’s neural activity can be also characterized by intrinsic temporal autocorrelation in milliseconds to seconds and minutes range. These timescales can be measured by “auto-correlation window” (Honey et al., 2012), and scale-free or fractal properties like power-law exponent or Hurst exponent (He, 2014; He et al., 2010). This makes clear that the brain’s “intrinsic” time (i.e. its “inner duration”) is highly structured and fine-grained organized. We will see further down that such temporal structure and organization in the brain’s neural activity is central for consciousness.

Thirdly, the range of frequencies and the intrinsic temporal organization of the brain’s neural activity strongly influence the processing of extrinsic stimuli. The different frequencies with their respective cycle durations provides “windows of opportunity” (Lakatos et al., 2013, 2008; Schroeder and Lakatos, 2009) to acquire and encode extrinsic stimuli and their temporal sequences. Therefore, there appears to exist

intrinsic “temporal receptive windows” that matches with the physical features of the extrinsic stimuli in hierarchy timescales (Chen et al., 2015; Hasson et al., 2015; Honey et al., 2012; Murray et al., 2014).

How about the “intrinsic” space of the brain activity, i.e. its “spatial extension”? The brain shows an extensive structural connectivity that links across neurons, regions and networks. This structural connectivity provides a “hardware”, through which the neurons could functionally communicate (e.g. functional connectivity). Although there is strong dependency of functional connectivity on structural connectivity (Honey et al., 2009), the divergence between them seems to be consciousness relevant (Tagliazucchi et al., 2016). Finally, it shall be mentioned that the brain’s “intrinsic” space is also related with its small-world organization (e.g. spatially scale-free) with various features including modularity, centrality and so on (Bassett and Sporns, 2017; Sporns and Betzel, 2016).

We so far have described the “temporal duration” and “spatial extension” of the brain’s neural activity, and how they construct the brain’s “intrinsic” time and space. One also needs to consider that the brain and its “intrinsic” time and space are “located” in the “extrinsic” time and space encompassing our body and the world (Park and Tallon-Baudry, 2014; Park et al., 2014). Empirical data suggest that the brain’s “intrinsic” time and space align themselves to the “extrinsic” time and space in order to constitute “world-brain relation” (see below for details of “temporo-spatial alignment”). Such “world-brain relation” allow us to experience ourselves including our body within and as part of the temporo-spatially more extended world.

2. Neural predispositions: from “temporo-spatial nestedness” and “dynamic repertoire” of spontaneous activity to level/state of consciousness

2.1. Temporo-spatial nestedness: spontaneous activity, long-range temporal correlation (LRTC), cross-frequency coupling (CFC), and small-world properties

The brain’s spontaneous activity shows a sophisticated temporal structure that operates across different frequencies from infraslow over slow and fast frequency ranges (Fig. 2A). Importantly, the neural activity in these frequencies shows a fractal organization with a gradient fashion that slower frequency’s power is higher than that of faster ones, which can be described as “scale-free dynamics” (He, 2014). Scale-free activity has been further characterized by long-range temporal correlation (LRTC) which can be seen across widespread cortical regions (Bullmore et al., 2001; He et al., 2010; Linkenkaer-Hansen et al., 2001; Palva et al., 2013; Palva and Palva, 2012). Due to the fact that LRTC predominantly reflects irregular fluctuation in the infraslow frequency range (rather than the more regular oscillations in the faster frequencies), they were often conceived as mere “noise”. However, the 1/f noise-like signal was actually derived from the neural activity itself that is organized in a specific way (thus reflecting what is described as

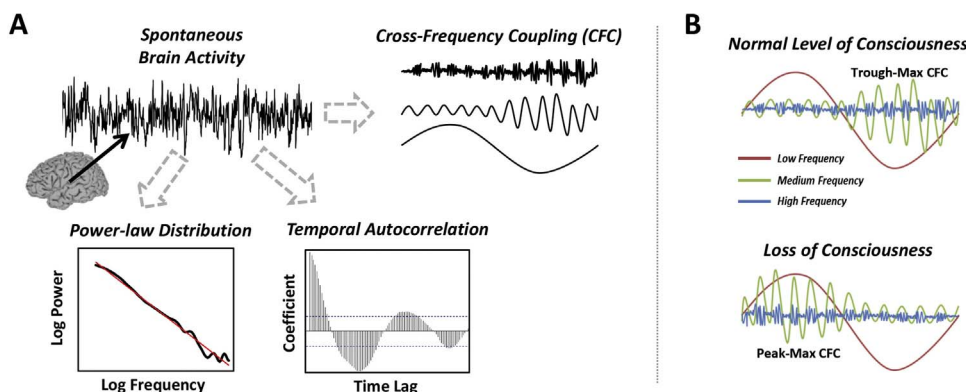


Fig. 2. Temporal nestedness and level of consciousness. A. The temporal structure of spontaneous brain activity is reflected by power-law distribution of the power-spectrum, autocorrelation function, and cross-frequency coupling (CFC) patterns. B. Different CFC relationship corresponds to different level or state of consciousness. A trough-max CFC reflects normal level of consciousness, while a peak-max CFC reflects loss of consciousness (modified and reproduced from Purdon et al., 2013).

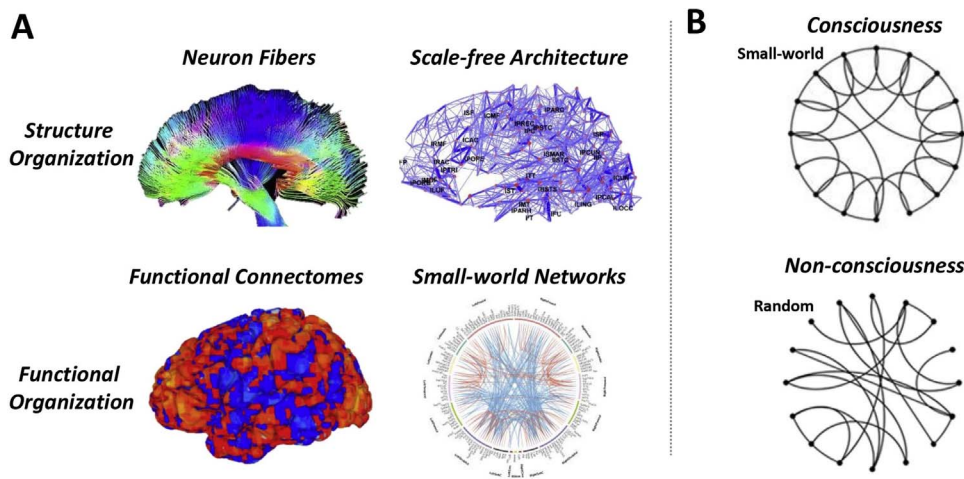


Fig. 3. Spatial nestedness and level of consciousness. A. The spatial architecture of brain's structural/anatomical connections and functional connectivity. Both of them show scale-free and small-world organization. B. Small-world organization is necessary for consciousness, while random organization leads to non-consciousness.

structured noise, i.e. “pink noise”). This can be distinguished from the noise related to our method of measurement (“white noise”) (He et al., 2010). The data shown below suggests that the structured $1/f$ noise-like-signal is central for the level/state of consciousness.

In addition to the scale-free fractal nature of LRTC, infraslow, slow, and faster frequencies are also coupled or nested with each other, namely cross-frequency coupling (CFC) (Aru et al., 2015; Bonnefond et al., 2017; Canolty et al., 2006; He et al., 2010; Hyafil et al., 2015; Lakatos et al., 2008; Tort et al., 2008). The CFC refers to a systematic relationship across frequencies where the phase of lower frequencies modulates the amplitude of higher ones in an upward progression. This has been shown in both slow/fast frequencies (Aru et al., 2015; Buzsáki et al., 2013; Hyafil et al., 2015) and infraslow ranges (Huang et al., 2015).

How about the spatial organization of the brain's spontaneous activity? There is extensive structural connectivity between neurons, regions and networks in the brain (Fig. 3A). That is superseded by functional connectivity that concerns the co-activation between different regions' neural activities (Honey et al., 2009). Interestingly, as in the temporal domain, both the structural and functional (connectivity) organization are spatially scale-free and fractal, which can be measured by small-world properties such as modularity, centrality, etc. (Bassett and Sporns, 2017). Therefore, the spatial organization of the brain's dynamic system exhibits nested “hierarchical modularity” architecture, which achieves an elegant balance between integration and segregation (Deco et al., 2015; Sporns and Betzel, 2016).

Spatial and temporal organization of neural activity are closely linked. One example is that different regions and networks show different timescales. For instance, the sensory regions show shorter timescale, while the DMN exhibits the longest timescale along with the strongest power in the infraslow frequency range (Hasson et al., 2015; Lee et al., 2014; Murray et al., 2014). Also, the faster frequencies are relatively spatially restricted and temporally regular, while the infraslow frequencies are more spatially extended and temporally irregular (Buzsáki and Draguhn, 2004; He et al., 2010). Therefore, analogous to the temporal side, one may speak of “spatial nestedness” that reflects a “hierarchy of timescales” on spatial grounds (Murray et al., 2014).

Taken together, scale-free dynamics with LRTC, CFC, and small-worldness establish a unique “integrated hierarchy of time and spatial scales” in our brain. We thereby speak of “temporo-spatial nestedness” of the brain's neural activity.

2.2. Temporo-spatial nestedness: neural predispositions of the level/state of consciousness (NPC)

How about the LRTC, CFC, and small-worldness during the loss of consciousness? Scale-free activity (as measured by power-law

exponent/PLE or detrended fluctuation analysis/DFA) is progressively reduced during the advancement of sleep stages N1 to N3 in the infraslow frequency range (Mitra et al., 2015; Tagliazucchi et al., 2013; Tagliazucchi and Laufs, 2014; Zhigalov et al., 2015). These studies observed reduction in infraslow scale-free activity globally as well as in specific networks like default-mode network (DMN) (including midline regions) and attention network (including lateral fronto-parietal regions).

While fMRI measures infraslow frequency range (< 0.1 Hz), EEG usually targets higher (1–180 Hz) frequency ranges. Interestingly, the misbalance between lower and higher frequencies, e.g. stronger delta (1–4 Hz) with weaker beta and gamma (20–60 Hz), was found in unresponsive wakefulness state (UWS) and anesthesia (Lewis et al., 2012; Purdon et al., 2013; Sarà et al., 2011; Sitt et al., 2014). Studies in especially anesthesia also showed abnormal coupling of the ongoing phase in slow frequencies (< 1 Hz) to either spiking rates (Lewis et al., 2012) or faster frequencies like alpha during the loss of consciousness (Mukamel et al., 2014).

Notably, an elegant EEG study by Purdon et al. (2013) showed that alpha amplitudes were maximal at low-frequency peaks during anesthetic-induced unconsciousness, whereas this relationship reversed during consciousness and transition period to unconsciousness. Moreover, the phase–amplitude and thus CFC relationship predicted recovery of consciousness (Purdon et al., 2013). Taken together, these findings show that the temporal and spatial organization of the brain's spontaneous activity by LRTC, CFC, scale-free, and small-world is central for the level/state of consciousness. Temporal nestedness of neural activity may thus not only organize and structure our brain's spontaneous activity but also yield the level/state of consciousness (Fig. 2B).

How about nestedness of neural activity on the spatial side? Barttfeld et al. (Barttfeld et al., 2015) showed reduced small-world organization in monkey anesthesia. Analogous findings were observed in human subjects (Uehara et al., 2014). It has been shown that dynamic functional connectivity was reduced in human anesthesia that resembled structural connectivity whereas in the awake state both structural and functional connectivity diverged transiently (Tagliazucchi et al., 2016). Liu et al. (2014) observed reduced functional connectivity in both anesthesia and unresponsive wakefulness state (UWS); however, only UWS showed decreased scale-free properties while the latter were maintained in anesthesia (Fig. 3B).

How can temporo-spatial nestedness of neural activity account for the level/state of consciousness? Temporo-spatial nestedness is a global feature of neural activity spanning across different timescales, frequencies and regions/networks. Temporally, it refers to the integration, i.e. coupling across infraslow, slow, and fast frequencies, while spatially different regions/networks are integrated and organized in terms of small-world properties. Hence, temporo-spatial integration of different

temporal and spatial scales allows constituting what we described as “temporo-spatial nestedness” of neural activity.

Analogously, the level or state of consciousness can be considered a global feature that integrates and operates across different intrinsic temporal and spatial scales. For instance, the level/state of consciousness remains continuous across both short and longer time intervals and also apply to proximal and distal spatial environment. Psychologically, the level/state of consciousness may thus include different time and space scales that are nested within each other and may operate in a scale-free way. As such, the level/state of consciousness may well correspond to the brain’s global integration of temporal and spatial dimensions. We suppose that integration of different temporal and spatial scales is a central mechanism for constituting temporo-spatial nestedness in neural activity. In other words, we suppose a correspondence of temporo-spatial scales between the brain’s spontaneous activity and the level/state of consciousness: the degree to which different temporal and spatial scales/ranges are integrated may correspond to the degree of temporal and spatial continuity of the level/state of consciousness. One may consecutively hypothesize that the fluctuations in the degree of temporo-spatial nestedness of the brain’s neural activity may correspond to the fluctuations in our level/state of consciousness across time and space.

Moreover, it shall be noted that the level/state of consciousness is not about specific contents but concerns ‘conscious experiences in their entirety, irrespective of their specific contents’ (Koch et al., 2016). We consider temporo-spatial nestedness represents the brain’s “neural activity in its entirety irrespective of specific contents. Therefore, temporo-spatial nestedness of the brain’s spontaneous activity is a necessary condition of possible consciousness – a neural predisposition of consciousness (NPC) (Northoff and Heiss, 2015).

Note that we here explicitly refer to the global temporo-spatial structure of the brain’s spontaneous activity rather than global activity or global metabolism (Schölvinck et al., 2010; Shulman et al., 2009) per se (or a specific neural network like the DMN; see above). Global activity or metabolism may well be present without a specific temporo-spatial structure. We suppose that it is the latter, the temporo-spatial structure (the degree of fractal and scale-free organization of the brain’s spontaneous activity) rather than the mere level of global activity or metabolism itself that is central for the level or state of consciousness. However, it shall be noted that sufficient metabolism and thus energy supply may be necessary to constitute complex temporal and spatial structure in the brain’s neural activity. That may explain the findings in specifically UWRS that the degree of glucose metabolism is usually a good predictor of the level/state of consciousness in these patients (Stender et al., 2014).

In sum, we demonstrate the central rule of LRTC, CFC, and small-world organization for the level/state of consciousness. The LRTC, CFC, and small-world organization are temporo-spatial mechanisms that constitute the spontaneous activity’s structure in terms of ‘temporo-spatial nestedness’. The level/state of consciousness is consequently a temporo-spatial phenomenon that can be traced back to the temporo-spatial nestedness of the brain’s spontaneous activity.

2.3. Temporo-spatial nestedness: “Dynamic repertoire”

Temporo-spatial nestedness of neural activity is closely related to what has been described as “dynamic repertoire” (Hudetz et al., 2015). Put in temporo-spatial terms, “dynamic repertoire” concerns the temporal and spatial range of the brain’s neural activity, i.e. its duration and extension. The “dynamic repertoire” of neural activity can be probed by external stimuli like a TMS pulse (Casali et al., 2013). If the spontaneous brain activity shows less complexity and reduced scale-free organization, e.g. during the loss of consciousness, then the brain shows a smaller range of possible temporal and spatial reaction to the TMS. This is well manifest in patients suffering from disorders of consciousness, whose response to the TMS pulse is temporally and spatially

limited, stereotypical, and less complex. This suggests the central relevance of the “dynamic repertoire” for the level/state of consciousness.

Recent empirical findings suggest that the spontaneous activity’s “dynamic repertoire” is reduced and thus more static and less dynamic in altered states of consciousness such as anesthesia, sleep and unresponsive wakefulness state (Bartfeld et al., 2015; Chennu et al., 2014; Hudetz et al., 2015; King and Dehaene, 2014; Marinazzo et al., 2014; Sarasso et al., 2015; Tagliazucchi et al., 2016). For instance, the variability of regional homogeneity (ReHo) and the degree to which the signal crosses a certain threshold, i.e. threshold crossing (Hudetz et al., 2015), as well as the dynamics of functional connectivity patterns decrease significantly during the loss of consciousness (Bartfeld et al., 2015).

The “dynamic repertoire” is also related with the “critical point” of a phase transition that can be seen on a diversity of complex systems (Haimovici et al., 2013; Tagliazucchi et al., 2016). The “critical point” may reflect an optimized range of temporo-spatial nestedness, which provides the largest possibility of spontaneous repertoire, and the largest capacity of the system for both maximum number of spontaneous configurations and external stimulus processing. The closer the brain’s global neural activity operates to the “critical point”, the larger its dynamic repertoire, and, as we suppose, the higher its possible level or state of consciousness. One may consequently assume that during loss of consciousness, the brain’s spontaneous activity cannot reach its “critical point” anymore. Hence, one would hypothesize that the more distant the brain’s global neural activity operates relative to its “critical point”, the lower the level/state of consciousness. This remains to be tested though. Moreover, the exact neural mechanisms on how the brain’s spontaneous activity can reach and approach its “critical point” remain unclear.

We now suggest that the range of the global neural activity’s “dynamic repertoire” predisposes the level/state of consciousness. The temporo-spatial range of the neural activity’s “dynamic repertoire” corresponds to the temporo-spatial range of the level/state of consciousness: the larger the range of the neural activity’s temporo-spatial scales with more fractal and complex organization, the larger its “dynamic repertoire”, which, in turn, translates into the level or state of consciousness. We, for instance, hypothesize that the decreased spatial extension and temporal duration of the TMS-evoked activity (Casali et al., 2013) is related to the decrease of temporo-spatial nestedness of the brain’s spontaneous activity. That can be well tested by investigating the spontaneous activity in the very same subjects. Also, future studies may apply multimodality approaches by combining TMS, EEG, MEG and fMRI to explore the temporo-spatial nestedness in more depth.

In sum, both temporo-spatial nestedness and “dynamic repertoire” concern the necessary conditions of the possibility level/state of consciousness rather than its actual manifestation – they are thus neural predispositions of the level/state of consciousness (NPC). Taken all together, we suppose that the level/state of consciousness is based on the integration of different temporal and spatial ranges which thereby allow for what is described as “temporal continuity” or “subjective feeling of continuity” across different temporal and spatial scales. Future studies may therefore directly compare the temporo-spatial fluctuations in the brain’s “dynamic repertoire”, i.e. scale-free activity, CFC, small-world, entropy and variability, with the fluctuations of the level/state of consciousness over time (and space). We suppose direct correspondence between both neural and conscious fluctuations, which, neuronally, can be traced to the temporo-spatial nestedness and “dynamic repertoire” of the brain’s spontaneous activity.

3. Neural prerequisites: from “temporo-spatial alignment” of spontaneous activity to content and form of consciousness

3.1. Temporo-spatial alignment: temporal alignment to single stimulus – phase preference and contents of consciousness

We so far focused only on the level or state of consciousness, which we supposed to remain independent of specific contents. However, consciousness can usually be characterized by specific contents that may originate either externally in the environment or internally within the own body or one’s mind. For instance, one can become conscious of a particular event in the environment (like the face or chair over there), within the own body (as the own heartbeat), or the own mind (like the own self or some thoughts as in mind wandering).

How must these stimuli and their respective contents be processed and aligned to the ongoing brain’s spontaneous activity, for becoming associated with consciousness? Recent studies using fMRI show that the contents of consciousness are dependent upon the state of the brain’s neural activity, i.e. state-dependence. Various studies demonstrated that pre-stimulus activity levels have an impact on the subsequent stimulus-induced activity and consciousness content (Boly et al., 2007; He, 2013; Hesselmann et al., 2008; Huang et al., 2015; Mathewson et al., 2009; Ploner et al., 2010; Qin et al., 2016; Sadaghiani et al., 2009; Sadaghiani and Kleinschmidt, 2013; Schölvinck et al., 2012; van Dijk et al., 2008). A recent study on visual perceptual awareness by Huang et al. (2017, unpublished) showed an even earlier pre-stimulus interval to predict consciousness. Huang et al. presented faces very shortly (using backward masking) and asked subjects whether they perceived the face or not. They demonstrated that the pre-stimulus activity levels (which is most likely related to the ongoing phases) in the medial prefrontal cortex (MPFC) 10–20 s prior to the onset of the actual stimulus predicted whether subjects consciously perceived the face or not. This effect was mainly observed in the very low infraslow frequency range – Slow 5 (0.01–0.27 Hz). The study is well in line with the central relevance of infraslow frequencies for consciousness. Another study showed that the infraslow frequency fluctuations (as measured in fMRI) in contralateral visual cortex influence the association of consciousness to the stimuli presented in respective other side (Wohlschläger et al., 2016).

Though not explicitly measured in fMRI, these pre-stimulus effects on consciousness suggest phase-related mechanisms, which have received much attention recently. The timing of the stimuli might fall into a specific part of the ongoing phase cycle like peak or trough, which, in turn, influences whether the stimuli will be subsequently associated with consciousness. One can therefore speak of “phase preference” as one example of “temporal alignment”. “Temporal alignment” describes that the timing on the ongoing spontaneous activity’s fluctuations, i.e. its cycle durations with phases aligned to the timing of the stimulus. The relevance of such “phase preference” for the contents of consciousness is indeed supported by various studies (see below). Such “phase preference” is merely passive, that is coincidental timing between ongoing phase cycle and stimulus onset. As merely passive, “phase preference” needs to be distinguished from more active “phase

shifting or locking” where the phase onset is actively shifted in relation to the onset of sequentially especially rhythmically presented stimuli (Lakatos et al., 2008; van Atteveldt et al., 2015).

A more direct evidence on the relevance of “phase preference” for conscious contents has been shown by Monto et al. (2008). They investigated high (1–40 Hz) and infraslow (0.01–1 Hz) frequencies using direct-current-coupled full-band electroencephalography (FbEEG) in human subjects. Subjects were delivered near-threshold somatosensory stimuli at random intervals (1.5–4.5 s) targeting their right index finger and were instructed to detect the stimulus yielding hits and misses. They observed a clear coupling of the phase of the infraslow fluctuations (ISF) to the hits and misses in the detection of the stimulus: the probability of a hit was highest during the rising phases of the ISF, while it was lowest during the falling ISF phases at the central (Cz) and fronto-central (Fpz) anterior midline electrodes. ISF phases also entrained high-frequency oscillations in the range between 1–40 Hz at Fpz and Cz. Amplitudes in the 1–40 Hz oscillations were highest in the rising phases of the ISF, while they were rather low in the falling ISF phases. This suggests that the stimulus-related higher frequencies are entrained by or nested in the phases of the lower ones in the ongoing spontaneous activity which seems to be central for perceptual awareness, and thus for associating consciousness to specific contents or stimuli.

The role of phase cycles in slow frequency range from 0.1 to 1–2 Hz in conscious contents is supported by other studies (Li et al., 2014) and other tasks (Kayser et al., 2015; Kösem et al., 2014; Lakatos et al., 2013; O’Connell et al., 2015; Palva et al., 2005; Stefanics et al., 2010; van Atteveldt et al., 2014; van Atteveldt et al., 2015). Moreover, the phase preference for conscious contents can also be observed in faster frequencies like alpha (Mathewson et al., 2009; Palva et al., 2005; Spaak et al., 2014) and gamma ranges (Fries et al., 2007; Singer, 2001).

Why and how are the phase cycles relevant for associating consciousness to contents? First and foremost, the different phases show different levels of excitability. The peak is rather low excitable while stimuli falling in the trough can induce higher levels of excitation and thus higher amplitude in stimulus-induced activity (Huang et al., 2015). While this is well known for faster frequencies ranging from 1–60 Hz, it is less studied in the infraslow range. One recent study by Huang et al. (2015) demonstrated that the phases in the infraslow frequency range, i.e., trough, peak, descending, or ascending, strongly modulate the amplitude of subsequent stimulus-induced activity. This suggests that different phases in the infraslow frequencies also show different levels of excitability as it is, analogously, the case in faster frequencies. Moreover, the results described above suggest that the different levels of excitability within different phases are relevant for associating the stimuli (and their respective contents) with consciousness.

How is that related to specifically the contents of consciousness? The temporal alignment to single stimuli as in “phase preference” allows to bind and align the single stimuli to the ongoing spontaneous activity of the brain (Fig. 4). Such “binding” between stimulus and neural activity is dependent upon the degree of “temporal correspondence” between stimulus and spontaneous activity’s phase cycles: the timing of the stimulus must “fit” or “correspond” to the timing of the

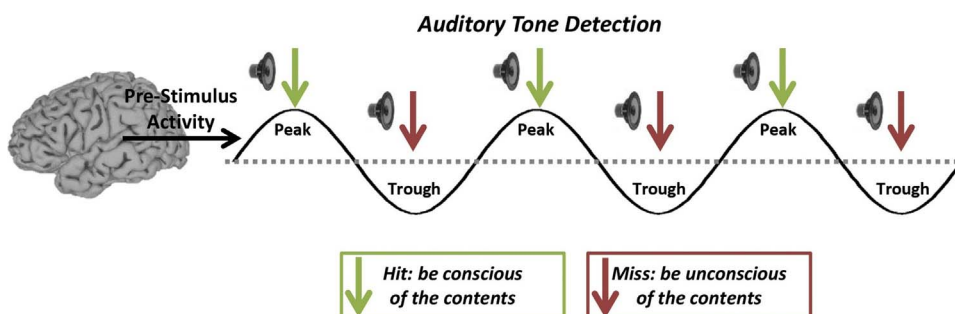


Fig. 4. Temporo-spatial alignment for single stimulus. The detection of auditory near-threshold stimuli is associated with the state of pre-stimulus spontaneous activity in the auditory cortex. Human subjects tend to report “hear” the stimulus (hits) when the stimulus was presented during the peak period of pre-stimulus activity, while subjects tend to “miss” the stimulus when it was presented during the trough period of pre-stimulus activity (modified from Sadaghiani et al., 2009).

ongoing phase cycle in the spontaneous activity. Hence, we consider “temporal correspondence” between phase timing and stimulus onset with subsequent “phase preference” an enabling condition or neural prerequisite of the contents of consciousness (preNCC).

In addition to the impact of the spontaneous activity’s phases, we also need to consider the impact of the stimulus itself including its spatiotemporal features. A stimulus with high intensity and/or long duration (Dehaene and Changeux, 2011; Li et al., 2014) can more easily induce phase shift than a stimulus with low intensity. That, in turn, will allow for increased “binding” between stimulus and spontaneous activity, which makes it more likely that such stimulus can be associated with consciousness. What we described as “temporal correspondence” between stimulus and neural activity is thus a two-way interaction or balance in which both stimulus and spontaneous activity “have a say”. Both stimulus and spontaneous activity and, more specifically, their balance, can exert impact and consequently determine whether a specific content is associated with consciousness.

3.2. Temporo-spatial alignment: temporal integration and cognitive unity of consciousness

What is the role of the infraslow fluctuations for the contents of consciousness? The infraslow and slow frequencies show long cycle duration (like 100 s in the case of 0.01 Hz) which are ideal for integrating different stimuli (Kringelbach et al., 2015). The relevance of long periods for stimulus processing and integration is further supported by the fact that the latency of metastability of infraslow frequency fluctuations lies around 20 s (Ponce-Alvarez et al., 2015; Tognoli and Kelso, 2014): these long periods can provide the temporal reference for encoding and aligning to longer stimulus sequences (like melodies or movies), which then, in their “temporal durations”, may “resonate” with the ones of the ongoing cycle durations in the brain’s spontaneous activity (Chen et al., 2015; Hasson et al., 2015; Kringelbach et al., 2015). The long cycle durations of the infraslow and slow frequencies may thus provide “windows” for stimulus integration – this has been described as “temporal receptive window (TRW)” (Hasson et al., 2008) (Fig. 5).

The TRW describe the temporal windows in the brain’s neural activity within which different stimuli and their respective contents can be merged and integrated (Hasson et al., 2015). The TRW allows to bind stimuli together based on their temporal properties regardless of their specific contents: stimuli that are temporally proximal and fall within the TRW are more likely to be bound and integrated comparing to stimuli that are temporally rather distal and may therefore fall outside the temporal range of the TRW. Such “temporal integration” must be distinguished from “content-based integration” that are more based on binding specific contents. In the case of multi-sensory integration, for instance, auditory contents have a higher likelihood of being bound to other auditory contents when compared to, for instance, visual or tactile contents. The content-based integration here is thus based predominantly on “contents” themselves rather than the content’s temporal properties (Mudrik et al., 2014).

How is such processing by the long cycle durations of the infraslow frequency fluctuations related to the contents of consciousness? Rather than concerning single contents of consciousness, the long cycle durations may allow for integrating and grouping different stimuli into different contents. For instance, all stimuli (and their respective contents) that fall into the long period of high excitability may be integrated with each other and thus constitute what is often described as the “cognitive unity” of consciousness in especially philosophy (Bayne, 2011; Searle, 2004). In contrast, stimuli falling outside the appropriate windows may not be integrated within that very same “cognitive unity”. Hence, the “cognitive unity” may ultimately be based on temporal (and spatial) mechanisms – “temporo-spatial alignment”.

Taken together, we suppose that the long cycle durations of infraslow frequency fluctuations are ideally suited for integrating different stimuli (and their respective contents) on purely temporal grounds thus enabling “temporal integration”. They thus provide a “temporal reference frame” (Kayser et al., 2012) for encoding stimuli’ sequences including the integration of various stimuli and their contents into one cognitive unity.

3.3. Temporo-spatial alignment: spatial alignment – contents of consciousness

How are such temporal alignment and its role in consciousness related to the spontaneous activity’s temporo-spatial nestedness? As described above, high degrees of scale-free activity indicate relatively stronger power in infraslow frequency fluctuations when compared to slow and faster frequencies. This is for instance the case in the default-mode network (DMN) (Fox and Raichle, 2007; Greicius et al., 2003; Raichle et al., 2001) and cortical midline structures (CMS) including ventro- and dorsomedial prefrontal cortex, medial parietal cortex, anterior and posterior cingulate cortex (Northoff and Bermpohl, 2004).

The regions in DMN and CMS show stronger LRTC (He, 2011; Huang et al., 2016) and longer auto-correlation windows (ACWs) than other regions, e.g. sensory regions (Murray et al., 2014). These regions are capable of encoding long stimulus sequences as marked by what Hasson described “temporal receptive window” (TRW) (Hasson et al., 2008). The findings clearly indicated that different regions show different temporal features in their neural activity – spatial differentiation goes along with temporal differentiation. Based on especially the findings by the group around Hasson (see Hasson et al., 2015 for an excellent summary of their various studies), the different regions’ varying temporal features are associated with the encoding and processing of stimuli’ sequences of different lengths. Interestingly, a recent study suggested that the content heterogeneity and stimulus-independence are central features of the DMN as opposed to sensory regions at the lower end of the hierarchy (Margulies et al., 2016). This is well compatible with the opposite temporal features of DMN and sensory regions. The stronger power in infraslow frequencies makes the DMN more independent of specific stimuli and specific temporal features, which allows for encoding more heterogeneous contents with different temporal features. Moreover, one would suppose that such

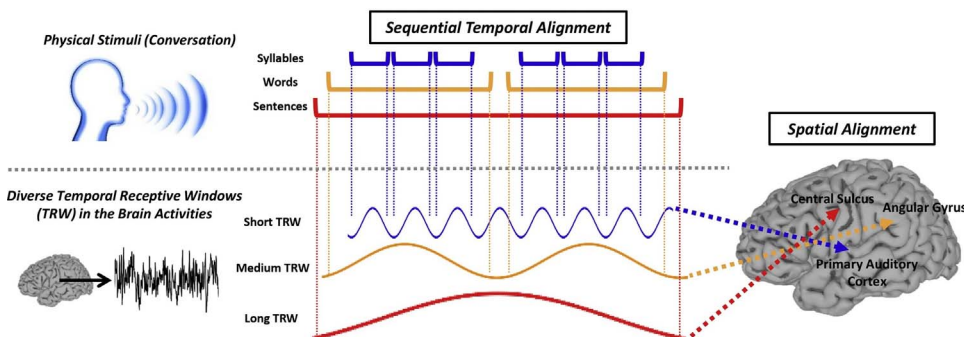


Fig. 5. Temporo-spatial alignment for sequential stimulus. On the left and middle panels, the spontaneous brain activity consists of a wide variety of temporal receptive windows (TRWs), which correspond to different timescales of the extrinsic physical stimuli, thus described as “sequential temporal alignment”. On the right panel, different brain areas show different lengths of TRWs with a fine-grained hierarchical organization, thus described as “spatial alignment”.

encoding is related to phase preference and/or phase shifting in the infraslow frequency range (which remains to be investigated though) and thus, more generally, to temporal alignment as described above.

How about the contents of consciousness? Based on the specific temporal features, one would assume that the CMS and DMN play a crucial role in aligning, integrating and unifying different temporally extended stimuli and contents in consciousness – they may thus account for the above-described “cognitive unity” of consciousness. This is in line with the special role of the CMS, which have often been associated with internally-generated contents such as mind wandering (Andrews-Hanna et al., 2014; Christoff et al., 2016), mental time travel or episodic simulation (Benoit and Schacter, 2015; Schacter et al., 2012) and self-consciousness (Huang et al., 2016; Northoff and Panksepp, 2008). In contrast, sensory regions and their shorter intrinsic time windows may rather allow for the temporal alignment to single stimuli with low degree of temporal extension – this may be related with the so-called “sensory unity” of consciousness (Bayne, 2011). Overall, the different temporal features of different regions may thus serve as preNCC.

3.4. Temporo-spatial alignment: stochastically-based alignment to body and world – “form” of consciousness

In addition to single or a group of stimuli, temporo-spatial alignment may also occur over longer period of lifetime to stimulus’ sequences occurring in both body and world (Fig. 6). For instance, a recent MEG study reported alignment, i.e. cross-frequency coupling, between the stomach’s infraslow frequency’s phase and the brain’s alpha amplitude in insula and occipital regions (Richter et al., 2017). Analogous alignment was observed between heart and brain in fMRI studies (Chang et al., 2013; Jennings et al., 2016), demonstrating a correlation between the variability of subcortical-cortical functional connectivity in the brain and variability of the heart rate.

This was further confirmed by EEG studies. Lechinger et al. (2015) recently reported a study on the relationship between heart rate and phase locking in the brain during awake and asleep states. Moreover, the phase onset of especially the delta/theta frequency (2–6 Hz) was locked to the onset of the heartbeat. Most interestingly, the phase locking of the delta/theta frequency to the heart beat was reduced during sleep stages (N1 to N3). This was the case during NREM sleep only, while the REM sleep pattern resembled the one in the awake state. These data suggest that the degree of temporo-spatial alignment of the brain’s neural activity to the body/heart is related to consciousness.

How is such temporo-spatial alignment between the brain’s neural activity and the temporo-spatial features of the body related to

consciousness? Park et al. (2014) observed that the amplitude of the heart-evoked potential (HEP) in the brain predicted conscious detection of visual stimuli: the amplitude of the HEP was significantly different between hits and misses with hits showing higher amplitude than that of misses. Accordingly, the way of the brain processed the heartbeat influenced whether consciousness was associated with the visual stimuli.

Park et al. (2014) further showed that the HEP and its effects on conscious detection was most predominantly located in the medial prefrontal cortex (MPFC). In other words, the HEP differences between hits and misses during the detection task corresponded to the coupling or association between HEP and spontaneous brain activity. This suggests that the temporal structure of heartbeat and brain’s spontaneous activity is closely related with each other thus showing “temporal correspondence” between brain and heart. Following Park and Tallon-Baudry (2014), such brain-heart coupling provides a “neural subjective frame” of the body in the brain’s neural activity that is central for consciousness (see Blanke et al., 2015 for the central role of the body and its representation in the brain as well as various theories on embodiment and embeddedness; Noë and Thompson, 2004; Thompson and Varela, 2001).

Analogous long-term stochastic temporo-spatial alignment can be observed in the case of exteroceptive stimuli from the world. Various lines of data showed active phase shifting in the brain’s neural activity which follows the rhythmic structure of exteroceptive stimuli in the environment (Lakatos et al., 2013; Lindenberger et al., 2009; Stefanics et al., 2010; van Atteveldt et al., 2015). The same applies to social stimuli related to other persons (Hasson and Frith, 2016). Albeit tentative, temporo-spatial alignment to exteroceptive and social stimuli seems to be disturbed in psychiatric disorders like schizophrenia (Lakatos et al., 2013; Northoff and Duncan, 2016) or bipolar disorder (Martino et al., 2016). For instance, Lakatos et al. (Lakatos et al., 2013) demonstrated that schizophrenic patients no longer show phase shifting following exteroceptive stimuli; instead, as suggested by the authors, these patients’ brains may align their phase onsets rather to interoceptive stimuli.

What do these data tell us about consciousness? The brain’s temporo-spatial alignment concerns here are the alignment to stochastically-based stimulus sequences over longer periods of time, namely “long-term temporo-spatial alignment”. These long stochastically-based sequences are usually not conscious as such; they provide the background or the “form” of our specific conscious contents (Northoff, 2014).

What do we mean by the concept of “form” as third (besides level/

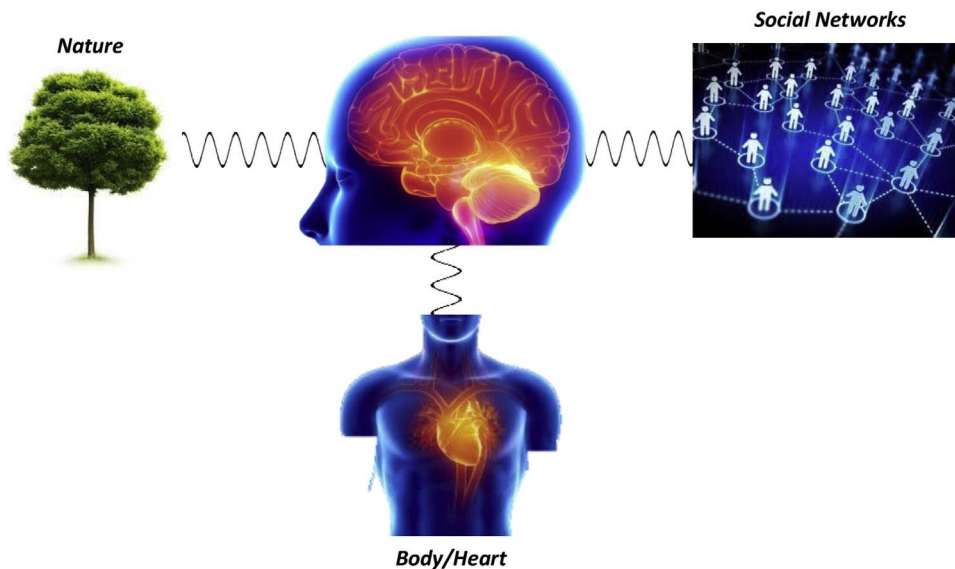


Fig. 6. Schematic illustration of stochastically-based alignment to body and world over long period of lifetime. Such long-term temporo-spatial alignment provides the alignment of the brain to the world. This world-brain relation constitutes the background of consciousness.

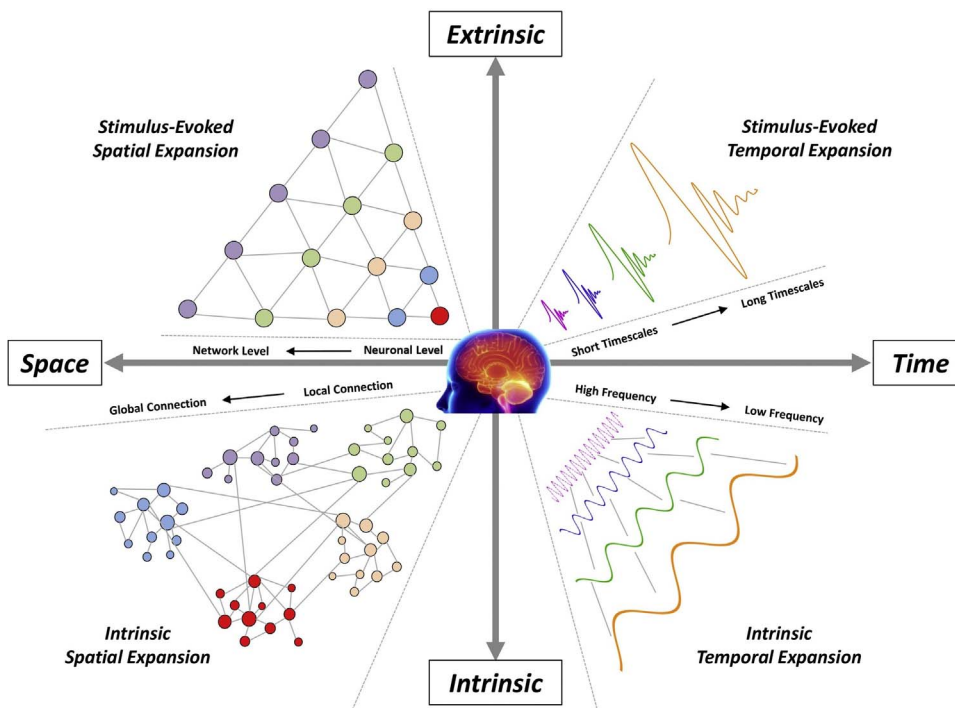


Fig. 7. Schematic illustration of temporo-spatial expansion in both intrinsic and extrinsic brain activity. In the stimulus-evoked spatial expansion, the evoked activity is hierarchically processed and “broadcast” from local neurons to brain networks. In the stimulus-evoked temporal expansion, neuronal spikes (millisecond timescale) can be extended to slow cortical activities (second to minute timescales). In the intrinsic spatial expansion, functional connectives assemble from local neural circuits to global large-scale brain networks. In the intrinsic temporal expansion, high frequency fluctuations are expanded and nested with low-frequency fluctuations.

state and contents) dimension of consciousness? We do not only experience the single content itself in consciousness. Instead, the single content is embedded in a variety of different contents that, in our experience, remain in the background. However, that background contents are connected to the specific content with both being organized and structured in a specific way thus showing content-background (or figure-background) configurations. This relationship between specific and background contents is what we describe as “form” of consciousness. Most generally, the various contents in the world and the world itself (including our body as part of the very same world) provide the background of consciousness. Therefore, consciousness is not “located” in our brain but extends beyond our brain by including the world – we do experience the specific content in consciousness as part of the world.

How can the world and its various background contents be included in our consciousness? We suppose that it is likely due to the temporo-spatial alignment of our brain’s spontaneous activity to the stochastic sequences of stimuli and their subsequent integration by the long cycle durations of the spontaneous activity fluctuations. Such long-term temporo-spatial alignment provides, as we suppose, the alignment of the brain to the world. This world-brain relation, in turn, constitutes the background of consciousness for our experience of specific contents in the very same consciousness.

In sum, we suppose that temporo-spatial alignment itself can occur on different scales, short- and long-term. Short-term temporo-spatial alignment allows for the binding between single stimuli thus constituting specific contents in consciousness, while long-term temporo-spatial alignment allows for establishing a world-brain relation that provides the background contents and “form” of consciousness. This allows us to experience the specific contents including our bodies and ourselves as part of the world in consciousness. On a more conceptual level, long-term temporo-spatial alignment with “form” of consciousness between world, body, and brain may account for the bodily and ecological (and social) nature of consciousness, and thus for what is described as “embodiment” (Park and Tallon-Baudry, 2014), “embeddedness” (Thompson and Varela, 2001), “enactment” (Noë and Thompson, 2004) and “extendedness” (Clark and Chalmers, 1998) in philosophy. We suppose that all these different concepts can be traced to the one of “world-brain relation” which then can be understood in

both empirical (as here) and ontological (as in philosophy) senses.

4. Neural correlates: from “temporo-spatial expansion” of stimulus-induced activity to phenomenal features of consciousness

4.1. Temporo-spatial expansion: stimulus-induced activity – “temporal duration” and “spatial extension”

We so far discussed that the temporo-spatial nestedness of the brain’s spontaneous activity provides a neural predisposition of the level/state of consciousness (NPC). The temporo-spatial alignment of the brain’s spontaneous and/or pre-stimulus activity to single stimuli and long-term stimulus sequences in our body and the world is considered as a neural prerequisite of consciousness (preNCC). This leaves open the neural correlates of consciousness (NCC) – the neural mechanisms that are sufficient to associate specific contents with consciousness – that shall be the focus in the following.

How is the stimulus processed in neural terms such that it can be associated with consciousness? The data showed that the amplitude of stimulus-evoked neural activity can be considered a marker of consciousness: the higher the amplitude in response to the stimulus, the more likely the stimulus will be associated with consciousness (Koch et al., 2016; Tsuchiya et al., 2015). In addition, various lines of data showed that, comparing to unconsciousness processing, stimulus-induced activity during consciousness lasts longer and spatially more extended. This has been reviewed extensively in recent papers (Dehaene et al., 2014; Koch et al., 2016); for this reason we here only highlight some results on “temporal duration” and “spatial extension” (Fig. 7).

Li et al. (2014) measured slow cortical potentials in MEG during presentation of near-threshold visual stimuli. The MEG results showed long lasting event related magnetic fields (ERMF) between 300 ms and 2–3 s post-stimulus during seen trials when compared to unseen ones. The long lasting ERMF do not resemble oscillations but the slow DC-type drift, making it likely reflect slow cortical potentials in the slow frequency range between 0.1 and 5 Hz. Interestingly, the long lasting ERMF was specific for subjective awareness, e.g. seen vs unseen,

whereas they neither surfaced in objective performance, e.g. distinction between correct and incorrect trials, nor in confidence judgments. The long-lasting ERMF changes during seen trials were accompanied by widespread activity changes in temporal and fronto-parietal cortices. One can therefore suppose that slow cortical potentials shape stimulus-induced activity and its association with consciousness; this is further supported by the findings in phase and power analysis in the same study (Li et al., 2014).

The central role of temporo-spatial expansion is impressively demonstrated in the TMS-EEG experiments by the group around Massimini (Casali et al., 2013; Massimini et al., 2010). They applied TMS pulse (in premotor and parietal cortical regions) during both conscious and unconscious states in UWRS, anesthesia, and sleep. The degree of temporo-spatial expansion of TMS-induced activity varied considerably between conscious and unconscious states. During the conscious state, the TMS-pulse induced long duration and spatially extended activity. In contrast, both temporal duration and spatial extension of TMS-induced activity were much restricted during the unconscious state in anesthesia, UWRS, and sleep.

Why and how is it possible that the same TMS pulse leads to different temporo-spatial features of the stimulus-induced activities during conscious versus unconscious states? We assume that this is related to the spontaneous activity itself as well as its neural interaction with the TMS pulse, i.e. rest-stimulus (or rest-pulse) interaction (Northoff et al., 2010; Huang et al., 2015). The fact that stimulus-induced activity expands during consciousness suggests that the stimulus can better suppress the ongoing spontaneous activity: the better the stimulus interacts with the spontaneous activity and suppresses its ongoing fluctuations, the more likely the stimulus can expand the temporal duration and spatial extension of its own neural activity. Such suppression of the ongoing spontaneous activity by the stimulus can be measured by trial-to-trial variability (TTV), which has been shown on both cellular (Churchland et al., 2010) and regional (Ferri et al., 2015; He, 2013; Huang et al., 2015) levels of neural activity. The more the stimulus suppresses the variability of the ongoing spontaneous activity, the more (negative) interaction between spontaneous and stimulus evoked activity (He, 2013; Huang et al., 2015). While the exact neural mechanisms of such suppression of spontaneous activity fluctuations by the stimulus remain unclear, one would tentatively hypothesize that the temporo-spatial expansion of stimulus-induced activity is related to the suppression of ongoing activity and rest-stimulus interactions.

4.2. Temporo-spatial expansion: expansion vs integration – information integration theory (IIT)

How does the supposed temporo-spatial expansion of stimulus-induced activity as NCC stand in relation to integration and the Information Integration Theory (IIT) (Tononi et al., 2016; Tononi and Koch, 2015)? Putting in a nutshell, the main thesis of the IIT is that consciousness is based on information integration which has been mathematically formalized in the *phi* index, while, empirically, it has been operationalized by the perturbation complexity index (PCI) (Casali et al., 2013). One should also note that the concept of information in the IIT does not refer to information in terms of specific contents as traditionally or commonly understood (Tononi and Koch, 2015). Rather, within the context of the IIT, information refers to “how a system of mechanisms in a state, through its cause-effect power, specifies a form (*‘informs’ conceptual structure*) in the *space of possibilities*” (Tononi and Koch, 2015, p.8; italics by the present authors). Let us explicate that quote in the temporo-spatial terms of the TTC in the following; we will focus on those concepts highlighted by italics

How does information as *system of mechanisms in a state* specifies a form in the *space of possibilities* stand in relation to the here suggested “temporo-spatial expansion”? The data suggest that the stimulus both suppresses and enhances the neuronal features of the brain’s spontaneous activity. Temporo-spatial expansion is thus dependent and

ultimately based upon temporo-spatial nestedness and alignment: without proper degrees of temporo-spatial nestedness and alignment, the stimulus-induced activity will not be temporo-spatially expanded. One may assume that the constellation of the various temporo-spatial mechanisms (which, as we predict, will be complemented by various other temporo-spatial mechanisms in the future) corresponds to what Tononi described as “system of mechanisms”. We suggest that such “system of mechanisms” operates on temporo-spatial grounds hence our suggestion of the various “temporo-spatial mechanisms”.

What exactly is meant by “a state”? We suggest that “a state” refers to the brain’s spontaneous activity and, more specifically, its degree of temporo-spatial nestedness. The various temporo-spatial mechanisms, as suggested here, operate within the “space of the brain’s spontaneous activity and its temporo-spatial structure”: both temporo-spatial alignment and temporo-spatial expansion are based and dependent upon the spontaneous activity’s temporo-spatial nestedness. However, at the same time, the very same temporo-spatial nestedness is modulated by especially longer stochastically-based stimulus sequences; the “state”, i.e. the spontaneous activity’s temporo-spatial nestedness as we say, is not fixed but highly dynamic and malleable by itself.

How can we conceive the concepts of “*form (‘informs’ conceptual structure)*” and “*space of possibilities*” as raised in IIT in the temporo-spatial context of TTC? The TTC suggests that temporo-spatial alignment of the brain’s neural activity to the temporo-spatial structure of body and world provides a stochastically- and temporo-spatially-based “form” as background and third dimension (besides level/state and content) of consciousness. Therefore, we suggest that what the IIT describes as “form” can be traced to the stochastically-based virtual temporo-spatial structure or organization between brain, body, and world (i.e. the form of consciousness). More specifically, what Tononi describes as “conceptual structure” may then be traced to what we describe as “form” characterized by “temporo-spatial and stochastically-based structure” as ranging in a virtual stochastically-based way between world and brain (i.e., world-brain relation).

The very same “temporo-spatial and stochastically-based structure” as ranging between brain, body, and world provides the neural predisposition and prerequisite of consciousness (NPC and preNCC). This “temporo-spatial and stochastically-based structure” renders possible certain ways of temporo-spatial expansion and stimulus-induced activity while excluding others. If, for instance, the spontaneous activity’s various frequencies are already suppressed and non-reactive in the resting state, the stimulus will not be able to enhance them to expand its own stimulus-induced activity; this, in turn, makes impossible for its association with consciousness. Accordingly, what Tononi describes as “*space of possibilities*” may find its more specific neuronal mechanisms in temporo-spatial nestedness and alignment providing the NPC and preNCC – the “space of possibilities” is thus a space of possible temporo-spatial configurations.

In sum, we suppose that the here suggested temporo-spatial approach to consciousness (TTC) is well compatible with the IIT. “Integration” as in IIT is supposed to occur on temporal and spatial grounds rather than on sensory or cognitive grounds (Cromwell and Panksepp, 2011; Mudrik et al., 2014). Moreover, we regard the concrete temporo-spatial determination of specific neuronal mechanisms, i.e. temporo-spatial mechanisms, involved in consciousness as complementary to the more abstract notion of “information” in IIT. Future investigation may want to apply some of the mathematical and operational measures of the IIT in the context of the presumed temporo-spatial mechanisms of TTC.

4.3. Temporo-spatial expansion: phenomenal features of consciousness – “neuronal-phenomenal correspondence”

We so far discussed various neuronal mechanisms like temporo-spatial expansion and information integration. This leaves open the phenomenal features of consciousness including their relation to these

neuronal mechanisms. That shall be the focus in the following.

What are the phenomenal features of consciousness and how are the neuronally instantiated? This is the central question in both neuroscience and philosophy of consciousness. Phenomenal features refer to experience which is subjective rather than objective. Philosophers often describes phenomenal features by their qualitative character – qualia as the “what it is like” of experience (Nagel, 1974). Other phenomenal features concern the directedness of experience towards a specific content, e.g. intentionality (Searle, 2010), self-perceptiveness with first-person perspective, and others (Northoff, 2014, 2016).

Without going into detail, these phenomenal features must be distinguished from the cognitive features of consciousness. Phenomenal features concern the experience of a content as conscious whereas cognitive features allow to access and subsequently report that very same content. The distinction between phenomenal and cognitive features of consciousness is more or less mirrored in the conceptual distinction between non-cognitive and cognitive consciousness (Cerullo et al., 2015).

How can temporo-spatial expansion of stimulus-induced activity serve as neural correlate of the phenomenal features of consciousness? Buzsáki says that “perception goes *beyond* the stimulus” (Buzsáki, 2006). We now suggest that such “*beyond*” is central for the phenomenal features of consciousness and that it consists in temporo-spatial features. The stimulus itself can be characterized in temporal and spatial terms by its duration and extension. That contrasts with the experience or consciousness, within which the very same stimulus usually lasts longer and extends beyond its mere physical duration and extension. For instance, even though physically absent, we still hear the last tones of the melody and still see the last scene of the opera in a more temporally and spatially extended sense. In brief, the temporo-spatial features of the stimulus in consciousness thus expand “*beyond*” the ones featuring the stimulus in purely physical terms in that the former show longer “temporal duration” and more distributed “spatial extension”.

Where is such “temporo-spatial expansion” “*beyond*” the stimulus’s own physical duration and extension in consciousness coming from? We tentatively suggest that it comes from or, put differently, added to the stimulus by the brain’s spontaneous activity. The brain’s spontaneous activity shows a large temporal and spatial scale that extends far beyond the one of the single stimulus. For instance, the stimulus may show a duration of 100 ms which corresponds to alpha frequency or a duration of 1 s as mirroring delta frequency. The spontaneous activity, in contrast, includes a much wider variety of different frequencies as ranging from infraslow frequencies to faster ones. This carries major implications for how the stimulus is processed by the brain’s spontaneous activity, i.e. so-called “rest-stimulus interaction” (Northoff et al., 2010). When interacting with the spontaneous activity, the stimulus and its more limited temporo-spatial scale interact with a much larger temporo-spatial range of the brain’s spontaneous activity. This, in turn, makes possible to integrate, nest and contain the former within the latter. Such “nesting” or “embedding” may, for instance, be manifest in the stimulus-induced modulation of the spontaneous activity’s scale-free activity, which allows expanding the stimulus beyond its own original temporo-spatial scales.

Taken together, we hypothesize that the degree of “temporo-spatial expansion” of the stimulus beyond its own or original temporo-spatial features is closely related to the association of the stimulus/contents with the phenomenal features. Phenomenal features may then be regarded stochastically-based temporo-spatial features that show a certain degree of “temporo-spatial expansion” beyond the stimuli’s own temporo-spatial features on the purely physical level. There may thus be a “neuronal-phenomenal correspondence” between phenomenal features and the temporo-spatially expanded stimulus-induced activity. “Neuronal-phenomenal correspondence” in this sense yields “neuro-phenomenal hypothesis” (Northoff, 2014) while conceptually it may be described as “isomorphism” (Fell, 2004), “operational time-space” (Fingelkurts et al., 2013), or “identity” (Tononi et al., 2016).

Note that such “neuronal-phenomenal correspondence” consists between the brain’s neuronal activity and phenomenal features of consciousness. In contrast, “neuro-phenomenal correspondence” does not consist between the stimulus itself, i.e. its physical features in terms of time and space, and the phenomenal features of consciousness. There is thus a discrepancy between physical and phenomenal features of the stimulus – “physical-phenomenal discrepancy”. Taken together, we suppose that the temporo-spatial gap between physical and phenomenal features can be “filled” or bridged by the brain’s spontaneous activity and its temporo-spatial features. We thus assume that the temporo-spatial features of the brain’s neural activity provide a “common currency”, “missing link” or “glue” between the stimulus itself and the phenomenal features of consciousness.

5. Neural consequences: from “temporo-spatial globalization” of stimulus-induced activity to cognitive features of consciousness

5.1. Temporo-spatial globalization: stimulus-induced activity – early, posterior and medial cortical activity vs. late and lateral prefrontal cortical activity

How can we investigate and operationalize consciousness? The traditional way is to ask subjects whether they see or hear something and thus to make a judgment – this has recently been described as “report paradigm” (Tsuchiya et al., 2015). However, the judgment or report itself may introduce a cognitive component that may not belong to consciousness *per se*. The neural mechanisms underlying such judgment or report may thus be a neural consequence rather than neural correlate of consciousness (Aru et al., 2012). Therefore, “report paradigms” have been contrasted with “no-report paradigms” where the subjects do not need to report or give a judgment.

No-report paradigms reveal different spatial and temporal pattern than report paradigms. Several studies demonstrated that early components (like P50 and N100) of stimulus-induced activity (around 100 ms to 200–300 ms) indicate the presence and experience of a specific content in consciousness even if that the very same content may not yet be accessible for subsequent reporting (Andersen et al., 2016; Palva et al., 2005; Pitts et al., 2014a,b; Rutiku et al., 2016; Schurger et al., 2015). The central role of these electrophysiological markers of early stimulus-induced activity like N100 are reduced if not abolished in altered states of consciousness like anesthesia, slow wave sleep, and vegetative state (Bachmann and Hudetz, 2014).

How about the spatial side? “Report paradigms” show extensive involvement of especially the lateral prefrontal and parietal cortical regions (Tsuchiya et al., 2015). In contrast, “no-report paradigms” do not show prefrontal-parietal recruitment but rather posterior cortical regions at the interface between parietal, occipital and temporal cortex, described as “hot zones” (Koch et al., 2016).

Moreover, we need to consider the distinction between medial and lateral prefrontal regions. Lateral prefrontal regions are recruited during judgment, e.g. in “report paradigms”, as they are related to various cognitive functions including working memory. In contrast, due to the lower cognitive load during the absence of judgment, “no-report paradigms” lead to stronger involvement of medial prefrontal regions like the ventromedial prefrontal cortex (Northoff and Bermpohl, 2004). This is well compatible with the involvement of the midline regions in various forms of spontaneous mental activity associated with consciousness.

What does the operational distinction between “report and no-report paradigms” and their different neuronal correlates imply for our characterization of consciousness? The “no-report paradigms” reveal earlier event-related potentials as well as posterior cortical regions and/or cortical midline regions. It is mostly likely associated with the phenomenal features of consciousness, thus speak of neural correlates of consciousness (NCC) as detailed in the previous section. In contrast, if stimulus-induced activity is further temporally and spatially expanded

and lateralized to fronto-parietal cortical regions, the cognitive features of consciousness may predominate while the phenomenal features recede in the background. The late event-related potentials like the P3b and lateral prefrontal-parietal regions seem to be related to the cognitive functions rather than consciousness itself. They may thus index the ability to be aware of certain contents.

5.2. Temporo-spatial globalization: global neuronal workspace theory (GNWT) – cognitive features of consciousness

How can we specify the neural consequences of consciousness? Relying on “report paradigms”, the various findings supporting the Global Neuronal Workspace Theory (GNWT) showed later components like P3b and prefrontal cortical involvement (Dehaene et al., 2014). We will not recapitulate the various findings that support the GNWT as it has been reviewed in detail elsewhere (Dehaene et al., 2014; Dehaene and Changeux, 2011). The question is not so much whether late prefrontal activity is related to consciousness in general but rather to what feature of consciousness it is related. That shall be the focus in the following.

The GNWT postulates that the stimuli and their respective contents become globally available for cognition. Such globalizing and sharing is supposedly made possible by the architecture of the brain with especially lateral prefrontal and parietal cortex as a “global workspace” where the different functional systems of the brain (like memory, evaluative/reward, attentional, motor, and perceptual systems) converge and overlap. We describe that as “spatial globalization” of stimulus-induced activity (Fig. 8). Moutard et al. (2015) proposed a concept of “non-linear ignition”: the transition from local-regional to global prefrontal-parietal activity must be ignited by the stimulus in a non-linear rather than linear way. The exact neuronal mechanisms of such “non-linear ignition” of lateral prefrontal-parietal cortical activity remain unclear though.

In addition to its spatial component, the GNWT also considers temporal measures like late event-related potentials and high frequency oscillations like Gamma frequency band. Analogous to “spatial globalization”, such extension of neural activity to different temporal domains from the early sensory-based ERP like N100 (Bachmann and Hudetz, 2014) to later ERP (P3b) and higher frequencies may be described by the term of “temporal globalization”. Such temporal globalization seems to be deficient in altered states of consciousness where

the temporal extension of later ERP is reduced, and higher frequencies’ power is reduced too (Koch et al., 2016; Sitt et al., 2014).

Which feature or aspect of consciousness does “temporo-spatial globalization” of stimulus-induced activity (as suggested in GNWT) target? Relying on “report paradigms”, the GNWT indexes consciousness by accessing and reporting the contents of consciousness. The lateral prefrontal-parietal cortex and the late components of stimulus-induced activity from 300 ms to 500 ms like P300 (or even longer up to 800 ms) are strongly associated with cognitive functions like selective attention, expectation, self-monitoring, and task planning and reporting (Tsuchiya et al., 2015). These cognitive functions may allow to access and reporting the stimuli and their respective contents in consciousness. On the neuronal level, temporo-spatial globalization of stimulus-induced activity occurs later as a consequence of earlier neural processes such as alignment and expansion. We therefore suppose that consciousness comes prior to cognition and serves as its trigger or initiator rather than cognition being prior to consciousness. Therefore, temporo-spatial globalization of stimulus-induced activity as required for accessing and reporting the contents in consciousness must be distinguished from consciousness itself, thus speak of the “neural consequence of consciousness” (NCCcon).

6. Conclusion

Time and space are the central and most basic building blocks of nature; as the brain is part of nature, this also applies to the brain in general and, more specifically, how it constitutes neuronal activity. For this reason, the TTC conceives both brain and consciousness in primarily temporo-spatial terms – consciousness is a temporo-spatial phenomenon that is based on and emerged from the temporo-spatial features of the brain’s neural activity.

We postulated four different temporo-spatial neuronal mechanisms, which are central in constituting the brain’s inner time and space, thus, in turn, generating different dimensions of consciousness. (i) Temporo-spatial nestedness is related to the level/state of consciousness as NPC. (ii) Temporo-spatial alignment accounts for the content and form of consciousness as preNCC. (iii) Temporo-spatial expansion is relevant for the phenomenal consciousness as NCC. (iv) Temporo-spatial globalization accounts for the cognitive features of consciousness mirroring NNCcon. The four mechanisms together amount to what we describe as “temporo-spatial theory of consciousness” (TTC).

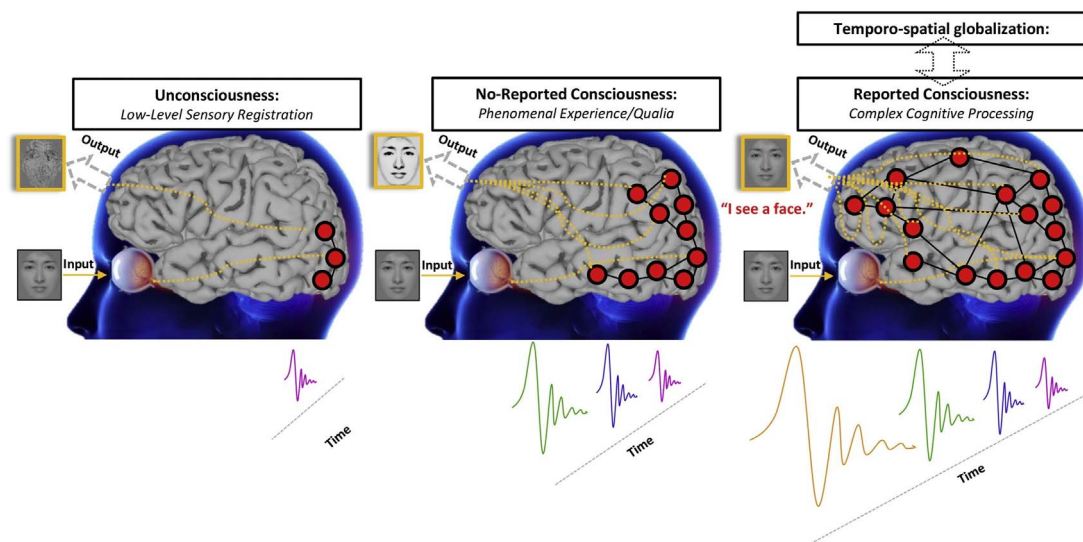


Fig. 8. Temporo-spatial globalization. On the left panel, the content of external inputs (e.g. face) remain unconscious during low-level sensory registration, with limited temporo-spatial expansion, in the brain. On the middle panel, subjective and phenomenal experience occurs when temporo-spatial expansion in the brain activity reaches a certain extent, e.g. activation spreads to the posterior “hot zones”. This relates to the “no-report” consciousness. On the right panel, the subjects are able to “report” the content of external inputs when the temporo-spatial expansion is globalized (e.g. the involvement of lateral fronto-parietal networks). This “temporo-spatial globalization” is concomitant with complex cognitive processing.

How are the four different temporo-spatial mechanisms related to each other? The four mechanisms can be distinguished from each other by their temporal and spatial scales. “Temporo-spatial nestedness” is supposedly based on the spontaneous brain activity, which has the largest temporal-spatial scales relative to other mechanisms. We consider “temporo-spatial nestedness” as the most basic and fundamental mechanism that bridges all the other mechanisms. In this sense, the nestedness of the brain activity is central for yielding consciousness and binding its different dimensions.

7. Limitations and outlook

Finally, it shall be mentioned that we are well aware that the TTC as formulated here finds itself in a rather immature state leaving out several issues:

- (i) The relationship between consciousness and self (which also has a long philosophical history) is left open in TTC; this is especially relevant given that the brain’s spontaneous activity strongly overlaps with self and self-related processing, i.e. “rest-self-overlap” (Qin and Northoff, 2011). The self may thus be one dimension or, even stronger, predisposition of consciousness that needs to be considered in the TTC in the future;
- (ii) The social aspect of consciousness as it has been formulated in the “attention schema theory” (Graziano and Webb, 2015) is neglected here – the TTC considers the social aspect and thus the relationship between different persons and their brains in the temporo-spatial terms of alignment to body and world as shown above – more detailed work is needed in investigating the temporo-spatial features of inter-personal relationships;
- (iii) We here focused only on systems level of the brain while neglecting its cellular and molecular levels with their potential relevance for consciousness (e.g. Changeux, 2017); the TTC would conceive different levels from genetic over molecular and cellular to regional, network, and global levels in temporal and spatial terms – the better the different temporo-spatial scales of the different levels are integrated and nested into each other, the more likely consciousness will occur;
- (iv) The coding of the brain’s neural activity was completely neglected. One of the major theories is predictive coding (Friston, 2005) which would probably be related to both temporo-spatial alignment and expansion; however, it is primarily a theory of brain activity rather than a theory of consciousness;
- (v) The temporo-spatial mechanisms suggested here can be tested in various neurologic and psychiatric disorders. Specifically, we suppose the following relationships: (i) temporo-spatial nestedness is impaired in patients suffering from disorders of consciousness corresponding to abnormal level/state of consciousness; (ii) temporo-spatial alignment is altered in psychiatric patients (e.g. schizophrenia, depression and bipolar disorder) corresponding to abnormal form of consciousness; (iii) temporo-spatial expansion and globalization are impaired in neurologic lesion patients that show specific changes in content-related phenomenal features and/or cognitive aspects of consciousness.
- (vi) How the TTC is related to and possibly account for more philosophical questions like the “hard problem” and mind-body problem? The TTC takes the stance that time and space are not only empirically but also ontologically relevant, i.e. reflecting existence and reality. Time and space constitute the brain’s existence and reality – the brain’s neural activity is temporo-spatial – as it were otherwise it would not exist. If the brain no longer constitutes its own inner time and space, the brain is dead, i.e. it ceases to exist. This requires a temporo-spatial “ontology of brain” which may also be highly relevant for consciousness and the mind-body problem. Consciousness is then primarily temporo-spatial and does no longer require the assumption of the existence and reality of a

mind – the mind-body problem can be replaced what one of us describes as “world-brain problem”.

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