

# Neuroscience and Whitehead I: Neuro-ecological Model of Brain

Georg Northoff<sup>1</sup>

Received: 4 December 2015 / Accepted: 16 March 2016 / Published online: 12 April 2016  
© Springer Science+Business Media Dordrecht 2016

**Abstract** Neuroscience has made enormous progress in understanding the brain and its various neuro-sensory and neuro-cognitive functions. However, despite all progress, the model of the brain as well as its ontological characterization remain unclear. The aim in this first paper is the discussion of an empirically plausible model of the brain with the subsequent claim of a neuro-ecological model. Whitehead claimed that he inversed or reversed the Kantian notion of the subject by putting it back into the ecological context of the world, the so-called reformist subjectivist principle. Based on empirical evidence about the experience-dependence of the brain's spontaneous activity, I argue for an analogous inversion or reversion with regard to the model of brain: empirical evidence is well compatible with a neuro-ecological model which extends beyond and integrates both Humean neuro-sensory and Kantian neuro-cognitive models. I conclude that a neuro-ecological and process-based model of brain and its relationship to the world may offer a novel model of brain that carries major ontological implications as they shall be discussed in the second paper.

**Keywords** Kant · Whitehead · Brain · Neuro-ecology · Resting-state · Process philosophy

---

✉ Georg Northoff  
georg.northoff@theroyal.ca;  
<http://www.georgnorthoff.com>

<sup>1</sup> Mind, Brain Imaging and Neuroethics, Institute of Mental Health Research, University of Ottawa, Ottawa, Canada

# 1 Introduction

## 1.1 General Background

Neuroscience has made major progress in the last 20 years in understanding the brain and its neural activity. Major discoveries show for instance the neuronal mechanisms underlying various kinds of perceptual and cognitive functions. However, despite all the progress, the central question of how the brain's neuronal activity is related to mental features, like consciousness, remains open. This question is not only empirically relevant for neuroscience in order to reveal the so-called neural correlates of consciousness (Crick and Koch 2003; Koch 2004; Northoff 2014a, b, c) but touches also upon theoretical issues like the model of brain as well as ontological questions regarding how to characterize the brain's existence and reality.

The model of brain presupposed most often in past and present neuroscience is akin to the model of mind put forward by David Hume (2012). Hume conceived the mind as passive in that its activity is sufficiently determined by the external sensory stimuli without any active contributions by the mind itself. Analogously, the brain and its neural activity are characterized by external stimuli and therefore in a passive way amounting to what recently has been described as an extrinsic model of brain (Northoff 2012c, 2016a; Raichle 2009, 2010, 2015). However, most recently, the discovery of neural activity within the brain itself independent of any specific external stimuli, e.g., the brain's spontaneous activity (see below for definition at the end of the introduction) as it is described, has led to suggestions for an intrinsic rather than extrinsic model of brain (Northoff 2012c; Northoff 2014a; Raichle 2009, 2010).

As noted by recent investigators (Churchland 2012; Fazelpour and Thompson 2015; Northoff 2012a, b, 2014a, b, c, 2016b), such an active rather than a passive model of brain featured by its spontaneous activity is somewhat akin to the model of mind suggested by Immanuel Kant (1998). Kant suggested that the mind shows spontaneous activity that shapes the mind's response to external stimuli and is indispensable, e.g., necessary for mental features like consciousness. Which model of brain is empirically most plausible—do we need to base our empirical-experimental investigation upon a Humean or Kantian model of brain or a yet to be defined alternative model of brain? The question for the model of brain is the major aim in this first paper.

## 1.2 General and Specific Aim and Main Assumption

The *general aim* in this paper is to develop a tentative model of brain in neuro-ecological and process-based terms. Such neuro-ecological model of brain requires a process-based ontology as developed by Whitehead. This provides an alternative to the most often presupposed neuro-cognitive model and property-based characterization of brain in the current philosophical (and neuroscientific) debate about mental features and their relationship to the brain (see for instance Churchland

2012; Thagard 2012). I here focus exclusively on the brain itself and the development of a neuro-ecological model and process-based characterization. In contrast, I leave open the explicit discussion of how the brain stands in relation to mental features like consciousness which ontologically touches upon the mind-brain or mind–body problem (see for instance Griffin 1998 and Pred 2005 for a discussion of the mind–body problem in a process-based ontological context) (see Northoff 2016b for a further discussion of this question).

The *specific aim* in this paper is to investigate different models of brain, e.g., neuro-sensory (Hume) and neuro-cognitive (Kant), and to develop a neuro-ecological (Whitehead) model of brain. Based on recent empirical evidence, I suggest that neither the Humean neurosensory nor the Kantian neuro-cognitive model of brain is empirically plausible. Instead, both need to be extended and put into the wider context of a neuro-ecological model of brain as based on Whitehead. Such neuro-ecological model conceives the brain and its spontaneous activity within the ecological context of the environment which, philosophically, is well compatible with some of the concepts (like prehension and his understanding of the notions of subject and object) as developed by Whitehead. The fundamental concepts by Whitehead will be introduced in part I while empirical data will be presented in part II. That serves as springboard to develop a neuro-ecological model of the brain as in part III.

### 1.3 Definitions

One may want to shed a brief light on the definition of the brain's spontaneous activity. One can define the concept of spontaneous activity in a purely neuronal (or even metabolic-energetic) sense independent of any associated cognitive and mental features like task-related thought, mind wandering, self-relatedness etc. (see Northoff 2014a; Raichle 2015). In that case the spontaneous activity features only the brain itself in exclusively neuronal terms while its psychological, e.g., cognitive, and mental, e.g., consciousness features, are neglected (see for instance Raichle 2015). Alternatively, one may focus more on the psychological, e.g., cognitive, features of spontaneous activity as it is often done in psychological investigation (paralleling more or less Kant's focus on the cognitive features of the mind's spontaneous activity). I here refrain from such psychological, e.g., cognitive, and wider definition of spontaneous activity. Instead, I here presuppose a narrow determination of spontaneous activity that focuses only on its neuronal features independent of its psychological (and mental) features (see Raichle 2015).

One may also doubt whether the spontaneous activity remains really independent of external stimuli. The operational definition of the spontaneous activity, as it surfaces in the concept of the resting state, is that it shall remain independent of specific tasks or stimuli (see Logothetis et al. 2009; Northoff 2014a) at one particular discrete point in time and space. This nevertheless opens the door for unspecific stimuli that may occur temporally in a less discrete and more continuous way like the continuous input of the heartbeat to the brain. The difference between spontaneous and stimulus-induced activity may thus not be absolute, e.g., consisting in the presence or absence of stimuli or tasks per se, but rather relative, e.g., as

related to spatiotemporal differences (see below as well as Klein 2014; Northoff 2014a). It is such a relative, e.g., spatiotemporal sense, of the concept of spontaneous activity as distinguished from stimulus-induced activity that I presuppose here.

One may also shed a brief light on the concept of model. While I am not able to go into detail about the concept of model, I understand models here as theoretical frameworks whose validity can be tested by comparing them with empirical data. Taken in a Whiteheadian sense, models may be conceived as abstractions in that they are detached or abstracted from specific processes which allows them to integrate various lines of different processes under one “umbrella”, e.g., model. Models are thus approximations that remain open to continuous specification and correction in the light of novel empirical data.

Before going ahead, we shall briefly touch upon the notion of the brain. The concept of the brain may be restricted to the human brain which presupposes a rather narrow notion of brain. Alternatively, one may also include animal brains; that opens a heterogeneity though since there are animals with a brain somewhat resembling the human brain like non-human primates as well as creatures like *C. elegans* that only possess about 300 neurons. If one excludes the latter and focuses only on those animals with a brain resembling the one of humans, one may presuppose a moderate concept of the brain (as distinguished from narrow and wide notions). If, in contrast, one opts to include any creature with any kind of nerve cells, one may suppose a wide concept of the brain. For the sake of simplicity, I here suppose a moderate notion of the brain.

## 2 Part I: Process-Based Ontology: Subject (Kant) Versus World (Whitehead)

Kant conceived the subject by activity or spontaneous (see below), which he deemed to be central for yielding mental features like consciousness. However, the question arises how such a spontaneous subject stands in relation to the world, namely whether the subject can be characterized in an ecological way. This is the question Whitehead raised which I will discuss in this part of my paper.

### 2.1 “Reformed Subjectivist Principle” and “Ontological Inversion” of Kant

David Hume conceived of mere stimuli originating in the external world as sufficient for our perception and cognition of objects and events in that very same world. Our mind merely puts these different stimuli together by associating them. This means that the activity of the mind is completely and exclusively determined by the stimuli from the external world, the world’s contribution as I will describe it in the following. Kant opposed such a view of the mind. He argued that we would not cognize and, even more important, know anything about the world if the mind were merely associating stimuli from the external world, the world’s contribution.

Mere association of the various stimuli from the world is simply not sufficient for obtaining knowledge about the world.

In order to obtain possible knowledge about the world, our mind itself needs to provide additional input, an intrinsic contribution by the subject, the subject's contribution. Based on his transcendental reasoning, Kant (1998) assumed that the contribution of the mind, the subject's contribution, must consist in the categories that provide a logical form or template that allows structuring the world's contribution in such way that we can perceive and cognize and ultimately know the world including its various events and objects. Kant focused therefore on the epistemological question of the necessary mental conditions of possible knowledge, for which reason one may speak of mental predispositions of knowledge.

How does Kant characterize the subject's contribution? He argues that the subject provides activity or spontaneity to the otherwise merely passive or receptive processing of the stimuli from the world. The subject is continuously active as for instance in its thoughts that remain independent of any external stimuli from the world; for that reason the subject can be characterized by spontaneity. Moreover, the subject provides homogenous unity within which the heterogeneous diversity of the different stimuli from the world must be integrated in order to yield mental features like self and consciousness. Such unity can also be understood in terms of a spatiotemporal structure as it will become particularly relevant when transposing Kant's model to the brain (see below).

Where does the subject's contribution originate and how is it constituted? Though strongly debated within the Kantian literature, the exact origin and constitution of the subject's contribution, e.g., the categories and their logical forms and templates, remains unclear. Kant himself seemed to have argued for an innate origin and constitution of the subject's contribution.

This is the moment where Whitehead steps in. He argues that we need to put back the subject and its contribution into the ecological context of the world. For that we need to invert or revert the relationship between subject and world: Kant conceived the world to originate within the subject, whereas Whitehead argues to invert the relationship between world and subject when assuming the subject to be constituted and originate within the world; he writes "The philosophy of organism is the inversion of Kant's philosophy. The Critique of Pure Reason describes the process by which subjective data pass into the appearance of an objective world. The philosophy of organism seeks to describe how objective data pass into subjective satisfaction, and how order in the subjective data provides intensity in the subjective satisfaction. For Kant, the world emerges from the subject; for the philosophy of organism, the subject emerges from the world—a superject rather than a subject" (Whitehead 1929/1978: 88) (see below for further explanation of the term superject).

How though can the subject, including the subject's contribution to its own cognition and knowledge of the world, emerge from that very same world? Whitehead argued that we need to reform the notion of subject. Kant assumed the subject to be a fixed, static and lasting entity that remains the same through time. Whitehead opposed such a view, and considered the subject and subjectivity in general as changing rather than fixed, dynamic rather than static, and perishing

rather than lasting. This leads him to assume what he describes as the “reformed subjectivist principle” (Whitehead 1929/1978: 157, 160, 167, 189): the “reformed subjectivist principle” states that metaphysically there is nothing but the dynamic construction process of actual entities without there being anything else like a prefigured subject as a template that precedes or is prior to those dynamic construction processes (as Kant seems to assume).

In sum, one may want to speak of an “ontological inversion” in Whitehead. Kant considers the subject a contribution to our cognition of the world, while Whitehead regards the subject merely as a result, a “superject,” of the continuous ongoing construction processes in the world. The subject is here put in the ontological context of the world and its construction processes as distinguished from Kant’s more epistemological context; for that reason one may characterize Whitehead’s inversion as ontological.

## 2.2 Dynamic Construction Processes in the World: Actual Entities, Occasions and Prehension

Whitehead is known for his process philosophy. Rather than assuming fixed, static substances and properties as basic ontological features, he suggested dynamic and flexible construction processes as the basic ontological features of existence and reality in the world. In order to account ontologically for such construction processes of existence and reality, he introduced concepts like ‘actual entities’, ‘actual occasions’, and prehension that shall be briefly explained in the following (without though going into the details of his account).

What are “actual entities”? One may consider the concept of “actual entities” to refer to the basic ontological building blocks of existence and reality in the world. To understand what that means we briefly have to reflect about past philosophy. Past philosophers, such as Descartes, determined actual entities in terms of substances, including for instance both mental, i.e. immaterial, and physical, i.e. material, substances. Within the framework of such substance or property-based ontology, brain and subject are conceived as substances or properties: the brain is usually characterized as a physical substance or property whereas the subject is featured by either a mental substance or property (as in Descartes and variants of dualism) or as mere physical property (as linked to the brain).

How about Whitehead? Whitehead rejected any determination of actual entities in terms of either substances or properties. He argued that actual entities consist in ongoing processes that are continuously changing rather than being fixed, dynamic rather than static, and perishing rather than enduring. These dynamic and continuously changing processes that underlie the construction of events and occurrences are the ontological building blocks of existence and reality in the world rather than properties or substances as assumed by past philosophers (or events as in event ontology as assumed by current day philosophers). Whitehead refers to these dynamic and continuously changing processes as what he describes as “actual occasions”. Any event or occurrence in the world, like your actual experience of reading this paper or the falling of a tree across the road, can be considered to be a manifestation of these dynamic construction processes, e.g., actual occasions:

“‘Actual entities’—also termed ‘actual occasions’—are the final real things of which the world is made of. There is no going behind actual entities to find anything more real. They differ among themselves: God is an actual entity, and so is the most trivial puff of existence in far-off empty space. [...] The final facts are, all alike, actual entities [...] The notion of ‘substance’ is transformed into that of ‘actual entity’” (Whitehead 1929/1978, 18f.).

Whitehead assumes that each actual occasion is generated on the basis of the former actual occasion so that there are continuous construction processes that mediate between different actual occasions and their respective actual entities. To denote the transitions from one actual entity to another, he introduces the concept of ‘prehension,’ which specifically refers to the dynamic processes between the actual entities. John Cobb (2008: 31) describes the concept of prehension in the following quote: “prehensions are the way that what is there becomes something here. A prehension is the bond between two actual occasions. The past occasion shares in the constitution of the new occasion. From this perspective, we can say that something there becomes something here. This is the “causal efficacy” of the past occasion for the new one. Returning to the point of the new occasion, we can say that the new occasion draws the past occasion into itself. Thus one and the same relation can be viewed as the causal efficacy of the past or a prehension in the present” (Cobb 2008: 31).

Without going into extensive detail, one may want to characterize the concept of prehension by three different features: (1) prehensions mediate between two actual occasions and make thereby possible the constitution of a new occasion; (2) prehensions feature an internal non-symmetrical relation: there is an internal, i.e. constitutive relation, between the past occasion and the later or present occasion with the two standing always in an asymmetrical relation to each other where the former is present in the latter while the latter, the later or present occasion, does not surface in the former; (3) prehensions link different temporal dimensions by providing internal asymmetrical relations between past, present, and future: due to the continuously changing dynamic construction processes with the construction of ever changing occasions, a future occasion may become a present occasion which in turn will fade away and thereby become a past occasion. Prehension thus allows for constructing both continuity and distinction between the three temporal dimensions of future, present, and past with regard to occasions.

### 2.3 Subject as Superject and Actual Occasion

Whitehead assumes the above described dynamic construction process, including actual entities, actual occasions, and prehensions, to operate on all levels of ontological reality and existence. This includes the subatomic, i.e. quantum level, the atomic or micro-level, and also higher macro-levels including the level of humans and persons extending to societies as wholes (where he speaks of “societies” and “nexus”). Taken in this sense, the subject is ultimately nothing but an actual occasion that results from previous actual occasions, and so forth. The subject understood in this way is then no longer a fixed, enduring, and static entity in terms of a mind, a monad, a subject as taken in the Kantian sense. Instead, the

subject is now nothing but an actual occasion that is continuously changing, dynamic and not enduring as in the sense of Kant.

Whitehead introduced the concept of “superject,” which describes the new occasion as resulting from past occasions on the basis of prehension. In addition to the enduring, static, and fixed features of the traditional notion of subject, the concept of superject also entails the rejection that the subject is the agent of all action and movement. The notion of agent presupposes a stable fixed and enduring entity that can serve as the origin and cause of action and cognition. If, however, there is no such stable fixed enduring entity anymore, any assumption of an agent as cause and origin of action and cognition becomes impossible. There is simply no subject or agent anymore to which action and cognition could be ascribed.

Instead of the subject as agent being the source of all action and movement and the resulting events or occurrences, action and movement occur prior to and through the subject with the latter being the dynamic and changing manifestation of the continuously ongoing actions and movements. Since it is based on actual occasion, the subject as superject is based on prehensions and their different features: The superject is an actual occasion that, as based on prehension, is internally, e.g., constitutively, though asymmetrically related to past occasions, meaning that the superject is intrinsically and asymmetrically linked to its past that surfaces in the present while the latter does not surface in the former. However, despite the fact that the past surfaces in the superject as based on the present occasion, the superject cannot be reduced to its past occasions because of the continuously ongoing change and the dynamic construction processes. Accordingly, the superject is intrinsically temporal while it is not determined by one particular temporal dimension, i.e. past, present, or future, but rather by their continuous relationship.

How about the relation between subject and object? Traditionally, philosophy opposes the concepts of subject and object. Kant, for instance, conceived the subject as the subject of cognition and knowledge that targets the object as originating in the world. Hence, subject and object are signified by different epistemological roles and origins: the subject is the active agent and source of cognition and originates in the mind (as often believed to be outside the world), whereas the object is the passive recipient of cognition, which originates in the world.

This dichotomy between subject and object changes once one re-determines the subject as superject. In this case, subject and object are no longer mutually exclusive but rather complementary with their relationship no longer fixed. The subject as superject signifies an actual occasion in the present that results from a past actual occasion that signifies an object for the former. However, based on prehension, even the present actual occasion will become a past actual occasion and thus an object. The concepts of subject and object are consecutively functions of one and the same underlying dynamic construction process in terms of actual occasions and prehensions. Subject and object are no longer mutually exclusive as in Kant but rather complementary as distinct aspects or stages of one and the same underlying dynamic construction processes. Accordingly, the concepts of subject and object can be conceived as dynamic features rather than as either epistemological (as in Kant) or ontological properties (as in Descartes 2008), who assumes first and third-



person ontology as an ontology of subject and object (see also Wiehl 1990: 219, 220).

Whitehead defines the subject as superject and thus as an actual occasion based on prehension of past actual occasions. Since there is continuous construction of actual occasions, the subject as superject underlies and consists in dynamic construction processes including their internal asymmetrical relations to past actual occasions and temporal characterization. Most importantly, the construction of an object as past actual occasions entails the perishing of the subject as the present actual occasion (see Ford 1998: 237). There is consecutively no longer a fixed, static and enduring subject anymore as in the sense of Kant. Instead, the subject as superject is transitory rather than enduring. Such determination of the subject opens the door for conceiving the dynamic construction processes themselves prior to and independent of both subject (as superject and outcome of these processes) and object. Whitehead complained therefore about an “excess of subjectivity” in Kant (Whitehead 1929/1978: 15) which, one may add metaphorically, blurred Kant to see the ontological ground behind the epistemological curtain.

### 3 Part II: Empirical Evidence—Experience-Dependence of the Brain’s Spontaneous Activity as “Basis or Bottom Layer”

After having discussed the transition from subject to world (as Whitehead’s inversion of Kant), we are now ready to focus on the brain and how it relates to the world. Analogous to the question for the relationship between subject and world, as raised by Whitehead, one may want to focus on how the brain and its spontaneous activity stand in relation to the world. This shall be the focus in this second part, which I will also discuss recent empirical evidence.

#### 3.1 The Brain’s Spontaneous Activity I: Spatiotemporal Structure

In order to develop an empirically plausible model of brain, we need to understand some empirical features of the brain’s spontaneous activity. This shall be the focus in this subsection. The brain’s spontaneous activity exhibits a certain spatial and temporal structure. Neuroimaging techniques like fMRI and EEG focused initially strongly on stimulus-induced activity that concerns the brain’s response to sensorimotor, cognitive, affective or social stimuli or tasks, i.e. stimulus-induced or task-evoked activity. However, for all the progress in investigating the brain’s stimulus-induced activity and its various functions, how the brain yields its neural activity remains still unclear. Recent neuroimaging has shifted to the brain’s spontaneous activity, its so-called resting state activity that can be characterized by a particular spatial and temporal structure.

Roughly, the brain’s spontaneous activity or resting state activity describes the brain’s neural activity in the absence of any specific tasks or stimuli (Logothetis et al. 2009). Initially it was thought that resting state activity is contained to particular neural networks like the DMN (see also Klein 2014). However, it soon became clear that the resting state activity is not limited to the DMN but pervasive

throughout the whole brain. Specifically resting state activity seems to be organized in different neural networks including the central executive network (CEN), salience network (SN), and the sensorimotor network (SMN) (see Klein 2014). Even in regions as dependent on external stimuli as the sensory cortices there is neural activity, e.g., resting state activity in the absence of any sensory stimuli. There is continuous neural activity throughout the whole brain going on in the absence of external stimuli.

In order to better understand how the brain's resting state activity is related to the world, we need to better understand the empirical details of its spatial and temporal structure. This, as well shall see, carries important implications for the model of the brain. Hence let us start with some empirical details. Spatially, the brain's intrinsic activity can be characterized by different neural networks such as the default-mode network (DMN), the cognitive-executive network (CEN), the salience network (SN), and the sensorimotor network (see Cabral et al. 2014; Deco et al. 2013; Ganzetti and Mantini 2013; Menon 2011; Raichle 2009; Raichle et al. 2001). The DMN concerns mainly cortical midline regions and the bilateral posterior parietal cortex (Buckner et al. 2008; Raichle et al. 2001). These regions seem to show high resting state activity, dense functional connectivity, and strong low frequency fluctuations (0.001–0.1 Hz) in the resting state.

The executive network comprises the lateral prefrontal cortex, the supragenual anterior cingulate, and posterior lateral cortical regions as core regions, as these are involved in higher-order cognitive and executive functions. The executive network is often subdivided into the fronto-parietal network and dorsal attention network (Ganzetti and Mantini 2013). The salience network includes regions like the insula, the ventral striatum, and the dorsal anterior cingulate cortex, which are associated with reward, empathy, intero/exteroception and other processes involving salience (see Menon 2011; Wiebking et al. 2011). Finally, there is the sensorimotor network that is often subdivided into the auditory, somatomotor, and visual networks (see for instance Ganzetti and Mantini 2013 for a recent review).

In addition to the strong functional connectivity between regions within each network, there are also plenty of interactions between networks. For instance, the DMN and the executive network are often observed to be anticorrelated meaning that the functional connectivity of their respective regions correlates negatively with each other (Ganzetti and Mantini 2013).

Most importantly both functional connectivity within and between networks is not static but rather dynamic being subject to continuous changes and temporal variation, as induced either spontaneously or by specific stimuli or tasks (Di and Biswal 2013; Hutchison et al. 2013). The degree of change in the resting state activity within the various regions, its variability, may by itself be important and be coupled to the functional connectivity between regions in though yet unclear ways (Di et al. 2013). Due to the various neural networks and their dynamic functional connectivity within and between networks, the brain's resting state activity seems to generate a particular spatial structure.

### 3.2 The Brain's Spontaneous Activity II: Experience-Dependence

Where does the spatiotemporal structure in the brain's spontaneous activity originate and how does it come into the brain? Based on recent empirical data, Sadaghiani and Kleinschmidt (2013) suggest that the spontaneous activity's spatiotemporal structure is dependent on prior experience of the respective subject. Severe life trauma in early childhood may affect the exact spatial structure of the spontaneous activity like the balance between for instance DMN and CEN. They consequently speak of the experience-dependent nature of the spontaneous activity's spatiotemporal structure.

How can we further detail the experience-dependence of the spontaneous activity's spatiotemporal structure? For that I turn to a recent psychological and imaging study by Duncan et al. (2015). Duncan investigated healthy college students, i.e. without any neurologic, psychiatric or medial disease, with a psychological questionnaire that assessed early childhood trauma, the Childhood Trauma Questionnaire (CTQ). Using fMRI he measured the spatiotemporal structure of the resting state activity, as indexed by entropy. Roughly, entropy reflects the statistically-based degree of complexity (or disorder) of the signal (as measured in fMRI) across time (and space) within the brain and, more specifically, how much the signal at one point in time (and space) is different from the signal obtained at the subsequent and later points in time. Therefore, one can say that entropy can be regarded as a statistically-based measure of the spatiotemporal structure of the brain's resting state activity.

How did the early childhood trauma affect the entropy, i.e. the spatiotemporal structure, of the brain's intrinsic activity in a particular region, namely the perigenual anterior cingulate (PACC; it is highly relevant for processing personal relevance or self-relatedness; see Northoff 2014b, 2006) in later adulthood? The subjects who scored high for early childhood trauma showed higher degrees of entropy in the PACC intrinsic activity in early adulthood. Specifically, we observed significant correlation between PACC entropy and their questionnaire score: the higher the degree of early childhood trauma, the higher the degree of PACC entropy in the brain's intrinsic activity later at early adulthood. This result suggests that higher degrees of early childhood trauma became encoded into the temporal structure, i.e. entropy of the brain's intrinsic activity at the time and persisted until early adulthood.

More generally, events in the world impact and modulate the brain's intrinsic activity in such way, i.e. in a statistically-based and spatiotemporal way, that they can become traumatic events for the respective person. The spatiotemporal structure of the brain's intrinsic activity may therefore serve as "spatiotemporalized memory" of how the world impacted and modulated the brain and its spontaneous activity's spatiotemporal structure. Such "spatiotemporalized memory" seems to be encoded implicitly and automatically in terms of spatiotemporal features rather than in terms of specific contents in the traditional concept of memory, e.g., cognitive memory as one may want to say (see Sadaghiani and Kleinschmidt 2013).

Framing it in terms of Whitehead, one may be inclined to say that what I describe here as "spatiotemporalized memory" may be featured by what he calls "subjective

form” whereas “cognitive memory” may correspond to his concept of “objective content”: the way the spatiotemporal structure is arranged and organized is subjective according to the life experiences of the respective subject, e.g., person while the cognitive memory concerns contents as they are shared across different subjects, e.g., persons. Whitehead also characterized such basic level of experience as in “spatiotemporalized memory” by emotions rather than cognition. Our empirical example does indeed show that such “spatiotemporalized memories” are highly emotional, e.g., affectively loaded, as manifest in the subject’s abnormal reaction to aversive stimuli (see below). However, the exact empirical relationship between the brain’s resting state and affect/emotions remains unclear at this point in time.

### 3.3 The Brain’s Spontaneous Activity III: Layers of Neural Activity

How did Niall Duncan further support his assumption that events in the world, i.e. early childhood trauma, impact and modulate the brain’s intrinsic activity? In addition to temporal measures of neural activity, i.e. entropy, using magneto resonance spectroscopy (MRS), Duncan also included biochemical measures, such as the resting state concentration of glutamate in the same region of the brain, the perigenual anterior cingulate cortex (PACC). Glutamate is a biochemical that is well known to be centrally involved in developing neural pathways from early childhood right after birth. Due to the neurodevelopmental role of Glutamate, one may assume that early childhood trauma may also affect the levels of Glutamate later in early adulthood.

Indeed, Duncan observed direct relationship between early childhood trauma and glutamate: the higher the degree of childhood trauma (as measured with CTQ), the lower the resting state concentration of glutamate in PACC. This suggests that a particular event in the world can impact and modulate the biochemical features of the brain’s intrinsic activity, its level of glutamate, in such way that the respective event may later be regarded as traumatic. Though the exact empirical relationship between early childhood trauma and Glutamate remains to be investigated, it is nevertheless clear that events in the world can also modulate and impact biochemical measures in the brain.

We have, however, omitted the question of how the changes in the brain’s intrinsic activity as related to early childhood trauma impact and modulate its subsequent functioning in later adulthood. To begin to answer this question, Duncan et al. (2015) included yet another component in their imaging experiment in fMRI, namely a task that applied aversive stimuli (a short painful tactile stimulus to the index finger) and measured its stimulus-induced or task-evoked activity. Neural activity (as with fMRI) was measured specifically during the anticipation of aversive stimuli.

Most interestingly, we observed that neural activity in the right anterior insula and the motor cortex during the aversive anticipation correlated significantly with all three measures: early childhood trauma, Glutamate concentration, and degree of entropy. Specifically, it correlated with the relationship between early childhood trauma: the higher the degree of early childhood trauma, the lower the degree of

stimulus-induced activity in right anterior insula and motor cortex during the anticipation of (a certain) aversive stimulus. Finally, using complex connectivity analysis, they demonstrated that the aversion-related neural activity in motor cortex and right anterior insula was modulated by the resting state activity in PACC and its degree of entropy.

The results by Duncan et al. (2015) are supported by other results from Nakao et al. (2013). The fMRI as used by Duncan et al. (2013) measures specifically infraslow frequency fluctuations (IFF) in neural activity (0.01–0.1 Hz). The role of IFF was specifically targeted in another study by Nakao et al. (2013). Using another technique, e.g., near infrared spectroscopy (fNIRS), they observed that resting state IFF in the lowest range ( $<0.04$  Hz) mediated, e.g., correlated with specifically early life events in childhood rather than late life events in recent adulthood.: the less power in the IFF in medial prefrontal cortex, the higher the degree of early childhood trauma. Since the IFF are major constituents of the spontaneous activity's spatiotemporal structure, e.g., its “temporal basement”, these findings against suggest that they encode early life events.

Moreover, the results demonstrated that the resting state changes in IFF this impacted decision making in adulthood: the higher the early life events, the more subjects relied on external rather than internal criteria in decision making, and the less power of IFF during rest and task. This means that their spontaneous activity's spatiotemporal structure could no longer serve as foil or template for providing criteria that serve to make decisions. More generally, the encoding of early life events into the spontaneous activity's spatiotemporal structure impacts our decision making in adulthood.

Taken together, the studies by Duncan et al. (2015) and Nakao et al. (2013) (and others; see Sadaghiani and Kleinschmidt 2013) show three different layers of neural activity. There is first and foremost the individually varying layer of stimulus-induced or task-evoked activity in response to aversive stimuli (Duncan et al. 2015) or a decision making task (Nakao et al. 2013) in the adult subjects. This is the layer that is most visible to us as outside observers at our present moment in time and can be probed easily by applying the respective stimuli or stimuli. One may thus want to speak of stimulus-induced or task-evoked activity as the “surface layer” of the brain.

Secondly, we can observe inter-individual differences in glutamate levels and entropy in the spontaneous activity of adult subjects. This second layer is more hidden and can be accessed rather indirectly through the stimulus-induced or task-evoked activity. One may therefore want to speak of a “hidden layer” in the brain's neural activity.

Thirdly, our results demonstrate that the inter-individually varying levels of glutamate and entropy and IFF (as well as the differences in stimulus-induced activity in response to aversive stimuli or decision making tasks) in adulthood are related to early childhood trauma. These findings reveal a third layer of the brain's neural activity where its spontaneous activity is closely intertwined with its respective environmental context as manifest in the encoding of early life events. Since the encoding occurs early in life and provides the neural basis for later

adulthood, one may want to speak here of a ‘basis or bottom layer’ in the brain’s neural activity.

### 3.4 The Brain’s “Basis or Bottom Layer” I: “Life Events as Real” Versus “Life Events as Perceived”

I shall here focus on third layer of the brain’s neural activity, the ‘basis or bottom layer’ that allows for the direct interaction between the brain’s spontaneous activity and environmental events in early childhood, in the following. Why? The interaction between the brain’s spontaneous activity and its environmental context in early childhood may be conceived as the most basic and fundamental layer since it affects and reverberates throughout both the second layer, e.g., spontaneous activity including its glutamate and entropy levels, and the first layer, e.g., stimulus-induced activity in response to aversive stimuli in later adulthood. What must happen during the interaction between spontaneous activity and environmental events in early childhood such that it affects spontaneous and stimulus-induced activity in later adulthood? For that we need to be clear what exactly the questionnaires of early life events, such as the CTQ as used by Duncan et al. (2015) measures.

The CTQ measures how an adult person perceives events in early childhood and more specifically whether she/he perceives them as traumatic. For instance, one and the same environmental event, e.g., bullying, may be perceived by one subject as traumatic. In contrast, another subject may have experienced the same kind of event, e.g., bullying, not at all as traumatic as it will be indicated in the CTQ. The CTQ thus measures the events as they are perceived by the subjects, e.g., whether they are perceived as traumatic, for which reason one may want to speak of “life events as perceived”. In contrast, the CTQ does not measure the life events as they are by themselves amounting to “life events as real” independent of the way subjects perceive them.

This entails that the concept of traumatic life events is strongly tied to the subjects and their perception: life events are not traumatic by themselves but become so only on the basis of their perception by the subjects. Traumatic “life events as perceived” are not merely “given” as such by the environment itself and then encoded (or represented; see below) by the brain. Instead, traumatic life events result from the interaction between environment and brain. The data suggest that certain not yet fully clear “neuro-ecological construction processes” (see below for details) mediate the encoding of life events into the brain’s spontaneous activity and its spatiotemporal structure in such way that they become (and are consequently perceived as) traumatic life events. The difference between “life events as real” and “life events as perceived” can consequently be traced to the difference between the environment itself and the environment-brain interaction.

How can we describe these “neuro-ecological construction processes” in empirical terms? Take the results by Duncan et al. (2015). The levels of entropy and glutamate in the spontaneous activity do not reflect the life events themselves independent of the subjects and their perception, e.g., “life events as real”. Instead, the changes in entropy and glutamate index the life events as they were encoded

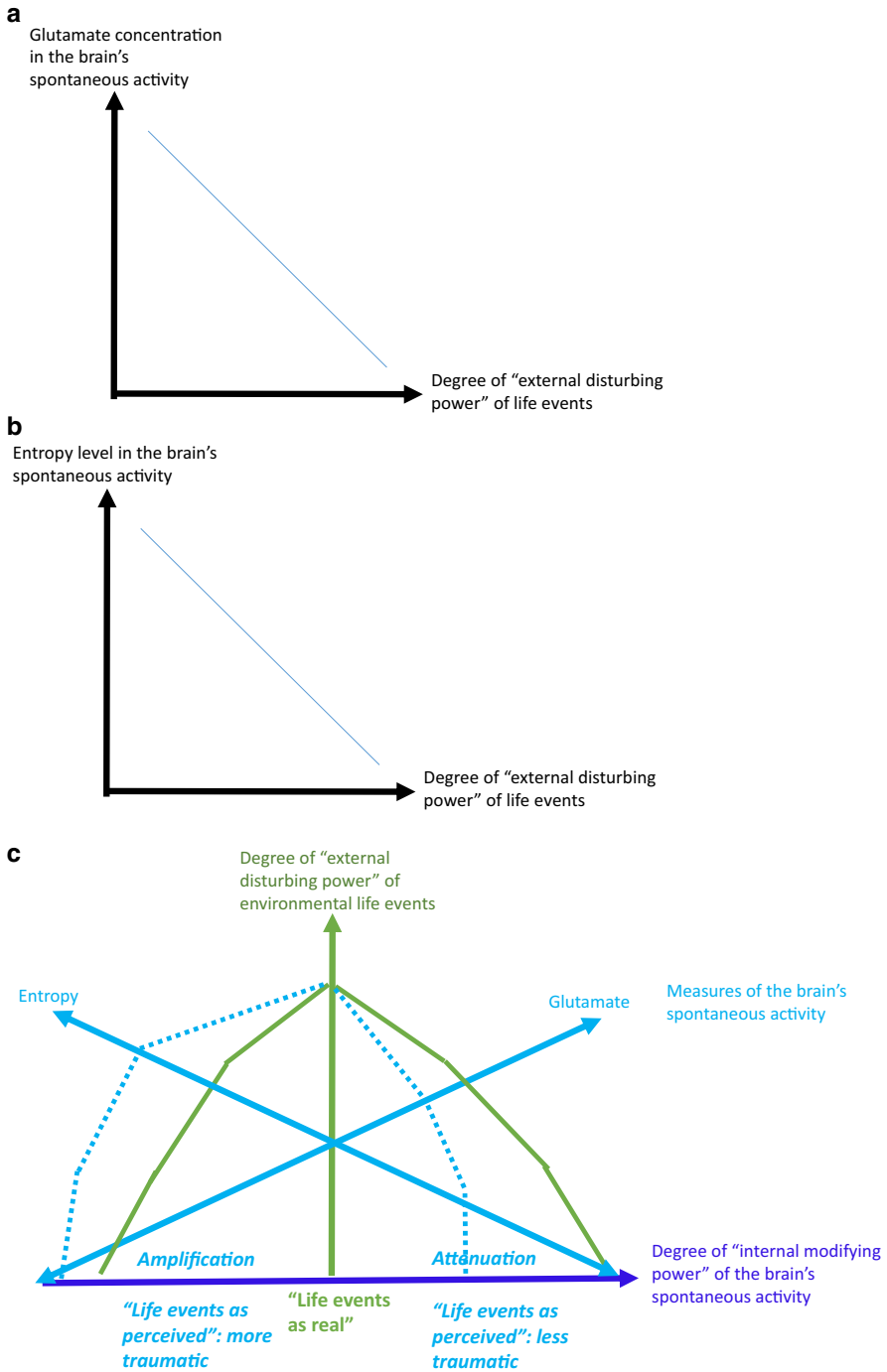
(and constructed) (in early childhood) and are now (in adulthood) (re-constructed) and perceived (e.g., experienced) by the subjects. During its encoding, the brain's spontaneous activity must have somehow modified the “life events as real” in such a way that they were transformed into “life events as perceived” and subsequently perceived as traumatic. Given the empirical findings by Duncan et al. (2015) and Nakao et al. (2013), one may be inclined to assume that the spontaneous activity's glutamate, entropy, and IFF (infraslow frequency fluctuations) play an essential role in such modification during the encoding of early life events as “life events as perceived”.

### **3.5 The Brain's “Basis or Bottom Layer” II: “Active Modification by Amplification or Attenuation”**

The modification of the early life events during their encoding by the brain's spontaneous activity is only possible if the latter directly interacts with the respective environmental context, e.g., the world. How can we detail such direct interaction between environmental context and the brain's spontaneous activity in empirical terms? Let us develop a scenario with three different subjects, which, despite being hypothetical, is nevertheless based on the data described above. A first subject may perceive the event of bullying as highly traumatic while a second subject may completely overlook or neglect and thus not even perceive that very same event. Finally, a third subject may perceive the same event but may not be affected by it thus remaining indifferent.

How can we conceive the interaction between environment and brain and thus the “neuro-ecological construction processes” with their encoding of environmental events by the brain's spontaneous activity in the three subjects? The first subject must have encoded the life event in a rather strong and thus amplified sense as indexed by high levels of entropy and low levels of glutamate in its spontaneous activity at adulthood. The opposite will be the case in the second subject that may have encoded the same life event in a rather attenuated sense as it shows high levels of glutamate and low levels of entropy. Finally, the third subject may have encoded the life event itself without strong amplification or attenuation as it may show intermediate levels in both entropy and glutamate.

The differences in encoding of one and the same life event suggests that the spontaneous activity is not modified by the environmental context in a merely passive way entailing “passive modification” of the former by the latter (as for instance suggested in the neuro-sensory model of brain; see below). Instead, the brain's spontaneous activity itself actively impacts and modifies the encoding of the life event into its own spatiotemporal structure entailing what I describe as “active modification” as distinguished from “passive modification”. As demonstrated in the three hypothetical subjects, such active modification can lead in its extremes to either amplification or attenuation of the life event during its encoding into the brain's spontaneous activity. I therefore speak of “active modification by amplification or attenuation” during the encoding of the environmental events by the brain's spontaneous activity.





◀ **Fig. 1** **a** Relationship between the brain's concentration of Glutamate and the "external disturbing power" of life events. **b** Relationship between the brain's level of entropy and the "external disturbing power" of life events. **c** Relationship between "life events as perceived" and the brain's spontaneous activity

How can we describe the brain's capacity for "active modification by amplification or attenuation" in more detail? Let us rephrase things in energetic terms. From the viewpoint of the brain, the life events in the environment exert an external power or energy that disturbs or perturbs the ongoing spatiotemporal dynamics in its spontaneous activity. Life events in the environment exert an "external disturbing power" on the brain's spontaneous activity. How can the brain's spontaneous activity deal and cope with the life events' "external disturbing power"? Either the brain is completely and arbitrarily affected by the life events' "external disturbing power" in which case it encodes the life events as they are by themselves into its spontaneous activity, e.g., as "life events are real".

Alternatively, the brain may exert itself a power by itself by means of which it can modify, e.g., amplify or attenuate, the impact of the life events "external disturbing power"; the life events are then encoded as "life events as perceived" rather than as "life events as real". The brain's modifying power may consist in its spontaneous activity (including its spatiotemporal structure) which may therefore be featured by an "internal modifying power". The spontaneous activity's "internal modifying power" prevents that the brain is affected and thus perturbed by the life events' "external disturbing power" in an arbitrary way. The evolutionary biologist William Powers points out the importance of such "internal modifying power" for organisms in general: "That world, on the other hand, is relatively incapable of altering the actions of organisms in an arbitrary way. This is the asymmetry of which I speak. It arises from the fact that organisms can draw on *internal power* supplies which are independent of the *energy contained in disturbances*" (Powers 1995: 126; *italics mine*).

How can we apply this to the data reported above? Specifically, such "internal modifying power" may be manifest in the levels of glutamate, entropy, and IFF. Glutamate mediates the brain's spontaneous activity on a neuronal level and thus the encoding of life events. At the same time, glutamate is directly coupled to the brain's energetic metabolism since it is converted from glutamine that is closely linked to the brain's energy and power supply. Our results suggest the following relationship: the less glutamate, the less glutamine is converted into glutamate, the less energetic supply is transformed into neuronal activity, the less the "external disturbing power" of life events can be modified, e.g., attenuated, during their encoding by the brain's spontaneous activity and its "internal modifying power", and the more the life events are perceived as traumatic. In short, low glutamate concentration may index low levels in the brain's "internal modifying power" (see Fig. 1a).

How about entropy? Entropy indexes the spatiotemporal structure of the brain's spontaneous activity: the more entropy, the less spatiotemporal structure, the less the brain's spontaneous activity can modify, e.g., attenuate the life events during their encoding, and the more traumatic the life events are perceived. Accordingly,

higher degrees in the spontaneous activity's entropy may index low levels in the brain's "internal modifying power" and subsequently a higher likelihood of being more strongly affected by the life events "external disturbing power". Finally, the data by Nakao et al. (2013) suggest that increased power in infraslow frequency fluctuations (IFF) may increase the brain's "internal modifying power" which, in turn, attenuates the effects of the life events' "external disturbing power" (See Fig. 1b).

In sum, the data and their interpretation suggest that the brain's spontaneous activity is both passively affected, or shaped, by environmental events and, at the same time, actively modifies, e.g., amplifies or attenuates that very same affection. What I described above as "neuro-ecological construction processes" may now be specified by the direct encounter and interaction between the environmental life events' "external disturbing power" and the brain's "internal modifying power" as related to its spontaneous activity's spatiotemporal structure. Specifically, the balance between the environmental life events' "external disturbing power" and the brain's "internal modifying power" may determine to which degree the "life events as perceived" deviate from the "life events as real" and consequently the degree to which life events are encoded and subsequently perceived as more or less traumatic (see Fig. 1c).

#### **4 Part III: Model of Brain—Neuro-sensory (Hume), Neuro-cognitive (Kant), and Neuro-ecological (Whitehead) Model**

##### **4.1 Passive Model of Brain: Neuro-sensory Model (Hume)—Stimulus-Response Determination of Stimulus-Induced Activity**

What model of brain is implied by the above discussed data? For that I first compare models of brain as they can be traced loosely to Hume's and Kant's models of mind.

Let us start with a Humean model of brain. In a nutshell, Hume argued that the mind passively receives external sensory stimuli and makes subsequent judgments from the resulting sense data (Hume 2012). Let us focus on especially the first aspect of Hume's model of mind, the passive receiving and processing of sensory stimuli. Such passive receiving and processing of sensory stimuli implies that the brain's neural activity is necessarily and sufficiently dependent upon the external stimuli it receives from body and environment. The resulting neural activity, stimulus-induced activity as it is called, is taken to be determined entirely by the external stimulus; the brain itself just passively processes the external stimuli and does not actively participate in constituting its own neural activity. Neural activity is consequently fully, that is necessarily and sufficiently, determined by stimulus-induced activity as related to single stimuli.

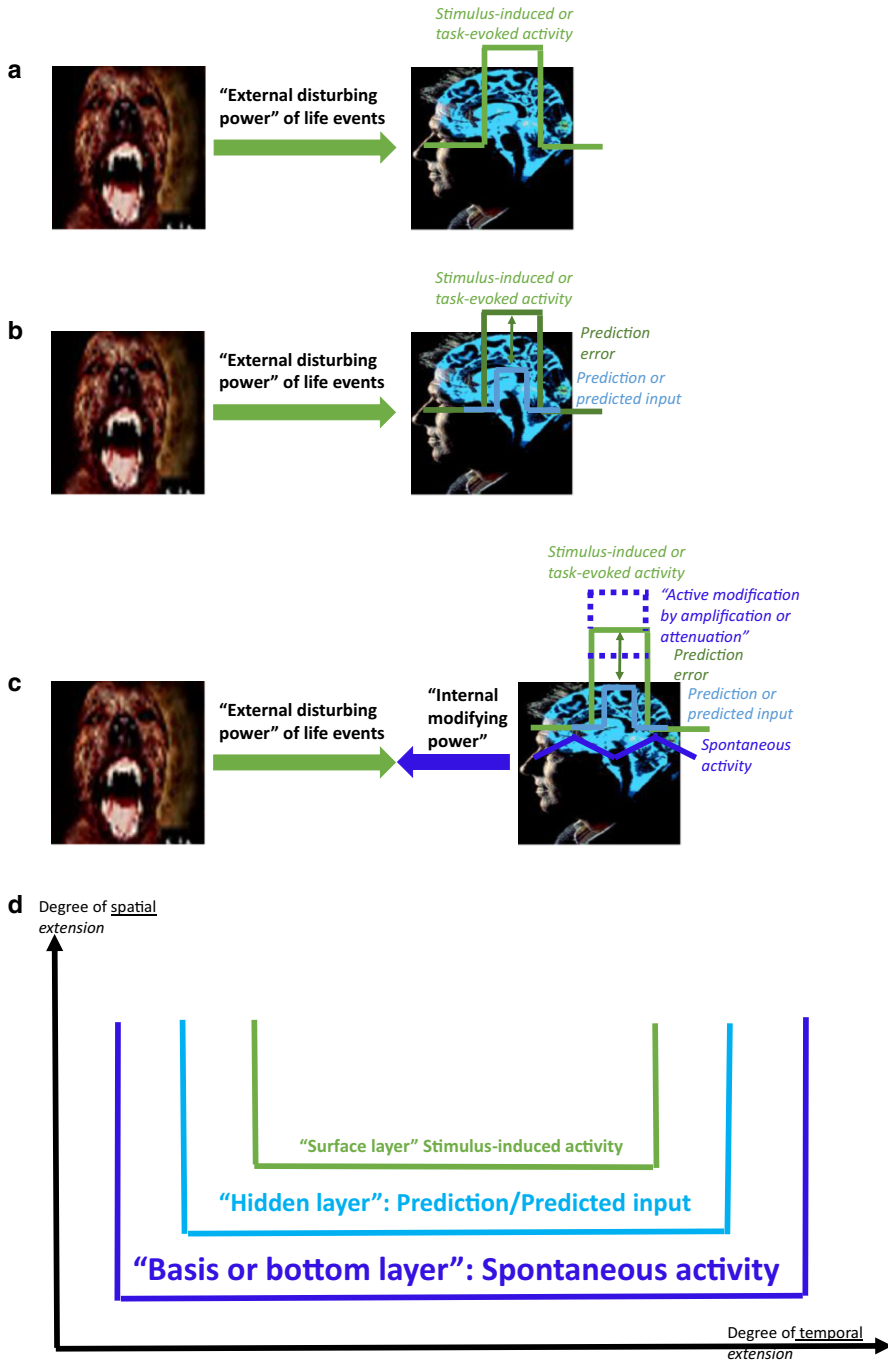
Even if such brains were showing spontaneous activity in such model of brain, the brain's spontaneous activity will have no impact on the stimulus-induced activity which superimposes on the former in a purely non-additive way. The brain itself has thus no impact on the degree of stimulus-induced activity the stimuli elicit in the brain. This makes it clear that stimulus-induced activity is passive in that it

remains fully or sufficiently determined by the external stimuli themselves. Moreover, the external stimuli and their associated stimulus-induced activity are also sufficient for the subsequent cognition, e.g., the association and judgment as postulated by Hume. Though implicating spontaneous activity and cognition, a Humean model of brain can ultimately be characterized as passive and sensory-based model of brain whose neural activity is mainly based on response to stimuli, e.g., stimulus-response-based. Since it is based on sensory functions and external sensory stimuli, I describe such Humean model of brain as “neuro-sensory model of brain” in the following (see Fig. 2a).

How does such neuro-sensory model of brain stand in relation to the empirical findings discussed above? This model can well account for the stimulus-induced activity in relation to aversive stimuli (or decision making task) which mirrors the first layer, e.g., the “surface layer”, of the brain’s neural activity (see above). The neuro-sensory model conceives the external stimuli or task as both necessary and sufficient for stimulus-induced or task-evoked activity. Given that all subjects in both studies received one and the same stimuli, e.g., aversive, or tasks, e.g., decision making, the neuro-sensory model implies that the resulting stimulus-induced or task-evoked activity should be the same across subjects. This was not the case in the empirical findings though. In both studies, the stimulus-induced or task-evoked activity showed considerable inter-individual variation with different subjects showing different degrees (which were related to the degree of early childhood trauma). This is not compatible with the neuro-sensory model that entails inter-individual similarity rather than inter-individual variation in stimulus-induced or task-evoked activity.

The same holds for the brain’s spontaneous activity as the second or “hidden layer” of the brain’s neural activity. Due to the fact that the external stimulus or task is conceived as necessary and sufficient, the stimulus-induced activity should only be dependent upon the aversive stimulus (or decision making task) itself but not on the spontaneous activity, e.g., its levels of glutamate and entropy. That is not the case in the empirical data though. The findings clearly demonstrate that the degree of stimulus-induced or task-evoked activity is related to, e.g., correlates with the spontaneous activity’s entropy and glutamate levels. There are additional (at least necessary) conditions of stimulus-induced or task-evoked activity that extend beyond the stimuli or tasks themselves and dent into the spontaneous activity. Since the neuro-sensory model is based solely on stimuli or tasks in terms of stimulus-response, it cannot accommodate these observations.

How would the neuro-sensory model account for the relationship to early childhood trauma? The neuro-sensory model would clearly admit that early life events can be encoded by the brain and its spontaneous activity. However, it would presuppose “passive modification” of the brain’s spontaneous activity by the environmental life events. The levels of glutamate and entropy should then index the real life events as they were independent of the subject and its perception, e.g., “life events as real”. This, as elaborated above, is not the case though. The levels of glutamate and entropy do not reflect the life event itself, or as “real,” but rather the degree to which the brain’s spontaneous activity actively modifies, e.g., amplifies or attenuates, the impact of the life events on the brain during their encoding resulting



◀ **Fig. 2** **a** Neuro-sensory model of brain (Hume) as passive and stimulus-response-based. **b** Neuro-cognitive model of brain (Kant) as active and prediction-based. **c** Neuro-ecological model of brain (Whitehead) as modifying and ecological. **d** “Spatiotemporal nestedness” between the different layers of the brain’s neural activity

in “life events as perceived”. Presupposing “life events as real” rather than “life events as perceived”, the neuro-sensory model fails to account for the brain’s active modification by attenuation or amplification and thus the complex neuro-ecological construction processes. More generally, the neuro-sensory model fails to consider the third layer of the brain’s neural activity, the “basis or bottom layers” where it stands in direct relationship with the environment.

In sum, the neuro-sensory model fails to account for the empirical findings on all three layers of the brain’s neural activity. The neuro-sensory model cannot accommodate the observed inter-individual variation in stimulus-induced activity on the first layer, the “surface layer”. Moreover, the second layer, the “hidden layer” of the brain’s spontaneous activity, including its modulation of stimulus-induced or task-evoked activity cannot be accommodated either. Finally, the third or “basis or bottom layer” where the spontaneous activity stands in direct relationship to the environment is completely neglected in the neuro-sensory model.

#### **4.2 Active Model of Brain I: Neuro-cognitive Model (Kant): Co-determination of Stimulus-Induced Activity**

Kant rejected such passive model of mind when he argued that the mind itself provides an active causal impact in processing sensory stimuli (which, as Kant argued, is central for constituting mental features) (Kant 1998). Instead of a passive model of mind, he therefore opted for an active model of mind in which the mind itself and its particular contribution are necessary in processing sensory stimuli. Briefly, Kant argued that the mind itself shows spontaneous activity independent of external stimuli by means of which the mind provides a unity into which all external stimuli need to be integrated in order to elicit mental features—the mind structures and organizes the external stimuli into a synchronic and diachronic unity. Accordingly, sensory stimuli are not processed in a passive and thus receptive way, e.g., without any contribution by the mind itself, in such active model of mind. Kant’s active model of mind can therefore be characterized by assuming that the mind’s participation, e.g., its active contribution, is necessary in order to process sensory stimuli and constitute mental features.

How does such Kantian model of the mind stand in relation to the brain? Recently, the focus in neuroscience is on the brain’s spontaneous or resting state activity. The concept of spontaneous activity concerns the neural activity in the brain that remains independent of and prior to specific stimuli or tasks (Northoff 2014a). Brain imaging demonstrated that neural networks like the default-mode network (DMN) shows particular high levels of resting state activity (see Raichle 2009; Raichle et al. 2001). Spontaneous activity is not restricted to specific regions or networks though but is present throughout the whole brain including all regions and networks (Northoff 2014b). Recently, the spontaneous activity in the brain has

been assumed to be central for mental features like self (Northoff 2012c, 2014a, b, c, 2016a; Whitfield-Gabrieli et al. 2011) and mind wandering and random thoughts (Christoff et al. 2009), consciousness (Huang et al. 2014; Huang et al. 2016; Northoff 2012c, 2014b).

The possible involvement of the brain's spontaneous activity in generating mental features like self and consciousness has prompted various authors to conceive the brain analogous to the model of the mind suggested by Kant. Kant emphasized the cognitive functions of the mind in his endeavor to reveal the subject's contribution to the constitution of mental features. This position is well reflected in current philosophical accounts of Kant's concept of the mind (see for instance Brook 1994) and has recently been extended to the brain. Referring explicitly to Kant, Churchland (2012), for instance, characterizes the brain in terms of cognitive functions that he deems to be central for our cognition and knowledge of the world. The Kantian model of brain (Northoff 2012c) or a "Kantian brain" as Fazelpour and Thompson (2015) say can thus be characterized as cognition—rather than sensory-based model of brain. For that reason I speak of a neuro-cognitive model of brain in the following and distinguish it from the neuro-sensory model of brain.

However, the simple presence of spontaneous activity and cognitions themselves does not yet turn the Humean passive model of brain into an active model. For that the spontaneous activity must impact and modulate the processing of external stimuli and their stimulus-induced activity in such way that the latter could not be elicited without the former which has indeed been supported on empirical grounds in recent studies (see He 2013; Huang et al. 2016). Due to such interaction between spontaneous activity and stimulus-induced activity (with the latter then also interacting with the subsequent spontaneous activity), there are no clear-cut boundaries between both forms of neural activity (see for instance Klein 2014; Northoff 2014a). The spontaneous activity directly impacts stimulus-induced activity as its necessary (though non-sufficient) condition: the stimulus-induced activity is not merely added to or superimposed upon the brain's spontaneous activity, e.g., additive interaction, but is actively shaped, e.g., impacted by the latter entailing non-additive interaction (see Huang et al. 2015) (which makes the distinction between the two forms of neural activity impossible) (see Fig. 2b).

We so far discussed the active model of brain on a purely neural level, the level of spontaneous activity and its interaction with stimulus-induced activity. How about the active model of brain on a more cognitive or psychological level? For that I turn to predictive coding (Friston 2009, 2010; Hohwy 2013, 2014). According to predictive coding, the brain generates predictions or anticipations internally, referred to as the predicted input, which are then matched and compared with the actual input. The difference between the predicted and actual input, the so-called prediction error, determines the degree of neural activity, i.e. stimulus-induced activity. Since the brain refers to itself, i.e. its internally generated predicted inputs, when determining the impact of the actual contribution and subsequent stimulus-induced activity, Hohwy (2013, 2014) characterizes the brain as a "self-evidencing system" (cf. Clark 2013), who determines the brain and its predictive coding not

only as “self-evidencing” but also as embedded into the world and thus as “world-evidencing”).

The predicted input and its modulation of stimulus-induced activity in terms of the prediction error is well in accordance with an active model of brain. The brain itself and its spontaneous activity generate a prediction or anticipation of the stimulus, e.g., the predicted input (Northoff 2014a), which impacts and modulates the stimulus-induced activity as it is manifest in the prediction error. The stimulus-induced or task-evoked activity are then no longer solely determined by the stimulus or task itself, e.g., in terms of stimulus-response, but rather co-determined by stimulus/task and brain/predicted input. Specifically, the balance between the stimulus/task and the “internal modifying power” of the predicted input are manifest in the prediction error: if the stimulus/task is strong, the impact of (especially a weak) predicted input as based on the spontaneous activity may be low so that the prediction error is rather high (since it deviates from the predicted input). Conversely, a weak stimulus/task may be more likely to be “overridden” by a strong predicted input, e.g., spontaneous activity, entailing a low prediction error (e.g., not differing much from the predicted input).

In a nutshell, the example of predictive coding shows in a paradigmatic way that stimulus-induced or task-evoked activity is co-determined by both stimulus/task and brain’s spontaneous activity/predicted input. Such co-determination (and co-dependence) of stimulus-induced or task-evoked activity on both the stimuli/tasks and the brain itself, e.g., the spontaneous activity’s predicted input, is a hallmark feature of the active or neuro-cognitive model of brain. The co-determination and co-dependence distinguishes the neuro-cognitive model of brain as active model from passive or neuro-sensory model.

### 4.3 Active Model of Brain II: Neuro-cognitive Model (Kant)—Innateness of Spontaneous Activity

How can the neuro-cognitive model account for the above described empirical findings? The neuro-cognitive model presupposes direct interaction or impact of the spontaneous activity with/on the neural processing of external stimuli like aversive stimuli and their subsequent stimulus-induced activity. Due to such co-determination (and co-dependence), the neuro-cognitive model can well account for the observed correlation of the spontaneous activity’s glutamate and entropy levels with the degree of stimulus-induced activity during aversion. Most importantly, the co-determination (and co-dependence) makes possible to account for the inter-individual variation in stimulus-induced or task-evoked activity. Different subjects may show different levels of entropy and/or glutamate in their spontaneous activity which, in turn, leads to different predicted inputs that impact subsequent stimulus-induced activity in different ways. The neuro-cognitive model thus traces the inter-individual variation in stimulus-induced activity (in response to aversive stimuli) to the spontaneous activity and its inter-individually varying entropy and glutamate levels. This puts the active or neuro-cognitive model in a superior position to the passive or neuro-sensory model with regard to the first layer of the brain’s neural activity, the “superficial layer” of stimulus-induced activity.



How about the second layer, the “hidden layer” of the brain’s spontaneous activity? Both studies demonstrated inter-individual variation in entropy, glutamate and IFF in the brain’s spontaneous activity. Where do these inter-individual variations come from? The proponent of the neuro-cognitive model may want to argue in two directions, assuming either innateness or representation as explanatory frameworks.

Let us start with innateness. The inter-individual differences in the spontaneous activity’s levels of entropy, glutamate, and IFF may be an innate or intrinsic feature of the respective individual subject’s brain and its spontaneous activity that may for instance be genetically determined. Hence, the assumption of such innateness can well account for the inter-individual differences in the levels of entropy, glutamate, and IFF as observed in both studies. In contrast, the relationship of these inter-individual variations in adult spontaneous activity’s glutamate, entropy, and IFF to early traumatic life events remains unclear: if the spontaneous activity (and its measures like glutamate, entropy, and IFF) is truly innately or intrinsically, e.g., genetically determined, it should remain unrelated, e.g., independent, to their respective environmental context, e.g., the early childhood life events. This puts the assumption of innateness at odds with the finding of a correlation between early childhood traumatic life events and the spontaneous activity’s levels of glutamate, entropy, and IFF in adulthood.

In sum, the assumption of innateness can account for inter-individual variations in spontaneous activity whereas it fails to accommodate its relationship to early childhood life events. More generally, innateness as one possible core feature of neuro-cognitive model can account for the spontaneous activity as the “hidden layer” of the brain’s neural activity. In contrast, it remains unable to explain the third layer of the brain’s neural activity, the “basis or bottom layer” with the direct relationship between environment and brain.

#### **4.4 Active Model of Brain III: Neuro-cognitive Model (Kant)— Representation of “Life Events as Perceived” by Cognitive Functions**

Due to the shortcoming of innateness, the neuro-cognitive proponent may want to revert to the assumption of representation of the early childhood life events in the spontaneous activity. The life events are represented as traumatic in the brain’s spontaneous activity, more specifically its levels of glutamate, entropy, and IFF. Such representation is possible on the basis of the brain’s cognitive functions (like decision making, working memory, attention etc.). One would then expect that the early childhood life events correlate with the cognitive functions and its related stimulus-induced or task-evoked activity. The study by Nakao et al. (2013) shows that this is indeed the case with both behavioral and neural correlates of decision making being related to early childhood traumatic life events: the more traumatic the early life events, the more decision making was tilted towards external (rather than internal criteria) and the lower the IFF power in medial prefrontal cortex (see above). Accordingly, these findings seem to lend support to the assumption of representation and its cognitive mechanisms for mediating early childhood traumatic life events.



Why do the very same life events also correlate with the spontaneous activity and its levels of glutamate, entropy, and IFF though? If the assumption of representation were true, one would expect the early life events to only correlate with stimulus-induced/task-evoked activity and its related cognitive functions (like decision making). In contrast, there should be no correlation with spontaneous activity (and its levels of glutamate, entropy, and IFF) since the latter remains prior to and independent of cognitive functions. This result, however, is not in accordance with the data though. Both studies (Nakao et al. 2013, Duncan et al. 2015) and others (Sadaghiani and Kleinschmidt 2013) show direct relationship between early life events and spontaneous activity with the latter then correlating with stimulus-induced/task-evoked activity and related cognitive functions. This suggests that there is an additional layer in the spontaneous activity that is more basic and fundamental than representation and its cognitive functions. As mentioned above, this is the third layer, the “basis or bottom layer” of the brain’s neural activity where its spontaneous activity is closely intertwined with its respective environmental context.

We need to consider this “basis or bottom layer” of the brain’s neural activity in order to account for how the adult brain’s spontaneous activity can be related to early childhood life events. As pointed out above, this leads us to the “neuro-ecological construction processes” as they can be featured by “active modification by amplification or attenuation”. Importantly, “active modification by amplification or attenuation” allows for the encoding of life events as “life events as perceived” (rather than “life events as real”) by the brain’s spontaneous activity. Such encoding, as the data show, impacts in turn subsequent stimulus-induced/task-evoked activity and its representation of the encoded life event, e.g., the “life event as perceived” by the various cognitive functions (like attention, decision making, working memory, etc.).

One could thus say that the representational approach in particular and the neuro-cognitive model in general neglect the very ground or bottom upon which they stand: the “neuro-ecological construction processes” between environment and brain without which there would be no encoding of life events into the brain’s spontaneous activity and thus no “life events as perceived” for representation by stimulus-induced/task-evoked activity and related cognitive functions. Metaphorically speaking, both representational approach and neuro-cognitive model only consider the upper neuro-cognitive half of the “life events as perceived”, e.g., their perception and cognition. In contrast, they neglect their lower neuro-ecological half, e.g., the processes on the basis of which they are generated and result from the brain’s modifications of the “life events as real”.

In sum, the neuro-cognitive model can account well for the impact of spontaneous activity on stimulus-induced activity. Taken in this sense, the neuro-cognitive model advances over the neuro-sensory model that can only account for the impact of the external stimuli on stimulus-induced activity. However, the neuro-cognitive model remains insufficient when it comes to the encoding of environmental life events by the spontaneous activity. Neither the assumption of innateness nor the neuro-representational account can account for the “active modification by amplification or attenuation” during the encoding of environmental life events by

the brain's spontaneous activity. Accordingly, while being to accommodate both "superficial and hidden layers" of the brain's neural activity, e.g., stimulus-induced and spontaneous activity, the neuro-cognitive model fails when it comes to the third layer, the "basis or bottom layer" of encoding and neuro-ecological construction processes. This leads us to the neuro-ecological model of brain as it shall be sketched in the following.

#### **4.5 Environmental Model of Brain I: Neuro-ecological Model (Whitehead)—Spatiotemporal Nestedness Between the Different Layers of Neural Activity**

We saw above in the first part that Whitehead inverts the Kantian concept of the subject by putting it into the environmental or ecological context of the world. The same, analogously, can now be done in the case of the brain and its spontaneous activity. The brain's spontaneous activity and its spatiotemporal structure are dependent upon and put within their respective environmental context which allows for their direct interaction in terms "active modification by amplification or attenuation". This, as discussed above, is supported by our findings with the correlation between early life events, e.g., "life events as perceived", and the spontaneous activity's levels of glutamate and entropy. Theoretically, this implies that the model of brain must consider the ecological (or environmental) context for which reason, I will speak of a "neuro-ecological model of brain" in the following (see Fig. 2c).

The neuro-ecological model considers the relationship between ecological context, or the environment, and brain as most basic and fundamental. Importantly, this relationship is not characterized by "passive modification" of the brain's spontaneous activity by the environmental context. Instead, the brain's spontaneous activity exerts an active impact on the degree to which the environmental events impact and modifies the spontaneous activity, e.g., "active modification by amplification or attenuation", resulting in encoding of "life events as perceived" rather than "life events as real". This makes it clear that the neuro-ecological model of brain can well account for the empirical findings of the correlation between early childhood life events and adult spontaneous activity, e.g., its levels of glutamate, entropy, and IFF. More generally, the neuro-ecological model of brain can well accommodate the observations of the experience-dependence and thus the ecological dependence of the brain's spontaneous activity.

The assumption of such neuro-ecological relationship makes it also possible to account for the inter-individual variation in the spontaneous activity's entropy, glutamate and IFF levels without reverting to either innateness or representation. Due to different relationships to their respective environmental contexts (and life events), the spontaneous activity in different individuals may show different levels of glutamate, entropy, and IFF (as related to prior life experiences and, in part, genetic predisposition). The balance between the life events' "external disturbing power" and the spontaneous activity's "internal modifying power" is consequently different between different individuals (as well as different at different points in time within each individual; that shall be neglected here though for the sake of

simplicity): even one and the same life event may be encoded in different ways by the brain's spontaneous activity in different individuals and consequently be perceived in different ways reflecting what I described above as "life event as perceived". How does the neuro-ecological model of brain stand in relation to the neuro-sensory and neuro-cognitive models? At first glance, all three models seem to be mutually exclusive or contradictory. However, taking a deeper look, they are complementary and extend each other rather than contradictory and exclusive in terms of their (i) empirical, (ii) conceptual, and (iii) spatiotemporal frameworks. Let us start with the empirical framework.

The neuro-sensory model is limited to external stimuli and their impact on stimulus-induced activity. This is extended in the neuro-cognitive model that puts both external stimuli and stimulus-induced activity into the context of the brain's spontaneous activity and how it impacts the former. Empirically, the neuro-cognitive model thus extends the neuro-sensory model by incorporating both, stimulus-induced and spontaneous activity. This is even more extended in the neuro-ecological model. Now the brain's spontaneous activity is by itself put into the ecological context of the environment raising the question of how the former actively modifies the impact of the latter by its own "active modification by amplification or attenuation". The neuro-ecological model thus extends the neuro-cognitive model by incorporating all three, the brain's stimulus-induced activity, the brain's spontaneous activity, and the brain's relation to and encoding of its respective ecological environment. This makes it clear that the three models of brain are not contradictory and exclusive in their empirical frameworks but rather complementary.

Complementarity can also be observed on the conceptual level with regard to the notion of activity. The neuro-sensory model attributes activity only to the stimulus in that it induces activity, e.g., stimulus-induced activity in the brain. The brain itself, in contrast, remains passive in this model. This is different in the neuro-cognitive model. Now the brain is itself attributed activity in terms of its spontaneous activity that co-determines stimulus-induced activity in an active way. That activity is extended even further in the neuro-ecological model: the brain's spontaneous activity does not only co-determine stimulus-induced activity but also its own relation to its respective environmental context by "active modification by amplification or attenuation".

Finally, there is also complementarity and extension on spatiotemporal grounds. The neuro-sensory model of brain focusing on the "surface layer" is limited to the discrete points in time and space at which stimuli occur and induce the usually rather short-lasting (e.g., 100–2000 ms) and spatially restricted (e.g., specific regions in the brain) stimulus-induced activity. The spatial and temporal dimensions are extended in the neuro-cognitive model of brain: the "hidden layer" of the spontaneous activity with its continuous changes shows a wider spatial distribution throughout the whole brain (rather than being limited to specific regions in the brain) and recruits a much longer temporal scale (from seconds to minutes if not hours, days, and years) when compared to stimulus-induced activity (see also Klein 2014). Finally, the neuro-ecological model targeting the "basis or bottom layer" of the brain entails an even larger spatiotemporal framework in that it relates and

aligns the brain's spontaneous activity beyond itself to the more extended temporal and spatial scales in the environment (as to life events in early childhood) (see Fig. 2d; Table 1).

Taken together, the different layers of the brain's neural activity, e.g., “surface layers”, “hidden layer”, and “basis or bottom layer,” seem to be characterized by different spatiotemporal scales, e.g., short, intermediate, and long. The empirical data as described above suggest that all three spatiotemporal scales are closely related to each other with the early childhood life events being related to the spontaneous activity which in turn is related to the stimulus-induced activity. Such a close relationship suggests that the three spatiotemporal scales of the different layers of the brain's neural activity are spatiotemporally nested within each other: the long spatiotemporal scale of the neuro-ecological “basis or bottom layer” nests the intermediate spatiotemporal scale of the neuro-cognitive “hidden layer” which, in turn, nests the short spatiotemporal scale of the neuro-sensory “surface layer”. Briefly, I assume what I describe as “spatiotemporal nestedness” between the three different layers of the brain's neural activity and their respective models. We will see further down that such spatiotemporal nestedness can be extended to the ontological domain as in the context of an ontology of brain.

#### 4.6 Environmental Model of Brain II: Neuro-ecological Model (Whitehead)—Process-Based Characterization of the Brain's Spontaneous Activity

Let us return to the neuro-ecological model of brain in order to describe it in more conceptual detail. One may want to describe the events occurring in early childhood as actual events in process-based ontological terms like actual events, occasion, prehension, and superject as introduced by Whitehead. The actual events in early childhood are constituted by dynamic construction processes in the world referring to what Whitehead describes ontologically as actual occasion (See above). One may now raise the question how these actual occasions that occur in the world can enter and be manifest into the brain and its spontaneous activity's spatiotemporal structure. One may want to say that the brain and its spontaneous activity participate in the ongoing dynamic construction processes, the actual occasions, in the world in

**Table 1** Comparison between different models of brain

	Neuro-sensory model (Hume)	Neuro-cognitive model (Kant)	Neuro-ecological (Whitehead)
Neural activity	Response-based	Anticipation-based	Process-based
Impact of the brain itself	Passive: external stimuli as sufficient	Active: spontaneous activity as necessary	Dynamic: temporal and spatial processes
Basis of brain's neural activity	Neuro-sensory—small spatiotemporal range	Neuro-cognitive—medium spatiotemporal range	Neuro-ecological—large spatiotemporal range
Relationship to world	Sensory stimulation of brain by world	Cognitive representation of world by brain	Ecological, e.g., spatiotemporal nestedness of brain within world

a neuro-ecological way, e.g., “neuro-ecological construction processes”: the dynamic construction processes in the world occur through the brain (rather than within the brain as a Kantian might say) and do therefore become manifest and articulated (and presented rather than represented as a Kantian might say) in a neuro-ecological (rather than purely neuronal way) way in the latter’s spontaneous activity and its spatiotemporal structure (as empirically manifest in entropy and glutamate).

I so far discussed the question how the early childhood events are encoded into the spontaneous activity’s spatiotemporal structure. That leaves open yet another question though: how is it possible that the early childhood events and their encoding into the spontaneous activity’s spatiotemporal structure are still present in adulthood? Process ontology may want to rely here on the concept of prehension. Prehension refers to those processes that mediate between different actual occasions and hence ultimately also between early childhood and adulthood. We recall from above that prehension can be characterized by three features, (1) mediation between different actual occasions with the constitution of new ones; (2) asymmetrical relation between past and actual occasions; and (3) linkage between different temporal dimensions. Let us specify that with regard to our childhood trauma example.

The spontaneous activity’s spatiotemporal structure clearly mediates between the actual occasion in early childhood, e.g., the traumatic event, and the actual occasions in adulthood like the reaction to aversive stimuli. This is empirically evidenced by the finding that the degree of childhood trauma (and the degree of entropy in the spontaneous activity’s spatiotemporal structure) correlated with, e.g., predicted the degree of task-evoked activity in response to the aversive stimulus during adulthood. The past actual occasion, the traumatic event, is thus mediated by prehension, the spontaneous activity’s spatiotemporal structure, in such way that it constitutes a new actual occasion, the aversive reaction.

Importantly, the relationship between past and actual occasion is asymmetrical. The past occasion, e.g., the traumatic early childhood event impacts the actual occasion, the aversive reaction. In contrast, the latter, the task-evoked activity in response to the aversive stimulus cannot change the traumatic childhood event and hence the spontaneous activity’s degree of entropy. There is thus an asymmetrical relationship between the spontaneous activity’s spatiotemporal structure and subsequent task-evoked or stimulus-induced activity which is rather akin to what is described in prehension. Finally, the spontaneous activity’s spatiotemporal structure links and bridges different temporal dimensions: the past as the early childhood event is linked to the present aversive reaction in adulthood.

Whitehead himself would probably speak of a “historic route of inheritance” from the actual occasion in early childhood event over the actual occasion in the brain’s spontaneous activity and the actual occasion of glutamate and entropy in adult spontaneous activity to the actual occasion of stimulus-induced activity in response to aversive stimuli/decision making task and its related behavioral manifestations (like more externally guided decision making): “Common sense, physical sense, and physiological theory, combine to point out a historic route of inheritance, from actual occasion to succeeding actual occasion, first physically in

the external environment, then physiologically—through the eyes in the case of visual data—up the nerves, into the brain” (Whitehead 1929/1978: 171).

In sum, I here suggest a neuro-ecological model of brain as distinguished from both neuro-sensory and neuro-cognitive models. The neuro-ecological model of brain is supported by empirical evidence. Ontologically, such neuro-ecological model is well compatible with a process-based participation of the brain in the world’s ongoing dynamic construction processes as featured by actual entities, occasion, and prehension (which may need to be elaborated on in further detail in the future though).

#### **4.7 Environmental Model of Brain III: Neuro-ecological Model (Whitehead)—Temporal Resolution of the “Brain Paradox” (Schopenhauer)**

We recall that Whitehead reversed Kant’s notion of subject by putting the subject back into the ecological context of the world. This led him to conceive the relationship between subject and object in a dynamic (rather than static) way where a subject is constituted out of an object while later perishing back into becoming mere object. How can we now apply such scenario to the brain and our example of childhood trauma?

Let us start with the first scenario, the actual events in early childhood. The events in early childhood can be regarded as an object in the world and its ongoing dynamic construction processes, the actual occasions. Due to the brain’s participation in the world’s dynamic construction processes, the events, e.g., the object, become manifest and articulated in the spontaneous activity’s spatiotemporal structure that therefore can be conceived as subject or superject. The brain and its spontaneous activity’s spatiotemporal structure does here indeed take on the role of the subject as superject, e.g., as the result of the ongoing dynamic construction processes in the world. One may consequently want to say that the object, e.g., the world’s dynamic construction processes, is articulated and manifested (or presented) in the subject as superject, the brain and its spontaneous activity’s spatiotemporal structure. The world as object consequently provides the ecological context for the brain as subject or superject.

The roles of subject and object may change in adulthood though. Now the spontaneous activity’s spatiotemporal structure provides the (neuronal) context for the subject’s aversive reaction to aversive stimuli and its task-evoked or stimulus-induced activity. The spontaneous activity’s spatiotemporal structure takes on the role of the object now which is manifest and articulated within the task-evoked or stimulus-induced activity in response to aversive stimuli, the superject or subject. This has been described empirically as rest-stimulus interaction that refers to how the resting state impacts stimulus-induced activity and thus the processing of stimuli (Huang et al. 2016; Northoff et al. 2010). Presupposing a process-based ontological framework, one may want to say that such rest-stimulus interaction can be characterized by transforming a subject or superject, e.g., the pre-stimulus resting state, into a mere object while, at the same time making possible the constitution of

a novel superject or subject, e.g., the stimulus-induced or task-evoked activity in response to the aversive stimulus.

Empirical evidence suggests that stimulus-induced activity also impacts the subsequent resting state entailing stimulus-rest interaction (Northoff et al. 2010; Schneider et al. 2008). Such stimulus-rest interaction is evidenced by the observation that the post-stimulus resting state level is different from the pre-stimulus resting state levels with different stimuli exerting different impact on subsequent resting state activity levels. In that case the stimulus-induced activity as superject or subject is transformed into an object that in turn makes possible the constitution of a novel superject as subject, e.g., the post-stimulus resting state activity level. In the same way there is continuous change between rest-stimulus and stimulus-rest interaction, there is also continuous dynamic change in the roles of the brain's neural activity as object and subject which is very much akin to Whitehead's characterization of the subject as superject.

The conception of subject and object as dynamic features of the ongoing processes of the brain may also provide a novel approach to what has been described as "brain paradox". The nineteenth century German philosopher Arthur Schopenhauer (1966) raised the question for how we can reconcile the double role of the brain as both object and subject which is often coined as the "brain-paradox": "But in so far as the brain knows, it is not itself known, but it is the knower, the subject of all knowledge. But in so far as it is known in objective perception, that is to say, in the consciousness of other things, and thus secondarily, it belongs, as organ of the body, to the objectification of the will" (Schopenhauer 1966, Vol II, 259).

How does the neuro-ecological model of brain address the brain-paradox? The paradoxical nature of the assignment of both subject and object to the brain stems from the hidden assumption that both, subject and object, are mutually exclusive: the brain can only be subject but not object or, alternatively, the brain can only be object but not subject. The mutual exclusivity of the brain as object and subject is ultimately based on the view of the brain as static, fixed, and non-spatiotemporal entity: if the brain is static, fixed and non-spatiotemporal, it cannot take on different roles like subject or object (even if these were flexible and changing as suggested by Whitehead). The brain-paradox thus rests ultimately on a particular view of the brain entailing either a neuro-sensory or neuro-cognitive model of brain.

The neuro-ecological model of brain rejects such a view. Here, as it will be elaborated further down, the brain is viewed in a process-based way as dynamic rather than static, changing rather than fixed, and spatiotemporal rather than non-spatiotemporal. This makes it possible for the brain to take on different roles like subject and object: subject and object are now just distinct aspects of one and the same underlying process at its distinct stages such that what is actually a subject in the present moment transforms into an object when the former recedes into the past. The notions of subject and object are thus put into a temporal context of continuous changes, e.g., processes which makes it possible to assign them to distinct stages of one and the same underlying process.

Presupposing such process-based perspective, the brain-paradox ceases to be paradoxical. The brain's neural activity, e.g., its spontaneous and stimulus-induced activity, are now conceived in the temporal context of ongoing processes and their

dynamic change including continuously changing roles of subject and object. The characterization of the brain by both subject and object is then no longer paradoxical but rather a proper characterization for the continuous change of the brain's neural activity, e.g., spontaneous and stimulus-induced activity with their continuously changing roles and constellations (as indicated above). Accordingly, the characterization of the brain by both subject and object may reflect the process-based, e.g., temporal and dynamic character of the brain's neural activity rather than a paradox. Viewed in such process-based context, one can resolve the “brain-paradox” on temporal grounds where it may then be replaced by the concept of “brain processes”.

## 5 Conclusion

I raised the question for a model of the brain that is both empirically and ontologically plausible. I compared different models of brain, e.g., neuro-sensory, neuro-cognitive, and neuro-ecological, with regard to recent empirical data on early childhood trauma and the brain. This let me suggest that the neuro-ecological model of brain is empirically more plausible when compared to neuro-sensory and neuro-cognitive models. Such neuro-ecological model of brain can ontologically be described in process-based terms like prehension as based on Whitehead's process-based philosophy.

Why is the model of brain relevant for philosophy? Philosophy is not so much concerned with the empirical realm as neuroscience but rather, among others, with ontological issues of how for instance brain and body are related to the mind. This touches upon the question of an ontology of brain. This shall be discussed in the second paper. I will point out that a process-based ontology of brain carries major implications for how to conceive the relationship between world and brain, the world-brain relation as I call it, which them may be featured in spatiotemporal terms. The world-brain relation, in turn, may provide a novel view on mind–body relation and this the mind–body problem in the spatiotemporal and process-based terms of an ontology of brain. This will be discussed in the second paper.

**Acknowledgments** I thank two anonymous reviewers for their excellent suggestions which were all included in this version of the paper. I also thank Alex Gomez-Marin and Ronnie Desmet for very helpful and constructive comments on an earlier draft, Nils Frederic Wagner and Johanna Pokorny for helpful English corrections and Wendy Carter for sorting the references. Finally, I am thankful for helpful comments to a talk of mine on Whitehead and brain at the recent Whitehead conference in June 2015 in Claremont/California as well as a talk at the College de France in Paris/France in January 2016.

## References

- Brook A (1994) Kant and the mind. Cambridge University Press, Cambridge
- Buckner RL, Andrews-Hanna JR, Schacter DL (2008) The brain's default network: anatomy, function, and relevance to disease. *Ann N Y Acad Sci* 1124:1–38
- Cabral J, Kringelbach ML, Deco G (2014) Exploring the network dynamics underlying brain activity during rest. *Prog Neurobiol* 114:102–131. doi:[10.1016/j.pneurobio.2013.12.005](https://doi.org/10.1016/j.pneurobio.2013.12.005)



- Christoff K, Gordon AM, Smallwood J, Smith R, Schooler JW (2009) Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proc Natl Acad Sci USA* 106(21):8719–8724. doi:[10.1073/pnas.0900234106](https://doi.org/10.1073/pnas.0900234106)
- Churchland PM (2012) *Plato's camera: how the physical brain captures a landscape of abstract universals*. MIT Press, Cambridge
- Clark A (2013) Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behav Brain Sci* 36(03):181–204
- Cobb J (2008) *Whitehead word book*. sq. (trad. française légèrement modifiée: *Lexique whiteheadien*, Editions Chromatika, 2010, pp 87–88). Cette caractéristique s'appliquant à tous les animaux dotés d'un système nerveux central, 45
- Crick F, Koch C (2003) A framework for consciousness. *Nat Neurosci* 6(2):119–126. doi:[10.1038/nn0203-119](https://doi.org/10.1038/nn0203-119)
- Deco G, Jirsa VK, McIntosh AR (2013) Resting brains never rest: computational insights into potential cognitive architectures. *Trends Neurosci* 36(5):268–274
- Descartes R (2008) *Meditations on first philosophy: with selections from the objections and replies: with selections from the objections and replies*. Oxford University Press, Oxford
- Di X, Biswal BB (2013) Dynamic brain functional connectivity modulated by resting-state networks. *Brain Struct Funct* 220:1–10
- Di X, Kim EH, Huang CC, Tsai SJ, Lin CP, Biswal BB (2013) The influence of the amplitude of low-frequency fluctuations on resting-state functional connectivity. *Front Hum Neurosci* 7:118. doi:[10.3389/fnhum.2013.00118](https://doi.org/10.3389/fnhum.2013.00118)
- Duncan NW, Hayes DJ, Wiebking C, Tiret B., Pietruska K, Chen DQ, Rainville P, Marjańska M, Ayad O, Doyon J, Hodaie M, Northoff G (2015) Negative childhood experiences alter a prefrontal-insular-motor cortical network in healthy adults: a multimodal rsfMRI-fMRI-MRS-dMRI study. *Hum Brain Mapp* 36(11):4622–437. doi:[10.1002/hbm.22941](https://doi.org/10.1002/hbm.22941)
- Duncan NW, Wiebking C, Tiret B, Marjańska M, Hayes DJ, Lyttleton O, Doyon J, Northoff G (2013) Glutamate concentration in the medial prefrontal cortex predicts resting-state cortical-subcortical functional connectivity in humans. *PLoS One* 8(4):e60312. doi:[10.1371/journal.pone.0060312](https://doi.org/10.1371/journal.pone.0060312)
- Fazelpour S, Thompson E (2015) The Kantian brain: brain dynamics from a neurophenomenological perspective. *Curr Opin Neurobiol* 31:223–229
- Ford LS (1998) Structural affinities between Kant and Whitehead. *Int Philos Q* 38(3):233–244
- Friston KJ (2009) Modalities, modes, and models in functional neuroimaging. *Science* 326(5951):399–403
- Friston K (2010) The free-energy principle: a unified brain theory? *Nat Rev Neurosci* 11(2):127–138
- Ganzetti M, Mantini D (2013) Functional connectivity and oscillatory neuronal activity in the resting human brain. *Neuroscience* 240:297–309
- Griffin DR (1998) Unsnarling the world-knot: consciousness, freedom, and the mind–body problem
- He BJ (2013) Spontaneous and task-evoked brain activity negatively interact. *J Neurosci* 33(11):4672–4682
- Hohwy J (2013) *The predictive mind*. Oxford University Press, Oxford
- Hohwy J (2014) The self-evidencing brain. *Noûs* 1–27. doi:[10.1111/nous.12062](https://doi.org/10.1111/nous.12062)
- Huang Z, Dai R, Wu X, Yang Z, Liu D, Hu J et al (2014) The self and its resting state in consciousness: an investigation of the vegetative state. *Hum Brain Mapp* 35(5):1997–2008. doi:[10.1002/hbm.22308](https://doi.org/10.1002/hbm.22308)
- Huang Z, Zhang J, Longtin A, Dumont G, Duncan NW, Pokorny J, Qin P, Dai R, Ferri F, Weng X, Northoff G (2015) Is there a nonadditive interaction between spontaneous and evoked activity? Phase-dependence and its relation to the temporal structure of scale-free brain activity. *Cereb Cortex pii:bhv288* (Epub ahead of print)
- Huang Z, Zhang J, Wu J, Qin P, Wu X, Wang Z, Dai R, Li Y, Liang W, Mao Y, Yang Z, Zhang J, Wolff A, Northoff G (2016) Decoupled temporal variability and signal synchronization of spontaneous brain activity in loss of consciousness: an fMRI study in anesthesia. *Neuroimage* 124(Pt A):693–703. doi:[10.1016/j.neuroimage.2015.08.062](https://doi.org/10.1016/j.neuroimage.2015.08.062)
- Hume D (2012) *A treatise of human nature*. Courier Dover Publications, New York
- Hutchison RM, Womelsdorf T, Allen EA, Bandettini PA, Calhoun VD, Corbetta M et al (2013) Dynamic functional connectivity: promise, issues, and interpretations. *Neuroimage* 80:360–378
- Kant I (1998) *Critique of pure reason*. In: Guyer P, Wood AW (eds). Cambridge University Press, Cambridge
- Klein C (2014) *The brain at rest: what it's doing and why that matters*
- Koch C (2004) *The quest for consciousness*. Oxford University Press, Oxford

- Logothetis NK, Murayama Y, Augath M, Steffen T, Werner J, Oeltermann A (2009) How not to study spontaneous activity. *Neuroimage* 45(4):1080–1089. doi:[10.1016/j.neuroimage.2009.01.010](https://doi.org/10.1016/j.neuroimage.2009.01.010)
- Menon V (2011) Large-scale brain networks and psychopathology: a unifying triple network model. *Trends Cogn Sci* 15(10):483–506. doi:[10.1016/j.tics.2011.08.003](https://doi.org/10.1016/j.tics.2011.08.003)
- Nakao T, Matsumoto T, Morita M, Shimizu D, Yoshimura S, Northoff G, Morinobu S, Okamoto Y, Yamawaki S (2013) The degree of early life stress predicts decreased medial prefrontal activations and the shift from internally to externally guided decision making: an exploratory NIRS study during resting state and self-oriented task. *Front Hum Neurosci* 7:339. doi:[10.3389/fnhum.2013.00339](https://doi.org/10.3389/fnhum.2013.00339) (eCollection 2013)
- Northoff G (2012a) Immanuel Kant’s mind and the brain’s resting state. *Trends Cogn Sci* 16(7):356–359. doi:[10.1016/j.tics.2012.06.001](https://doi.org/10.1016/j.tics.2012.06.001)
- Northoff G (2012b) Autoepistemic limitation and the brain’s neural code: comment on “Neuroontology, neurobiological naturalism, and consciousness: a challenge to scientific reduction and a solution” by Todd E. Feinberg. *Phys Life Rev* 9(1):38–39. doi:[10.1016/j.plprev.2011.12.017](https://doi.org/10.1016/j.plprev.2011.12.017)
- Northoff G (2012c) Psychoanalysis and the brain—why did Freud abandon neuroscience? *Front Psychol* 3:71. doi:[10.3389/fpsyg.2012.00071](https://doi.org/10.3389/fpsyg.2012.00071)
- Northoff G (2014a) *Unlocking the brain: volume 1: coding*, vol 1. Oxford University Press, Oxford
- Northoff G (2014b) *Unlocking the brain. Volume II: consciousness*. Oxford University Press, Oxford
- Northoff G (2014c) *Minding the brain: a guide to philosophy and neuroscience*. Palgrave Macmillan, Basingstoke
- Northoff G (2016a) Is the self a higher-order of fundamental function of the brain? The “basis model of self-specificity” and its encoding by the brain’s spontaneous activity. *J Cogn Neurosci* 1–20 (Epub ahead of print)
- Northoff G (2016b) *Neurophilosophy and the healthy mind. Learning from the unwell brain*. Norton Publisher, New York
- Northoff G, Heinzel A, de Greck M, Bermpohl F, Dobrowolny H, Panksepp J (2006) Self-referential processing in our brain—a meta-analysis of imaging studies on the self. *Neuroimage* 31(1):440–457
- Northoff G, Qin P, Nakao T (2010) Rest-stimulus interaction in the brain: a review. *Trends Neurosci* 33(6):277–284
- Powers WT (1995) The origins of purpose: the first metasystem transitions. *World Futur J Gen Evol* 45(1–4):125–137
- Pred R (2005) *The dynamic flow of experience*. MIT Press, Cambridge
- Raichle ME (2009) A brief history of human brain mapping. *Trends Neurosci* 32(2):118–126
- Raichle ME (2010) Two views of brain function. *Trends Cogn Sci* 14(4):180–190
- Raichle ME (2015) The restless brain: how intrinsic activity organizes brain function. *Philos Trans R Soc Lond B Biol Sci* 370(1668):20140172
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL (2001) A default mode of brain function. *Proc Natl Acad Sci USA* 98(2):676–682
- Sadaghiani S, Kleinschmidt A (2013) Functional interactions between intrinsic brain activity and behavior. *Neuroimage* 80:379–386. doi:[10.1016/j.neuroimage.2013.04.100](https://doi.org/10.1016/j.neuroimage.2013.04.100)
- Schneider F, Bermpohl F, Heinzel A, Rotte M, Walter M, Tempelmann C et al (2008) The resting brain and our self: self-relatedness modulates resting state neural activity in cortical midline structures. *Neuroscience* 157(1):120–131
- Schopenhauer A (1966) *The world as will and representation* (trans: Payne E), vol I and II. Dover Publisher, New York
- Thagard P (2012) *Cognitive science of science: explanation, discovery and conceptual change*. MIT Press, Cambridge
- Whitehead AN (1929/1978) *Process and reality: an essay in cosmology*. In: Griffin DR, Sherburne DW (eds). The Free Press, New York
- Whitfield-Gabrieli S, Moran JM, Nieto-Castañón A, Triantafyllou C, Saxe R, Gabrieli JD (2011) Associations and dissociations between default and self-reference networks in the human brain. *Neuroimage* 55(1):225–232
- Wiebking C, de Greck M, Duncan NW, Heinzel A, Tempelmann C, Northoff G (2011) Are emotions associated with activity during rest or interoception? An exploratory fMRI study in healthy subjects. *Neurosci Lett* 491(1):87–92. doi:[10.1016/j.neulet.2011.01.012](https://doi.org/10.1016/j.neulet.2011.01.012)
- Wiehl R (1990) Whiteheads Kant-Kritik und Kants Kritik am Panpsychismus. In: Holzhey H, Rust A, Wiehl R (eds) *Natur, Subjektivität, Gott: zur Prozessphilosophie Alfred N. Whiteheads*. Suhrkamp, Frankfurt