CORRESPONDENCE

Integrating subjective and objective—spatiotemporal approach to psychiatric disorders

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TO THE EDITOR:

The excellent perspective by Kyzar and Denfield [1] points out nicely the necessity for integrating subjective and objective approaches in the investigation of psychiatric disorders. They make especially the point of considering phenomenological approaches like the subjective experience of abnormal time speed in mania or major depressive disorder (MDD). Despite the excellent reflections on integrating phenomenology and modern neuroscience, we do believe their perspective is incomplete because two important questions of modern psychiatry remain unanswered: First, the question regarding an integrated brain-mind model that underlies and guides our methodological approaches like neurophenomenology. Second, how can we link the subjective experience to neuronal activity in mental disorders and can that yield the still lacking neuro-experiential markers for clinical differential-diagnosis? Based on earlier and most recent neuroscientific studies, we suggest that a number of conceptual, methodological and clinical pathways should be undertaken to answer the two above mentioned questions:

In order for brain and experience to be related with each other, they must share some features. Current models usually consider them as radically different like subjective vs objective, as pointed out by Kyzar and Denfield [1]. One may then either reduce the mind to cognitive function and its neural correlates [2] or consider it as an add-on [3]. Given that the former approach reduces the mind to the brain's function, one can speak of *"function-based approach"* [4] while the latter associates the mind with cognition, e.g., *"cognitive neuroscience approach"* [5]. Both approaches are contrasted with the *"phenomenological approach"* [6], which poses the primacy of subjective experience (rather than function or cognition). However, none of the three models provides an answer to the question how brain and mind are connected in MDD, mania and schizophrenia (SZ). We are aware that this question is one of the most complex questions in psychiatry and one may speculate whether it will ever be resolved. The so-called Cartesian dualism was first described by René Descartes (1596–1650) in his book *"Meditations on first Philosophy"* [7] published in 1641. In his book, Descartes argued that there are two kinds of human foundation: physical (body) and mental (mind). For centuries, this strict separation between body and mind (e.g. problem of incommunicability) led the way for both clinical and scientific psychiatry [8–10]. Although this dualistic concept of psychiatric illness has been discussed and criticized by many [11–13], it was only about two decades ago that the first studies attempting to overcome this dualism were conducted (for history of the different concepts of mind and body see Berrios [10]).

Recently, the first author of this commentary developed a novel phenomenological-neuroscientific model [14] that might help to overcome the body-mind problem in psychiatry. Here, the temporal and spatial configurations of the brain's neural activity are directly related to and manifest in the experience of the subjects' inner time and space – time-space are shared by brain and experience as their *"common currency"*. For instance, as also pointed out by Kyzar and Denfield [1], mania and MDD are characterized by the experience of abnormal inner time speed, that is, as either too slow or too fast [15, 16]. But where is such slow time speed in experience in MDD and mania coming from? A recent fMRI study by Northoff et al. [17] investigated time speed in the brain's neural activity by quantifying the brain signal variability (SD) and the amplitude of low frequency fluctuations (ALFF): if neural activity is variable and changes a lot over time, there is a certain time speed. If it is not variable and does not change over time, there is a rather slow time speed in neural activity. In particular, this study [17] showed opposite patterns of the somatomotor/sensory SD ratio in Slow5 (0.01–0.027 Hz) in manic and depressed bipolar disorder (BD) patients and healthy subjects. In depressed BD patients, their neural variability and thus time speed was very low/slow in those regions, e.g., somatomotor/sensory cortex, that constitute the brain's inner time speed and rhythm and are modulated by subcortical dopamine and serotonin [18] – decreased sensorimotor activity (and altered serotonin) in depressed BD patients is thus well in line with their perception of decreased time speed and prolonged duration [19]. While opposite changes in sensorimotor cortex, e.g., increased activity [20], in mania lead to opposite pattern in time perception with increased time speed and shortened duration [19].

If the brain's inner time speed is too slow, one would expect that MDD patients remain unable to properly react in their neural activity to fast external stimuli. A recent fMRI study by Lu et al. [20] using fast visual negative emotional stimuli showed that MDD patients were not able to properly increase their neural activity in various default-mode and sensorimotor regions when compared to healthy controls. What is even more interesting is that the lower task-related neural activity in default-mode and sensorimotor regions correlated with psychomotor retardation. Abnormally low neuronal response to specifically fast (but not slow) negative (but not neutral) stimuli is thus closely related to decreased speed in motor behavior, e.g., psychomotor retardation – that further supports the relationship of neuronal and behavioral speed featured by abnormal slowness on both levels in MDD [20]. Decreased speed also characterizes the cognitive level in MDD. A phenomenological-psychological study investigated the changes of internally- and externally-oriented thought contents over time in healthy controls, MDD, and depressed BD patients [21]. Thought contents in MDD and depressed BD were more focused on internally-oriented cognition (like their own self as distinguished from environmental contents) which, especially in MDD, lasted longer, were slower and showed lower power (when calculating

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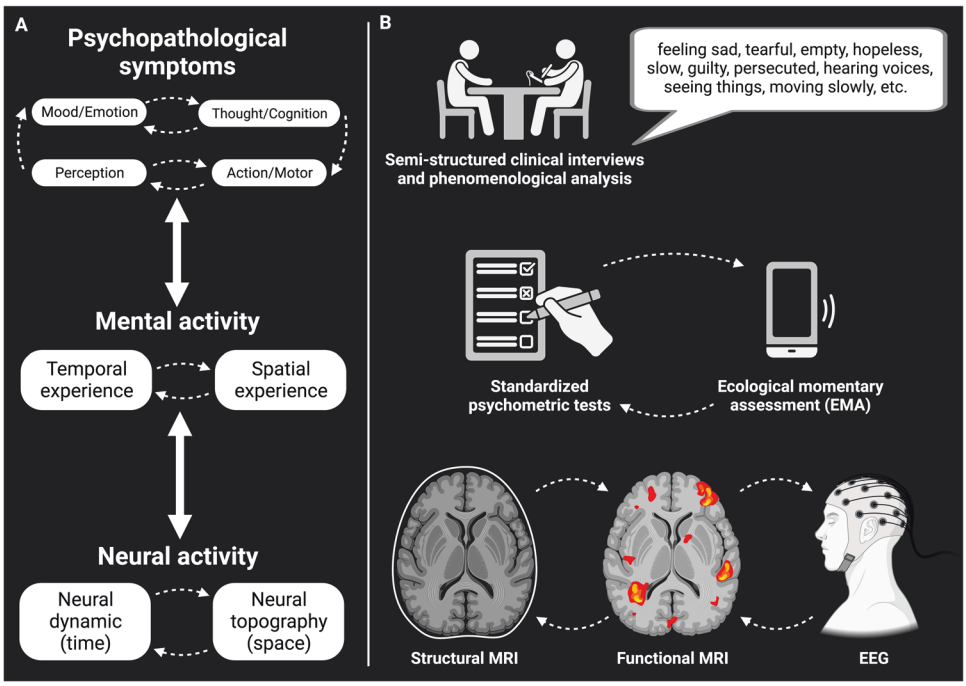

Fig. 1 The different psychopathological symptoms are shaped by both neural and mental activity providing their connection as "common currency". A The commonly shared features of symptoms, mental activity, and neural activity, that is, spatiotemporal features as their "common currency". **B** It illustrates how that can be tested on the corresponding levels of symptom questionnaires/interviews, psychometric tests, and brain data.

the time series of thought changes in power spectral density). These measures of thought dynamic were also related to symptom severity and specifically ruminations/brooding [21] - this suggests the importance of decreased thought speed for MDD symptoms. Finally, abnormal slowness in MDD can also be observed in affect/emotion which show decreased changes over time (in especially early depressive stages) as recently demonstrated in a psychological study [22]. Together, the various findings suggest that increased slowness with reduced time speed is manifest in MDD in both brain [20] and experience [16, 19] as well as in various functions (like emotions [22], thoughts [21], movement [20], and perception [20]). Moreover, these findings also hold the promise of providing differential-diagnosis markers. The mentioned thought dynamic study could well differentiate between depressed MDD and depressed BD [21] while a recent scale for space-time experience in psychosis (STEP) clearly distinguished SZ and affective psychosis [23]. Albeit tentatively, these findings suggest differential temporal features in MDD, e.g., abnormal slowness, and SZ which rather shows temporal fragmentation with temporal imprecision in the millisecond range – this predominates in both experience [23] and time perception of SZ [15, 24]. Temporal imprecision can also be observed in the brain's neural activity of SZ (but not in MDD) as it shows decreased and imprecise synchronization with the timing of external stimuli, e.g., entrainment, in delta, theta and alpha frequency bands [25, 26] as well as in timing changes in the dynamic and hierarchy of neural networks [24, 27]. The differential findings in the (neural and experienced) timing of MDD and SZ raise the specter of the possible diagnostic specificity and differential-diagnostic relevance of temporal (and spatial) disturbances in different psychiatric and neurological disorders like SZ, MDD and Parkinson's disease [18].

In conclusion, the spatiotemporal approach, e.g. Spatiotemporal Psychopathology (STPP) [28], could provide an opportunity of an integrated brain-mind model in psychiatric disorders (see Fig. 1 for overview). This may make it possible to more closely link and connect neural and mental levels through their shared changes in the different time-space dimensions (like precision, speed, etc.). Future interdisciplinary and multimodal studies are needed that develop systematic quantitative instruments for the assessment of the different time-space experiences in the different psychiatric disorders as it has already been done recently for psychosis [23], but is still outstanding for other psychiatric disorders. That needs to be accompanied by developing and applying measures of the temporal dynamic (like the power spectrum) and spatial topography (like global signal topography) on both neural and mental levels. This would allow developing a truly neurophenomenological approach by integrating phenomenology, psychiatry and neuroscience (as pointed out by Kyzar and Denfield [1]). Even more important, STPP could provide an opportunity to gain novel insights into neuro-mental markers for the differential diagnostic work-up of psychiatric disorders.

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COMPETING INTERESTS

The authors declare no conflict of interest.

ADDITIONAL INFORMATION

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