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EDITORIAL

Sensorimotor Neuroscience in Mental Disorders: Progress, Perspectives and Challenges

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The research in the field of sensorimotor functioning[1–4] in distinct psychiatric disorders has grown exponentially in the last 3 decades (see also recent reviews[2,4–9]), spurring a discussion[10,11] about the scientific and clinical relevance of sensorimotor neuroscience in mental disorders. We propose that the future research on sensorimotor dysfunction will need to consider distinct multi-omics layers to succeed in the development of innovative prevention and diagnostic strategies in the identification of novel targets for psychopharmacological research and therapy as well as of treatment response biomarkers in mental disorders. Building on the previous findings of the sensorimotor neuroscience, we suggest that a number of conceptual, methodological, and clinical pathways should be undertaken to succeed in these ambitious aims:

(1) *Broader use of the "sensorimotor domain" of the Research-Domain-Criteria (RDoC)-Initiative:* Currently, there is an urgent scientific need to conceptualize known both intrinsic (reflecting vulnerability and emerging illness) and antipsychotic drug-exacerbated (contributing to dysfunction/impairment) sensorimotor abnormalities in terms of the RDoC sensorimotor domain and vice versa. For instance, future studies examining catatonia and parkinsonism should focus on the construct "motor actions" and on its subconstruct "initiation." In the next step, more fine-grained units of analysis for this domain should be "circuits" (eg, basal ganglia, supplementary motor area) characterized by neuroimaging and "behavior" (eg, catatonic stupor and psychomotor retardation) assessed by clinical rating scales and instrumental assessments.

(2) *Prevention and early recognition of sensorimotor abnormalities:* A recent umbrella review[12] highlighted a role of genetic variations on the risk for drug-related movement disorders. Furthermore, the prescription of antipsychotics for non-psychotic symptoms in youth (0–20 years)[13] is a growing concern, because antipsychotics can interfere with neuronal development in the adolescent brain. A critical translational infrastructure for the understanding of the vulnerability for sensorimotor abnormalities are deeply phenotyped individuals, both healthy persons with subtle sensorimotor abnormalities and patients with target sensorimotor abnormalities, as provided by longitudinal studies focusing on developmental trajectories of different sensorimotor abnormalities from early childhood to late adulthood (eg, ref.[14]).

(3) *Multimodal research on pathomechanism of sensorimotor abnormalities:* In the past 2 years, multivariate data fusion approaches[15,16] decisively provided a more comprehensive understanding of brain structure and intrinsic neural activity in schizophrenia spectrum disorders (SSD) patients with different categories of sensorimotor abnormalities.[17,18] Furthermore, Wolf and colleagues[19] were the first to investigate relationships between sensorimotor dysfunction and cognitive/perceptual anomalies in SSD. Future neuroimaging studies should consider in more detail functional and structural network changes (a) in relation to specific sensorimotor signs and symptoms, (b) through targeted neuromodulatory pharmacology focusing on dopaminergic and GABAergic transmission (or plasticity-promoting agents such as cannabidiol) in transdiagnostic population exhibiting sensorimotor abnormalities, and (c) across multiple sensorimotor domains to disentangle conceptual, symptomatic and network overlap between different categories of sensorimotor abnormalities.

(4) *Multilayer therapy of sensorimotor abnormalities:* Future drug development studies should explicitly use RDoC sensorimotor domain to (a) identify transdiagnostic study samples with purely sensorimotor dysfunction rather than individuals fulfilling criteria for specific diagnostic categories, (b) obtain approval for novel drugs for major sensorimotor abnormalities, (c) prove effectiveness of psychotropic medication along multiple units of analysis, and (d) monitor treatment outcome when the sensorimotor function is taken into account besides conventional primary and secondary endpoints. Also, future clinical trials should evaluate the safety and efficacy of established pharmacological compounds (eg, vesicular monoamine transporter 2) in different indications (eg, Tourette syndrome,[20] catatonia, akathisia) and other potentially promising pharmacological compounds (eg, naringin,[21] N-acetylcysteine or cannabidiol). Finally, non-invasive brain stimulation techniques[1] should be evaluated through systematic multimodal assessment of intervention effects on brain and multi-omics biomarkers.

(5) *Elimination of pitfalls of previous studies on sensorimotor domain:* There are only few preclinical models and genetic studies,[12] offering a scientific discussion of a narrow set of sensorimotor abnormalities emphasizing multimodal MRI techniques. Therefore, the recent neurobiological evidence on neurological soft signs, parkinsonism, and catatonia needs to be replicated and expanded by preclinical models (eg, ref.[22]) and independent transdiagnostic samples using corresponding RDoC constructs and subconstructs. Both genuine and drug-induced sensorimotor signs/symptoms should be monitored by multi-level instrumental assessments[23] in real-world setting and how they change over time. This aspect makes epidemiological and patient cohort studies even more important.

Finally, our personal view, which in full accordance with the ECSP consensus,[1] is that sensorimotor neuroscience will open door for different areas of scientific and clinical application of precision psychiatry such as allocation of patient subgroups to specific treatment and prediction of its response as well as identification of individual at risk for developing a mental disorder and/or medication side effects.

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