Commentary

Biological Psychiatry: GOS

Understanding Motor Abnormalities in Psychiatric Disorders as Altered Sensorimotor Processing

Nuttida Rungratsameetaweemana

A major challenge in psychiatric research is to characterize and relate heterogeneous symptoms to changes in underlying neural computations (1). Identifying the mechanisms underlying motor abnormalities in particular has been a central yet unsolved problem critical for the successful development of effective treatment strategies for several neuropsychiatric conditions. One way in which these abnormalities can be characterized is to conceptualize motor behavior as a product of a perceptual decision-making process. Within this framework, the execution of specific motor responses is triggered by a decision choice that is informed by analyses of incoming sensory information. As sensory environments are highly dynamic and often ambiguous, the brain must rapidly and efficiently generate informative sensorimotor associations that can then be used to guide optimal selection and execution of motor responses. In this sense, some cognitive deficits and distinct motor abnormalities as observed across various psychiatric and neurological conditions might be the results of disruptions associated with the sensorimotor integration process.

Probing motor abnormalities in this way allows for psychiatric disorders to be conceptualized not as unitary conditions but rather as clusters of multiple behavioral and cognitive phenotypes. This formulation also suggests areas in which psychiatric research can benefit from experimental and analytical techniques originating in cognitive and computational neuroscience for the purpose of investigating the bases of sensorimotor integration. Specifically, several computational models of decision making have suggested mechanisms by which optimal selection of decision choices and motor responses can be achieved on different timescales and under various constraints (2–4). Examining such models by systematically modifying parameters could generate testable hypotheses. One might then, for example, evaluate these predictions by comparing psychophysical and neural responses between healthy control subjects and patients with psychiatric conditions. Using similar approaches, past work has provided evidence linking alterations in the decision-making process to heterogeneity in the motor abnormalities observed across disorders (5–7).

Gilles de la Tourette syndrome (GTS) is a neurodevelopmental disorder with onset in early childhood and is characterized by multiple motor and vocal tics (8). The condition can result in poor quality of life and risk of social and emotional stigma, especially when tics persist into adulthood. Comorbidities such as attention-deficit/hyperactivity disorder or obsessive-compulsive disorder also present critical challenges in the management of the motor abnormalities of GTS. Because the pathophysiology of GTS remains elusive, current management strategies primarily involve behavioral methods, psychoeducation, and pharmacotherapy. An improved understanding of the neural dynamics that give rise to the generation of tics could benefit the development of effective evidence-based treatments for GTS (8). Consequently, it is useful for neurocognitive models of GTS to explicitly consider how the binding of sensory input and motor output becomes altered during decision making and results in disrupted generation and expression of motor responses.

In the current issue of *Biological Psychiatry: Global Open Science*, Beste *et al.* (9) present evidence suggesting that motor symptoms observed in GTS arise from alteration in sensorimotor processing that occurs during perceptual decision making. Specifically, when incoming sensory information triggers a motor response, binding can occur where the specific action becomes associated with particular features of the input. This process can facilitate decision making when the same stimulus is encountered again and the same motor response is required. However, strong binding can compromise performance when the formation of new sensorimotor associations is needed. Beste *et al.* (9) propose that strong sensorimotor binding may relate to the motor abnormalities in GTS. Given that GTS develops in early childhood, the present investigation focuses on adolescents with GTS. The goal was to assess whether the generation of tics was related to neural dynamics associated with aberrant sensorimotor processing. Thirty-two adolescents with GTS and 27 typically developing youths performed a decision-making task in which participants responded to two visual stimuli that were presented sequentially. The motor response (R1) required for the first stimulus (S1) was determined by a binary cue presented at the beginning of each trial. Thus, R1 was independent of S1. Participants then saw another stimulus (S2) and executed a binary response (R2) based on the orientation of S2. By manipulating the similarity between the two stimuli and between the two responses on each trial, the authors could evaluate the strength of sensorimotor binding by assessing performance in each task condition. Electroencephalography (EEG) was concurrently recorded as participants performed the task such that the temporal dynamics of neural responses associated with sensorimotor integration could be measured. First, the authors showed that neural oscillatory activity within the theta and beta bands was involved in the sensorimotor processing in

SEE CORRESPONDING ARTICLE ON PAGE 123

https://doi.org/10.1016/j.bpsgos.2021.06.006
ISSN: 2667-1743

both the GTS and control groups. This finding is consistent with the importance of the theta and beta band activity in broad cognitive functions including working memory, cognitive control, and rule-based learning.

Beste *et al.* (9) then used whole-brain EEG reconstruction methods to evaluate if the integration process was governed by distinct patterns of neural oscillatory activity across the widely distributed brain networks in GTS and control subjects. The results revealed similar functional activation patterns in the beta band where the neural oscillation was primarily associated with inferior parietal and temporal regions in both GTS and control subjects. However, the oscillatory activity in the theta band differed between GTS and control subjects. Specifically, the theta band activity was associated primarily with superior frontal regions in control subjects. In contrast, the spatial pattern of the theta band activity in the GTS group was associated with parietal and inferior frontal regions.

Notably, despite the observed difference in theta band activity, Beste *et al.* (9) found similar behavioral patterns between the two groups. It is possible that performance based on binary responses may not be sufficiently sensitive to capture alteration in the sensorimotor processing of adolescents with GTS. Modification of the current task by increasing the complexity of sensory stimuli and motor responses may allow for differential behavioral performance between the two groups to be observed. For example, future studies could incorporate a multiple-alternative forced choice or a continuous response scheme in which the precision and reaction times of motor responses could be concurrently assessed in a more fine-grained fashion. In addition, while EEG-based source reconstruction provides some insights into the spatial organization of neural activity, careful interpretation of the results is necessary given the inherently low spatial resolution associated with EEG signals. Future studies could apply similar reconstruction methods to neuroimaging data with higher spatial resolution, such as functional magnetic resonance imaging and magnetoencephalography data. Such analysis could further elucidate the brain-wide dynamics that underlie sensorimotor processing in GTS. Finally, future research is needed to determine if the present findings reflect a general computation typically underlying the motor abnormalities of GTS or a modality-specific computation unique to the processing of visual stimuli. For example, future research investigating the psychophysical and neural dynamics associated with sensorimotor integration during auditory decision making could provide further insights into the general mechanisms that become altered and lead to motor symptoms in GTS.

Perceptual decision making is a core cognitive function important for the generation of adaptive behavior. As such, healthy and disrupted motor behavior can be conceptualized in a framework whereby perceptual and cognitive components of action are integrated. By evaluating motor abnormalities associated with adolescent GTS in the context of underlying sensorimotor integration, Beste *et al.* (9) demonstrated distinct signatures of GTS in the theta band oscillation. These findings add to a growing literature that underscores the importance of experimental paradigms of decision making and neuroimaging methods in improving our understanding of GTS (10). The present investigation also provides a rationale for integrating neuroscientific techniques with clinical or neurobiological data to elucidate potential mechanisms associated with GTS as well as other psychiatric disorders. Finally, methods used in the present investigation could potentially be incorporated in current clinical practice to improve the overall diagnosis, treatment strategies, and clinical outcomes for GTS as well as other psychiatric and neurological conditions that include motor abnormalities as hallmark features.

Acknowledgments and Disclosures

This work was supported by National Institute of Biomedical Imaging and Bioengineering Grant No. R01EB026899-01, National Institute of Neurological Disorders and Stroke Grant No. R01NS104368, and mission funding from the U.S. Army Research Laboratory.

I thank Larry R. Squire for the helpful discussion and Deanna M. Barch for editorial assistance.

The author reports no biomedical financial interests or potential conflicts of interest.

Article Information

From the Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, California, Human Research and Engineering Directorate, U.S. DEVCOM Army Research Laboratory, Aberdeen Proving Ground, Maryland, and the Neuroscience Center for Research and Innovation, Learning Institute, King Mongkut's University of Technology Thonburi, Bangkok, Thailand.

Address correspondence to Nuttida Rungratsameetaweemana, Ph.D., at nrungrat@salk.edu.

Received Jun 17, 2021; accepted Jun 18, 2021.

References

1. Huys QJM, Maia TV, Frank MJ (2016): Computational psychiatry as a bridge from neuroscience to clinical applications. Nat Neurosci 19:404–413.
2. Sterzer P, Voss M, Schlagenhauf F, Heinz A (2019): Decision-making in schizophrenia: A predictive-coding perspective. Neuroimage 190:133–143.
3. Rungratsameetaweemana N, Squire LR, Serences JT (2019): Preserved capacity for learning statistical regularities and directing selective attention after hippocampal lesions. Proc Natl Acad Sci U S A 116:19705–19710.
4. Cavanagh SE, Lam NH, Murray JD, Hunt LT, Kennerley SW (2020): A circuit mechanism for decision-making biases and NMDA receptor hypofunction. Elife 9:e53664.
5. Ferrazzoli D, Ortelli P, Madeo G, Giladi N, Petzinger GM, Frazzitta G (2018): Basal ganglia and beyond: The interplay between motor and cognitive aspects in Parkinson's disease rehabilitation. Neurosci Biobehav Rev 90:294–308.
6. Heerey EA, Bell-Warren KR, Gold JM (2008): Decision-making impairments in the context of intact reward sensitivity in schizophrenia. Biol Psychiatry 64:62–69.
7. Henco L, Diaconescu AO, Lahnakoski JM, Brandi ML, Hörmann S, Hennings J, *et al.* (2020): Aberrant computational mechanisms of social learning and decision-making in schizophrenia and borderline personality disorder. PLoS Comput Biol 16:e1008162.
8. Robertson MM, Eapen V, Singer HS, Martino D, Scharf JM, Paschou P, *et al.* (2017): Gilles de la Tourette syndrome. Nat Rev Dis Primers 3:16097.
9. Beste C, Mückschel M, Rauch J, Bluschke A, Takacs A, Dilcher R, *et al.* (2021): Distinct brain-oscillatory neuroanatomical architecture of perception-action integration in adolescents with Tourette syndrome. Biol Psychiatry Glob Open Sci 1:123–134.
10. Cavanna AE, Ganos C, Hartmann A, Martino D, Pringsheim T, Seri S (2020): The cognitive neuropsychiatry of Tourette syndrome. Cogn Neuropsychiatry 25:254–268.