Commentary

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Performance Monitoring and Mental Health During the COVID-19 Pandemic: Clarifying Pathways to Internalizing Psychopathology

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The COVID-19 pandemic has caused widespread stressful events around the world, including job loss and financial strain, interpersonal conflicts, and separations from loved ones, as well as tremendous physical health effects and loss of life (1). Indeed, the pandemic's effects have been so pervasive that it is hard to imagine that many people have made it through fully unscathed. Not surprisingly, the pandemic is associated with high rates of internalizing disorders (2), but its impacts on psychopathology are complex. For example, we observed variability in symptom change early in the pandemic, such that depressive symptoms increased from pre-pandemic levels in young adults, but symptoms of social anxiety decreased (3). This suggests that the reduced social demands that accompanied restrictions to mitigate spread may have been protective for some people early on. Studies integrating pre-pandemic data with longitudinal follow-up assessments during the pandemic provide unique insights into vulnerabilities that underlie internalizing psychopathology in the context of stress exposure. This work is critical for identifying mental health needs during the pandemic and has broader implications for understanding pathways to psychopathology.

A large body of published literature indicates that event-related potential markers of performance monitoring (i.e., the error-related negativity [ERN] and correct response negativity [CRN]) may reflect a vulnerability for internalizing psychopathology, particularly anxiety disorders. CRN and ERN are elicited over frontocentral sites approximately 0 ms to 100 ms after a person responds to a target stimulus and makes an error, respectively. The ERN/CRN are thought to reflect activation of the anterior cingulate cortex to drive adaptive behavioral responses to meet the demands of the situation and avoid negative outcomes (4). An enhanced ERN is observed in patients with anxiety disorders and has been shown to prospectively predict anxiety in youth (4), suggesting a potential early-emerging vulnerability that predisposes to anxiety in combination with other proximal risk factors. At the same time, there is debate about the specific processes reflected by a heightened ERN and why people with enhanced performance monitoring are vulnerable to internalizing psychopathology (5). In addition, although the ability to improve prediction of psychopathology risk with neural measures is a major advancement in clinical neuroscience, in order to translate this work to improve intervention efforts we ultimately need to understand how processes measured in the laboratory manifest in daily life and shape people's experiences of the world.

In the current issue of *Biological Psychiatry: Global Open Science*, Riesel *et al.* (6) examined the ERN and CRN assessed pre-pandemic as prospective predictors of internalizing symptoms early in the pandemic. Although the ERN and CRN were not directly related to internalizing symptoms during the pandemic, both neural measures were associated with greater perceived COVID-19 risk, such that those with heightened pre-pandemic performance monitoring reported an elevated perceived risk of COVID-19 infection and anticipated a more severe course of illness. Riesel *et al.* (6) also observed indirect effects of ERN/CRN on internalizing symptoms through the perceived risk of COVID-19 infection and subjective experiences of stress in a serial mediation model. People who were more reactive to their performance pre-pandemic, in some cases years before the pandemic, reported experiencing COVID-19 as more threatening, and this was then associated with greater subjective stress and increases in internalizing symptoms. Interestingly, this pathway was supported for internalizing symptoms that were broadly defined, including trait anxiety, depressive symptoms, and obsessive-compulsive symptoms, even accounting for the same symptom dimension at baseline.

Through this longitudinal study, Riesel *et al.* (6) offer insights into why enhanced ERN/CRN assessed in the laboratory may underlie some forms of internalizing psychopathology. Enhanced performance monitoring at the neural level may reflect hyperreactivity to the potential risks associated with one's behavior, and the results of Riesel *et al.* (6) demonstrate that it also relates to concerns about external risks, like becoming infected with COVID-19. In some ways, it is surprising that reactivity to internal threats, such as one's own performance on a flanker task, generalizes to perceptions of risk due to an external threat in this way. This may be due in part to perceptions of one's control over avoiding COVID-19 infection through masking, vaccination, and social distancing, and the potential impacts of making a mistake in this context. Future research could investigate this possibility by testing the extent to which performance monitoring predicts perceived risk in the context of threats that are fully independent of one's choices and behaviors, like natural disasters or terrorist attacks.

At a broader level, Riesel *et al.* (6) highlight the complex relations between brain function, stress, and internalizing psychopathology. Neural measures tend to be modestly

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associated with symptom measures when examining direct associations, highlighting the need to consider multiple neurobiological and contextual factors that shape individual risk. Experiences of stress are known to impact brain function, suggesting that changes in neural processes underlying performance monitoring and threat reactivity in response to stress may serve as mechanisms of stress effects on internalizing symptoms. At the same time, individual differences in brain function, including performance monitoring, have been shown to moderate the effects of stressors on internalizing symptoms, in line with vulnerability stress models (7). But as Riesel *et al.* (6) show, our experiences of stress—and their subsequent effects on psychopathology—also depend on how our brains interpret the world and shape our behaviors. There is not a single direct pathway to internalizing psychopathology—instead, bidirectional and dynamic associations between experiences and brain function shape risk across the lifespan. Further longitudinal research could advance these ideas through tests of multiple theories of the associations between stress, neural processes, and internalizing symptoms (e.g., mediation, moderation, stress generation), as well as the extent to which these pathways change across development depending on the timing and type of experiences.

Despite the lack of direct effects from ERN/CRN to internalizing symptoms, Riesel *et al.* (6) add to the evidence of prospective associations between neural markers of performance monitoring and later internalizing symptoms. This raises questions about the clinical translational implications. One possibility is that an enhanced ERN/CRN could be used to identify people at greatest risk for internalizing symptoms during times of stress, and thus in need of preventive interventions. Efforts have begun to establish norms for the ERN (8), which could ultimately allow for the identification of those at risk, although challenges remain in terms of variability across tasks, systems, and processing parameters. In addition, the extent to which neural measures of performance monitoring can accurately predict future internalizing psychopathology at the individual level beyond more easily administered clinical measures remains to be evaluated.

In addition to identifying those who are at greatest risk, understanding the role of performance monitoring in internalizing psychopathology has the potential to provide new insights into intervention targets. This raises questions about the level at which to intervene and the most effective timing for interventions to mitigate risk. In terms of the level, are interventions that reduce ERN/CRN magnitude likely to be more effective than those targeting subjective experience (e.g., perceived risk)? There is mixed evidence regarding the extent to which the ERN/CRN can be altered through intervention. Established treatments like cognitive behavioral therapy and selective serotonin reuptake inhibitors do not seem to modify the ERN, despite effects on symptoms (9). There is promising emerging support for briefer targeted interventions, although longer-term clinical benefits have yet to be determined (10). In terms of timing, when can an enhanced ERN/CRN be reliably detected as a risk marker, and what is the optimal developmental period for intervening to change performance monitoring? Performance monitoring may be most modifiable early in development, but if an enhanced ERN/CRN on its own is not necessarily a problem, intervening at the time of more proximal triggers for psychopathology (e.g., stressful events) may be more useful, particularly when intervention resources are limited.

Relatedly, like many individual difference traits and neural processes, both "too much" and "too little" are associated with psychopathology. For example, in the case of performance monitoring, although an enhanced ERN relates to many internalizing symptoms, reduced ERN is linked to substance abuse, attention-deficit/hyperactivity disorder, and psychopathy, among others (4). This highlights further complexity in identifying intervention targets, raising the questions of who would benefit from interventions to reduce the ERN/CRN and what is the optimal magnitude to protect against psychopathology risk.

The COVID-19 pandemic has had devastating impacts on people's lives and well-being around the globe. Longitudinal research like that of Riesel *et al.* (6) offers unique insights into how people are coping in this specific context as well as a broader understanding of pathways to internalizing psychopathology. Ultimately, this work has the potential to advance the knowledge of processes that make some people particularly vulnerable to the effects of stress on mental health, leading to new approaches for identifying those at greatest risk and the development of targeted, precision medicine approaches to intervention. Yet there is currently a major gap between cognitive and affective neuroscience research and approaches to intervention and prevention. As we as a field face the current mental health crisis, there is an urgent need to begin to bridge this gap, translating neuroscience innovations in ways that mitigate risk and reduce the burden of internalizing psychopathology.

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