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EDITORIAL

Mental health during the COVID-19 pandemic, impact of childhood trauma in psychiatric disorders, and predictable biomarkers for bipolar disorder

Kenji Hashimoto[1]

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We have been experiencing the coronavirus disease 2019 (COVID-19) pandemic since the early 2020. Patients with major mental disorders are recognized as a risk for adverse outcomes. Using the Goettingen psychosocial Burden and Symptoms Inventory (Goe-BSI), Bartels and colleagues evaluated psychosocial burden, psychiatric symptoms, and resilience at the end of the first (April/May 2020) and the second lockdown in Germany (November/December 2020) [1]. Psychosocial burden varied significantly overtime with an increase from the pre-pandemic to the initial phase, followed by a steady decrease across both lockdowns, normalizing in November/December 2020. Furthermore, female gender, high adjustment disorder symptom load at baseline, and psychiatric comorbidities were risk factors for high levels and an unfavorable course of psychosocial burden. Most psychiatric symptoms changed minimally, while resilience decreased over time. It is of interest to investigate a turning point at which coping capacities are depleted [1].

The COVID-19 pandemic causes short-term and long-term health problems in survivors after infection of SARS-CoV-2 (severe acute respiratory syndrome-coronavirus-2). A recent systematic review using 57 studies with COVID-19 survivors ($n = 250{,}351$) reported that the median proportion of COVID-19 survivors experiencing at least 1 PASC (post-acute sequelae of COVID-19) was 54% at 1 month (short-term), 55% at 2–5 months (intermediate-term), and 54% at 6 or more months (long-term) [2]. The most common sequelae were neurological and psychiatric symptoms. In this issue, Poletti and colleagues report cognitive functioning 6 months following hospital discharge for COVID-19 [3]. Neuropsychological and psychiatric evaluations were evaluated for COVID-19 survivors, healthy control group, and patients with major depressive disorder (MDD). Seventy-nine percent of COVID-19 survivors at 1 months and 75% at 3- and 6-month follow-up showed cognitive impairment at least one cognitive function. COVID-19 survivors performed worse than healthy controls but better than MDD patients in psychomotor coordination and speed of information processing. There were no differences in verbal fluency and executive functions between COVID-19 survivors and MDD patients, which were lower than healthy controls. There were also no differences in working memory and verbal memory between COVID-19 survivors and healthy controls. Interestingly, depression was the best predictor of cognitive performance. The data suggest that COVID-19 sequelae include signs of cognitive impairment which persist up to 6 months after hospital discharge [3].

Environmental factors across the lifespan, such as maltreatment during childhood and stressful life events in adulthood, contribute to the development of psychiatric disorders such as MDD. The stress sensitization model shows that early adversity (e.g., childhood stress) sensitizes individuals to subsequent proximal stress (e.g., stressful life events in adulthood), increasing their vulnerability to psychiatric disorders. In this issue, Lin and colleagues report association among childhood adversity, adulthood adversity, and suicidal ideation [4]. Among 1,084 MDD patients, 48.6% had suicidal ideation and 65.6% experienced life adversity during their childhood or adulthood. Interestingly, patients with suicidal ideation were more likely to report childhood adversity or adulthood adversity than patients without suicidal ideation. Furthermore, patients with both childhood adversity and adulthood adversity were associated with suicidal ideation. This study suggests a hypothesis of stress sensitization on suicidal ideation in patients with MDD [4]. Collectively, application of stress sensitization model in suicidality could contribute to the identification of suicidal risk and prevention of suicidal behavior in MDD patients.

✉ Kenji Hashimoto
hashimoto@faculty.chiba-u.jp

[1] Division of Clinical Neuroscience, Chiba University Center for Forensic Mental Health, 1-8-1 Inohana, Chiba 260-8670, Japan

Co-occurrence of psychiatric disorders including severe post-traumatic stress disorder (PTSD), somatic symptoms, and dissociation in the aftermath of trauma is associated with poor treatment outcome. In this issue, Kratzer and colleagues explored direct connections between PTSD, somatic symptoms, and dissociations to gain a deeper insight into the pathological processes underlying their comorbidity that can inform future treatment plans [5]. Using a partial correlation with regularization, they found that muscle or joint pain was among the most central symptoms. Furthermore, physiological reactivation was central in the full network and together with concentrations problems acted as bridge between PTSD symptoms and somatic symptoms. Traumatic events had a severe and detrimental effect on mental and physical health, and their consequences worsen each other trans-diagnostically on a symptom level. Collectively, strong connections between physiological reactivation and pain with other symptoms could inform treatment target prioritization [5].

Schizotypy is defined as a constellation of personality traits which could mirror the subclinical domain of schizophrenia in general population. Accumulating evidence suggests a relationship between childhood trauma and schizotypy. In this issue, Dizinger and colleagues report sex-adjusted connections between childhood adversity and trauma subdomains (emotional/physical/sexual abuse, emotional/physical neglect) and positive (magical ideation, perceptional aberration) as well as negative schizotypy (physical/social anhedonia) [6]. The well-fitting path model using total samples showed a link of emotional abuse to magical ideation and a link of emotional neglect to social anhedonia. In females, physical abuse predicted magical ideation, while emotional neglect forecasted physical anhedonia and social anhedonia. In males, sexual abuse predicted perceptive aberration, and emotional abuse forecasted magical ideation. The study provides valuable insights into the sex-specific relationships between specific childhood adversity and trauma domains and schizotypal traits [6].

MDD and bipolar disorder (BD) are etiologically related, but clinically distinct mood disorders. Their shared clinical features result in high rates of misdiagnosis due to a lack of biomarkers that allow their differentiation [7]. Brain-derived neurotrophic factor (BDNF) and its precursor proBDNF play an important role of mood disorders such as MDD and BD [8]. Schröter and colleagues demonstrated a significant difference in BDNF DNA methylation CpG 5-2-1 in MDD and BD [9], although further study using large sample size is needed. In this issue, using Forward-Stepwise Selection of binary logistic regression, Wu and colleagues report peripheral biomarkers to predict the diagnosis of BD from MDD in adolescents [10]. Age, direct bilirubin, lactic dehydrogenase, free triiodothyronine, and C-reactive protein were the final factors included the models. The total predictable model showed good accuracy and external validation for distinguishing BD from MDD in adolescents. Further study using a large-scale multicenter sample is needed to ascertain predictable peripheral biomarkers for distinguishing BD from MDD in adolescents.

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Declarations

Conflict of interest Dr. Hashimoto is the inventor of filed patent applications on "The use of *R*-ketamine in the treatment of psychiatric diseases", "(*S*)-norketamine and salt thereof as pharmaceutical", "*R*-ketamine and derivative thereof as prophylactic or therapeutic agent for neurodegeneration disease or recognition function disorder", "Preventive or therapeutic agent and pharmaceutical composition for inflammatory diseases or bone diseases", "*R*-ketamine and its derivatives as a preventive or therapeutic agent for a neurodevelopmental disorder", and "TGF-β1 in the treatment of depression" by the Chiba University. Dr. Hashimoto has also received speakers' honoraria, consultant fee, or research support from Abbott, Daiichi-Sankyo, Meiji Seika Pharma, Seikagaku Corporation, Sumitomo, Taisho, Otsuka, Murakami Farm, and Perception Neuroscience.

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