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Neurobiology of “Positive Psychiatry”

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Psychiatry, like rest of medicine, has traditionally focused on study, diagnosis, and treatment of diseases. Whereas positive psychology has become a part of the lay lexicon, positive psychiatry has received far less attention even among professionals. Positive psychiatry may be defined as the science and practice of psychiatry that seeks to understand and promote well-being through assessment and interventions involving positive psychosocial factors.¹ It differs from positive psychology in having a greater focus on biology, medicine, and healthcare including mental illnesses. Multiple meta-analyses have shown that higher levels of positive factors such as social support, resilience, and optimism have a significant beneficial impact on health and longevity.² The effect sizes for the influence of social relationships on mortality equal or exceed the effect sizes of interventions to treat traditional risk factors like smoking, obesity, sedentary behavior, and hypertension.³ The overall US healthcare system, focused on treatment of diseases in individual patients by individual clinicians, has proven largely inefficient, and has created major disparities. These problems will only worsen as the population grows and the gap between the need for and the supply of healthcare professionals expands. Moreover, our goal should not be merely to reduce severity of psychopathology but also to enhance well-being. It is thus important to increase research on promoting mental health and preventing mental illnesses—ie, positive psychiatry. This does not mean replacing the current healthcare system including pharmacological and psychosocial interventions, but rather to supplement it with greater emphasis on wellness-focused factors at individual and public health levels. Prevention of all types—primary, secondary, and tertiary, will reduce the number of people requiring healthcare, thereby making the system less expensive and more efficient.

In 1998, the World Health Organization (WHO) highlighted the role of social determinants of health—ie, nonmedical factors that influence health outcomes and health disparities, such as education, income, employment, access to nutrition and healthcare, and living environment.⁴ There are also unique social determinants of mental health including social isolation/loneliness, homelessness, stigma against mental illnesses, mental healthcare inequities, and a flawed American legal system that tends to criminalize psychopathology.⁵ Equally important are positive psychosocial determinants mentioned earlier, which impact physical, cognitive, and mental health in people with or without illnesses.

The study by Hettwer et al. (this issue) is an excellent illustration of the neurobiology of positive psychiatry, specifically resilience in persons at high risk for schizophrenia.⁶ Using structural magnetic resonance imaging (MRI), these investigators found a significant correlation between an established schizophrenia polygenic resilience score (PRSResilience) and cortical volume, especially in the fusiform gyrus, in healthy individuals. This finding provides a novel link between the vulnerability–stress model, visual cognition, and schizophrenia resilience model. The authors postulate that impaired perceptual organization can negatively affect adaptive behavior and social interactions, producing a vicious cycle of increasing psychosocial stress, defective information processing, and risk of psychosis. In contrast, resilience mechanisms may increase perceptual and cognitive capabilities, thereby reducing the stress induced by perceptual impairments, and initiate a virtuous cycle. Thus, resilience is not just the flip side of vulnerability but a positive and protective factor that prevents progression of neuropsychopathology. Similar phenomena are likely in individuals at risk for bipolar and other mental disorders too, and have clear intervention implications.

As mentioned above, there are also other psychosocial determinants of health that are highly relevant for mental health. A particularly important one is loneliness/social isolation, which increases the risk of heart disease, obesity, diabetes, major depression, anxiety disorders, and dementia.⁷ During the past 2 decades, rising levels of loneliness and social isolation have contributed to an unprecedented decline in average life span in 2015–2017. The COVID-19 pandemic and the resulting social distancing guidelines have further increased the levels of loneliness in the population. This has contributed to skyrocketing of the numbers of deaths of despair from opioid and other substance use during the past year.

Fortunately, there are positive psychosocial determinants of health that can overcome the deleterious health effects of loneliness. Two prominent determinants in this context are social connections and wisdom. Social connections are a critical determinant of health and longevity.⁸ Strong evidence suggests that high-quality close relationships and feeling socially connected to the people in one's life are associated with a significantly reduced risk for many diseases and all-cause mortality. There is perhaps no other known factor that has the magnitude of the impact on length and quality of life across the entire life span as social connections.⁸ Several psychosocial, pharmacological, and technology-focused intervention trials are underway globally to develop ways of mitigating loneliness and enabling positive social relationships.

Wisdom is a complex personality trait comprised of specific components including empathy/compassion, emotional regulation, and self-reflection.⁹ Investigations suggest that prefrontal cortex (especially dorsolateral and ventromedial portions and anterior cingulate), insula, and limbic striatum are principal brain regions underlying wisdom traits. Importantly, several cross-sectional studies and a longitudinal one have shown a significant inverse association between loneliness and wisdom, especially its compassion component. There is considerable overlap in the brain regions putatively involved in wisdom and loneliness. An electro-encephalography (EEG) study found that these 2 constructs had contrasting emotional associations with activation of temporoparietal junction.¹⁰ Finally wisdom is potentially modifiable. A meta-analysis of 57 randomized controlled trials of behavioral and psychosocial interventions showed that nearly half of the studies reported improved levels of empathy/compassion, emotional regulation, and spirituality, with moderate to large effect sizes.¹¹ Increase in these components was generally associated with increase in well-being—opposite of the commonly reported associations of loneliness.

How the various psychosocial factors affect health is not yet well understood, although biological processes play a crucial role. For example, epigenetic mechanisms can alter the ability to cope with social stressors, which act on neural systems underlying physiological, psychological, and cognitive processes, thereby increasing or

reducing an individual's susceptibility to adverse effects of future environmental stressors.¹² A person's genes and their interactions with environmental factors (along with stochastic events) help shape the brain circuitry and neurochemical functions manifested behaviorally in psychological traits and processes. Resilience has been linked to adaptive changes in brain circuits that regulate emotions like fear as well as social behaviors. Resilient individuals appropriately adjust their emotional resources to meet the environmental demands, thereby preventing development and progression of pathology.

Another mechanism that is attracting increasing attention regarding putative neurobiology of psychosocial determinants of health is microbiome-related gut–brain axis.¹³ This involves bidirectional signaling between the gastrointestinal and central nervous systems, regulated at neural, hormonal, and immunological levels. Schizophrenia and bipolar disorder are associated with greater gastrointestinal inflammation and permeability, reduced microbial diversity, and possible global community differences compared to healthy subjects.¹⁴ Animal studies show that the collective genomes of the microbes that live inside and on the human body affect the development and function of regions of the “social brain,” including prefrontal cortex, hippocampus, hypothalamus, and amygdala.¹³ The microbiome influences the concentrations and signaling of molecules that affect social behavior, including glucocorticoids, sex hormones, neuropeptides, and monoamines. Human studies suggest that the microbiome is involved in emotional processes such as those in depression. The gut microbiome in early infancy may play a role in the development of social and emotional traits. A recent study reported that lower levels of loneliness and higher levels of wisdom, compassion, social support, social engagement, and well-being were associated with greater phylogenetic richness and diversity of the gut microbiome.¹⁵ The mechanisms by which psychosocial factors may be related to gut microbial diversity are unknown. Conceivably, perceived social support may buffer the negative effects of chronic stress on pro-inflammatory markers. Alternatively, microbiome may help shape social behavior, potentially leading to social isolation and loneliness or to social connectivity and wisdom. Obviously, the published microbiome research has limitations in terms of sample sizes, effect sizes, and cross-sectional designs. Nonetheless, if established, these findings have potential clinical implications for developing therapeutic and preventive interventions to enhance psychosocial and cognitive functioning. For example, specific psychobiotics (ie, probiotics and prebiotics that exert psychological effects via microbiome–gut–brain axis) could be a novel treatment option for behaviors like loneliness.

Psychiatry is in early stages of biopsychosocial research in positive psychiatry but studies like Hettwer et al.'s⁶ suggest an exciting new frontier of innovative science to enhance overall functioning and well-being in

people with and without serious mental illnesses through multipronged strategies. Neuropsychiatric innovations in prevention and intervention can help significantly reduce the toll of mental illnesses and enhance the mental well-being of the general population. From a public health perspective, an important target should be the most disenfranchised groups in the society such as the homeless, the incarcerated, and the marginalized populations at risk for serious mental illnesses. A major barrier is that the existing healthcare system is not set to make the necessary changes. Yet, there is substantial reason to begin testing implementation of this long-neglected approach that has clear promise. Positive psychiatry, through illness prevention and wellness promotion, can help make the healthcare less burdensome and more effective. The statement “we need more research” has become a cliché, but it applies to this topic area strongly and urgently.

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Conflict of interest

The authors declare no conflict of interest.

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