



Viewpoint

The impact of COVID-19 on mental health: The interactive roles of brain biotypes and human connection

Sarah L. Hagerty^{a,b,*}, Leanne M. Williams^{a,b,**}^a Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, Stanford, CA, USA^b Mental Illness Research Education and Clinical Center (MIRECC), Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

ARTICLE INFO

Keywords:

COVID-19

Precision psychiatry

Personalized medicine

Neural taxonomies

Social connection

ABSTRACT

COVID-19 along with the mitigation strategies being used to address the virus pose significant threats to our individual and collective mental health. As the crisis evolves and persists, it will be increasingly important for the research community to conduct investigations that address the mental health consequences of COVID-19. The causes of mental health effects in the context of COVID-19 are multifactorial and likely include biological, behavioral, and environmental determinants. We argue that the COVID-19 crisis significantly threatens our basic human need for human connection, which might serve as a crucial environmental factor that could underlie the overall insult to our mental health. Furthermore, “brain styles,” which we have previously conceptualized as “biotypes” that are informed by a neural taxonomy, might interact with the universal threat to our need for human connection to explain the mental health consequences of COVID-19 from a precision psychiatry perspective. The goal of this viewpoint is to inspire research on the mental health consequences of COVID-19 from an individualized, brain-based perspective that honors the profound threat that the virus poses to our basic human motivations.

The COVID-19 pandemic is, by definition, a significant threat to humanity. The pandemic is straining our healthcare and economic systems in ways that are significant and obvious. Beyond these domains, COVID-19 poses a profound threat to our most basic human motivations, especially human connection. While the threat to human connection is nearly universal, the specific pathways by which COVID-19 impacts our mental health are likely variable across individuals. In this viewpoint, we argue that research on the mental health consequences of COVID-19 should be sensitive to the universally experienced insults to our basic human motivations while simultaneously honoring the nuanced variable nature of COVID-19's mental health determinants from a precision psychiatry perspective. To support this effort, we advance hypotheses on how personalized brain profiles interact with our core need for human connection in the context of COVID-19 to underlie some of the mental health consequences of the pandemic. The research community could benefit from considering these issues as we begin to study the impact of COVID-19 on psychiatric well-being. Ultimately, developing a deeper understanding of how biological, behavioral, and environmental mechanisms vary across individuals and underlie the mental health consequences of COVID-19 could result in personally tailored interventions

and precision insights.

1. Human connection: A core human motivation

Initially posited in his seminal 1943 paper, Maslow's Theory of Human Motivation outlines a set of basic human needs that are organized into a hierarchy of relative prepotency, anchored by physiological needs and self-actualization as the lowest order and highest order needs, respectively (Maslow, 1943). First, Maslow posits that, at the most basic level, humans are driven to satisfy *physiological needs* that sustain life, including air and food. Second, humans are motivated to pursue *safety*, which is reflected by our preference for order, certainty, and comfort over unfamiliarity, inconsistency, and chaos. Third emerges a deep hunger for *love and belonging*, which becomes gratified by connecting physically and emotionally with other people. Fourth, we have a need to perceive ourselves with high evaluation and to feel respect for our self and others, which Maslow labels our *esteem* need. Finally, if one is fortunate enough to have these foundational needs met, they will be greeted with a new discontent, which is satisfied by meeting one's true potential. Maslow refers to this ultimate sense of fulfillment as the pursuit

* Corresponding author. Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, Stanford, CA, USA.

** Corresponding author.

E-mail address: shagerty@stanford.edu (S.L. Hagerty).<https://doi.org/10.1016/j.bbih.2020.100078>

Received 27 April 2020; Accepted 3 May 2020

Available online 7 May 2020

2666-3546/Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

of self-actualization.

COVID-19 stands to threaten all layers of Maslow's Hierarchy, and deficits across each of these core needs have deleterious consequences for our mental health. Particularly salient, however, is the profound impact of COVID-19 on satisfying our need for human connection, a need the Maslow labeled *love and belonging*. Maslow's original theory posited that needs follow a stepwise progression, such that higher order needs emerge as each preceding motivation becomes satisfactorily met. By this interpretation, human connection could be mistaken for a relatively higher order motivation that is perhaps necessary to *thrive* but not necessary to *survive*. In contrast, some have argued that social connection is the most essential need for survival among humans (Lieberman, 2013). Empirically, studies highlight the essential role of physical social contact and emotional social connection in species' survival (Harlow & Zimmermann, 1959). In line with this latter stance, the reality of our species experiencing a collective deficit in human connection has substantial implications for our mental health and our overall human experience.

The current level of profound human disconnection has environmental, biological, and behavioral determinants. One obvious environmental determinant is nearly universal in nature. That is, individuals across the United States and the globe are increasingly being encouraged or required to stay in their homes, separated from friends, family, and colleagues, with the narrow exception of leaving to engage in essential activities. While these mitigation techniques are currently necessary from a public health perspective, this unprecedented level of physical isolation is incompatible with our basic human instincts and motivations. In addition to this near ubiquitous environmental threat to connection, unmet need for human connection is further reinforced by biological and behavioral mechanisms that vary between individuals. Below, we outline how neurobiologically based psychiatric taxonomies could interact with COVID-19, human connection, and mental health.

2. Brain styles and the impact of COVID-19 on human connection

Along with other groups, we have characterized "biotypes" that are informed by a neural taxonomy and which we conceptualize as brain styles that contribute to the manifestation of mental health dysfunction (for review: Williams, 2017). In concert with the pervasive threat to human connection posed by COVID-19, these brain styles could be determinative of how individuals experience the pandemic from a mental health perspective. Here, we briefly describe three such brain styles and posit evidence-informed hypotheses on how each brain style might interact with deficits in human connection to underlie mental health challenges in the context of COVID-19. As outlined below, a confluence of literature suggests that these brain styles hinder human connection. We argue that COVID-19 could act as a catalyst that might exacerbate these human connection deficits via pathways that vary across brain styles. Given the relationship between human connection and mental health (Eisenberger, 2012), these dynamics may have profound implications for the mental health consequences of COVID-19. It is not our objective to comprehensively discuss the full range of consequences that each brain style has on human connection and mental health. Rather, we attempt to highlight several hypotheses that could be empirically tested as researchers investigate the neural, behavioral, and environmental mechanisms involved in the mental health consequences of COVID-19, including how these dynamics vary across individuals.

2.1. "Rumination" brain style

Rumination, a clinical construct commonly associated with depression, is a style of responding to distress that involves repetitively and passively focusing on the experience of distress. A ruminative thinking style is thought to have neural determinants, and our group has posited that these neural patterns comprise a ruminative brain style (for review: Williams, 2017). Specifically, a ruminative brain style is one that has previously associated with altered connectivity of the default mode

network of the brain (Williams, 2017). An overabundance of connectivity has been associated with rumination about internal concerns and worries about the future, whereas too little connectivity has been associated with an overgeneralized sense of self so that achieving an internal sense of control may be difficult (Williams, 2017). In addition to affecting how individuals see and feel about themselves, rumination also has deleterious consequences for how individuals relate to others. For example, ruminators are perceived by others as having a number of undesirable qualities, including dependency and neediness, being perseverative on worries and negative events, aggressive, and ruminators are seen as generally less favorable by others. As a result, ruminators are less likely to receive emotional support from others, and more likely to experience social friction, especially during times when they are in need of support (Nolen-Hoeksema and Davis, 1999).

Importantly, individuals who are characterized by a ruminative brain style could experience an exacerbation of rumination consequences due to COVID-19. Specifically, a ruminative style could exacerbate an individual's perceived threat to their physical health. Some empirical evidence supports this hypothesis, as a ruminative thinking style has been associated with a tendency to focus on health concerns. For example, prior work has found that individuals with a ruminative thought style are more likely to incorporate health concerns into autobiographical memory, and this could exacerbate their sense of vulnerability to illness and health-related anxiety (Sansom-Daly et al., 2016). Thus, individuals with a ruminative brain style could reasonably experience an increased need for social support while simultaneously encouraging social friction and negative perceptions from others as their ruminative tendencies become exacerbated by the health threats posed by COVID-19. Therefore, individuals with preexisting ruminative tendencies may be at particular risk of experiencing a deficit in human connection during COVID-19. Importantly, ruminative thought tendencies have been associated with deleterious mental health consequences, including depression, depressive affect, life satisfaction, and overall poor psychological health (Ysseldyk et al., 2007), and exacerbation of a ruminative thought style could negatively impact mental health via decreased social connection in the context of COVID-19.

2.2. "Anhedonia" brain style

Anhedonia is behaviorally characterized by a relative failure of experiencing pleasure from activities or stimuli once enjoyed. Neurobiologically, anhedonia is associated with variability across neurobiological substrates, including under-engagement of the brain's reward network. Specifically, hypoactivation across the striatum has been consistently associated with anhedonia, and our group conceptualizes hypoactivity within reward networks to be broadly consistent with an anhedonia brain style (Williams, 2017). Anhedonic states may be propagated by a "vicious cycle," in which an underactive reward system dampens an individual's motivation to engage in activities that are usually experienced as pleasurable (Husain and Roiser, 2018), as these efforts are not reinforced with a requisite sense of reward, including anticipatory reward. In the context of this dysfunctional reinforcement cycle, sources of stimulation become increasingly limited and the anhedonia worsens (Berridge and Robinson, 2003).

Under normative conditions, social interaction activates reward circuitry in the brain, and motivates approach-oriented decision making toward further social connection (Ruff and Fehr, 2014). An individual experiencing anhedonia, however, demonstrates dampened reward in response to social connection and interactions (Dodell-Feder and Germine, 2018). There is some evidence that individuals characterized by an anhedonic brain style show neural patterns of diminished reward in response to social connection. For example, individuals who fit an anhedonic brain style demonstrate hypoactivation of reward networks in response to socially rewarding stimuli (Williams, 2017). Moreover, anhedonia has a functional impact on engagement in social connection, as social anhedonia has been associated with decreased social support

and impaired functioning in social domains (Blanchard et al., 2011).

Cruelly, COVID-19 sets the perfect stage for the propagation of social anhedonia cycle. Due to social distancing ordinances, exposure to usual sources of rewarding stimulation, including sources of human connection, are markedly reduced in our current reality. As reviewed above, reduced exposure to rewarding stimuli seems to fuel a cycle of anticipatory reward deficits, diminished motivation for engaging in social interaction, and blunted reward (Dodell-Feder and Germine, 2018; Ruff and Fehr, 2014). Thus, individuals who are already primed for blunted anticipatory reward, such as individuals with an anhedonic brain style, could experience an even greater degree of amotivation to connect with others. In further support of this hypothesis, chronic deprivation of social interaction is experienced as a stressor, and animal models suggest that consistent exposure to stress exacerbates reward deficits in the context of anhedonia, which is mediated by modifications in the brain's reward circuitry (Willner et al., 1992). Due to the interplay among these neural and behavioral processes, individuals with an anhedonic brain style are at risk for social withdrawal. Thus, individuals with an anhedonic brain style may experience exacerbated threat to their core need for human connection during COVID-19. Exacerbation of anhedonia has deleterious consequences for mental health, as anhedonia has been associated with depression, suicide, and overall poorer quality of life (Winer et al., 2016). Furthermore, exacerbation of anhedonia during the pandemic could also negatively impact mental health via diminished social connection, as social disconnection is associated with deleterious mental health consequences (Eisenberger, 2012).

2.3. "Threat dysregulation" brain style

Individuals vary on how they interpret stimuli that they encounter in their internal experience and external environment. Some individuals have a bias towards attending to threatening stimuli in their environment. Neurobiologically, this tendency could result from heightened reactivity within the brain's threat networks. Consistent with the idea of a threat dysregulation brain style, attentional bias towards threat appears to have neural signatures. Specifically, a threat dysregulation brain style has been characterized by hyperactivation of the amygdala (Williams, 2017) and hypoactivation in the medial prefrontal, including anterior cingulate, cortex (Williams, 2017) in response to threatening stimuli. Subsequent work highlights how this brain-mediated attentional bias towards threat emerges as a transdiagnostic trait that commonly appears among individuals with clinical anxiety of various types (Abramowitz and Blakey, 2020). In addition to contributing to psychiatric dysfunction, threat dysregulation impacts our social relationships and connections with others, as individuals who experience an overactive threat response are more likely to withdraw from social relationships and connections (Pérez-Edgar et al., 2011). The relationship between overactive threat appraisal, anchored in neural dysregulation, and social disconnection could be reinforced in a cyclical manner. That is, individuals who report high perceived social isolation are particularly attuned to social threats and rejection, which leads individuals to think and act more negatively towards others, thus fueling further social disconnection (Cacioppo et al., 2014).

At present, the brains of individuals are constantly being prompted to evaluate threat in their environment given the pervasive presence of COVID-19 in our collective awareness and our natural tendency to evaluate and categorize threats that we encounter. For example, we are being confronted with internal stimuli (e.g., signs of illness symptoms) and external stimuli (e.g., possible contaminated surfaces, other people), which are likely to be perceived by our brain as threatening cues related to COVID-19. Some evidence suggests that a bias to threat expressed in behavioral responses and allocation of attention is exacerbated by stress (Mogg et al., 1990). Importantly, COVID-19 is a significant source of stress and poses a well-defined threat. Thus, individuals with a threat dysregulation brain style may experience an heightened allocation of attention to potential sources of threat during the pandemic. Given the

relationship between attentional biases to threat bias and social (dis) connection (Pérez-Edgar et al., 2011), individuals with a threat dysregulation brain style may be at particular risk for experiencing deficits in human connection during the pandemic. Threat bias alone has deleterious implications for mental health, as behavioral biases towards threat are associated with elevated anxiety and depression (Ruhe et al., 2019). Additionally, a threat dysregulation brain style could negatively impact mental health via social disconnection given the association between social connection and psychiatric health (Eisenberger, 2012).

3. Significance

In this viewpoint we argue that the mental health consequences of COVID-19 are partially determined by an interaction between precision brain profiles and the universal threat to human connection posed by the virus. We argue that this perspective is a useful way to conceptualize the mental health consequences of the pandemic as it captures the depth of COVID-19's threat to the human experience and generates hypotheses on the mental health implications of COVID-19 from a nuanced, precision psychiatry perspective. In advancing this viewpoint at this crucial juncture of the pandemic, we aim to inspire the development of research questions on the mental health implications of COVID-19. It is our hope that evidence-informed hypotheses, including those that we offer in this article, will be tested empirically as researchers integrate research aims on COVID-19 into existing protocols and future studies. Ultimately, understanding the impact of COVID-19 on mental health from a personalized, brain-based perspective could lead to the development and implementation of maximally effective intervention strategies. Additionally, understanding the impact of COVID-19 in this way could provide crucial insights on the ways in which the pandemic stands to impact the trajectory of individuals' mental health beyond the era proximal to COVID-19. Finally, by grounding our perspective in a discussion of core human needs, we aim to highlight the responsibility incumbent upon researchers to honor the profound threat that COVID-19 poses to what makes us human when pursuing research in these areas.

Declaration of competing interest

Authors report no conflicts of interest.

References

- Abramowitz, J.S., Blakey, S.M., 2020. Overestimation of threat. In: *Clinical Handbook of Fear and Anxiety: Maintenance Processes and Treatment Mechanisms*. American Psychological Association, pp. 7–25. <https://doi.org/10.1037/0000150-001>.
- Berridge, K.C., Robinson, T.E., 2003. Parsing reward. *Trends Neurosci.* 26 (9), 507–513. [https://doi.org/10.1016/S0166-2236\(03\)00233-9](https://doi.org/10.1016/S0166-2236(03)00233-9).
- Blanchard, J.J., Collins, L.M., Aghevli, M., Leung, W.W., Cohen, A.S., 2011. Social anhedonia and schizotypy in a community sample: the Maryland Longitudinal Study of Schizotypy. *Schizophr. Bull.* 37 (3), 587–602. <https://doi.org/10.1093/schbul/sbp107>.
- Cacioppo, J.T., Cacioppo, S., Boomsma, D.I., 2014. Evolutionary mechanisms for loneliness. *Cognit. Emot.* 28 (1), 3–21. <https://doi.org/10.1080/02699931.2013.837379>.
- Dodell-Feder, D., Germine, L., 2018. Epidemiological dimensions of social anhedonia. *Clinical Psychological Science* 6 (5), 735–743. <https://doi.org/10.1177/2167702618773740>.
- Eisenberger, N.I., 2012. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. *Nat. Rev. Neurosci.* 13 (6), 421–434. <https://doi.org/10.1038/nrn3231>.
- Harlow, H.F., Zimmermann, R.R., 1959. Affectional responses in the infant monkey. *Science* 130 (3373), 421–432.
- Husain, M., Roiser, J.P., 2018. Neuroscience of apathy and anhedonia: a transdiagnostic approach. *Nat. Rev. Neurosci.* 19 (8), 470–484. <https://doi.org/10.1038/s41583-018-0029-9>.
- Lieberman, M.D., 2013. *Social: Why Our Brains Are Wired to Connect*. OUP, Oxford.
- Maslow, A.H., 1943. A theory of human motivation. *Psychological review* 50 (4), 370.
- Mogg, K., Mathews, A., Bird, C., Macgregor-Morris, R., 1990. Effects of stress and anxiety on the processing of threat stimuli. *J. Pers. Soc. Psychol.* 59 (6), 1230–1237. <https://doi.org/10.1037/0022-3514.59.6.1230>.
- Nolen-Hoeksema, S., Davis, C.G., 1999. "Thanks for sharing that": ruminators and their social support networks. *J. Pers. Soc. Psychol.* 77 (4), 801–814. <https://doi.org/10.1037/0022-3514.77.4.801>.

- Pérez-Edgar, K., Reeb-Sutherland, B.C., McDermott, J.M., White, L.K., Henderson, H.A., Degnan, K.A., Hane, A.A., Pine, D.S., Fox, N.A., 2011. Attention biases to threat link behavioral inhibition to social withdrawal over time in very young children. *J. Abnorm. Child Psychol.* 39 (6), 885–895. <https://doi.org/10.1007/s10802-011-9495-5>.
- Ruff, C.C., Fehr, E., 2014. The neurobiology of rewards and values in social decision making. *Nat. Rev. Neurosci.* 15 (8), 549–562. <https://doi.org/10.1038/nrn3776>.
- Ruhe, H.G., Mocking, R.J., Figueroa, C.A., Seeverens, P.W., Ikani, N., Tyborowska, A., Browning, M., Vrijnsen, J.N., Harmer, C.J., Schene, A.H., 2019. Emotional biases and recurrence in Major Depressive Disorder. Results of 2.5 years follow-up of drug-free cohort vulnerable for recurrence. *Front. Psychiatr.* 10.
- Sansom-Daly, U.M., Bryant, R.A., Cohn, R.J., Wakefield, C.E., 2016. Rumination and self-defining memories in the context of health concerns. *Memory* 24 (7), 939–948. <https://doi.org/10.1080/09658211.2015.1059860>.
- Williams, L.M., 2017. Defining biotypes for depression and anxiety based on large-scale circuit dysfunction: a theoretical review of the evidence and future directions for clinical translation. *Depress. Anxiety* 34 (1), 9–24. <https://doi.org/10.1002/da.22556>.
- Willner, P., Muscat, R., Papp, M., 1992. Chronic mild stress-induced anhedonia: a realistic animal model of depression. *Neurosci. Biobehav. Rev.* 16 (4), 525–534. [https://doi.org/10.1016/S0149-7634\(05\)80194-0](https://doi.org/10.1016/S0149-7634(05)80194-0).
- Winer, E.S., Drapeau, C.W., Veilleux, J.C., Nadorff, M.R., 2016. The association between anhedonia, suicidal ideation, and suicide attempts in a large student sample. *Arch. Suicide Res.* 20 (2), 265–272. <https://doi.org/10.1080/13811118.2015.1025119>.
- Ysseldyk, R., Matheson, K., Anisman, H., 2007. Rumination: bridging a gap between forgiveness, vengefulness, and psychological health. *Pers. Individ. Differ.* 42 (8), 1573–1584. <https://doi.org/10.1016/j.paid.2006.10.032>.