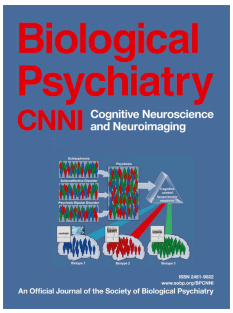

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Paul D. Hastings, Amanda E. Guyer, Luis A. Parra

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Conceptualizing the influence of social and structural determinants of neurobiology and mental health: Why and how biological psychiatry can do better at addressing the consequences of inequity

Paul D. Hastings*[a,b], Amanda E. Guyer[b,c], & Luis A. Parra[d]

[a] Department of Psychology, University of California Davis, USA

[b] Center for Mind and Brain, University of California Davis, USA

[c] Department of Human Ecology, University of California Davis, USA

[d] Brown School of Social Work, Washington University in St. Louis, USA

* Corresponding author

Paul D. Hastings

Center for Mind and Brain

267 Cousteau Place

Davis, CA 95618

Phone: 530-601-1835

Email: pdhastings@ucdavis.edu

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Abstract

Psychiatry and allied disciplines have recognized the potency of structural and social determinants of mental health, yet there has been scant attention given to the roles of neurobiology in the links between structural and social determinants and mental health. In this article, we make the case for why greater attention must be given to structural and social determinants of biological psychiatry by researchers, practitioners and policy-makers. After defining these terms and theoretical frameworks for considering their relevance in biological psychiatry, we review empirical research with marginalized and minoritized racial, ethnic, gender, sexual and economic communities that reveals the ways in which structural and social determinants affect neurobiological functioning with implications for mental health. We give particular emphasis to developmental science and developmentally-informed research, as structural and social determinants influence neurobiological adaptation and maturation across the lifespan. We conclude with recommendations for advancing research, practice and policy connecting biological psychiatry with structural and social determinants of health. Foremost among these is diversifying the ranks of biological psychiatry, from the classrooms through the laboratories, hospitals and community health centers. Transforming and advancing the understanding of the structural and social determinants of neurobiology and mental health is most likely to come through transforming the discipline itself.

Disparities and inequities in mental health across diverse marginalized and minoritized communities are well-documented(1,2). Recognition of structural and social determinants of mental health is increasing(3,4). Many theories posit that the development and functioning of the brain and peripheral biological systems play key roles in the links between inequities and worse mental health across the lifespan(5,6). Yet, until recently, the roles that neurobiology play in the developmental processes linking structural and social determinants with mental health have received relatively little attention.

We present arguments and evidence in support of committing greater attention to structural and social determinants of biological psychiatry. First, we provide a brief overview of theoretical frameworks linking structural and social determinants with mental health via neurobiology, which cohere around a developmental perspective on health. As developmental scientists, this perspective is reflected in the second section, a review of relevant research examining structural and social determinants in relation to brain structure and function, diurnal and acutely reactive hypothalamic-pituitary-adrenal (HPA) axis functioning, and tonic (baseline) and phasic (reactive) aspects of the autonomic nervous system (ANS) and immune (inflammatory) system. Third, the paper concludes with suggestions for translating these perspectives and empirical findings into actions for advancing research, training, practice and policy in biological psychiatry and allied disciplines.

Definitions and perspectives

Interpretations of "structural and social determinants" vary, and our perspective is informed by multiple sources(7–9). Consideration of this topic requires acknowledgement of the current and historically-perpetuated geographical, political, economic and societal conditions into which one is born and within which one lives. These conditions variably constrain or

provide access to opportunities that promote healthy biopsychosocial adjustment. Collectively, one's life conditions are seen as the roots of one's health, including neurobiological and mental health(10–12), and these conditions vary across racial, ethnic, national, gender, sexuality, economic and other individual and community characteristics. Recognizing that variability exists in individuals' life conditions necessitates also recognizing that lives begin on an uneven playing field for healthy development.

Structural and social determinants are overlapping and interdependent constructs. Whether a measure or phenomenon is understood as operating at the structural or social level, or both simultaneously, can depend on how narrow or broad a lens one brings to that understanding. Acknowledging others may use the terms differently, or apply additional distinctions (i.e., institutional, systemic)(7), we define structural determinants as encompassing the political, economic and social policies, practices and values that function at national and local levels to affect the availability of resources, civil rights and protections, and overall cultural climate within which people live. When these determinants reinforce power structures that disadvantage some groups and place them in subordinate and under-resourced positions relative to more dominant groups, such as the gender wage gap, redlining and neighborhood segregation, and voter suppression, the disadvantaged individuals and groups are structurally minoritized(7,9,13,14). Social determinants include people's daily lived experiences resulting from these structural conditions, such as personal material resources, education and employment, neighborhood resources, health care access, and inclusive versus discriminatory treatment by others. More neurobiological research has focused on social than structural determinants(13), although the latter may be the primary drivers of national and global health inequities(4,9).

Several theoretical models position structural and social determinants as contributors to neurobiology and mental health. McEwen's(15,16) model of allostatic load (AL) posits that prolonged stress system activation due to chronically aversive life conditions eventually disrupts the ability of stress systems to flexibly modulate activity in response to daily challenges(17), thereby eroding healthy functioning. The stress sensitization hypothesis contends that varying exposures to chronic or severe stressors in early life primes biological stress systems for exaggerated reactivity in adolescence and adulthood(18), which Hostinar and colleagues(19) extended to distinguish multiple biopsychological repertoires of acute stress responses that may underlie resilience versus distinct psychopathologies. Meyer(20), Myers(21) and others have proposed minority stress models that apply these views directly to the experiences and development of marginalized populations. Informed by an intersectional perspective on the synergistic consequences of having multiple identity characteristics(22), such as being racially marginalized and devalued for being transgender, minority stress models posit that both direct experiences of discrimination and lack of resources (social determinants) and overarching life conditions that maintain disadvantage, marginalization and disempowerment (structural determinants) are neurotoxic, undermining mental health through their biological effects(23,24).

These models of biological embedding, or "stress getting under the skin"(25), implicitly or explicitly reflect a lifespan developmental perspective. Structural and social determinants are relatively severe, chronic and stable – often, multi-generational – conditions. These may influence developing neurobiological systems underlying mental health throughout the lifespan. This perspective pertains even when considering adult populations, and research indicates that adverse social and economic conditions in the first two decades of life predict mental and physical health disparities in adulthood and older age(26,27). In the following review, we

consider the evidence that structural and social determinants affect neurobiological maturation, and affect mental health through neurobiology, with particular focus on the first two decades of life.

Evidence for relations between social and structural determinants and neurobiology

Of the social determinants, most research has focused on either household economic resources, or individuals' experiences of discrimination. Considering economics and the brain first, being raised in poverty is associated with structural and functional changes including reduced hippocampal volume, altered prefrontal cortex (PFC) activity to emotional and cognitive tasks, and reduced connectivity between PFC and the amygdala(28–30), potentially attributable to experiencing more stressors in the home(31). Childhood poverty continues to leave a mark on the brain in adulthood. Men raised in highly disadvantaged neighborhoods demonstrated less differentiation in structural brain networks(32) and middle-aged individuals from lower SES backgrounds have been found to have lower resting state connectivity and reduced cortical thickness(33), neural indices of less functionality and organizational efficiency. Conversely, increasing economic resources for impoverished children promotes healthier brain development. The Baby's First Years randomized controlled trial of monthly cash transfers to low-income new mothers showed that financial support to families enhanced infants' electroencephalography (EEG) power in high-frequency bands associated with better cognitive, language, and social-emotional functioning(34). For U.S. Mexican-origin adolescents living in poverty, increasing family income from 10 to 16 years predicted stronger resting state functional connectivity between the posterior cingulate gurus and insula and right inferior frontal gyrus, regions of the default mode network that supports social cognition(35); income changes were not associated with connectivity for youths living in financially secure families.

Economic hardship is linked with altered stress responses, including both reduced (hypocortisolism)(36) and exaggerated (hypercortisolism)(37) diurnal and acute HPA activity, which can incur myriad physical and mental health problems(15,16,38). Diurnal hypercortisolism is more prevalent in infants and younger children living in poverty(39), whereas hypocortisolism emerges after more time spent in poverty(40,41), potentially reflecting the cumulative toll of AL. Exemplifying early-emerging stress activation, Fernald and Gunnar(42) reported that hypercortisolism in preschool-aged children living in low-income families in rural Mexico was alleviated through a cash-transfer program, compared to children in families that were not enrolled in the program. Exemplifying the suppressive effect of more chronically endured poverty, U.S. Mexican-origin adolescents who lived in deep poverty from 10 to 16 years evinced HPA hyporeactivity (decreasing cortisol) following a social exclusion task, whereas youths who had not experienced poverty evinced cortisol increases from before to after the social challenge(43).

Childhood poverty predicts elevated tonic and reactive cardiovascular activity, especially blood pressure(12,44), in adolescence and adulthood. Effects are less consistent in pre-adolescent children(45–47), suggesting that ANS effects emerge over prolonged exposure to poverty, or that adolescence may be a sensitive period for the effects of poverty on cardiovascular health(30). Similarly, socioeconomic status (SES) in childhood and adolescence is inversely associated with chronic inflammation, both concurrently and into adulthood(48–51). These associations hold after accounting for changes in occupation and education over time(52), and appear to magnify with age(53). Studies of AL involving activity across multiple systems (i.e., HPA, ANS, immune) are consistent; children raised in poverty have increased AL in late adolescence(54,55) and adulthood(27).

Similarly to poverty, experiences of discrimination that target persons based on their non-majority social status constitute severe and pervasive sources of social stress that affect numerous biological systems(56). Interpreting acute negative treatment as racial/ethnic discrimination evokes elevated anterior cingulate cortex (ACC) activity associated with emotion regulation in both Black adults in the U.S.(57) and Turkish adults in Germany(58), potentially reflective of stress and coping efforts. Experiencing more chronic racial discrimination predicts reduced total brain volume in Black youths with depression symptoms(59), disrupted white matter microstructure in Black women with trauma histories(60), and increased activation and connectivity of multiple regions involved in vigilance, arousal and emotion regulation in Black adults with trauma histories(61,62). Such findings reveal the cumulative toll of racial discrimination on brain health.

Numerous studies indicate that marginalized individuals evince flatter diurnal cortisol slopes, especially for those who have experienced more discrimination(23,63), manifested as both hypocortisolism(64,65) and hypercortisolism(66,67). Hypercortisolism also is evidenced by increased hair cortisol concentrations in adults who experienced more discrimination(68). Racial discrimination experiences in early adolescence, but not early adulthood, predicted diurnal hypocortisolism in Black adults 20 years later(69); pubertal maturation and identity formation processes may make early adolescence a particularly sensitive period for the neurotoxic effects of discrimination. Yet, Black mothers' experiences of discrimination predicted their infants' elevated acute cortisol reactivity at 12 months(70), indicating discrimination has effects across the lifespan, and again suggesting that stressful life contexts may initially increase HPA activity, before tonically suppressing it after chronic exposure.

Sexual and gender identity discrimination is associated with disrupted adrenocortical functioning in lesbian, gay, bisexual, transgender, and queer (LGBTQ+) youths and adults. Sexual or gender minority status disclosure may increase discrimination exposure(71), and being "out" was associated with elevated cortisol and distress(72,73). Conversely, those who are not "out" may perceive greater risk with disclosing(74). Unlike other marginalized identity characteristics, family members typically do not share the sexual or gender identity of LGBTQ+ individuals. Lack of family support predicted stronger HPA reactivity in LGB young adults(75). Identifying with multiple minoritized characteristics can carry biological burdens(23,76). LGBTQ+ Latinx young adults who experienced both heterosexist and racist discrimination were challenged in forming an integrated intersectional identity, which in turn predicted hypocortisolism(24).

Across adolescence and adulthood, discrimination is associated with activity of the cardiovascular and immune systems(49,56,77). As evidence of discrimination's cumulative impact, African American adults' experiences of discrimination predicted greater chronic inflammation only for those who also had experienced higher levels of discrimination 18 years earlier, in pre-adolescence(78). This "double-hit model" again indicates that early adolescence may be a susceptible period for the pernicious neurobiological effects of discrimination against core identity characteristics. Indeed, meta-analyses have shown that, from adolescence through late adulthood, chronic inflammation increased more in racially minoritized and impoverished versus majority and economically secure groups(53). Inflammatory markers also were elevated in LGBTQ+ individuals versus heterosexual and cisgender individuals(79), possibly exacerbated by lack of family support(80) and discrimination experiences for those who are "out"(81).

Fewer studies have directly addressed links between structural determinants and neurobiology. Unequal prevalence of ethnic and racial minority groups across neighborhoods, often the intentional result of policy decisions pertaining to zoning, mortgages, and highway construction(7), during early adulthood predicted Black participants' reduced brain volume in middle adulthood(82), and was concurrently linked to increased inflammation and AL in adults(83). This latter finding was true for all racial/ethnic groups, over and above SES; hence, neighborhood segregation takes a biological toll on both advantaged majority group members and less advantaged and marginalized peoples. Structural racism quantified at the state level (e.g., racial differences in incarceration rates) predicted reduced hippocampal volume for Black and Latinx, but not White, pre-adolescents living in states with greater structural racial/ethnic stigma, independent of personal experiences of discrimination(84); a similar effect was noted for girls, but not boys, living in states with more structural gender stigma. Analogously, LGB young adults who had spent their adolescence living in counties and states that were more stigmatizing of LGBTQ+ people had hyporeactive cortisol responses to an acute stressor, relative to LGB individuals who had been raised in less stigmatizing environments(85). Similarly, beyond individual characteristics and state-level poverty, state-level structural racism predicted elevated prevalence of myocardial infarction for Black adults living in more versus less racist states; a weaker opposite tendency was noted for White adults(86).

As noted previously, chronic structural stressors may suppress HPA axis activity, whereas acute structural stressors may have the opposite effect. We found that young adults in California evinced diurnal hypercortisolism immediately following the 2016 Pulse Nightclub Massacre in Florida, which gradually declined over the subsequent two months(87). This could be seen as indicative of peripheral biological impacts from structural determinants related to lax

gun control laws and strong beliefs in gun ownership rights that contribute to the U.S. public health crisis of mass gun violence(88–90). This stress activation response was equally evident in those who shared or did not share identity characteristics with the majority of the 49 victims of the massacre (LGBTQ+, Latinx, male), paralleling evidence of elevated distress symptoms in the general Florida population following the massacre(91). Again, such findings suggest that structural inequities may undermine the well-being of all people, not only the marginalized peoples who are most directly disadvantaged by those inequities.

SES is a multifaceted construct that can demarcate exposure to various determinants (92), including where families live. Disparities between neighborhoods prospectively predict the prevalence of psychiatric disorders(93–96). Whether neighborhood-level measures should be considered structural or social determinants is debatable. Local crime rates, median household value and unemployment affect individuals' daily experiences, and are the products of municipal, state and national laws, policies and practices(7). Neighborhood characteristics have been associated with the neurobiology underlying mental health. Independent of family economic resources, living in neighborhoods with greater poverty, deterioration and crime during childhood(97,98) or adolescence(99–101) was associated with patterns of neural reactivity indicative of accelerated brain maturation and either dampened or sensitized neural reactivity in multiple brain regions that control behavior and emotion. For example, reduced inferior frontal gyrus (IFG) activation during a Go/No-Go task accounted for the association of greater neighborhood poverty and poorer response inhibition in children and adolescents(101). Considering peripheral effects, as with lower family SES, lower neighborhood SES was associated with diurnal hypocortisolism in adolescents(102). Neighborhood SES also is conflated with variation in exposure to pollutants that can have neurotoxic effects(103). Independent of

family and neighborhood SES, greater neighborhood level exposure to air (e.g., fine articulate matter, PM2.5) and water (e.g., lead, arsenic) pollutants from 10 to 16 years predicted stronger sympathetic and weaker parasympathetic influence over ANS activity at 17 years in U.S. Mexican-origin adolescents, which could increase risk for myriad illnesses in adulthood(104). Hence, neighborhood economic disadvantage exposes developing neurobiological systems to multiple kinds of threats.

Social and structural determinants, neurobiology, and mental health

Decades of research show that the central and peripheral systems impacted by structural and social determinants are intricately linked to mental health(2,5,23,105). Multiple neurobiological processes are theorized to function as mechanistic biomarkers, conveying structural and social determinants' effects on mental health(15,18,19,21,106). Evidence indicates that links between childhood adversities (e.g., family poverty) and later psychopathology are mediated through accelerated maturation of emotion processing via frontolimbic functional connectivity, and deficits in reward processing via functional connectivity of the salience network and amygdala(107). SES has consequences for family processes(92), and links between family SES and brain functioning and development are themselves mediated by effects of economic adversity on family functioning(108). The clinical implications of these effects on connectivity may be realized in transdiagnostic, symptom-relevant manifestations such as emotion dysregulation, attention inflexibility, and inefficiencies and biases in processing information. Considering other neurobiological mechanisms, diurnal hypercortisolism accounted for the association between heterosexist discrimination and elevated depressive symptoms in LGB young adults(109). Neurobiological mediation is not always evident, however. In U.S. Mexican-origin adolescents, greater exposure to social threats including discrimination and

crime predicted both internalizing problems and multi-system coupling of PFC and ANS reactivity to emotional faces, but multi-system coupling did not mediate links between these social determinants and mental health(110). Stronger down-regulatory coupling of increased PFC activity with less ANS reactivity may have been an adaptation to chronically threatening contexts that could carry longer-term risks to mental health in future(111).

Building on biopsychosocial models of mental health(112,113), researchers have begun to examine the combined or moderating roles of social and structural determinants and brain structure and function in adolescent mental health(114). U.S. Mexican-origin adolescents with larger hippocampal volumes showed more depressive symptoms when they experienced more neighborhood crime, but fewer symptoms when less exposed to crime(115). Neighborhood crime was unrelated to symptoms of adolescents with smaller hippocampal volumes, suggesting that larger hippocampi may potentiate the effects of these social determinants. In this same sample, greater neighborhood and school crime exposure also predicted elevated externalizing problems, but only for adolescents with reduced activity in the posterior cingulate cortex, temporoparietal junction, and amygdala when thinking about how another person's emotional cues made them feel, referred to as emotion introspection(116). Adolescents with weaker neural evidence of emotional awareness, potentially indicative of dampened engagement with others' emotional needs, appeared to be more affected by crime exposure.

A moderated-mediation pattern involving the subgenual ACC, hostile environments, deviant behavior and family connection also has been found with these Mexican-origin youths(117). Experiencing high levels of hostility at school predicted stronger subgenual ACC activation to social exclusion, which in turn predicted more deviant behavior. As found for attribution of racial discrimination(57,58), the brain's processing of social exclusion may be a

mechanism linking hostile experiences with deviant behavior, perhaps as the subgenual ACC becomes sensitized to social threat. This mediation effect was moderated, though. Adolescents who felt less family connection showed the most deviant behavior if they had high subgenual ACC reactivity to social exclusion, yet the least deviant behavior if subgenual ACC reactivity was low. Adolescents who felt more family connection were buffered from deviant behavior, regardless of their neural response to exclusion. Family connection functioned as a protective contextual factor, and could be a potential target for biologically-informed interventions.

Advancing the work on structural and social determinants: Challenges in the field

Given the accumulating evidence for the pervasive and enduring effects of structural and social determinants on neurobiology and mental health, an immediate reaction could be to "do more, do better." Certainly more research is needed, and, we would argue, particularly more research on (a) how the effects of structural and social inequities on multiple neurobiological systems shape the course of mental health disparities across development, (b) what can be done to mitigate said effects of these inequities, and (c) how to reduce or remove the inequities themselves. Yet, this reaction may be too superficial, as there are challenges to reaching an effective understanding of social and structural determinants within biological psychiatry. These include representation of diversity within researchers and the populations they study, biological reductionism, and access to care and training.

There is a woeful lack of representation of diverse communities, and particularly of racially and ethnically minoritized and economically marginalized peoples, within biological psychiatry(118,119), owing at least in part to histories of structural oppression and exclusion(120,121). Yet, there is a corollary of working in a homogenous profession: Most who have been privileged enough to do this work are, themselves, the products of the same systemic,

structural, and social determinants that have excluded and harmed those who are underrepresented(122,123). The effects of being the beneficiaries of these determinants are, to be sure, quite different than the effects discussed previously, but they are likely to include unrecognized biases in the questions we ask, the approaches used to address those questions, the populations studied, what is prioritized in the data generated, the interpretations of those data, and the evaluation of others' research(124–126).

One such bias is that, in studying neurobiology, many assume they are studying things that are objective, measurable, and interpretable as having consistent and specific meaning. We must escape assumptions of universality and biological reductionism. The same size of a brain region, the same magnitude of an ERP component, the same level of a circulating hormone will not necessarily have the same implication for mental health when observed between individuals with very distinct life histories. While plausible that some neurobiological processes may be expected to unfold in a similar manner regardless of life history, it requires additional research with diverse populations to assess where such commonalities exist.

Psychiatric providers and services are limited and impacted (e.g., regional access, insurance constraints) particularly in communities ridden with structural and social challenges. Marginalized communities have learned to mistrust researchers due to an extensive history of scientific abuses(118,127) and failures to keep personally identifiable biological data protected(128). This limits the pool from which to recruit research participants in clinical settings. Both psychiatric clinicians and researchers need training in understanding issues pertaining to cultural and diversity competency.

Actionable steps

Diversify biological psychiatry. The relatively scant empirical attention to structural and social determinants of neurobiology and mental health likely stems from limited diversity within the field of biological psychiatry(129). Most scientists have not come from marginalized, minoritized, or disadvantaged communities; consequently, they have not attended to the forces affecting those communities. Acknowledging that fact behooves the field to recruit, mentor, retain, and scaffold the success of researchers and scientist-practitioners who reflect the diverse populations with which the field should be engaging. This will require financial investments of fellowships and stipends to defray the high costs of education that individuals from economically marginalized backgrounds cannot be expected to shoulder, and also investments of time and effort for scientists from advantaged and majority positions to learn how to effectively mentor and scaffold people with different life experiences. Given their life experiences, this next generation of scientists may apply alternate theoretical frameworks, pose unasked questions, implement innovative approaches, achieve novel insights, and train future scientists differently. Compared to past and current scientific norms, such changes should be recognized as (at least) equally likely to be valid models of practicing biological psychiatry.

A more diverse biological psychiatry would more effectively engage and work with diverse communities. Engaging in community partnerships through participatory action research and citizen science approaches could help biological psychiatry better identify the mental health issues of greatest relevance to a given community, and the research procedures that community is more likely to accept and support(130–132). Community partnerships could shift the field from deficits-based to strengths-based models of adaptation and resilience by recognizing and incorporating community-specific assets into our understanding of the multiple paths toward mental health and well-being across diverse populations. This also could help to strengthen the

pipeline for engaging the interests of young people from diverse communities in the pursuit of biological psychiatry as a profession.

Integrate structural and social determinants into the biologically-informed practice of psychiatry. Psychiatrists could be better supported to consider the roles of structural and social determinants of mental health when working with those living in disadvantaged contexts. The Diagnostic and Statistical Manual of Mental Disorders (DSM–5(133)), used to define, classify, and diagnose mental disorders in the U.S., has pending the DSM-5-Text Revision (DSM-5-TR(134)) which will incorporate the impacts of racism and discrimination into the diagnosis and manifestations of mental disorders. This is a step in the right direction given the evidence reviewed above. Diagnostic tools could incorporate the impacts of structural and social determinants on mental health, for example, by including a life stress interview approach in assessments. Psychiatric service-providers' ability to better account for the life experiences of diverse clients, and what these may mean for their neurobiological adaptations to context, should contribute to more effectively person-centered care. For example, psychotherapy is less effective for Black youth living in more racist communities(135); more research, informed by models of structural and social determinants of mental health, is needed to develop adequate health practices for this underserved population.

Psychiatric assessment and diagnosis may be further aided by including biological assays of peripheral markers indicative of exposures to structural and social determinants of mental health. For example, testing blood for toxin exposure that can result in psychiatric symptom-like behaviors, such as lead or mercury(136), would be straightforward. More "big data" research with large samples of participants from diverse communities will be needed to confirm for whom specific neural and peripheral biomarkers of exposures to adversity actually do confer

susceptibility to mental health problems. From such efforts, physiological tests of hormones, cytokines and other biomarkers that can be assessed from minimally invasive biospecimens may also become informative components of community-appropriate assessments.

Preventive approaches to reduce suffering from mental disorders and promote good mental health must acknowledge that early-life periods constitute particularly key windows in which to apply prevention strategies(137). Implementing appropriate and valid screening measures, including assessments of contextual influences, in community settings frequented by all youth, such as schools, would reach those constituencies with less access to primary care. Prevention and intervention strategies must be designed with structural and social determinants in mind, and then evaluated for evidence of efficacy and effectiveness.

Translate research into structural and social action. Standard interventions for individuals' mental health problems typically treat the symptoms rather than the root causes of problems. Identifying and understanding neurobiological mechanisms by which adversity, classism, sexism, heterosexism, transphobia and racism contribute to mental health disparities(23) is necessary for developing systems-level interventions to disrupt these fundamental structural and social causes of disease at both individual and community levels(14,138). Bolstering anti-discrimination policies may help dismantle barriers to access to housing, employment, education and fair treatment among economic, ethnic, racial, sexual, and gender minorities. More inclusive laws, policies and practices support healthier brain and peripheral physiological development(84,85), which in turn promote better mental and physical health.

Examples of such laws and policies exist, but often are not upheld, and governments need to be held accountable in exercising these protective measures(139). This extends to violence prevention and gun control legislation, social safety net programs, natural disaster emergency

response programs, and pollution control efforts, all of which disproportionately adversely affect marginalized and minoritized communities(87,140–143). Simultaneously, new legislation being enacted in many jurisdictions that further marginalize already vulnerable populations, such as denying gender-affirming health care to transgender minors(144) or restricting school curricula from addressing the topic of structural and social determinants(145), are themselves imposing new structural inequities. Knowing the profound effects of structural and social determinants of mental health behooves psychiatric scientists and practitioners to become social and political advocates for positive change to improve the life contexts of those we study and treat.

Globalize biological psychiatry. Internationalizing basic research, translational efforts, and social policy changes should be a priority. Mental health research involving neurobiology is being conducted in low- and middle-income countries (LMICs)(146,147), yet it remains the case that biological psychiatrists overwhelmingly pursue their science in high-income countries. The majority of the world lives in LMICs, and they too are subject to structural and social determinants of neurobiology and mental health. There are mutual, bidirectional benefits to rectifying this disparity in empirical work across the global population. For example, increasing investment in the necessary physical and personnel infrastructure (equipment and training) for scientists and practitioners in LMICs to pursue biological psychiatry would advance theory, research, and practice with diverse cultures and communities, and would bring more diverse perspectives and approaches into scientific endeavors. The Fogarty International Center at the National Institutes of Health provides one example of how infrastructure and research grants can be targeted toward scientific capacity-building within LMICs.

More work remains to validate biological and psychiatric constructs across cultures and countries. The International Classification of Diseases (ICD-11)(148) is widely-used in Europe

and across the globe. Working to bridge future revisions of the DSM-5-TR and ICD-11 with globally-informed understandings of structural and social determinants of mental health could advance the training of clinicians and researchers by, for example, recognizing variations in the relevant criteria for diagnoses within different cultures and communities, and across the lifespan.

Globally, countries with steeper income gradients (more wealthy and more impoverished members, relative to fewer middle-income members) have overall worse health across the economic spectrum, compared to countries with less economic disparity(149,150). Even while acknowledging that marginalized and disempowered members suffer the most, living in a country with greater structural and social inequity is unhealthy for everyone in that country, paralleling research on the biological tolls of structural and social inequities(83,87). Translating biological psychiatry into advocacy for reducing collective stress stemming from economic and other disparities could promote better global mental health and well-being.

Conclusion

The increasing empirical attention from biological psychiatry to structural and social determinants is revealing that they have pervasive and life-long impacts on the brain and other neurobiological systems, with profound consequences for mental health. More research on these processes clearly is needed, and particularly for structural determinants, to advance both the science and the practice of biological psychiatry. Doing this work well will require creative thinking and novel approaches from scientists who have experience and understanding of these structural and social determinants, and competence at building effective research partnerships with communities who have been disadvantaged by structural and social inequities. Building diversity within biological psychiatry and allied disciplines by involving more people who identify as members of marginalized racial, ethnic, gender, sexual and economic groups will

require intentional efforts for culture change within the field. Although diversifying the ranks of scientists serves to increase scientific innovation, the work of scientists from underrepresented backgrounds is systematically devalued(126), contributing to their greater likelihood of leaving academia(129,131). To better promote national and global well-being, we need more research on the structural and social determinants of neurobiology and mental health, by the people who are best positioned to engage effectively with this challenging work.

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