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RESEARCH ARTICLE

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Mental health is biological health: Why tackling "diseases of the mind" is an imperative for biological anthropology in the 21st century

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Abstract

The germ theory of disease and the attendant public health initiatives, including sanitation, vaccination, and antibiotic treatment, led to dramatic increases in global life expectancy. As the prevalence of infectious disease declines, mental disorders are emerging as major contributors to the global burden of disease. Scientists understand little about the etiology of mental disorders, however, and many of the most popular psychopharmacological treatments, such as antidepressants and antipsychotics, have only moderate-to-weak efficacy in treating symptoms and fail to target biological systems that correspond to discrete psychiatric syndromes. Consequently, despite dramatic increases in the treatment of some mental disorders, there has been no decrease in the prevalence of most mental disorders since accurate record keeping began. Many researchers and theorists are therefore endeavoring to rethink psychiatry from the ground-up. Anthropology, especially biological anthropology, can offer critical theoretical and empirical insights to combat mental illness globally. Biological anthropologists are unique in that we take a panhuman approach to human health and behavior and are trained to address each of Tinbergen's four levels of analysis as well as culture. The field is thus exceptionally well-situated to help resolve the mysteries of mental illness by integrating biological, evolutionary, and sociocultural perspectives.

KEYWORDS
evolutionary medicine, mental health, psychopathology

1 | INTRODUCTION

During the 20th century, the biomedical sciences rapidly reduced the global burden of infectious disease, leading to dramatic increases in life expectancy (Murray et al., 2015). In the 21st century, chronic, non-infectious diseases have emerged as major contributors to global disease burden (Benziger, Roth, & Moran, 2016), with mental disorders playing a substantial role (Whiteford et al., 2013). The causes of most mental disorders, however, remain a mystery, and there has been little progress in reducing the prevalence of any of them.

Here we provide a comprehensive critique of mainstream research on mental disorders (see Figure 1). First, we review the contribution of mental disorders to the global burden of disease. Second, we explore the successes and failures of biological psychiatry, including psychopharmacology, imaging and other biomarker research, and genetic and epigenetic approaches. Third, we critique the theoretical foundations of psychiatric classification, reviewing different concepts of disorder and disease. Our goal in the first half of our article is to convince biological anthropologists that there is a genuine and widely-recognized theoretical crisis in mental health research.

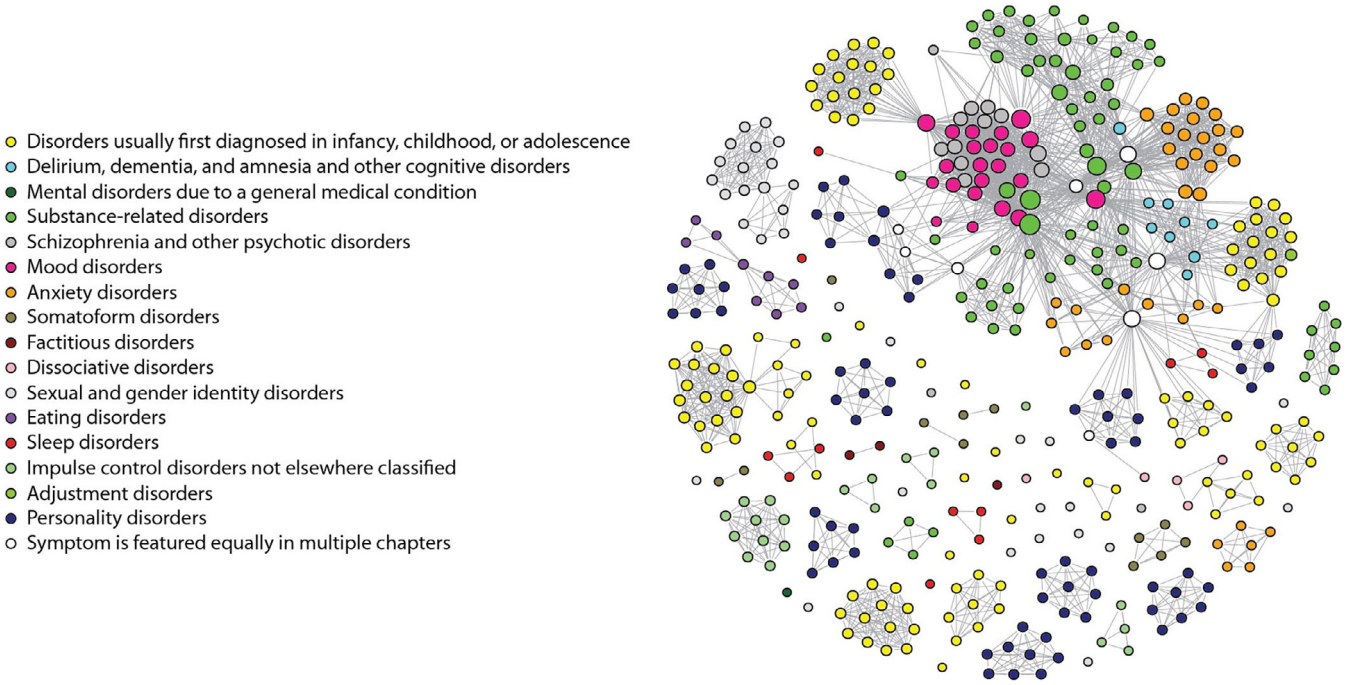

FIGURE 1 Symptoms of mental disorders as defined in the Diagnostic and Statistical Manual IV (DSM-IV). Each dot is one DSM-IV symptom. Symptoms are colored by the DSM chapter in which they occur most often. Symptoms that occur in the same disorder are connected by an edge. *Source:* Figure from Borsboom and Cramer (2013). An interactive version of this figure that identifies each symptom (node) is available in the supplementary material of Borsboom and Cramer (2013)

In the second half of our article, we sketch new approaches to mental health research from within mainstream psychiatry and clinical psychology, some of which are driven by the National Institute of Mental Health (NIMH). We then offer a provisional evolutionary schema for conceptualizing mental disorders that identifies one group as relatively rare disorders of development that are probably caused by genetic variants, one widespread group that comprises aversive but probably adaptive responses to adversity and therefore are likely not disorders at all, one group that is probably due to senescence, and one group that might be caused by mismatches between ancestral and modern environments. For each group, we review biocultural studies of mental health that provide fresh insights. Biological anthropologists are unique among the health-related researchers in that we take a panhuman approach to human health and behavior and are trained to address each of Tinbergen's four levels analysis (mechanistic, ontogenetic, phylogenetic, and function; for historical overview, see Beer, 2019) as well as culture. Thus, our field is exceptionally well-situated to help resolve the mysteries of mental disorders by integrating biological, evolutionary, and sociocultural perspectives.

2 | MENTAL DISORDERS AND THE GLOBAL BURDEN OF DISEASE

Although pathogens have been among the most powerful of selective forces shaping human evolution, their role in disease was recognized only recently in the late 19th century, leading to unprecedented improvements

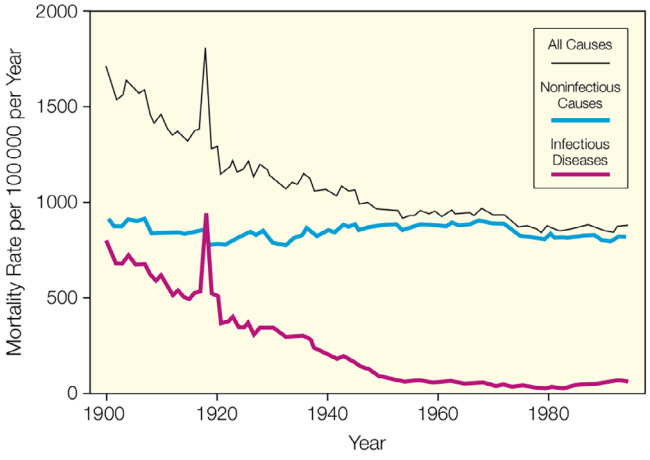

FIGURE 2 Crude mortality rates for all causes, noninfectious causes, and infectious diseases in the United States. *Source:* Figure from Armstrong, Conn, and Pinner (1999)

in human health. Immunization and sanitation programs and development of effective antibiotics sharply reduced the prevalence of, and mortality from, infectious diseases in high-income populations during the 20th century (Logan, 1950; Roser, 2018). In 1900, about half of all deaths in the United States were due to infectious diseases, but by the end of the century almost none were (Figure 2). Although high-income nations still disproportionately benefit from biomedical advances, the average life expectancy at birth has risen in every country since the 1940s (Roser, 2018). In an 1893 public address to Louis Pasteur, fellow microbiologist

Joseph Lister stated, "For centuries, infectious diseases have been shrouded, as it were under a dark curtain. In discovering the microbial origin of disease you have raised that dark curtain" (Schwartz, 2001).

Mental disorders, by comparison, are still shrouded under a dark curtain, and there has been little, if any, improvement in public mental health. The worldwide prevalence of mental, neurological, and substance abuse disorders, heretofore mental disorders, remained steady between 1990 and 2010. Disease burden is measured in disability adjusted life years (DALYs)—years of life lost to illness, disability, or death (Whiteford et al., 2013). Currently, mental disorders account for the fifth largest proportion of global DALYs (7.4%), behind cardiovascular and circulatory diseases (11.9%), common infectious diseases (11.4%), neonatal disorders (8.1%), and cancer (7.6%) (Whiteford et al., 2013; see Figure 3). Of the 7.4% of total DALYs attributable to mental

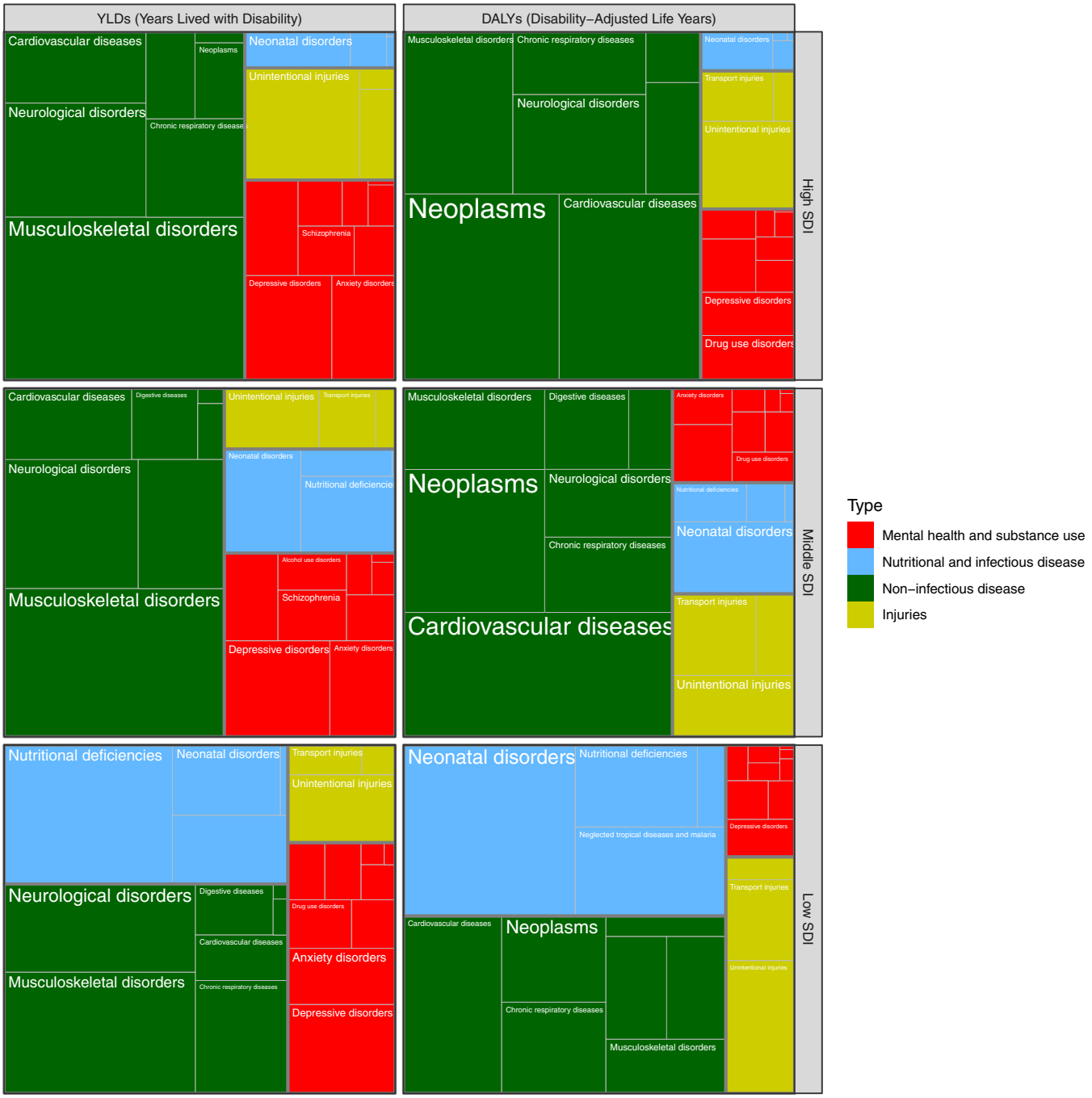

FIGURE 3 The proportion of disease burden attributable to four categories of diseases in countries with low, middle, and high levels of socioeconomic indices in 2017. Self-harm has been recategorized from the injury group to the mental health group. *Source:* Data from Global Burden of Disease (GBD; http://www.healthdata.org), accessed April 4, 2019. Socio-demographic Index (SDI): A summary measure that identifies where countries or other geographic areas sit on the spectrum of development. Expressed on a scale of 0–1, SDI is a composite average of the rankings of income per capita, average educational attainment, and fertility rates of all areas in the GBD study

and substance use disorders, the largest share by far, 40.5%, is due to depressive disorders. The remainder is due to anxiety disorders (14.6%), drug use disorders (10.9%), alcohol use disorders (9.6%), schizophrenia (7.4%), bipolar disorder (7.0%), pervasive developmental disorders (4.2%), childhood behavioral disorders (3.4%), and eating disorders (1.2%) (Whiteford et al., 2013). Much of the burden for depressive and anxiety disorders falls on young and middle-aged adults (see Figure 4).

A more recent analysis that expanded the definition of mental disorders to include suicide, self-harm, and dementias, and made other adjustments, estimated that mental disorders actually account for 13% of DALYs, on par with the top-ranked cardiovascular and circulatory disease category (Vigo, Thornicroft, & Atun, 2016). In a related study, Ferrari et al. (2014) estimated that two-thirds of suicide DALYs were attributable to mental disorders, notably depression. To put that in perspective, more people die by suicide than all wars and homicides combined (Lozano et al., 2013).

DALYs combine mortality and disability burden. The contribution of mental disorders to disease burden is primarily due to their contribution to the burden of disability, not mortality. Disability burden is measured in years lived with disability (YLDs). Mental disorders are the leading cause of disability overall, accounting for 22.9% of global YLDs, with musculoskeletal disorders a close second (21.3% of YLDs), and other non-communicable diseases, such as cancer and cardiovascular disease, a distant third (11.1% of YLDs) (Whiteford et al., 2013). The reanalysis of Vigo et al. (2016) puts the disability burden of mental illness even higher, at 32.4% of YLDs.

Most studies find that the prevalence of mood and anxiety disorders have remained constant over time (Bretschneider et al., 2018; Patten et al., 2016). From 1990 to 2010, for instance, the global prevalence of major depressive disorder (MDD) remained around 4.4% and for anxiety disorders was 4% (Baxter et al., 2014). There is little evidence that increased treatment rates reduce suicide rates (Nock et al., 2008), and there has been no appreciable decline in cross-national suicide rates, which vary dramatically across countries and regions (Lee, Roser, & Ortiz-Ospina, 2018). Meanwhile, there have been increases in the diagnosis and treatment of neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) in some Western populations, likely reflecting shifting diagnostic trends and growing public awareness (Myers et al., 2018; Olfson, Gameroff, Marcus, & Jensen, 2003; Russell, Collishaw, Golding, Kelly, & Ford, 2015; Visser et al., 2014; Xu, Strathearn, Liu, Yang, & Bao, 2018).

3 | BIOLOGICAL ANTHROPOLOGY: A WORLD OF UNTAPPED POTENTIAL

There is a long tradition of anthropological scholarship on psychological and behavioral variation and psychopathology across cultures, and many such works are classics of American anthropology. Ruth Benedict documented how different cultures differentially value particular behaviors and psychological states; whereas some cultures promote psychotropic drug use or ecstatic experiences, for example, other cultures discourage these (Benedict, 1934a, 1934b). Margaret Mead investigated the role of culture in shaping psychosexual development (Mead, 1928). Nancy Scheper-Hughes researched psychosis in rural Ireland (Scheper-Hughes, 2001) and the medicalization of suffering (Scheper-Hughes & Lock, 1986). Arthur Kleinman examined the influence of culture in shaping the illness experience (Kleinman, 1980, 1982). Cultural and medical anthropologists continue to prioritize research on mental illness (e.g., Jenkins, 2015; Kohrt & Mendenhall, 2016), but rarely integrate evolutionary, biological, and comparative perspectives.

Human biologists and biological anthropologists have focused considerable research efforts on fertility, nutrition, physical growth

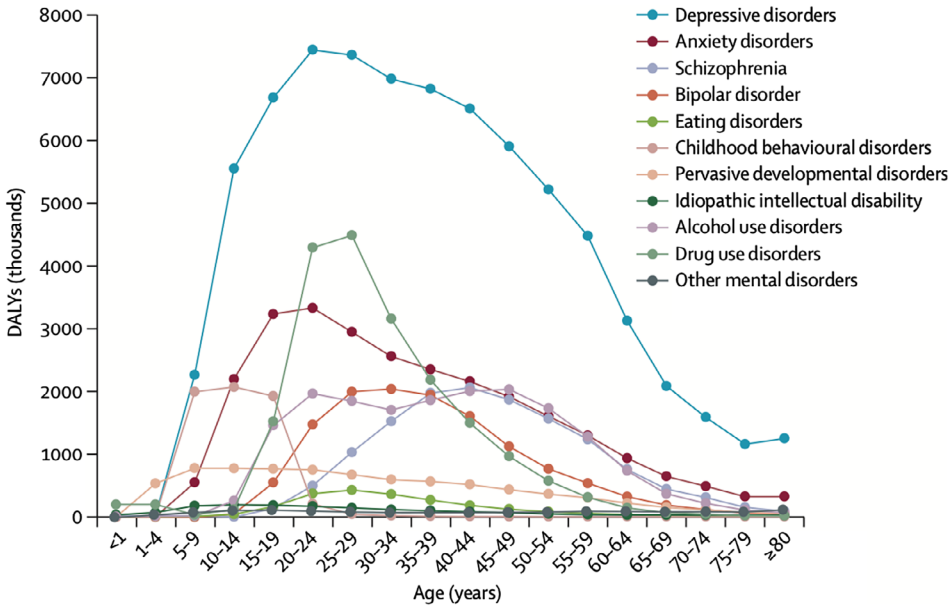

FIGURE 4 Disability-adjusted life years (DALYs) for each mental and substance use disorder in 2010, by age. *Source:* Figure and caption from Whiteford et al. (2013)

and development, and infectious and perinatal diseases in low and middle income countries and indigenous populations (e.g., Bogin, 1999; CLHNS, 2019; Gurven et al., 2017; Hill & Hurtado, 1996; Jasieńska & Ellison, 1998; Leonard & Godoy, 2008; Little, 1989; Sellen & Mace, 1997; Sugiyama & Snodgrass, 2019; Valeggia & Snodgrass, 2015; Vitzthum & Wiley, 2003). Despite the fact that most biological anthropologists interested in health conduct fieldwork in low- and middle-income countries, however, and that mental disorders are the first or second ranked cause of disability burden in most of these countries (see Figure 3), only a handful of biological anthropological studies have focused on mental health. These include Hadley and colleagues' work on depression and anxiety (Hadley & Patil, 2006, 2008; Patil & Hadley, 2008); Sullivan's biocultural research on schizophrenia in Palau (Sullivan et al., 2007; Sullivan, Allen, Otto, Tiobech, & Nero, 2000; Sullivan, Andres, Otto, Miles, & Kydd, 2007); McDade's investigation on social status, psychosocial stress, and culture change in Samoa (McDade, 2002); Flinn et al.'s work on the stress response (Flinn, Nepomnaschy, Muehlenbein, & Ponzi, 2011; Flinn, Quinlan, Decker, Turner, & England, 1996); Stieglitz et al.'s research on depression and immune function (Stieglitz et al., 2015); Wells et al.'s research on eating disorders (Wells et al., 2015), and several others (Adair et al., 2010; Fuller, Mccarty, Gravlee, & Mulligan, 2018; Mulligan, 2016; Patil, Maripuu, Hadley, & Sellen, 2015; Reyes-Garcı'a et al., 2010). In addition, many biological anthropologists and behavioral scientists have investigated how humans cognitively and behaviorally respond to environments of varying risk using a life history theory (LHT) framework (Belsky & Pluess, 2009; Ellis & Bjorklund, 2012; Nettle, 2010; Pepper & Nettle, 2017; Quinlan, Dira, Caudell, & Quinlan, 2016), which has implications for many symptoms of mental disorders. In their review of the health of indigenous populations, Valeggia and Snodgrass (2015) note some common risk factors for mental health issues, including rapid acculturation, lack of local control, urbanization, poverty, profound changes in traditional social roles, and violence due to colonial repression.

No coherent theoretical framework for understanding mental health has emerged from biological anthropology or related disciplines, however. Moreover, the tradition of Cartesian dualism that treats the mind and body as separate continues to hinder the full integration of mental health research into biological anthropology. Hence, there is a substantial but unrealized research potential for our discipline. The mainstream psychiatric paradigm has severe limitations, many of which might be addressed by theoreticians that take a panhuman, evolutionary and comparative approach to health and behavior and who recognize the importance of social relationships and culture, that is, biological anthropologists.

4 | A CRITIQUE OF BIOLOGICAL PSYCHIATRY

The brain is the most complex organ in the human body. Advocates contend that mental disorders should be regarded as biological diseases like any other, invoking the effectiveness of psychopharmaceutical drugs and the associations of mental disorders with hormonal, imaging, genetic, and epigenetic biomarkers, as evidence for this view (e.g., Kirsch, 2015). It is inarguable that mental health phenomena have a basis in biology, and that most (but not all) should be classified as biological dysfunctions. The track record of biological psychiatry, however, a field that investigates the neurophysiological and genetic bases of mental disorders, is poor. The leading objectives of the field are to develop diagnostic tests and effective treatments. Biological psychiatry is presently limited, though, by technologies that can assess physical variation in the brain at some levels of organization but not others. So far, there are no diagnostic tests, and treatments have limited efficacy.

4.1 | The limited efficacy of psychopharmaceuticals

In the early 2000's, well-intentioned campaigns aimed to reduce the stigma of mental illness by reframing depression, schizophrenia, and other disorders as “diseases like any other” (Pescosolido et al., 2010). A key tactic, eagerly adopted by drug companies, was to popularize “chemical imbalance” models. These campaigns failed on two counts. First, a systematic review found that an endorsement of biogenetic causes of mental disorders does not reduce stigma and, in fact, might even increase stigmatizing attitudes among mental health professionals and the mentally ill themselves (Larkings & Brown, 2018). Second, there is little evidence that psychopharmaceuticals correct specific chemical imbalances or neurobiological deficits.

The “chemical imbalance” theory of depression, for example, also known as the catecholamine, monoamine, or serotonin deficiency hypothesis, was based on the chemical action of the first generation of antidepressants, which were discovered serendipitously and found to act on monoamine pathways to increase monoamine concentrations (López-Muñoz & Alamo, 2009). We now know that the “chemical imbalance” hypothesis of depression is false. First, the fact that drugs that increase monoamine concentrations also reduce depressive symptoms (O'Donnell, 2011) is not strong evidence that depression is caused by a deficiency of monoamines. Aspirin reduces headache symptoms but headaches are not caused by an aspirin deficiency. Second, antidepressant drugs increase monoamine concentrations almost immediately (within minutes), but their antidepressant effects only appear after a few weeks (Frazer & Benmansour, 2002; Harmer, Goodwin, & Cowen, 2009). Third, other drugs, such as cocaine, increase monoamines (Kalsner & Nickerson, 1969; Kuhar, Ritz, & Boja, 1991) but are not effective antidepressants. Fourth, some antidepressant drugs, such as tianeptine, decrease monoamines (Baune & Renger, 2014; McEwen et al., 2010). Fifth, depletion of monoamines does not induce depression in non-depressed individuals (Ruhé, Mason, & Schene, 2007). In summary, although monoamines might play some role in depression, there is no evidence that depression is caused by a simple imbalance of serotonin, norepinephrine, or any other neurotransmitter or biochemical (Kendler, 2008; Lacasse & Leo, 2015, and references therein).

Despite the lack of evidence, the “chemical imbalance” model was successfully disseminated by the pharmaceutical industry via direct-to-

consumer advertising (Lacasse & Leo, 2005, 2015), infiltrating popular consciousness in the United States and influencing the culture of help-seeking and diagnosis (Angell, 2009; France, Lysaker, & Robinson, 2007). This, and the development of antidepressants with fewer adverse side effects, such as selective serotonin reuptake inhibitors, caused antidepressant prescriptions in many countries to increase several fold. In Australia, for example, antidepressant use increased 352% from 1990 to 2002, with a further 95% increase from 2000 to 2011. Similar increases in antidepressant and other treatments occurred in Canada, England, and the United States. There were also substantial increases in the use of psychological therapies. Nevertheless, no reduction in the prevalence of mood, anxiety, or substance use disorders was observed in any country (Jorm, Patten, Brugha, & Mojtabai, 2017).

The limited efficacy of commonly prescribed antidepressants has been recognized for at least two decades (e.g., Kirsch & Sapirstein, 1998). Analyzing both published and unpublished reports of antidepressant trials obtained from the U.S. Food and Drug Administration, Kirsch (2008) and Turner, Matthews, Linardatos, Tell, and Rosenthal (2008) uncovered strong biases in the published data in favor of positive treatment effects. After adjusting for unreported studies, they found effect sizes Cohen's d = .31 to .32, indicating a modest advantage of treatment over placebo. This corresponds to less than 2 points on the Hamilton Depression Scale (HAM-D), which ranges from 0 to 52. A 3-point difference on the HAM-D is a criterion for clinical significance for depression treatment (Kirsch, 2015; National Institute for Clinical Excellence, 2004). A recent exhaustive meta-analysis of published and unpublished antidepressant trials found an almost identical effect of antidepressants over placebo (Cipriani et al., 2018; see also Kirsch, 2015 for a discussion of active placebo).

Psychopharmaceuticals cause many adverse side effects, requiring serious risk–benefit analyses. For instance, antidepressants can cause insomnia, sexual side effects (e.g., decreased libido, erectile dysfunction), and weight changes, among others. Cartwright, Gibson, Read, Cowan, and Dehar (2016) found that among a sample of 180 long-term antidepressant users, 73.5% reported withdrawal symptoms and 43% reported feeling addicted to their medication. There is promising new evidence that the NMDA receptor antagonist ketamine can rapidly and effectively treat the symptoms of depression. The effects are short-lived, however, and ketamine is a drug of abuse (McGirr et al., 2015; see also Duman, 2018 for review). Risks associated with taking antipsychotics include: movement disorders such as parkinsonism, and even irreversible brain damage, such as tardive dyskinesia (repetitive, involuntary, purposeless movements, Bagnall et al., 2003; Muench & Hamer, 2010), loss of brain tissue volume (Dorph-Petersen et al., 2005; Ho, Andreasen, Ziebell, Pierson, & Magnotta, 2011; Moncrieff & Leo, 2010; Vita, De Peri, Deste, Barlati, & Sacchetti, 2015), metabolic syndrome (e.g., abdominal obesity, high blood pressure, high blood sugar) (de Hert, Schreurs, Vancampfort, & Winkel, 2009), and sudden cardiac death (Ray, Chung, Murray, Hall, & Stein, 2009). The short-term side effects of antipsychotics are notoriously unpleasant and include subjective feelings of reduced intelligence and creativity (Moncrieff, Cohen, & Mason, 2009), and the patient nonadherence rate for this class of medication is roughly 50% (Lacro, Dunn, Dolder, Leckband, & Jeste, 2002), the blame for which tends to fall on the patients (Haddad, Brain, & Scott, 2014). Finally, treating symptoms is not necessarily equivalent to correcting a biological dysfunction.

4.1.1 | Ethical Lapses: crossing the line between science and marketing

Moore and Mattison (2017) estimated that 16.7% of American adults filled at least one prescription for psychiatric drugs in 2013. Antidepressants were the most common at 12.0% (see also Pratt, Brody, & Gu, 2017) followed by anxiolytics, sedatives, and hypnotics (8.3%) and antipsychotics (1.6%) (Moore & Mattison, 2017). The substantial profits from these drugs (Lindsley, 2012) have had a corrosive influence on mental health research and treatment (Angell, 2005). As the former editor-in-chief of The New England Journal of Medicine, Marcia Angell, wrote,

> It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor… (Angell, 2009).

Medical professionals, many of whom are affiliated with prestigious research universities, are often paid tens of thousands of dollars to run or enroll patients in clinical drug trials or to advertise products at company-funded talks, creating serious conflicts of interest (Angell, 2009; Callaway, 2010). In a review of 397 psychopharmaceutical clinical trials published in high-quality psychiatry journals from 2001 to 2003, Perlis et al. (2005) found that 47% of the articles reported at least one author financial conflict of interest, which was associated with an increased likelihood of reporting positive drug outcomes among studies receiving industry support (see also Lexchin, Bero, Djulbegovic, & Clark, 2003; Lundh, Lexchin, Mintzes, Schroll, & Bero, 2017). In addition, several NIH-funded psychiatrists at top universities violated federal guidelines by failing to report financial support from companies whose drugs they were investigating (Harris, 2008; Kaiser, 2009).

Drug companies, on the other hand, engage in unethical marketing practices, such as paying physicians to give speeches promoting off-label treatments and to claim authorship for articles written by ghostwriters working for the industry, among other unscrupulous activities (Petersen, 2002, 2003; for further discussion on ghostwriting and the pharmaceutical industry see also Angell, 2009; Sismondo, 2007; Fugh-Berman, 2010). Between 1991 and 2015, there were 373 settlements involving drug companies and federal and state governments, resulting in industry fines totaling $35.7 billion (Almashat, Wolfe, & Carome, 2016).

To summarize, most psychopharmaceuticals are not very effective, their effects have been exaggerated by biased scientific publishing and advertising campaigns, they often have numerous harmful side effects, and the genuine effects that they do have do not provide compelling evidence for any specific etiology of any mental disorder.

4.2 | Imaging and other biomarkers of mental disorders

There are no biological tests for the diagnosis of mental disorders. In the 1970s and 1980s, the Dexamethasone Suppression Test showed promise as a biomarker of depression that predicted drug response, but further large studies found low-to-moderate specificity and sensitivity, and limited clinical utility (Kapur, Phillips, & Insel, 2012). Neuroimaging measures also show potential. Functional MRI and PET can resolve blood flow (an index of neural activity) in voxels as small as 1 mm^3, and numerous studies show statistical differences in neural activity between patients and controls. But these differences are not yet sensitive or reliable enough to serve as diagnostic tools (Abi-Dargham & Horga, 2016), perhaps because 1mm^3 of brain tissue contains a complex network of 60–70,000 neurons and tens to hundreds of millions of synaptic connections (Azevedo et al., 2009) that is essentially invisible with current technology.

4.3 | Genes, environment, and epigenetics: the heritability of phenotypes implicated in psychiatric disorders

The heritabilities of anxiety disorders, MDD, and post-traumatic stress disorder (PTSD) are low (e.g., the heritability of MDD is ~0.38), implying that environmental factors such as adversity play an outsized role (Kendler & Baker, 2007; Kendler & Gardner, 2016; Kendler, Gatz, Gardner, & Pedersen, 2006). Many mental illnesses, though, are highly heritable, suggesting that they are caused, in part, by genetic variation in, for example, neuroreceptors, neuropeptides, neurotransmitter transporters, and other proteins involved in neural function, and variation in their associated regulatory sequences. Approximately 50% of all genes in the human genome are expressed in the brain (Naumova, Lee, Rychkov, Vlasova, & Grigorenko, 2013). Many of these genes have variants, and it is widely believed that some of these variants (a) play an important role in psychiatric illnesses and (b) influence fitness via their influence on behavior (Keller, 2018). The heritability of schizophrenia is ~0.80, similar to the heritability of height (Cannon, Kaprio, Lönnqvist, Huttunen, & Koskenvuo, 1998; Hilker et al., 2018; Sullivan, Kendler, & Neale, 2003). ASDs (Colvert et al., 2015; Tick, Bolton, Happé, Rutter, & Rijsdijk, 2016), bipolar disorder (Wray & Gottesman, 2012), and obsessive–compulsive disorder (OCD) (Taylor, 2011) are also highly heritable, implying that genetic factors explain more variation in disease risk than environmental factors (Sullivan, Daly, & O'donovan, 2012). It is an evolutionary paradox that many mental disorders are both harmful and heritable, because deleterious alleles should be eliminated by purifying selection (Keller, 2018; Keller & Miller, 2006), an issue to which we shall return.

Most early research on the genetics of psychiatric disorders focused on the functional impact of "candidate" genes, which are typically selected based on prior knowledge of a gene's functionality (Johnson et al., 2017). There was a potential breakthrough when Caspi et al. (2003) reported that the short (S) allele of the serotonin-transporter-linked polymorphic region (5-HTTLPR), which is present at frequencies ranging from 0.08 to 0.44, depending on population (Haberstick et al., 2015), moderated the relationship between stressful life events and depression. This influential paper launched a series of follow-up investigations on 5-HTTLPR in humans and other animals including non-human primates (e.g., Shattuck et al., 2014). Unfortunately, the most recent collaborative meta-analysis on 31 datasets with 38,802 subjects with European ancestry did not support the hypothesis of a gene X environment interaction effect, with the researchers concluding, "… that if an interaction exists in which the S allele of 5-HTTLPR increases risk of depression only in stressed individuals, then it is not a broadly generalizable effect, but must be of modest effect size and only observable in limited situations" (Culverhouse et al., 2018). Another study found no support for several candidate gene or candidate gene-by-environment interaction hypotheses for major depression across multiple large samples (Border et al., 2019). Psychiatric genetics is moving away from candidate-gene studies due to their poor reproducibility, and toward alternative genetic methods (Keller, 2018).

Gene-mapping studies, such as genome-wide association studies (GWAS) and whole-genome sequencing studies, are used to detect associations between DNA sequence variations and phenotypic outcomes (Timpson, Greenwood, Soranzo, Lawson, & Richards, 2018). As the cost of conducting GWAS on sufficiently large sample sizes has decreased, these techniques have largely replaced candidate gene studies. GWAS have found that the effects of any single nucleotide polymorphism (SNP) on psychiatric illness is small, and it is now clear why candidate gene studies have not led to breakthroughs in identifying the etiology of mental disorders (Keller, 2018; McCarroll, Feng, & Hyman, 2014): single SNPs only account for <0.05% of the variance of the risk for depression and schizophrenia (e.g., Culverhouse et al., 2018; Keller, 2018).

Gene-mapping studies indicate a large mutational target for mental disorders, however, and the large target might resolve the paradox of the high heritability of psychiatric disorders. It is estimated that 8,300 common genetic variants distributed across the genome account for 50% of the genetic risk for schizophrenia, for instance, although each allele individually only has a very small effect (Alzheimer's disease [AD] is an exception to this pattern in that a few loci of large effect account for much of the variation). Common SNPs account for one-third to one-half of the heritability of many disorders, but more is known about common compared to rare SNPs since the latter require large sample sizes to detect significance. It is thought that some combination of common and rare variants, which include de novo SNPs and copy number variations, produce mental disorders in ways that are not yet understood (see Gratten, Wray, Keller, & Visscher, 2014 for review). Several studies, for example, indicate that multiple, unique rare structural variants confer risk for schizophrenia (International Schizophrenia Consortium and others, 2008; Walsh et al., 2008). One possibility is that rare structural variants might disrupt other genes, leading to pathogenesis (Walsh et al., 2008). Alternatively, mildly deleterious alleles might accumulate over time and by chance pass a threshold leading to phenotypes liable to behavioral or cognitive dysfunction (Gratten et al., 2014; see also Boyle, Li, & Pritchard, 2017 for the "omnigenic model of complex disease").

Additional complications include that the genetics of mental disorders evidences equifinality, in which different variants lead to a single disorder (Keller, 2018), and multifinality, in which a single variant or the same variants are risk factors for several different disorders (International Schizophrenia Consortium and others, 2009). Evidence for shared genetic variants across certain disorders (including schizophrenia, bipolar disorder, and depression; see Lee et al., 2013) might be explained by pleiotropy, epigenetic factors, variation in exposure to certain environmental inputs, weaknesses in the validity of our phenotyping methods, or some combination of these.

Mutation-selection-drift is thus a good null model by which to test alternative hypotheses about genetic variation such as, for example, balancing selection (Keller, 2018). Moreover, if polygenic traits are normally distributed, then the construct of mental disorders captures extreme variations of "normal" behavior, lending support to the view that psychopathology is dimensional, not binary categorical (Plomin, DeFries, Knopik, & Neiderhiser, 2016), a perspective we discuss in part II. In sum, even with all our advancements in gene sequencing technologies, we still know very little about the genetic architectures that contribute to behavioral, psychological, and other phenotypic outcomes (Gratten et al., 2014). Furthermore, as Sullivan, Allen, et al. (2007) caution, although schizophrenia and other mental disorders have similar symptom profiles in diverse populations, our understanding of these phenotypes is nevertheless heavily biased toward Western, Educated, Industrialized, Rich, and Democratic (WEIRD) populations (Henrich, Heine, & Norenzayan, 2010). Much biocultural research remains to be done, potentially by biological anthropologists.

4.3.1 | Environments are genetically heritable too

Mental disorders are the product of gene X environment interactions. Variation in mental disorders and other psychological traits (including personality) can be partitioned into a fraction due to genetic variation and a fraction due to environmental variation (see Plomin et al., 2016 for review). About 38% of the variation in experiencing depression, for example, is due to genetic variation, and 62% of the variation is due to environmental variation, such as variation in experiencing a divorce or other adversity. It turns out, however, that much that is considered environmental variation, such as getting a divorce, also has a genetically heritable component (Plomin, 2018; Plomin & Bergeman, 1991; Plomin, Lichtenstein, Pedersen, McClearn, & Nesselroade, 1990), and these heritable environments include family, neighborhood, work, and school environments (Plomin et al., 2016). In a systematic review of studies investigating the genetic heritability of measures of "environment," Kendler and Baker (2007) estimated the weighted heritability of all identified environmental measures (35 constructs in total including specific life events, family environment, and marital quality) to be 27%. Since divorce is a risk factor for depression and the risk of divorce is genetically heritable, some of the genetic heritability of depression includes the heritability of "environmental" risk factors for depression, such as divorce. Some of the heritability of depression could also be heritability in personality risk factors such as neuroticism (Fanous, Neale, Aggen, & Kendler, 2007).

Numerous studies indicate that most environmental effects on psychological traits are not shared by siblings who grew up in the same home. Thus, the aspects of the environment that influence adult outcomes are likely highly stochastic, idiosyncratic events that are difficult to capture methodologically (see Turkheimer, 2000 for review). As Plomin et al. (2016) observed, just as psychological traits are transmitted via many genes with small effects, the "nonshared environment" is the product of an untold number of experiences, most of which might have small effects.

4.4 | Summarizing biological psychiatry

Biological psychiatry has produced a wealth of information on the hormonal, neuroanatomical, genetic and epigenetic correlates of mental disorders, but this hard-won knowledge has not translated into improved diagnoses and treatments. In fact, it raises questions about the prevailing conceptualization and categorization of mental disorders. Family and twin studies indicate that heritable influences on mental disorders do not map onto mainstream diagnostic categories. In the words of Smoller et al. (2019, p. 4), "our genes don't seem to have read the DSM."

Although neuroscientists have uncovered much about the anatomy, neurochemical organization, and circuitry of the nervous system, the editors of the most recent edition of a key textbook on the subject made a sullen admission:

> …this explosion of knowledge of the brain has not been translated into fundamental advances in our understanding of the pathophysiology of most major psychiatric syndromes, the diagnosis of these syndromes based on their underlying biological mechanisms, or the treatment and prevention of mental illness (Charney, Buxbaum, Sklar, & Nestler, 2013, p. ix).

5 | A CRITIQUE OF THE THEORETICAL FOUNDATIONS OF THE DOMINANT PSYCHIATRIC RESEARCH PARADIGM

Critics from within medicine, psychiatry, and related fields are calling attention to the failure of psychiatric research to improve public health. Many critics argue that this failure is due, in large part, to fundamental flaws in the classification of mental disorders based on the DSM, and that psychiatric nosology (the classification of disease) is undergoing a crisis of confidence (for review, see Zachar & Kendler, 2017).

5.1 | The DSM stranglehold on research and policy

The DSM was meant to improve research, but it is now so deeply entrenched in healthcare and legal systems that reinforce its authority, that is difficult to make substantial changes on scientific grounds.

As we discuss later, scientifically questionable diagnostic categories are retained so that patients do not lose insurance coverage. The influence of the DSM is not limited to the US as it informs the International Classification of Diseases (ICD-11) (see Tio, Epskamp, Noordhof, & Borsboom, 2016). The Chair of the DSM-IV task force, psychiatrist Allen Frances, opined that it has achieved,

> …perhaps too much real-world influence as the arbiter of who gets what treatment and whether it will be reimbursed; who is eligible for disability benefits, Veterans Affairs benefits, and school and mental health services; and who qualifies to receive life insurance, adopt a child, fly an airplane, or buy a gun (Frances, 2013a).

Many now believe that the DSM is impeding research. The problems include excessive co-morbidity of DSM/ICD disorders, heterogeneity of mechanisms, and reification of disorders. The DSM/ICD categories do not map well onto emerging findings from genetics, systems neuroscience, and behavioral science, calling into question the underlying validity of the disease entities. It is therefore difficult to translate research from basic studies in animal models or in humans to a systematic understanding of pathology or to treatments directed at mechanisms (Cuthbert & Insel, 2013, and references therein).

Unlike most biomedicine that bases diagnoses on recognizable dysfunctions, psychiatry currently bases diagnoses on the number and types of symptoms. At the dawn of the scientific revolution, scholars aimed to identify "natural" classifications of, for example, plants, animals, and inorganic substances, and to discover their underlying causes. Mental disease classification systems were developed by Pinel, Kraepelin, Bleuler, and many others. These theoreticians, whose systems were forerunners of the current DSM, expected that a successful natural classification of mental diseases would lead to an understanding of their underlying causes, a gambit that succeeded for many other natural phenomena, such as insights gleaned from the periodic table of elements, and the influence of plant and animal taxonomies on Darwin's theory of evolution. Kraepelin acknowledged near the end of his career, however, that many of his classifications might not delineate natural disease groups (Zachar & Kendler, 2017).

By the 1950s in the United States, the early systems were replaced, in part, by psychoanalysis, which classified mental illnesses based on a psychoanalytic theory of causation that included repression of powerful emotions, often those experienced in infancy. The creators of the DSM-I and II (American Psychiatric Association, 1952a, 1952b), who adopted elements of this causation-based approach (Shorter, 2015), delineated only two broad diagnostic categories: The first concerned severe mental disturbances believed to have an organic etiology, and the second concerned less severe conditions such as "psychoneurosis" thought to be caused by social and environmental stressors (Kawa & Giordano, 2012). The lack of clear diagnostic boundaries and low diagnostic reliability under this system became an increasing source of criticism toward psychiatry in the 1970s when third parties such as government agencies and private insurance companies began paying for treatment (Eaton, South, Krueger, Millon, & Simonsen, 2010).

The introduction of the DSM-III in 1980 heralded a paradigm shift and laid the foundation of modern diagnosis. Its symptom-based approach, which had clear antecedents in the classification systems of Kraepelin and other eighteenth and nineteenth century theorists (e.g., Compton & Guze, 1995), replaced the psychoanalytic, causation-based approach of the DSM-I and II, which had poor empirical support (Mayes & Horwitz, 2005; but see Cooper & Blashfield, 2016). This strategy improved diagnostic reliability, placating third party payers and bolstering psychiatry's reputation.

Improving reliability was seen as an important step toward improving validity (Skodol & Spitzer, 1982; see also Horwitz & Wakefield, 2007). To date, however, there is no sign that the DSM has improved validity. The leader of the DSM-III effort, Robert Spitzer, and Michael First, editor of the DSM-IV, conceded:

> Despite the considerable advances in psychiatric research, disappointingly little progress has been made toward understanding the pathophysiological processes and cause of mental disorders. If anything, the research has shown the situation is even more complex than initially imagined, and we believe not enough is known to structure the classification of psychiatric disorders according to etiology (Spitzer & First, 2005, p. 1898).

Some have even argued that increased diagnostic reliability has come at the expense of diagnostic validity (Horwitz & Wakefield, 2007; Kendell, 1989). DSM-III diagnostic criteria were developed based on research in clinical populations, usually inpatients, that is, individuals who were already determined to be suffering severe psychopathology. The aim of this research was to reliably distinguish different types of illness from each other, not to distinguish the healthy from the ill (Horwitz & Wakefield, 2007). When the resulting DSM-III diagnostic criteria were first (mis)applied to nationally representative community populations, the vast majority of whom did not have a mental illness, over a quarter of the population (28.5%) was implausibly identified as suffering a mental illness in the previous year, and nearly half the population (48%) as having suffered a mental illness in their lifetimes (Regier et al., 1998). These excessively high rates raised concerns in Spitzer and others about false positives (Horwitz & Wakefield, 2007; Regier et al., 1998; Spitzer & Wakefield, 1999). As Regier, who would later go on to chair the DSM-5 effort, and colleagues noted (Regier et al., 1998, p. 114):

> Although it is possible that all of these community-based disorders are simply milder cases of essentially the same disorders seen in clinical settings, there are other possibilities as well. Based on the high prevalence rates identified in both the ECA [Epidemiological Catchment Area] and the NCS [National Comorbidity Survey], it is reasonable to hypothesize that some syndromes in the community represent transient homeostatic responses to internal or external stimuli that do not represent true psychopathologic disorders. The human organism has a

> limited repertoire of response patterns to various physical, biological, and emotional stresses. Transient changes in blood pressure, pulse rate, body temperature, anxiety, or mood are not always indicators of pathology but of appropriate adaptive responses. It is possible that many people with currently defined mental syndromes (in particular among the affective and anxiety disorders) not brought to clinical attention may be having appropriate homeostatic responses that are neither pathologic nor in need of treatment—e.g., other equivalents of grief reactions that meet clinical criteria but are not considered pathologic if they are time-limited.

Such eminently reasonable interpretations of "cases" in community populations have virtually disappeared from the scientific literature, and implausibly high prevalence rates are now reported without a bat of the eye. In 2017, for example, the U.S. government reported that one in five adolescent women suffered MDD in the past year (National Institute of Mental Health, 2019a), that is, putatively suffered a major disorder of the brain.

More than 30 years after the publication of the DSM-III, Insel and Cuthbert, then Directors of NIMH and NIMH Division of Adult Translational Research and Treatment Development, respectively, specifically named it as an "impediment to progress" (Cuthbert & Insel, 2013). Neurobiologist and former Director of NIMH Steven Hyman argued that the DSM is useful as a heuristic, providing a "common language" among clinicians and clinical researchers with generally good inter-rater reliability of diagnosis, but he criticized the widespread treatment of these disorders "as if they were natural kinds, real entities that exist independently of any particular rater (Hyman, 2010)." Hyman also observed that the complexity of neurobiology was the greatest obstacle barricading valid diagnostics, but added that the DSM itself compounds the problem, noting for instance, "…a fairly arbitrary decision was made to favour 'splitting' symptoms over 'lumping' them, which resulted in the creation of a large number of disorders (Hyman, 2007)."

The number of diagnostic categories has proliferated with each subsequent edition of the DSM. The first edition had 128 categories, and the most recent, the DSM-5, catalogs 541 diagnoses (Blashfield, Keeley, Flanagan, & Miles, 2014). Frances, Chair of the DSM-4 effort, has bemoaned the excess of diagnostic labels that increasingly medicalize what he considers "severe variants of normal behavior", adding that recent increases in the rates of ADHD, bipolar disorder, and ASDs are "market-driven diagnostic fads" (Frances, 2013a). According to him, the DSM-5 will lead to massive over-diagnosis and harmful over-medication (Frances, 2013b):

> Except for autism, all the DSM-5 changes loosen diagnosis and threaten to turn our current diagnostic inflation into diagnostic hyperinflation. Painful experience with previous DSMs teaches that if anything in the diagnostic system can be misused and turned into a fad, it will be. Many millions of people with normal grief, gluttony, distractibility, worries, reactions to stress, the temper tantrums of childhood, the forgetting of old age, and "behavioral addictions" will soon be mislabeled as psychiatrically sick and given inappropriate treatment.
>
> People with real psychiatric problems that can be reliably diagnosed and effectively treated are already badly shortchanged. DSM-5 will make this worse by diverting attention and scarce resources away from the really ill and toward people with the everyday problems of life, who will be harmed, not helped, when they are mislabeled as mentally ill.

Unlike the natural classifications of plants, animals, infectious diseases, and inorganic substances, which all played key roles in the discovery of underlying causal principles, such as the theory of evolution, the atomic theory of matter, and the germ theory of disease, the various classifications of mental disorders have failed, so far, to uncover their underlying causes. The current system has little claim to be a "natural" classification, and is instead deeply contingent on the specific history of psychiatry. As Kendler, a leading figure in psychiatry, notes, "Had we been in a parallel universe in which Emil Kraepelin, Eugen Bleuler, Kurt Schneider and Robert Spitzer never lived, DSM-IV would surely have differed in important ways" (Kendler, 2009, p. 1938).

5.2 | What is illness? constructivist vs naturalistic perspectives

The failures of psychiatry to uncover the cause of any mental disorder or improve public health can be traced, in no small part, to weaknesses in its theoretical foundations, starting with its concept of "illness." The large literature on concepts of illness generally falls into two camps: Naturalism, which emphasizes biological mechanisms and functions, and constructivism, which emphasizes normative and often culturally specific notions of health and disease (for review, see Murphy, 2015).

Perhaps the most influential Naturalistic account of illness comes from the philosopher Christopher Boorse, who argued that diseases are internal states that depress a functional ability below species-typical levels and are therefore as value-free (non-Constructivist) as are statements about biological functions (Boorse, 1977). Concerning the DSM, Spitzer endorsed a Naturalistic illness concept: "Our approach makes explicit an underlying assumption that is present in all discussions of disease or disorder, i.e., the concept of organismic dysfunction." (Spitzer, Endicott, & Franchi, 2018, p. 37; cited in Wakefield, 1992a, p. 235). But the concept of biological dysfunction is fuzzier than it seems. One intuitive view of biological dysfunction is that of statistical deviation from normal functioning (e.g., Caplan, Engelhardt Jr, & McCartney, 1981; Scadding, 1967; Taylor, 1971). Statistical deviance is certainly a feature of disease, but not all statistical deviances are diseases, as abnormalities in the structure or function of an organ or system can be functionally benign (Wakefield, 1992a, 1992b). Heavy calluses on the soles of the feet would be statistically deviant in shoe-wearing populations, for example, but typical in populations that go barefoot. Positioning of the heart on

the reverse side of the body, or situs invertus, is a rare but often asymptomatic condition (Wakefield, 1992b). Thus, a condition that deviates from some norm is not a disorder based on that fact alone. Many traits such as height and weight are harmful when they fall too many standard deviations into either the right or left tails of a distribution, whereas other traits, such as intelligence, appear harmful in one extreme but not in the opposite extreme. Body temperatures above 100F are also statistically abnormal, but are functional when they occur during an infection (i.e., fever; Kluger, Kozak, Conn, Leon, & Soszynski, 1998). Cataracts, on the other hand, are statistically "normal" in the elderly (prevalence >50% by age 80), yet they are still considered dysfunctions of vision.

Leaning toward the constructivist side, Sedgwick writes, "All sickness is essentially deviancy [from] some alternative state of affairs which is considered more desirable…" (Sedgwick, 1982, p. 32; cited in Wakefield, 1992b, p. 376, emphasis added). In some cases, threats to physiological function largely determine the desirability of conditions. Dental decay is undesirable because it erodes dental tissue, which is both painful and can impair mastication and in turn harm nutrition status. In other cases, social norms and attitudes set the value on certain "medicalized" conditions. Cesarean-sections are often performed unnecessarily because vaginal deliveries are incorrectly viewed as less safe (Cecilia De Mello, 1994; Rosenberg & Trevathan, 2018; Rosenberg & Veile, 2019). Cosmetic surgery trends vary across nations based on localized standards of physical attractiveness (Holliday & Elfving-Hwang, 2012; Tranter & Hanson, 2015), and many patients seek elective cosmetic surgeries to "correct" perceived deformities that fall within normal (and healthy) variation (Honigman, Phillips, & Castle, 2004) in order to enhance their social value in their cultural context (Haas, Champion, & Secor, 2008).

Constructivist criticisms of illness concepts in psychiatry have a long history, casting psychiatry as a social institution that enforces social norms rather than one that treats biological dysfunctions. Psychiatrist Thomas Szasz stated, "Mental illness exists or is 'real' in exactly the same sense in which witches existed or were 'real' (Szasz, 1960)." Sociologists like Foucault (Foucault, 1965, 1990) and Scheff (Scheff, 1971) framed the mentally ill as social deviants coerced into social roles and conditions that reinforce and legitimize their marginalization. Many psychiatric diagnoses and treatments appear to have been aimed, not at treating dysfunction, but instead at suppressing socially undesirable behavior.

The inclusion of homosexuality in the first two editions of the DSM is an oft-cited example of the role that social values play in shaping psychiatric diagnosis. Other now defunct mental disorders or classes of disorders that are medically questionable include moral insanity (Augstein, 1996), childhood masturbation disorder (Engelhardt, 1974; Foucault, 1990), and hysteria (Veith, 1965).

Gender identity disorder was only recently reclassified as gender dysphoria to remove the implication that gender nonconformity is a "disease" (American Psychological Association, 2015), but even this new label is inconsistent with the definition of mental disorder provided by the DSM-V, which requires that symptoms reflect a

> …dysfunction in the psychological, biological, or developmental processes underlying mental functioning… Socially deviant behavior (e.g., political, religious, or sexual) and conflicts that are primarily between the individual and society are not mental disorders unless the deviance or conflict results from a dysfunction in the individual, as described above. (emphasis added) (American Psychiatric Association, 2013, p. 20).

If gender nonconformity is not a disorder on its own, it is not clear why it, but not other sources of dysphoria (e.g., bereavement, job loss, sexual assault), requires a unique diagnosis, especially because it seems to fall under "conflicts that are primarily between the individual and society (American Psychiatric Association, 2013, p. 20)." The disease label was retained in the DSM-V despite some controversy, in part, to protect insurance coverage and access to care because gender nonconformity is associated with an increased risk for anxiety, depression, self-harm, and suicidal behavior, as is homosexuality (Haas et al., 2010; Marshal et al., 2011; Hughto, Reisner, & Pachankis, 2015; Reisner et al., 2016; see Zucker, Lawrence, & Kreukels, 2016 for review).

Critics of psychiatry highlight an essential point that mental disorders are defined by symptoms that, perhaps not coincidentally, represent socially devalued conditions such as poor hygiene, obsessive thoughts, inappropriate sexual behavior, delusion, hyperactivity, persistent low mood, impulsivity, odd thinking, exaggerated sense of self-importance, compulsive lying, attention-seeking, flat affect, and disassociation, to name only a few. The designation of these symptoms to "disorder" categories is currently independent of clear evidence for pathology.

Nevertheless, the view that mental illnesses only reflect culturally specific values or roles is not well supported. Schizophrenia, for instance, has high heritability and similar symptoms, prevalence, and poor social outcomes across diverse populations (Jablensky et al., 1992; Saha, Chant, Welham, & McGrath, 2005; Sullivan, Allen, et al., 2007; Whiteford et al., 2013). As we discuss in part II, a satisfactory synthesis of Naturalistic and Constructivist accounts of illness requires, somewhat ironically, evolutionary biology.

5.3 | Summarizing the critiques of the theoretical foundations of the DSM

The symptom-based classification system of Kraepelin and other leading nineteenth century psychiatrists did not reveal underlying causes of mental illness, and in the US at least, were partially superseded by a psychoanalytic approach. The rethinking of disorder classification embodied in the DSM-III involved a thorough rejection of the causal psychoanalytic theories embodied in the DSM-I and DSM-II, which the leaders of the DSM-III effort despised, and a return to a symptom-based system (Shorter, 2015; cf. Cooper & Blashfield, 2016), combined with investigations of new biomarkers and development of new drugs. But despite providing researchers with reliable diagnoses of (an increasing number of) disorders, this neo-Kraepelinian project fared no better than its nineteenth century forebears in discovering the causes of disorders or developing effective treatments, and many DSM "disorders" have dubious validity. Although no consensus on a better approach has yet emerged, many researchers sense that a Kuhnian paradigm shift is in the offing.

6 | PART II

In this section we review leading mainstream alternatives to the current DSM-based system, and then outline an evolutionary approach based on the "harmful dysfunction" illness concept (Wakefield, 1992a). We tentatively suggest that there is one group of disorders that are relatively rare, highly heritable, and tend to onset during development, which might be best explained by various genetic theories; a second group that are relatively common and seemingly caused by adversity, which might actually be aversive but adaptive defenses; a third group that is probably best explained by senescence; and a fourth group caused by mismatches between modern and ancestral environments. We highlight the research of biological anthropologists on each of these groups.

7 | TOWARD NEW THEORETICAL APPROACHES TO MENTAL ILLNESS WITHIN PSYCHIATRY AND CLINICAL PSYCHOLOGY

Dimensional or quantitative nosological approaches represent one major challenge to the DSM (Zachar & Kendler, 2017). In medicine, infectious diseases and cancers are typically framed in the categorical disease model, but other conditions such as hypertension and obesity are not discrete disease states but conditions associated with health risks that are continuous with normal variation. According to dimensional approaches to psychopathology, symptoms, such as anxiety or depressed mood, also exist on a continuum, with no categorical distinction between normal and abnormal levels. Moreover, the levels of different symptoms often covary, that is, there is substantial comorbidity. Factor analysis and similar statistical methods are therefore commonly used to identify dimensions of variation (Helzer, Wittchen, & Krueger, 2008). Two major dimensions often emerge: an internalizing dimension, which accounts for comorbidity among, for example, depressive, anxiety, post-traumatic stress, and eating disorders, and an externalizing dimension, which accounts for comorbidity among, for example, substance use disorders, conduct disorder, antisocial behavior, and ADHD. Thought disorder spectrum, which includes psychotic and bipolar I disorder, appears to be a third dimension, and some researchers also identify subfactors such as sexual problems and fear (Kotov et al., 2017). Other researchers claim that there is a single underlying dimension, *p*, that measures a person's liability to mental disorder, comorbidity among disorders, persistence of disorders over time, and severity of symptoms (Caspi & Moffitt, 2018; see also Rosenström et al., 2018; see Figure 5). Dimensional and network approaches still rely on the symptoms provided by the DSM, however, and thus inherit many of its weaknesses discussed earlier.

The NIMH proposed another new and still evolving approach, termed Research Domain Criteria (RDoC), which implicitly at least, is based on evolved functionality. RDoC currently involves a matrix that cross-tabulates different levels of measurements and markers—from genes and molecules to cells to physiology to cognition and behavior—with more-or-less functional domains relevant to mental disorders, such as positive and negative valence systems, motor systems, cognitive systems, and social processes (Cuthbert & Insel, 2013; National Institute of Mental Health, 2019b). The first dimension takes into account what biological anthropologists and other evolutionary biologists, following Tinbergen, call proximate-level mechanisms involving ontogeny and physiology (e.g., genes, molecules, and cells), and the second dimension roughly corresponds to function, that is, ultimate-level explanations involving phylogeny and adaptation, for example, fear or visual perception (Mayr, 1961). To investigate anxiety disorders, for instance, researchers might investigate the genetic, cellular, physiological, behavioral, and social processes related to fear and threat perception.

The dimensional and RDoC efforts reflect an increasingly popular perspective that mental disorders are not discrete phenomena but instead a consequence of complex systems in the individual and the environment that interact at many levels, from genes and molecules to cultural transmission, with feedback loops embedded between and within levels, for example, interactions among symptoms. There is therefore not likely to be a one-to-one correlation between an altered biological trait and a mental disorder (Kendler, 2008; Borsboom & Cramer, 2013; Borsboom, Cramer, & Kalis, 2019; see Figures 1 and 5d). For review and critique of network models, see Bringmann and Eronen (2018). Computational psychiatry is another approach that aims to develop computational models that could generate psychiatric symptoms, signs, and diagnostic outcomes from latent psychopathological states involving, for example, neuroreceptor deficits (Friston, Redish, & Gordon, 2017).

None of these approaches explicitly invoke evolutionary theory, however, and thus cannot take advantage of its powerful theoretical toolkit. Remarkably, they even lack a valid concept of disorder (Wakefield, 2014), and ignore the compelling social critiques of psychiatry.

8 | EVOLUTIONARY MEDICINE AND PSYCHIATRY: FUNCTION AND DYSFUNCTION

More than a century and a half after Darwin published *On the Origin of Species*, medicine, including psychiatry, should have incorporated evolutionary thinking into its theoretical foundations, but it has not (Nesse et al., 2010). It is therefore possible that the failures of psychiatry are traceable, in part, to its failure to make use of the scientific framework for understanding the origins and functionality of the human species, including the evolution and functions of the brain. Evolutionary medicine is a relatively new effort to rectify this shortcoming and synthesize medicine and evolutionary biology (Trevathan, 2007).

8.1 | An evolutionary concept of illness as 'harmful dysfunction'

All the approaches to mental illness have largely accepted psychiatrists' ad hoc discrimination of the mentally ill from the mentally healthy. If their underlying concepts of illness have been flawed, however, so too will their identifications of the ill, crippling efforts to determine causes.

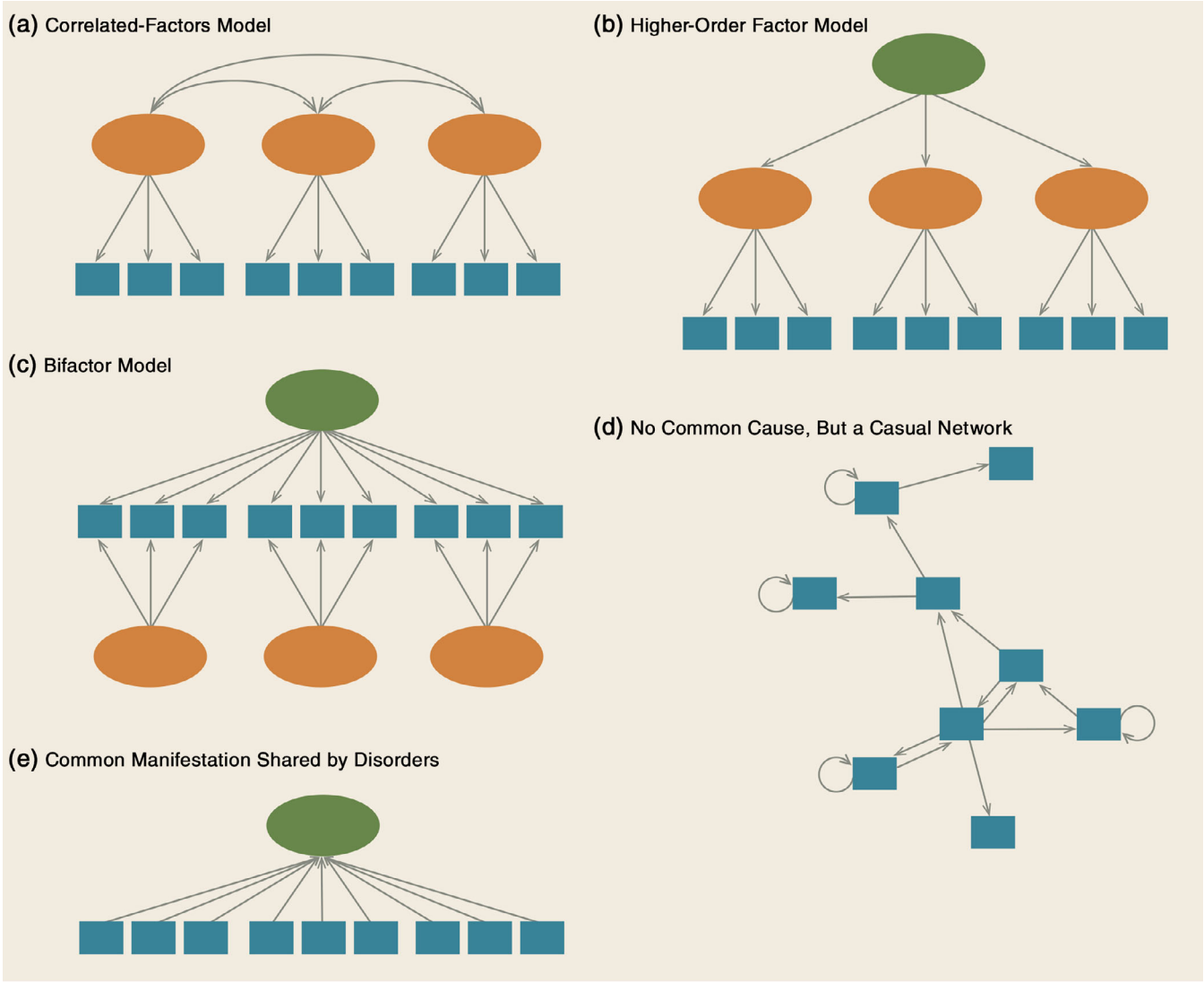

FIGURE 5 Panel (a) shows a correlated-factors model, which is the original structural model used in psychopathology research. In this model, the latent variables represent variance shared (or comorbidity) among the disorders within each of three spectra: internalizing, externalizing, and psychotic experiences. The high correlations between these latent traits suggested the possibility that they could be accounted for by a general factor of psychopathology, labeled "p." Panels (b) and (c) show two ways to conceptualize p, respectively. The higher-order factor model (panel b) shows that there is a second-order factor arising from the internalizing, externalizing, and psychotic experiences first-order latent variables; p represents the variance shared among the three spectra. The bifactor model (panel c) shows that there is one common liability to these three forms of psychopathology (p) as well as a set of independent factors that influence a smaller subset of symptoms and disorders. The use of the term "bifactor model" is an unwieldy historical and statistical legacy; it harkens back to the early days of intelligence research, which first proposed a general factor that is common to all items on a test (g) and more specific factors that are common to a smaller subset of related items and are thought to represent independent cognitive modules. Panel (d) shows an alternative conceptualization of positive correlations among disorders. Here there is no common cause, but instead there is a causal network in which disorders influence each other (straight arrows) and themselves (looped arrows) over time. Panel (e) shows that rather than a cause of disorders, p is constructed from the disorders, reflecting a common manifestation that is shared by the different disorders. *Source:* Figure and caption from Caspi and Moffitt (2018)

In our view, a more successful scientific approach to mental illness must start with an illness concept grounded in the evolved functionality of the human organism (Naturalism). It is not clear that a purely Naturalistic illness concept completely escapes the Constructivist critiques, however, because efforts to "treat" some putative biological dysfunctions, such as homosexuality, might have much more to do with their social undesirability than with their supposed harm to the individual.

Wakefield's *harmful dysfunction* illness concept (Wakefield, 1992a) combines the Constructivist and Naturalist accounts with the concept of adaptation from evolutionary biology (Darwin, 1859; Williams, 1966). It was formulated to help disentangle true disease states from conditions, like homosexuality, that are merely considered socially undesirable. "Harmful" signifies an individual, social, or cultural value judgment, whereas "dysfunction" represents the failure of a trait to perform its evolved function, a matter for scientific inquiry. Thus, a

broken femur is a disease state because it involves both an objective dysfunction of the femur, an adaptation for locomotion, that in turn impairs one's ability to perform individually and socially valued tasks such as one's job, and is therefore deemed harmful.

Traits that are biologically dysfunctional but socially benign, or that are biologically functional but socially harmful, are not illnesses. Birthmarks appear to be a dysfunction of skin growth, for example, but because they are typically not regarded as harmful, they are not illnesses. Similarly, being born with one kidney instead of two indicates some genetic or developmental dysfunction, but because this condition is not harmful, it is also not an illness. Even if homosexuality is caused by a biological dysfunction, it is not harmful and is therefore not an illness. Aggression and lying, on the other hand, might be socially harmful (and might lead to physical harm), but because they are not biological dysfunctions, they are not illnesses. Moreover, physical pain, sadness, disgust, and fear are aversive, but aversiveness alone does not implicate a dysfunction; in these cases, in fact, aversiveness is functional. Only conditions that are both biological dysfunctions *and* harmful, like cancer, infectious diseases, and neurodegenerative diseases, are illnesses. There has been a robust debate regarding this concept (see, for example, Clark, 1999; Wakefield, 1995, 2000), but in our view Wakefield has convincingly rebutted most objections.

9 | A PROVISIONAL EVOLUTIONARY SCHEMA OF MENTAL DISORDERS

The nascent disciplines of evolutionary medicine and evolutionary psychiatry have not reached even a rough consensus on the cause(s) of any mental disorder. Here we very tentatively offer a provisional evolutionary schema with the important caveat that because most research has used DSM categories, our schema relies on them too.

The causation model employed by early versions of the DSM classified disorders into organic vs. reactive, with the former seen as bearing little relation to life events and circumstances, and the latter rooted in life events and circumstances. Although it is now clear that all disorders have both environmental and genetic components, some disorders, such as autism and schizophrenia, have high heritability, onset during development, and are relatively rare; some, such as Alzheimer's, are virtually absent prior to old age; and some, such as anxiety and depression, have low heritability, are relatively common, can onset throughout the adult life course in response to adversity, and involve symptoms that have face validity as functional responses to adversity.

Using the harmful dysfunction illness concept, we therefore propose that there is a group of mental disorders that are probably best explained by genetic-based developmental dysfunctions; a group that is probably caused by senescence; a group that might be caused by mismatches between modern and ancestral environments; and a group that are probably not disorders but instead are aversive and socially undesirable but nevertheless adaptive responses to adversity (with a few disorders that do not clearly belong to any of these groups). We restricted our schema to disorders analyzed in a recent large GWAS study so that heritability estimates were easily comparable (Brainstorm Consortium et al., 2018; see Figure 6).

10 | DEVELOPMENTAL DISORDERS

Most mammals, including humans and most primates, have distinct pre-reproductive (infancy and childhood) and reproductive (adult) stages (Pagel & Harvey, 2002). Gene regulatory networks (GRNs) govern development through differential gene expression. Subsets of genes are activated in different cells at different stages of development to generate cellular and anatomical features that serve the fitness interests of the organism during that life stage (Rebeiz, Patel, & Hinman, 2015). In humans, several developmental schemes have been proposed, with transitions from one stage to the next mediated by various hormones (for review, see Bogin, Varea, Hermanussen, & Scheffler, 2018). Mutations or other disruptions of the GRNs that govern the development of cognitive functions necessary during each stage would cause cognitive/emotional dysfunctions that appear during that stage.

10.1 | Disorders of early development

ASD and Tourette's disorder are members of a neurodevelopmental class of disorders in the DSM-5 (American Psychiatric Association, 2013) (we address ADHD, another member of this group, below). Neurodevelopmental disorders are characterized by childhood onset and cognitive or motor functional delays or impairments (Thapar, Cooper, & Rutter, 2017). ASD and Tourette's are highly comorbid, although the symptoms of ASD are pervasive over the lifecourse, the motor tics associated with Tourette's tend to subside in adulthood (Hallett, 2015). Neurodevelopmental disorders are male-biased (Arnett, Pennington, Willcutt, DeFries, & Olson, 2015; Baio, 2012; Hallett, 2015; Pinares-Garcia, Stratikopoulos, Zagato, Loke, & Lee, 2018). These conditions are highly heritable and, other than ADHD, relatively rare (Figure 6), which suggests that they might be explained by multiple mutations that cumulatively interfere with the early development of one or more cognitive functions.

A recent large GWAS study of ASD found multiple significant loci (Grove et al., 2019), with ASD subtypes having different genetic architectures. Specifically, common variants associated with high-functioning subtypes were positively associated with high IQ and educational attainment. Other subtypes seem to be more strongly associated with spontaneous mutations. Functional information on the identified loci implicate processes relating to pre- and postnatal brain development and neuronal function.

10.1.1 | Autism and theory of mind deficits

The autism literature is rather unique in that some of the most influential theoretical approaches draw heavily from cognitive and

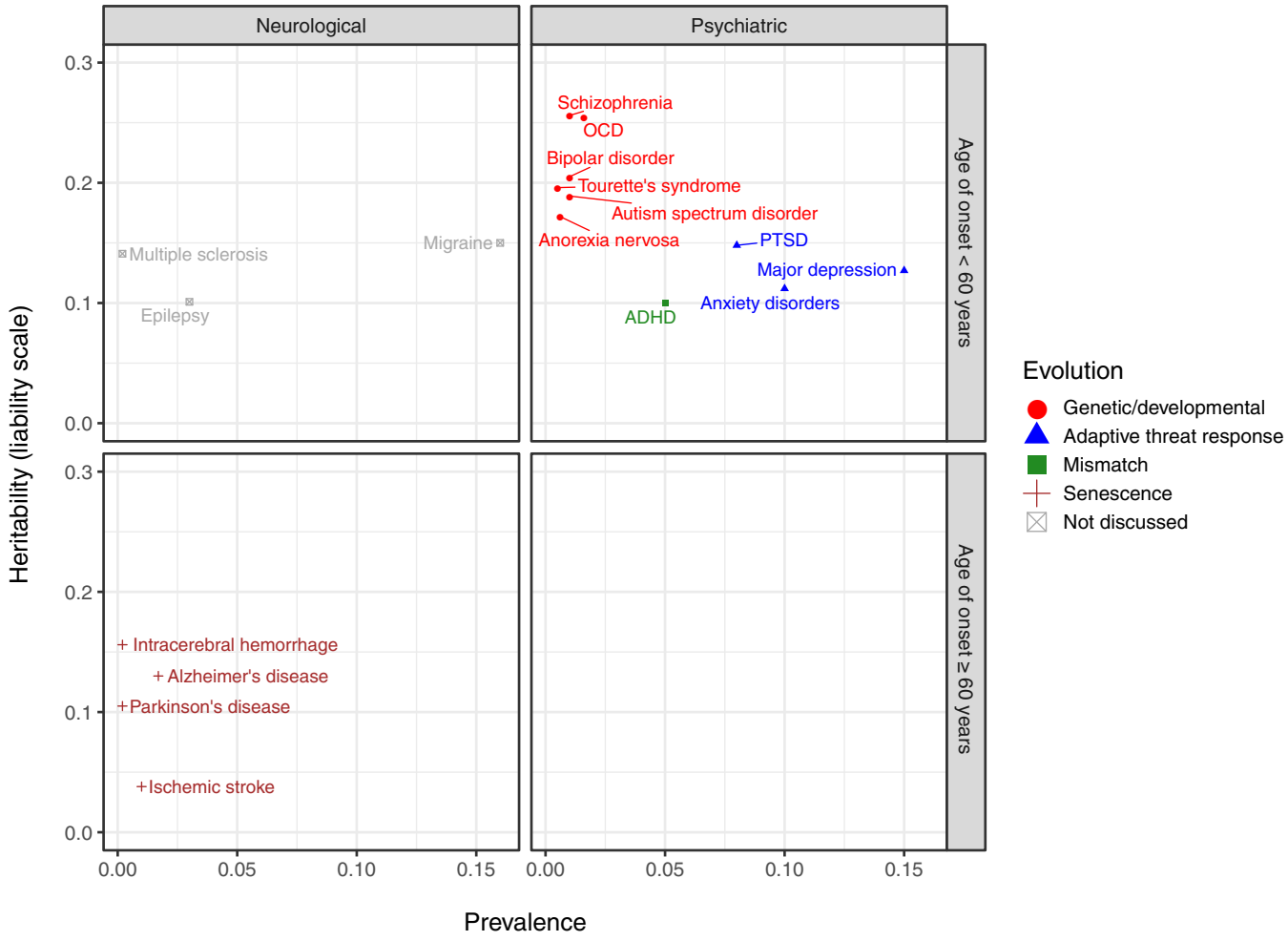

FIGURE 6 A provisional evolutionary schema of nervous system disorders traditionally categorized as neurological (left) and psychiatric (right), based on their heritability, population prevalence, and age of onset. Heritability is on a liability scale. The colors represent the classification scheme (see text). ADHD, attention deficit hyperactivity disorder; OCD, obsessive–compulsive disorder; PTSD, post-traumatic stress disorder. *Source:* Data from Brainstorm Consortium et al. (2018), table S1

evolutionary psychology. Baron-Cohen, Leslie, and Frith (1985), inspired by the Premack and Woodruff (1978) discovery that chimpanzees might have a "theory of mind" (ToM) capability similar to humans, proposed that autism represents a dysfunction of an evolved ToM "module." ToM refers to the cognitive ability to infer the mental states of others, and more generally reflect on the connection between one's own or others' mental states and actions. It is thought to have evolved in response to social selection pressures, and elements of ToM appear in infancy and early childhood (Perner & Roessler, 2012). ToM is thus one of the foundations of the social intelligence hypothesis (Brüne, 2005; Byrne & Whiten, 1990).

ASD seem to be characterized, in part, by a difficulty in inferring the mental states of others, and hence might reflect a dysfunction of the ToM, sometimes referred to as "mindblindness" (Baron-Cohen, 2000; Baron-Cohen et al., 1985; Baron-Cohen & Hammer, 1997). This hugely influential hypothesis has generated a vast research literature. Nevertheless, the theory has weaknesses. It does not explain the non-social deficits in ASD, the difficulty that many individuals with ASD have in responding emotionally to others, and the fact that other disorders also seemed to involve ToM deficits. Empathizing–systemizing (E–S) theory was developed to address these shortcomings. It proposes that ASD involves developmental delays and deficits in empathy, including emotional responses to the mental states of others, combined with average or even above average abilities in systematizing, that is, analyzing or constructing rule-based systems. E–S theory led to the popular yet controversial extreme male brain theory of autism, which is built on evidence that female sex is associated with an empathizing cognitive style whereas male sex is associated with a systematizing cognitive style. According to this theory, autism represents an extreme systematizing cognitive style (Baron-Cohen, 2002; Baron-Cohen & Hammer, 1997; Baron-Cohen, Knickmeyer, & Belmonte, 2005).

10.2 | Disorders of later development

Another group of disorders with relatively low prevalence and high heritability, such as bipolar disorder, OCD, and schizophrenia

(Figure 6), are rare in childhood and typically onset during late adolescence or early adulthood, suggesting that they might involve mutations in GRNs governing the transition to sexual maturity. From an evolutionary perspective, sexual maturation involves a number of relatively new social and environmental challenges, such as intrasexual competition for mates, management of mating relationships, increased contributions to subsistence, increased autonomy, increased influence on group decisions, and increased childcare responsibilities. Physiologically, sexual maturation in females involves the onset of ovulation, breast development, widening of the hips, and increases in body fat, and in males increases in muscle mass, lowering of voice pitch, and appearance of facial hair (Bogin et al., 2018). Cognitively, this transition involves enhancements in abstract and hypothetical thinking (including planning for the future), processing speed, theory of mind, and perspective taking (Bogin et al., 2018; Smetana and Villalobos 2009; Yurgelun-Todd, 2007).

As many researchers have noted, several symptoms of this group of disorders appear to involve dysfunctions of evolved social strategies or behavioral defense systems (Brüne, 2015, and references therein). These systems might be activated or upregulated in the transition to adulthood when individuals enjoy less protection and provisioning by parents and face new responsibilities, competitive challenges, and threats. Dysfunctions in these systems would therefore first be apparent during or shortly after sexual maturation.

10.2.1 | Obsessive–compulsive disorder

OCD, with a mean age of onset of about 19 (Ruscio, Stein, Chiu, & Kessler, 2010), is characterized by obsessional fears concerning physical and/or moral contamination and compulsions to perform acts and/or rituals to relieve the obsessions. Fiske and Haslam (1997), an anthropologist and clinical psychologist, respectively, argued that humans have an evolved capacity to invent, perform, and transmit rituals, which play crucial roles in key life transitions and social relationships, such as the transition to adulthood (e.g., rites of passage) and mating (e.g., marriage rituals). These rituals often involve behaviors that are similar to behaviors observed in OCD, which therefore might be a dysfunction of the psychological processes that support culturally meaningful rituals.

To test their hypothesis, Fiske and Haslam (1997) coded the presence or absence of OCD-like behaviors in ethnographic texts from 20 cultures involving ritual and non-ritual activities, as well as the presence or absence of behaviors characteristic of other disorders (e.g., anxiety, depression, schizophrenia). OCD symptoms included a focus on numbers or colors with special significance, repeating activities, measures to prevent harm, ordering or arranging things, saying special prayers or incantations, and washing and grooming. They found that features resembling OCD symptoms were much more likely to occur in rituals than in work or other activities. Features resembling symptoms of other psychological disorders, on the other hand, were rarer and did not discriminate as well between rituals and other activities. In the vast majority of cultures sampled, rituals contained more OCD-like features than work or other activities. They conclude that, whereas rituals are highly regulated, socially sanctioned, and have a clear meaning for the participants, individuals with OCD might have a dysregulated disposition to perform socially meaningless rituals.

10.2.2 | Schizophrenia and bipolar disorder

Schizophrenia can first onset around 15–19 (Thomsen, 1996) with a drop in the rate of onset after age 35 (Angermeyer & Kühnz, 1988). It is characterized by positive and negative symptoms, and cognitive impairment. The positive symptoms include hallucinations; paranoid, somatic, grandiose, and erotic delusions; and disordered thoughts and speech. The negative symptoms include flat affect, anhedonia, withdrawal, and lack of motivation in starting and sustaining tasks–each of which are also features of depression. Poor executive functioning and problems with working memory are also features. ToM delays and deficits are also thought to help explain the social deficits in schizophrenia (Frith, 2004). Delusions, for instance, might be caused by misreading others' mental states as well as one's own (for review of research on ToM and schizophrenia, see Brüne, 2005). Paranoid and somatic delusions focus on imagined social and environmental threats, and grandiose and erotic delusions on aspects of social value. Evaluating threats and social value are both critical during the transition to sexual maturity and adulthood.

Sullivan et al. have been studying schizophrenia in Western Pacific cultures using a biocultural framework (Sullivan et al., 2000; Sullivan & Allen, 1999; Sullivan, Allen, et al., 2007). To characterize the expression of schizophrenia in these cultures, they employ psychiatric diagnosis, biomarkers such as smooth-pursuit eye-tracking, psychometric measures, self-reported substance use, and cultural and historical analyses. Across Micronesia, schizophrenia prevalence varies by a factor of four, ranging from a low of approximately 0.4% in the Marshall Islands in eastern Micronesia to 1.7% in the western island nation of Palau, and in Palau there is a marked 2:1 male bias in prevalence, much greater than seen elsewhere (Sullivan, Allen, et al., 2007). Previous researchers had suggested that the high prevalence in Palau was an artifact of the arrival and widespread use of exotic drugs. More generally, many researchers had argued that schizophrenia has a more benign expression in developing countries such as Palau.

Sullivan, Allen, et al. (2007) indeed found some important differences between Palauan participants compared to typical Western patient samples. Of the Palauan participants, 87% were living with families, similar to other developing settings, but quite different from Western settings. In general, women with schizophrenia seemed to fare better than the men; 48% of the women were married, for instance, compared to 10% of the men, and women had an average of 2.3 offspring (about the same as other Palauan women) compared to an average of 0.5 for men. Several researchers have suggested that customary obligations that are different for young men than for young women might protect Palauan females, but not males, from the onset of, or worsening of schizophrenic symptoms. Young Palauan women

generally maintain secure positions in the household and lineage by fulfilling domestic responsibilities, helping in childcare, and bearing children. Palauan men, on the other hand, have no meaningful identity until they earn an income, marry, have children, and engage in social, political, and economic relationships. Schizophrenia thus disrupts a man's ability to establish a secure social position through wage employment (Sullivan, Allen, et al., 2007).

The differences between schizophrenia in Palau and schizophrenia in other populations, however, were outweighed by the many similarities. Symptomatic expression of schizophrenia and prevalence of smooth-pursuit eye-tracking dysfunction in Palau were broadly comparable to other settings. As in other populations, drug use among those with schizophrenia was high. But contrary to the assumption that drug use worsens symptoms, or might even be responsible for the high prevalence of schizophrenia in Palau, drug use was associated with milder symptoms, probably because patients were self-medicating their symptoms with locally available psychoactive substances such as betel nut and cannabis (see also Sullivan & Hagen, 2002).

Despite fairly substantial differences in cultural context between Palau and other populations, Sullivan, Allen, et al. (2007) reject the hypotheses that schizophrenia in Palau has a unique diagnostic profile, that it has a unique bio-behavioral expression, and that it is a consequence of "development" such as the introduction of exotic psychoactive drugs. These results return focus to genetic factors.

Schizophrenia is associated with reduced fertility (Power et al., 2013), so the persistence of schizophrenia risk alleles is puzzling. Keller (2018) reviews two genetic hypotheses for schizophrenia: mutation-selection-drift, and balancing selection. In favor of mutation-selection-drift is evidence that schizophrenia risk alleles appear to be under weak-to-strong purifying selection. It is not clear, however, how a large number of risk alleles of small effect, the distribution of which would vary from individual to individual, would generate schizophrenia's common diagnostic profile. Balancing selection, in which selection maintains multiple alleles at a locus, is another possible mechanism. Schizophrenia alleles might provide benefits, such as enhanced immunity or creativity, that offset their costs. In favor of this hypothesis, two of the strongest schizophrenia risk alleles occur in immunity-related genes, and first-degree relatives of schizophrenics appear to be over-represented in creative professions (Keller, 2018). See also Burns (2004) and commentaries.

These hypotheses might also apply to bipolar disorder, as GWAS research suggests the bipolar disorder and schizophrenia share an underlying genetic risk (Prata, Costa-Neves, Cosme, & Vassos, 2019). Bipolar disorder, which usually onsets in late adolescence or early adulthood (Leboyer, Henry, Paillere-Martinot, & Bellivier, 2005; Nowrouzi et al., 2016), is characterized by rapid shifts between symptoms of mania and depression (Merikangas et al., 2011). Manic symptoms—elevated mood, high energy, reduced need for sleep, and increased risk-taking—are probably functional when "profitable" opportunities present themselves, but in bipolar disorder seem to onset regardless of such opportunities. Similarly, low mood, as we discuss in detail later, is probably functional when experiencing adversity, but dysfunctional in the absence of adversity.

As biocultural anthropologist Allen (1997) argued, schizophrenia (and perhaps bipolar disorder) appears to involve genetic disruption of the social competencies required for a successful transition to adult life in traditional societies, with, in the Palauan case at least, particularly negative consequences for men.

10.2.3 | Eating disorders

Restrictive eating disorders (i.e., bulimia nervosa and anorexia nervosa) also emerge in adolescence, and adolescent females tend to exhibit greater eating disorder symptomatology (Hay, Girosi, & Mond, 2015; Herpertz-Dahlmann et al., 2008; Nagl et al., 2016). Anorexia nervosa, characterized by food restriction, and bulimia nervosa, characterized by binging and purging, both concern extreme dietary regulation and are related to anxieties about weight gain and self-perceptions of needing to lose weight. Anorexia nervosa and bulimia nervosa are rare, but subthreshold symptoms are classified as separate eating disorders in the DSM and account for the majority of cases (Fairburn & Bohn, 2005; Le Grange, Swanson, Crow, & Merikangas, 2012).

There are several evolutionary hypotheses for eating disorders, including the thrifty genotype hypothesis, which sees disordered eating arising from a mismatch between resource-rich modern environments and ancestral environments in which malnutrition and starvation were ever present risks; intrasexual competition, in which slimness indicates youth, a trait preferred by men; and reproductive suppression, which sees anorexia as an adaptive attempt to suppress reproduction, or manipulation of reproductive status by parents or competitors (for brief review, see Rantala, Luoto, & Krams, 2019). Because restrictive eating disorders emerge in adolescence and are female-biased, they are probably developmental disorders related to sexual maturation and female competition in a novel environment (Nettersheim et al., 2018; Rantala et al., 2019, and references therein).

11 | AVERSIVE BUT POSSIBLY ADAPTIVE DEFENSES

MDD, anxiety disorder, and PTSD have relatively low heritability (Figure 6), indicating that environmental factors play a large role. In fact, as we reviewed earlier, some of the genetic heritability of these disorders includes the heritability of their environmental risk factors, such as divorce, so the role of environmental variation might be even larger than it seems. These disorders are also quite common. As we discussed earlier, when DSM-III criteria, which were developed within patient populations, were applied to community populations, they produced surprisingly high prevalence rates, raising concerns of false positives. In adults, depression, anxiety and PTSD commonly onset at any age in apparent response to various forms of adversity (Au, Dickstein, Comer, Salters-Pedneault, & Litz, 2013; Kendler & Gardner, 2016; Kendler, Karkowski, & Prescott, 1999). In conflict-affected countries, an estimated one in five people suffers from depression,

PTSD, anxiety disorders, and other disorders, compared to 1 in 14 worldwide (Charlson et al., 2019). Because many of their symptoms seem to be functional responses to threats, the hypothesis that they are functional responses to adversity is compelling. In fact, early on, prominent mental health researchers grappling with these high prevalence rates suggested exactly this (e.g., Regier et al., 1998).

Traits are selected because they increase reproduction, not necessarily survival, a subjective sense of well-being, or a prosocial disposition (Belsky, Schlomer, & Ellis, 2012; Nesse & Williams, 1994). One of the key insights of evolutionary medicine and the harmful dysfunction illness concept is that not all traits that are aversive or "harmful" are illnesses. Defense systems are adaptations that reliably activate in fitness-threatening situations in order to minimize fitness loss (Keller, 2018). Fever, for instance, is part of an evolved adaptive defense system against infections. Pain evolved to induce organisms to reflexively repel from tissue-damaging stimuli, and conditioned pain avoidance is a psychological adaptation that warns against re-encountering harmful stimuli. Just as these unpleasant adaptations protect humans against infections and other physical harms (Eccleston & Crombez, 1999; Merskey, 1986), sadness, low mood, anxiety, agitation, and hypervigilance, however aversive and socially undesirable, might well be adaptations that likewise defend against a variety of social and other harms, in part, by way of being unpleasant to the sufferer and her social partners.

Depression is characterized by persistent sadness, low mood, and anhedonia, which, like ordinary sadness and grief, are probably forms of "psychic pain" that adaptively focus attention on adverse events that would have reduced fitness, such as loss of a spouse, so as to mitigate the current adversity and avoid future such adversities (Andrews & Thomson Jr, 2009; Hagen, 1999, 2003; Horwitz & Wakefield, 2007; Nesse & Ellsworth, 2009; Panksepp, 2004; Syme, Garfield, & Hagen, 2016; Thornhill & Thornhill, 1989; Tooby & Cosmides, 1990; Wakefield, 1992a). In the large majority of cases, MDD symptom levels are proportionate to levels of adversity (Brown & Harris, 1978; Kendler, Karkowski, & Prescott, 1998), typically resolve within weeks or months (the median is 6 months; Ten Have et al., 2017), and the majority of sufferers will experience only a single episode in their lifetimes (Ten Have et al., 2018), features that are consistent with a functional emotional response to adversity.

Anxiety is characterized by fear or panic, irritability, hypervigilance, racing heart, loss of sleep, and other symptoms associated with fight or flight responses, which also seem to be functional responses to genuine social and environmental threats. PTSD diagnosis requires exposure to a traumatic stressor, and although some symptoms, such as inability to recall key features of the trauma and risky or destructive behavior, are not clearly functional, many other symptoms, such as avoidance of trauma-related stimuli, hypervigilance, negative affect, and unwanted upsetting memories, have face validity as functional responses to avoid future traumas. These characteristics suggest that these "disorders," which are highly comorbid (Ginzburg, Ein-Dor, & Solomon, 2010; Kaufman & Charney, 2000), might be functional responses to adversity.

Biological anthropologists have investigated numerous socioecological correlates of depression, anxiety, and PTSD in WEIRD and non-WEIRD settings, and their results confirm that various forms of adversity are strongly associated with, and probably cause, these putative defense responses. Worthman et al., for instance, have investigated the effects of conflict exposure on mental health including depression, anxiety, suicidality, and PTSD (Bhardwaj et al., 2018; Kohrt et al., 2008, 2009, 2012; Kohrt & Mendenhall, 2016). One study found that conflict exposure predicted anxiety in a dose–response relationship, whereas low socioeconomic status and non-conflict-related stressful life events predicted depression (Kohrt et al., 2012). Hadley et al. have found food insecurity to be a risk factor for elevated depression and anxiety symptoms in East African populations (Hadley & Patil, 2006, 2008; see also Hadley & Crooks, 2012 for review). Valeggia and Snodgrass (2015) review evidence that adversity experienced by indigenous populations, such as rapid acculturation, poverty, disruptive changes in traditional social roles, and violence, increase the risk of depression and suicide, and that greater involvement with native culture is protective.

Hagen, building on the psychic pain hypothesis, proposed that postpartum depression (PPD) is an adaptation that informs mothers that investment in a new offspring is unlikely to deliver fitness benefits, for example, because the infant has severe health problems, the mother has health problems, or the mother is not receiving sufficient investment from the father or other kin. There is little difference between PPD and MDD, so a more general version of this evolutionary model might apply to MDD (Hagen, 1999). Hagen and Barrett (2007) tested this hypothesis among Shuar mothers, finding that mothers who reported being sad when their infant was born had problems in their relationship with the father, were in poor health, or faced opportunity costs (e.g., already investing in young child). Stieglitz, Schniter, von Rueden, Kaplan, and Gurven (2014) similarly found that depression in older Tsimane adults was associated with disability and other factors that reduced their ability to invest in their adult offspring and other kin.

Some evidence of possible functionality of PTSD comes from research on transmission of stress responses from parents to offspring. PTSD is often used as a model of extreme stress exposure in research on the transmission of epigenetic signatures—thought to mediate the stress response—from parents to offspring, either through the gestational environment, gametes, or parenting effects (Bowers & Yehuda, 2016). Biological anthropologist Mulligan (2016) reviews the evidence that exposure to such traumas have adaptive and maladaptive impacts on health throughout the life course and across generations. In particular, they are associated with DNA methylation at specific genes and throughout the genome. Numerous studies have investigated the intergenerational transmission of trauma-related effects and/or vulnerability from survivors to their offspring in populations exposed to war trauma and threats of genocide (Evans-Campbell, 2008; Field, Om, Kim, & Vorn, 2011; Lehrner et al., 2014; Yehuda, Schmeidler, Wainberg, Binder-Brynes, & Duvdevani, 1998). Mulligan's research on women in the Democratic Republic of the Congo found evidence that maternal exposure to war trauma

produces DNA methylation changes at genetic sites that regulate the hypothalamic–pituitary–adrenocortical axis (e.g., NR3C1) in both mothers and newborns that correspond to infant DNA methylation status and health outcomes such as birth weight (Clukay, Hughes, Rodney, Kertes, & Mulligan, 2018; Kertes et al., 2016; Mulligan, D'Errico, Stees, & Hughes, 2012; Rodney & Mulligan, 2014). Other studies also look at the transgenerational impact of maternal psychosocial stress on the epigenome via the influence of the intrauterine environment, that is, fetal programming (Radtke et al., 2011; Rudahindwa et al., 2018). It is not yet clear if these effects are best interpreted as functional or dysfunctional responses to environmental threats. As Mulligan emphasizes, however, there would be a selective advantage for the fetus to accurately predict the postgestational environment based on intrauterine cues.

11.1 | Social conflicts of interest

As the work of biological anthropologists and many others make clear, PTSD, anxiety disorders, and major depression are strongly associated with, and probably caused by, adversity in WEIRD and non-WEIRD populations. Why, then, have mainstream mental health researchers become so reluctant to consider that these conditions might be functional responses to adversity? Critics of psychiatry, such as Szasz (1960) and Scheff (1971), have long maintained that psychiatry is an institution that often serves to control social deviance as much as it serves to identify and treat genuine pathology. This view has some support from evolutionary theory. Within a population, agents evolve strategies in competition with other agents with whom they have conflicts of interest over access to resources and mates. This is true even among close genetic relatives such as mothers and their fetuses (Haig, 1997), parents and offspring (Trivers, 1974), and siblings (Godfray & Parker, 1992). Hence, as Cosmides and Tooby (1999) observed in their comment on Wakefield's harmful dysfunction concept, "…what is desirable or harmful are rarely matters of harmonious consensus or intersubjective agreement, much less matters of fact (p. 456)."

Victims of adversity, in many cases, are socially powerless, and providing them the substantial help they need would impose costs on others. Even the loss of a loved one, a common risk factor for depression (Kendler, Myers, & Zisook, 2008), could lead to conflict if the depressed person consequently needs substantially more investment from her other social partners than they are able or willing to provide. This raises the concern that in some cases the label "mental illness" is applied to resolve conflicts in favor of some parties at the expense of others, and silence inconvenient cries for help.

We illustrate this possibility with two examples: suicidality and work-related depression. Major depression and suicidality are often caused by social conflicts, such as marital conflict, work conflict, and physical and sexual assault (Devries et al., 2011; Dworkin, Menon, Bystrynski, & Allen, 2017; Husky, Guignard, Beck, & Michel, 2013; Stein et al., 2010; Theorell et al., 2015), and biological anthropologists Stieglitz et al. (2014) have found that the association of conflict with depression is seen in the Tsimane, a non-WEIRD society. Depression is also associated with anger and hostility (Bertera, 2005; Gilbert, Gilbert, & Irons, 2004; Riley, Treiber, & Woods, 1989; Simon & Lively, 2010; Whisman & Uebelacker, 2009). Sexual assault in particular is a potent predictor of PTSD and suicidality (Dworkin et al., 2017).

Sad expressions and crying are low cost signals of need that are effective when there is little conflict between the signaler and his or her social partners. Victims of assault and other severe adversity, though, are often in conflicts with powerful others (Hagen, Watson, & Hammerstein, 2008; Syme et al., 2016; Syme & Hagen, 2018). These victims need help, but they are often not believed. We are testing the hypothesis that depression, non-fatal suicidal behavior, and self-harm are, in part, costly, credible signals of need that are effective despite high levels of conflict that would render low cost signals ineffective. The vast majority of suicidal behavior does not result in death. Hence, the non-zero risk of death might be a credible signal of need, which, in the majority of cases in which the victim survives, functions to convince skeptical others that the signaler's need is genuine. Syme et al. (2016) coded all instances of suicide in the probability sample of the Human Relations Area Files (HRAF). They found that social conflict, powerlessness, and threats to the victim's fitness were ubiquitously associated with suicidality across diverse cultures. If the victim survived, far more often than not he or she received important benefits, such as social pressure against an abuser or avoidance of an unwanted marriage.

Work-related depression is another example where the illness label might serve the interests of the powerful over the powerless. The economic cost imposed on employers by their depressed workers due to absenteeism and presenteeism (working while depressed), for example, is often raised to make the "business case" for depression research. A recent study of absenteeism and presenteeism costs due to depression across eight diverse countries found that the cost of absenteeism ranged from 0.01% of GDP in Korea to 0.66% of GDP in Brazil, and the cost of presenteeism ranged from 0.12% of GDP in Korea to 4.2% of GDP in South Africa, with the aggregate costs in the United States exceeding $84 billion/year (Evans-Lacko & Knapp, 2016). A highly effective antidepressant medication would represent an enormous economic benefit to employers.

There is substantial evidence, however, that work-related depression is associated with poor working conditions. A recent systematic review and meta-analysis of the relationship between the work environment and depression found moderately strong evidence that job strain, low decision latitude, and bullying were risk factors for work-related depression, and weaker but still positive evidence that effort-reward imbalance, low support, unfavorable social climate, lack of work justice, conflicts, limited skill discretion, job insecurity, and long working hours were risk factors (Theorell et al., 2015). The illness label for work-related depression alleviates employers from the responsibility to improve working conditions for depressed employees.

11.2 | Mental Health and Immunity

The increasing evidence that the immune system plays an important role in mental health also provides evidence for the role of conflict.

Exposure to acute and chronic social stressors involving conflict, threat, isolation, and rejection are associated with increased inflammation (Herbert & Cohen, 1993; Segerstrom & Miller, 2004; Kiecolt-Glaser, Gouin, & Hantsoo, 2010; see Slavich & Irwin, 2014 for review). Early evidence of an association between biomarkers of inflammation and depression (Maes, 1995; Smith, 1991) has led to a burgeoning field on the role of the immune system in depression, anxiety, and other stress responses. A team of biological anthropologists extended these findings to Tsimane forager-horticulturalists in Bolivia, providing evidence that this relationship is not unique to WEIRD populations (Stieglitz et al., 2015).

Numerous, closely related evolutionary theories have attempted to explain the association of inflammation and depression. Kinney and Tanaka (2009) proposed that depressive symptoms conserve energy to combat infection, discourage activities that promote transmission of infection, signal others to avoid contact, reduce the risk of conflict and therefore injuries, and reduce appetite to avoid exposure to pathogens (see also Anders, Tanaka, & Kinney, 2013). Raison and Miller (2017) propose similar ideas, adding that, ancestrally, social conflicts were good predictors of physical injury, and therefore preemptively activated the immune system (see also Raison, Capuron, & Miller, 2006; Raison & Miller, 2013). The latter idea is extensively developed by Slavich and Irwin (2014) in their "social signal transduction" theory of depression, which posits that social threat and adversity upregulates components of the immune system, generating sickness behaviors and depression. It has even been proposed that depression might be an exaptation of sickness behavior (Andrews & Durisko, 2017; Raison & Miller, 2017).

In our view, existing evolutionary theories of the relationship between inflammation and depression do not account for the psychic pain that characterizes depression. What do infections, or the threat of infections, have to do with profound psychic pain, guilt, and suicidal thoughts? A much more parsimonious explanation is simply that, as we reviewed earlier, depression is a functional response to social conflicts and other threats to fitness that, as others have argued, often resulted in physical injury, and do so today. After all, assault is one of the most potent risk factors for depression (Kendler et al., 1995), and violence in the context of interpersonal conflict is common. In a study among the Tsimane, 85% of female participants reported physical abuse by their husbands (Stieglitz, Kaplan, Gurven, Winking, & Tayo, 2011). Hagen and Rosenström (2016) proposed that physical formidability would protect against depression, and that the sex difference in depression was due, in part, to the sex difference in physical formidability. In a large, nationally representative US sample (NHANES), they found that grip strength, an index of upper body strength, had a strong negative association with depression that was not explained by numerous possible confounds, and that it mediated part of the effect of sex on depression.

From an evolutionary perspective, conflict should activate both psychological mechanisms to resolve or avoid the conflict (e.g., anger, fear, avoidance, depression), as well as immune mechanisms to protect against infections and initiate tissue repair should the conflict result in physical injury. Given that depression and anxiety are responsible for more than half the disease burden attributable to mental disorders (40.5 and 14.% of DALYs, resp., after adjusting for comorbidity; Whiteford et al., 2013), much that psychiatry considers to be pathological appears to be rooted in adversity and conflicts of interest (Hagen, 1999, 2003; Hagen et al., 2008; Hagen & Barrett, 2007; Hagen & Rosenström, 2016; Hagen & Thornhill, 2017; Horwitz & Wakefield, 2007; Rosenström et al., 2017; Wakefield, 2014). If so, research on depression, anxiety, and PTSD, should put greater emphasis on mitigating conflict and adversity and less on manipulating brain chemistry.

12 | SENESCENCE AND DEMENTIA

The prevalence of various forms of dementia, which are characterized by deficits in memory and cognitive function, increase dramatically with age. The DSM-5 classifies AD and other age-related dementias under neurocognitive disorders and the delineation of subtypes (e.g., cerebrovascular disease, Lewy body disease, frontotemporal degeneration) represents one of the few instances in which diagnosis is based on etiology (Sachdev et al., 2014).

Senescence is the process of organism deterioration with age. In humans, for example, the prevalence of numerous diseases, such as cancer and cardiovascular diseases, increases dramatically with age (Lozano et al., 2013). Senescence is now well-documented in a wide range of wild populations but is nevertheless quite variable across species (Lemaître et al., 2015). There are several evolutionary theories of senescence, most based on the observation that the force of selection decreases with age (Hamilton, 1966; Medawar, 1952). Medawar (1952) proposed that because the force of selection decreases with age, mutations with late-acting effects would accumulate, leading to deterioration of the organism. Williams (1957) expanded on this idea by proposing that genes often have multiple effects (pleiotropy). Genes that increase fitness early in life but decrease fitness late in life (antagonistic pleiotropy) would nevertheless be positively selected. Kirkwood (1977) instead proposed a "disposable soma" hypothesis in which a tradeoff between organism investment of resources in the germline (e.g., DNA repair) vs. investment in the soma leads to a sacrifice of late survival for reproduction (Kirkwood & Rose, 1991).

Biological anthropologist Fox (2018) evaluated eight evolutionary theories of AD. These included novel extension of the lifespan; lack of selective pressure during the post-reproductive phase; antagonistic pleiotropy; rapid brain evolution; delayed neuropathy by selection for grandmothering; novel alleles selected to delay neuropathy; by-product of selection against cardiovascular disease; and thrifty genotype. In addition, she evaluates a novel mismatch hypothesis: AD risk factors, including insulin resistance, estrogenic neuroprotection, inflammation, and ApoE (a genetic risk factor for AD) might have involved different fitness costs and benefits in the evolutionary past, such that AD risk may have been much lower. If so, disease onset would have been later in the lifespan, closer to age at mortality, diminishing the fitness effect of AD.

13 | MISMATCHES

Based on the harmful dysfunction concept, a mismatch between the current and ancestral environments could cause (a) dysfunction, or (b) harm, or both. The diagnostic status of ADHD has long been controversial because it might simply be a harmful (but not dysfunctional) mismatch between highly structured modern environments and less structured ancestral ones (Jensen et al., 1997). Typically diagnosed in childhood, ADHD has low heritability and a fairly high population prevalence of about 5–7.2% (Willcutt, 2012; Thomas, Sanders, Doust, Beller, & Glasziou, 2015; see Figure X), which means that, on average, there is about one child diagnosed with ADHD in each classroom. Symptoms include inattentiveness, hyperactivity, distractibility, impulsivity, and disorganization. These symptoms are specific to contexts requiring sustained attention and behavioral restraint such as the classroom or the workplace, and it is not clear how problematic this phenotype is in less structured environments. Given the intertwinedness of these symptoms to a particular environment, it is arguable that attention deficits only exist in relation to these novel highly structured environmental contexts. It is not that the modern environment causes ADHD, but rather that it sets tighter restrictions on what is normal or acceptable.

There is increasing evidence that an ADHD diagnosis results from a mismatch between normal child development and classroom environments. Several very large studies, for example, have now found that children relatively younger in age compared to their classmates (i.e., born later in the year) are at greater risk of being diagnosed with ADHD because the metric that teachers and parents judge them by is calibrated to children at slightly later stages of development (Caye et al., 2019; Karlstad, Furu, Stoltenberg, Håberg, & Bakken, 2017; Root et al., 2019). This provides clear evidence that this diagnosis, at least at times, pathologizes child behaviors that clearly fall within the normal spectrum, and that the skyrocketing use of powerful stimulants and other drugs to treat ADHD "symptoms" (Renoux, Shin, Dell'Aniello, Fergusson, & Suissa, 2016) requires a rethink.

ADHD is perhaps another example in which the illness label serves the interests of the powerful (e.g., teachers, parents) at the expense of the powerless (e.g., children). It is far easier to control rambunctious and inattentive children using medication than it is to restructure the school environment to accommodate normal variation in development.

13.1 | Substance use and coevolutionary arms races

Drugs of abuse, such as cocaine, activate brain circuitry related to reinforcing behaviors that increase access to food, sex, and other biological necessities. Because drug use is harmful, most substance abuse researchers subscribe to a mismatch hypothesis: humans did not evolve in an environment that contained hypodermic needles and purified psychoactive substances like heroin or cocaine. Since the advent of agriculture, according to this hypothesis, humans have domesticated plants that produce substances that hijack reward and reinforcement circuits, producing pleasure despite providing no fitness benefits (Hyman, 2005; Kelley & Berridge, 2002; Wise, 1996).

Hagen, Sullivan et al. dispute the mismatch hypothesis. They argue that all popular recreational drugs are plant defensive chemicals. Nicotine, cocaine, arecoline, THC, and caffeine are neurotoxic pesticides that evolved to defend plants from insect and other herbivores. Human ancestors co-evolved with plants that produced such defensive chemicals for hundreds of millions of years, and humans are well-adapted to them. Wild tobacco species, for example, were widely used by pre-Columbian Native American hunter-gatherers, and often contain levels of nicotine comparable to domesticated species (Hagen & Tushingham, 2019; Tushingham, Snyder, Brownstein, Damitio, & Gang, 2018). Hence, the widespread attraction to, and consumption of, compounds that evolved to deter consumption is a paradox (Sullivan, Hagen, & Hammerstein, 2008). One possible resolution of the paradox is that humans evolved to regulate intake of neurotoxic pesticides as an unconscious form of self-medication against their own parasites (Hagen et al., 2009; Hagen, Roulette, & Sullivan, 2013; Hagen & Sullivan, 2018; Sullivan et al., 2008). The drug toxicity perspective can also help explain the dramatic age and sex differences in drug use (Hagen et al., 2013).

14 | CONCLUDING REMARKS

Mental disorders cause a large fraction of disease burden, even in the low- and middle-income countries where biological anthropologists often conduct their research (Figure 3). This fraction will only increase as infectious disease burden continues to decrease. There is widespread agreement that many decades of research on mental disorders has failed to understand them or lessen the burden they impose on society. Understanding the complex, multi-level mechanisms that underlie mental disorders, and cognition and behavior more generally, cannot be achieved by focusing only on the lowest mechanistic levels (e.g., molecules, neurotransmitters) (Sapolsky, 2018). Nor can we rely solely on the descriptive symptom-based approach to mental disorders epitomized by the DSM.

We sketched a provisional evolutionary scheme that categorizes a group of relatively rare disorders, such as autism and schizophrenia, as disorders of development that involve dysfunctions of cognitive adaptations related to sociality and defenses against socioecological threats. These are highly heritable and probably caused, in large part, by genetic variants. There is a second group of disorders, such as Alzheimer's, that appear late in life and are probably explained by senescence. A third group of disorders, such as ADHD some eating disorders, might be explained by mismatches between modern and ancestral environments.

A final group of disorders, such as anxiety, depression, and PTSD, have low heritability, are caused by adversity, and involve symptoms that seem to be adaptive responses to adversity. Because they are relatively common throughout adult life, they account for a substantial fraction of disease burden attributable to mental illness. These might not be disorders at all, however, but instead aversive yet adaptive responses to

adversity. If so, this has several important implications. First, these conditions would largely indicate social problems, not medical ones, and therefore call for social, not medical, solutions. Research and social policy on these "disorders" should shift from altering brain chemistry to avoiding and mitigating adversity and resolving conflicts. Second, treatment would still be valuable, but could not ignore circumstances. A broken bone is a biological dysfunction, for example, but the physical pain it causes is not. Therefore, it would be unethical to provide pain medication without also setting the broken bone. Similarly, it would be unethical to suppress the psychic pain without addressing the source of adversity. Third, effective psychotropic medication that suppressed these emotions and behaviors would provide substantial benefits to those who are inconvenienced by them, raising the troubling specter of chemical forms of social control, which, at least in some cases, might already be occurring with the use of stimulants and other medications to treat ADHD.

The failure of science to identify the biological etiology of almost any mental disorder does not mean that discovery is out of reach. As psychologist Elliot Valenstein noted, "at some period in history the cause of every 'legitimate' disease was unknown, and they all were at one time 'syndromes' or 'disorders' characterized by common signs and symptoms (Valenstein, 2002, p. 150)." Before Robert Koch identified the tubercle bacilli as the causal agent of tuberculosis, it was not obvious that consumption, miliary disease, caseous pneumonia, intestinal tuberculosis, and scrofula were all forms of the same disease (Blevins & Bronze, 2010; Koch, Pinner, & Pinner, 1932). Likewise, the prevailing symptom-based approach might split conditions with shared etiology into separate disorders, as some argue is the case with schizophrenia and bipolar disorder (International Schizophrenia Consortium and others, 2009), or lump conditions with different etiologies into a single disorder as others argue is true of MDD and its subtypes (e.g., Milaneschi et al., 2016) and schizophrenia (Arnedo et al., 2015). Zachar and Kendler stated, "carving nature at its joints" with regard to psychiatric diagnosis requires "inference to the best explanation… the constant interaction between empirical evidence and clear conceptual thinking (Zachar & Kendler, 2007, p. 564)."

Mental health is biological health and should be a thriving area of research in biological anthropology. We offer the following six recommendations for biological anthropologists:

1. Consider investigating mental health issues in your study populations. As a starting point, there are several survey instruments, based on the DSM or ICD, that have been developed for cross-national research (e.g., WMH-CIDI; Kessler & Üstün, 2004). Keep in mind that symptom domains might be genetically and phenotypically dissociable (Warrier et al., 2019).
2. Do not shackle your research to DSM/ICD categories and its symptom-based approach. The DSM/ICD symptom-based categories were largely developed based on inpatient populations in urban psychiatric hospitals in 19th and 20th century Europe and the United States (Harrington, 2019; Shorter, 1997; Zachar & Kendler, 2017). As we discussed, it is far from clear that these categories correspond to distinct biological realities. It is possible that research in diverse populations that incorporates an evolutionary concept of cognitive/emotional function, and which considers a broader array of phenotypic markers and causal models, would better identify genuine cognitive/emotional dysfunctions.
3. Investigate the social contexts of, and social responses to, mental distress. Anthropologists have the advantage of participant observation. We can observe the social context and social consequences of these phenomena that are often "invisible" to researchers in psychiatry who rely on inpatient populations or epidemiological surveys. Ethnographic approaches are widely used by cultural and medical anthropologists to better understand mental distress (e.g., Jenkins, 2015; Kleinman, 1980; Scheper-Hughes, 2001). Data on the social contexts and consequences of psychological distress would help elucidate the etiological roles of adversity and conflict.
4. Use every empirical tool in the bioanthropology toolkit, for example, biomarkers, genetics, epigenetics, comparative evidence, ontogeny, behavioral observation, and cross-population comparisons.
5. Use every theoretical tool in the toolkit, for example, evolutionary theory, population genetics, Tinbergen's four levels of analysis, life history theory, and cultural transmission and evolution.
6. Collaborate with researchers from diverse theoretical and methodological backgrounds. Biological anthropology is inherently interdisciplinary, but we cannot do it all on our own. We need the expertise of psychiatrists and other biomedical specialists, psychologists, medical and cultural anthropologists, and others.

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Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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