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The Relevance of a Philosophical Toolkit to Advance Neuroscience

Psychoneural reduction revised: The case of suicidality in bipolar disorder

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Abstract

This paper uses suicidality in bipolar disorder (BD) to illustrate that multidimensional frameworks account for complex phenomena with cognitive, psychological, socioenvironmental and physiological components better than their reductionist counterparts. We challenge level-based reductionist models that regard a particular dimension as fundamental. To comprehensively understand complex psychiatric phenomena, multidimensional models that acknowledge the heterogeneity of aetiological factors, rather than homogenising them under a single dimension, must be utilised. Multidimensional models allow a better understanding of the individual context under which a psychiatric phenomenon arises, and the interrelationships between its different aetiological dimensions.

Suicidality in BD is used as a case study because it particularly highlights the interplay between biological, psychological, sociocultural and experiential factors. The multidimensional nature of suicidality is reflected by the heterogeneous strategies by which it is managed. Although similar to suicidality in other contexts, in BD suicidality has distinctive structural characteristics that emphasise its multidimensionality. Consequently, investigating suicidality in BD yields claims generalisable to suicidality as a whole alongside novel insights on BD-specific features. For instance, suicidality in BD has physiological causal factors, e.g., genetic predisposition and aggravation by symptomatic periods. However, its other features underscore the causal roles of cognitions. In persons with BD, suicidality can persist beyond depression and is sometimes experienced during mania, possibly due to suicidal ideation persisting beyond symptomatic periods. This indicates the need to account for cognitive or psychological causal factors.

Models of suicidality in BD typically adopt a non-level-based, non-reductionist approach, reflected in the diverse clinical strategies for managing suicidality in BD.

Abbreviation: BD, bipolar disorder.

KEYWORDS
bipolar disorder, multidimensional frameworks, reductionism and non-reductionism, suicidality

1 | INTRODUCTION

Contemporary psychiatry straddles being a branch of medicine, a scientific discipline, a social-political movement and a healthcare practice that relies heavily on practitioners' insights and experience. This compound identity stems from the need to address conditions whose correspondingly complex aetiologies encompass biological, psychological, social, environmental and experiential factors. It is thus reasonable to expect that where explanations about psychiatric phenomena are concerned, a *multidimensional* approach that regards aetiological factors as belonging to multiple, heterogeneous dimensions would be the default. However, this has not been the case: *reductionist* paradigms that reduce the diverse facets of psychiatric phenomena to a single *level* have long been influential. Consequently, psychiatric disorders have at times been construed as "nothing but" dysfunctions of the brain, or alternatively as the outcome of deleterious sociocultural or environmental living conditions. For instance, the former is especially pronounced in the National Institute of Mental Health's Research Domain Criteria (RDoC), while the latter is at the heart of the Neurodiversity paradigm and the Mad Pride movement. This in turn impacts how treatment programmes are designed. Depending on their orientation, reductionist-leaning clinicians may be predisposed to tout either pharmacological or psychosocial approaches as the exclusive means to alleviate psychiatric symptoms; however, this one-size-fits-all strategy is not always effective. Successful treatment largely hinges on addressing the most salient aetiological factors along their respective dimensions: symptoms caused predominantly by neurobiological dysfunctions are best minimized through medication, while talk therapy may be more appropriate for those arising due to adverse living conditions, and so forth.

Our goal in this paper is to show that multidimensional models are sometimes necessary for capturing the complexity of psychiatric phenomena, in contrast to reductionist models—particularly those endorsing *level-based* thinking that emphasize the primacy of a single dimension over others and thus regard all aspects of the phenomenon as "[traceable] back to one dimension only" (de Haan, 2020, 4). Reductionism has its roots in philosophical views seeking to resolve the "mind–body problem," i.e., by clarifying the relationship between the body and the mind. However, level-based reductionist models fail to capture the complexity of psychiatric phenomena, particularly the heterogeneous nature of aetiological factors and the complex dynamical interactions between them. Using *suicidality* in *bipolar disorder (BD)*/manic-depressive disorder as a case study, we demonstrate that multidimensional models fare significantly better than their reductionist counterparts at accounting for the diversity of causal factors underlying a psychiatric phenomenon. A further implication of multidimensional models for therapeutic practice is that they provide the clinician with comprehensive, holistic and individual-specific information about the circumstances under which a psychiatric condition has arisen, which can then be incorporated into developing strategies for managing it.

Suicidality covers "all the suicidal behavior/acts and suicidal thinking/thoughts referring to an intention to end life" (Nanayakkara et al., 2012, 334). It is the outcome of "a complicated sequence of cognitive and behavioural events, beginning with ideation through to planning and an intention to act" (Malhi et al., 2013, 559). Suicidality thus highlights the contributions of cognitive, psychosocial, behavioural and biological dimensions alike. These characteristics are further underscored in suicidality in persons with BD. Suicidality in BD illustrates the interplay between cognitive-affective, neurophysiological, environmental and social causal factors: it demonstrates the need to account for these components to comprehensively account for a complex phenomenon. This pluralistic framework is reflected in the heterogeneous interventions for managing suicidality, which can be pharmaceutical, technological, psychosocial, cognitive or a combination of all. It is also reflected in individual responsiveness to such interventions: for instance, suicidality in some persons may be alleviated by medication, while for others a cognitive approach, such as talk or group therapy, is more effective.

The main reason for the paper's focus on BD is that suicidality in BD has a more pronounced biological component than suicidality in many other contexts, thus underscoring the need to consider the physiological aspects of its aetiology alongside their psychosocial counterparts. This emphasis on the biological component balances established and widespread scientific and lay views that suicidality is the outcome of experiencing adverse psychological, social or environmental conditions. Thus, the case of suicidality in BD is especially suitable for our

purpose because its study and clinical management brings together several disciplines that focus on its various facets. Suicidality in BD is partly due to genetic factors (Kim et al., 2007), and can be aggravated by symptomatic periods. This suggests that its causality has a significant physiological component. However, some features of suicidality in BD underscore the causal roles of cognitions. Notably, suicidality can persist beyond depressive periods, and is sometimes experienced during manic periods (Dilsaver et al., 1994; Miklowitz & Gitlin, 2014). It is believed that this is due to the persistence of suicidal ideation, a cognitive phenomenon, thereby highlighting the need to appeal to cognitive concepts in accounting for suicidality. This is reflected in actual scientific practice: models of suicidality in BD typically adopt a pluralistic approach that does not reduce cognitive or mental factors to neurobiological ones or vice versa (Malhi et al., 2013). Rather, they are treated as different dimensions of a complex phenomenon that interact and influence each other. Moreover, recent studies have shown the promise of physical interventions on neuromodulation such as electroconvulsive therapy (ECT) in the treatment of suicidality in BD (Kucuker et al., 2021; Liang et al., 2018; Tondo & Baldessarini, 2016). Additionally, social and environmental interventions have been successful in suicide prevention more generally (Platt & Niederkrotenthaler, 2020). This demonstrates that multi-disciplinary, multidimensional explanations account for how cognitive, affective, psychosocial and environmental factors contribute to suicidality alongside genetic and physiological determinants more comprehensively and in more detail than level-based reductionist frameworks.

Suicidality in BD is distinctive in many ways, such as its heritability and genetic loading, occurrence during mania or outside of depression, response to antidepressants. Nevertheless, regardless of quantitative differences (e.g., rates of attempted and completed suicides, frequency of suicidal ideation, patterns in suicidality-related hospitalisation or demographics) and BD-specific characteristics, suicidality in BD does not differ drastically from suicidality in other contexts (Bottlender et al., 2000; Raja & Azzoni, 2004). Thus, although disorder-specific features have to be taken into consideration the arguments and conclusions of this paper are generalisable to suicidality as a whole, as well as to other conditions with biological, psychosocial and environmental components. Furthermore, suicidality is not alone in being clinically addressed from a multidimensional perspective: numerous other conditions are similarly managed, including BD itself (Miklowitz, 2019; Miklowitz & Gitlin, 2014).

The argument strategy is as follows. First, some major philosophical views on reductionism will be discussed (Section 2), to trace the development of level-based thinking and how it has impacted psychiatry. Following this is a discussion of suicidality in relation to BD (Section 3) and how it has been modelled (Section 4). The aim of Sections 3-4 is to illustrate how multidimensional models comprehensively account for the multidimensional nature of suicidality in BD. Preceded by a brief exposition of existing multidimensional frameworks in Section 5, in Section 6 we argue that multidimensional models are necessary to understand complex psychiatric phenomena such as suicidality in BD. A brief Section 7 concludes the paper.

2 | THE PSYCHONEURAL RELATION IN PSYCHIATRY

Three competing conceptualizations of mental illness dominated 20th-century psychiatry: the *medical model, antipsychiatry* and the *biopsychosocial model*. According to the medical model, mental illness is an organic disease just like any other disease studied and treated in medicine. Even though environmental and social factors may be relevant to the aetiology of the disease and its diagnosis, a disease is identified as a biological dysfunction that results from the interaction of genetic and environmental factors. Consequently, neurobiology is the relevant scientific discipline to advance psychiatry (Guze, 1978). The mirror image of the reductive medical model is antipsychiatry which denies any organic cause of mental illness. Psychiatry should instead be considered a practice of helping a struggling individual overcome personal, moral or other problems in living (Szasz, 1960). This conceptualization has been particularly influential in the disabilities rights movement. The biopsychosocial model is an alternative to both of these views as it promotes an integrated multidimensional conceptualisation of mental illness, and all diseases for that matter. According to this model, diabetes and schizophrenia are both experienced, identified and diagnosed as complex phenomena which require accounting for biological, psychological and social factors. Moreover, the success of the treatment of each depends to a large extent on the relationship between the physician and the patient (Engel, 1977). With certain modifications, all three of these views have their contemporary proponents. As we indicated earlier, our affinity is with a biopsychosocial approach. However, the main point we are making is that the debates between the proponents of the three models, while overlapping to various degrees with traditional philosophical debates over psychoneural reduction, do not involve any references to levels of any kind.

Level-based reduction has made its way into philosophy of psychiatry by way of philosophy of mind and systems biology. Traditional discussions of reduction in philosophy of mind are largely motivated by the need to articulate a solution to the mind–body problem, the problem that arises when assuming Descartes' substance dualism which postulates that the ideal (mind) and the material (body) substances which make up reality are so fundamentally different that it is not clear how the two can interact. How do our desires produce actions in our bodies and how do our bodily needs produce ideas in our minds, for example? One way to solve the problem is to show that the distinction is faulty. Either the world is completely ideal or it is completely material. While both options have their proponents, only the latter has gained credence in the analytic philosophy tradition which claims close allegiance with science. Thus, the debates have shifted towards the role of science, or scientific discipline(s), in shedding light on the true nature of the mind–body relation.

20th century psychology was the discipline identified as the science of the mind while physiology was the science of organisms in general. Human minds could now be studied by psychology, while their bodies by physiology. Those who sought to solve the mind–body problem through a scientific study, then aimed at articulating the relationship between psychology and physiology in order to provide a unified account of humans, including their minds and their bodies. Oppenheim and Putnam (1958) famously introduced their account of *intertheoretic reduction* as a model of unified science. In their view, the relationship between scientific disciplines, or branches, is defined by the theoretical vocabulary, or universe of discourse, corresponding to a level of the multilevel real world where every higher level can be decomposed into the entities of the level below it. Further, a scientific discipline has the potential to reduce the theories of a discipline of a higher level to the vocabulary of its own theories gradually level-by-level, starting with sociology through psychology, biology and chemistry all the way down to elementary particle physics. Any whole that can be decomposed to the parts of a lower level, in their model, belongs to that level even though its "proper" level is the highest level to which it belongs (Oppenheim & Putnam, 1958, 9–10). Thus the mind can be reduced to a physical entity as psychology can be reduced to neurophysiology, and ultimately physics. Early critics of this reductive view of mind and psychology objected that the reduction of the vocabulary of a higher level theory presupposes a direct correspondence to the vocabulary of a lower level theory in order for the reduction to be possible. Furthermore, this also presupposes identities between the corresponding properties at the psychological and neurological levels (Fodor, 1974, 101). Fodor famously considers this an absurdity and argues for the relative independence of the "special" sciences from physics. Rather than unity, he then advocates disunity of science.

The 20th-century philosophy of mind and philosophy of science have proposed numerous versions of reductive and non-reductive accounts of the psychoneural relation. However, the debates have degenerated into scholastic rhetoric and seem to be of little relevance to real-life experiences such as mental illness. Early 21st-century proposals that criticized both the proponents and the opponents of intertheoretic reduction have included *ruthless reduction* (Bickle, 2006), *nonreductive mechanistic explanations* (Craver, 2007) and *mechanistic reduction* (Bechtel, 2007). Variations of these three models of the psychoneural relation have dominated the reduction wars over the past two decades in philosophy of psychology and neuroscience. However, all three of them have assumed some kind of level-based model. Bickle proposes a direct jump from molecular/cellular interventions to behavioural observations without the need to go up and down the compositional ladder identified by Oppenheim and Putnam. Craver articulates an ontic account of compositional levels of mechanisms which are thus irreducible. Whereas Bechtel assumes an epistemic model of compositional levels and allows for reductive explanations in terms of the lowest compositional level of a given model. However, these level-based accounts of the psychoneural relation have, at best, shown to be insufficient to capture the complexity of psychiatric phenomena as it is widely acknowledged that comprehensive approaches to treatment that include psychosocial, pharmacological and lifestyle interventions may be more successful than "single-level" interventions (Miklowitz, 2019). We thus propose to use the term "dimension" to capture the ontic as well as disciplinary approaches to the study of complex psychiatric phenomena. Instead of the hierarchical organization of scientific disciplines and corresponding compositional levels of reality, we propose to consider biological dimensions as those aspects of reality that are detectable through the methods of biology, and psychological dimensions as those that are detectable through the methods of psychology, and so forth. This conceptualisation frees us from any commitment to arrange those aspects of reality in a hierarchical organisation, be it ontological or epistemological.

In what follows, we will review the literature on the modelling of psychiatric phenomena, and suicidality in people with BD more specifically. This kind of modelling draws from methods in genetics, physiology, pharmacology and psychology.

3 | BIPOLAR DISORDER AND SUICIDALITY

3.1 | Bipolar disorder

BD is a common, heritable and lifelong psychiatric condition. Due to its distinctive symptom profile, BD can provide novel philosophical standpoints on various dimensions of human experience and how they are impacted by the interplay between cognitive, psychological, socio-environmental and physiological factors.

BD is a spectrum of disorders characterised by alternating elevated and depressed periods, which in turn are accompanied by changes to neural activity, cognition, behaviour and personality (Angst, 2007). The symptomatic periods of BD are divided into *mania* (or its milder form of *hypomania*), *depression* and *mixed states*. Among the typical characteristics of manic or hypomanic periods are euphoric mood, increased energy or decreased need for sleep, rapid thinking, associational fluency, impulsivity and feelings of grandiosity. In some severe cases of mania, psychosis can occur. Common symptoms of depression include low mood, feelings of hopelessness or worthlessness, lack of energy or motivation, restricted thinking, rumination and cognitive slowness. Mixed states are periods that exhibit a combination of manic or hypomanic and depressed symptoms (for instance being in a low mood yet having increased energy). The fifth edition of the Diagnostic and Statistical Manual (DSM-V) categorises BD into different types, depending on severity, frequency and presentation of symptoms, which vary extensively between individuals. The trajectory of BD also varies from person to person: some have more severe and frequent manic or hypomanic periods, while for others depression is more common.

BD is associated with a predisposition towards suicidality. As previously mentioned, suicidality is an umbrella term that encompasses suicidal ideation, i.e., thoughts or preoccupation about suicide, and suicidal behaviour or actions and attempts related to suicide (Borders, 2020). The population with BD is one of the highest suicide risk groups, in comparison to the general population and all other psychiatric illnesses (Miller & Black, 2020). The suicide rate within the BD population is 10–30 times higher than that of the general population, with up to 20% of persons with BD dying by suicide and about 20–60% having attempted suicide at least once (Dome et al., 2019). A review by (Miller & Black, 2020) states that "about one-third to one-half of bipolar patients attempt suicide at least once in their lifetime and approximately 15-20% die due to suicide" (p. 2). Individuals with BD who have comorbid personality disorders, a history of suicidal behaviour or family histories of suicide or suicide attempts are more likely to themselves attempt or die by suicide (Miller & Black, 2020). It is also well established that genetic risk factors are involved in suicidality in BD (Kim et al., 2007). Additional factors contributing to suicidality in persons with BD include poor quality of life, relationships or social support and childhood abuse or neglect (Miller & Black, 2020).

3.2 | Symptoms/presentation and suicidality

Suicidality typically—but not exclusively—occurs during depression, wherein feeling low, a sense of hopelessness, rumination, mental pain and increased susceptibility to stress are common. Suicidality usually arises due to the interaction of these psychological and cognitive factors with stressful social and environmental circumstances, physiological states and other cognitions pertaining to taking one's own life (Jamison, 1995; Malhi et al., 2018). Emphasiing the cognitive dimension, Kay Redfield Jamison (Jamison, 1999, 91) writes that "much of the decision to die is in the construing of events, and most minds, when healthy, do not construe any event as devastating enough to warrant suicide." In addition to the aforementioned symptoms, depressed periods are also accompanied by negative construal of social or environmental circumstances, such that one is more likely to regard one's situation as hopeless or inescapable, while at the same time having a diminished ability to see other solutions to perceived problems (Jamison, 1999). Thus, during depression, a person may view death as the only escape from or solution to circumstances experienced as stressful and problematic, and may consequently contemplate suicide. Moreover, persons with BD are believed to be prone to suicidal ideation (Miklowitz & Gitlin, 2014), thereby increasing exposure to cognitive or psychological states that may be translated into suicidal actions. This tendency is further compounded when death is viewed as an end to one's problems and pain (Jamison, 1999).

Nevertheless, in persons with BD, suicidality is not limited to depressed periods. Mixed states, particularly those with a significant depressive component (sometimes referred to as *mixed depression*) are likewise high-risk periods for suicidality. Periods wherein a person with BD appears to be recovering from depression also pose a high risk (Jamison, 1999). Suicidality during mania is sparsely documented, but nevertheless occurs (Dilsaver et al., 1994; Malhi et al., 2018; Miklowitz & Gitlin, 2014). It has been proposed that "persons experiencing mania may have components of the suicidal process in mind but are incapable of putting them into action. It is only when they shift from the manic phase or a depressive or mixed

state that they may regain the capacity to do so" (Malhi et al., 2018, 341). This thus indicates that being in a depressed state is not a necessary condition for suicidality. Furthermore, in BD, the use of antidepressants (in contrast to mood stabilisers) can also lead to increased suicidality (Miklowitz & Gitlin, 2014). It is believed that the "emergence of suicidal ideation during antidepressant treatment might be genetically driven" (McGuffin et al., 2010, 276). When depressed, a person may experience suicidal ideation, but may not have sufficient energy or motivation to carry out suicidal actions to a lethal degree. However, when their energy and motivation increase (e.g., due to the effects of anti-depressants, during mixed depressions with manic/hypomanic components such as agitation or impulsivity, or when the depressed state is beginning to lift) they may become psychologically "strong" enough to complete suicide.

Rapid-cycling BD, defined as "presenting four or more manic or depressive episodes during at least 2 weeks" (Garcia-Amador et al., 2009, 74), compounds suicide risk and predisposition towards suicidality (MacKinnon et al., 2005). It has been found that rapid-cycling BD is associated with a higher rate of suicide attempts and a "marked increase of lifetime history of suicidal ideation" (Garcia-Amador et al., 2009, 76), in comparison to its non-rapid-cycling counterparts. A person with rapid-cycling BD is potentially faced with briefer asymptomatic periods and more frequent mood episodes throughout their life than their counterparts with non-rapid-cycling BD (Garcia-Amador et al., 2009). It can be inferred from the existing literature that rapid cycling results in exposure to the stressors associated with symptomatic periods, which in turn can aggravate any suicidal tendencies that may be present.

3.3 | Genetics and heritability

In BD, suicidality has a genetic component (Kim et al., 2007; McGuffin et al., 2010), although what aspects of suicidality are genetically transmitted is yet unclear. Nevertheless, "[a]ll the genetic epidemiology evidence suggests that suicide and suicidal behaviours are complex traits where there are probably multiple genes with each individual gene having a small effect" (McGuffin et al., 2010, 276). Among the candidate genes that stand out are those related to serotonin (McGuffin et al., 2010). There may be an overlap between genes that predispose towards suicidality and those that predispose towards affective disorders, although the extent of this overlap is yet unclear. It has been theorised that expressions of certain BD-related genes are associated with neural, physiological, cognitive, behavioural and personality processes, traits or patterns implicated in suicidality. For instance, some genes relevant to stress regulation increase the sensitivity of certain neural systems to stress, making them more reactive to stress-inducing factors in a manner that increases the predisposition to suicidality (Malhi et al., 2018; Mathews et al., 2013). The periodic dysregulation brought about by BD's symptomatic periods, physiological features and adverse life experiences—including those directly related to the experience of BD—can also bring about "abnormalities in the hypothalamic pituitary adrenal (HPA) axis as well as the serotonergic, dopaminergic, and noradrenergic systems" (Mathews et al., 2013, 204) implicated in suicidality. It is also hypothesised that candidate genes may affect the development of brain areas or neural activity in ways correlated with suicidality (Kim et al., 2007). Another possibility is that certain genes are related to the development of the personality traits impulsivity and aggressiveness—which are not uncommon in persons with BD, particularly during manic periods—and which have been identified as suicide risk factors. There are also findings that in BD, suicidal ideation that emerges upon treatment with antidepressants have a genetic basis (Laje et al., 2007), although it is yet unclear how the cognitive component, i.e., suicidal thinking, arises from these neurobiological interactions.

A family history of suicidality is one of the more consistent risk factors for suicide, in the BD population and in general. There is extensive evidence that suicidality aggregates within families (Brent & John Mann, 2005; Voracek & Loibl, 2007), partly due to genetically transmitted biological or psychiatric features, but also as a result of other heritable factors such as behavioural patterns. Nevertheless, not all families with a history of suicide have a history of psychiatric illness; likewise, a history of psychiatric illness is insufficient to account for aggregation of suicidality within families. It has been proposed that familial transmission of suicidality can be attributed to a combination of genetically inherited responses to stress, the presence of psychiatric disorders, imitation of behaviour and cognitive patterns and exposure to similar environments and the stressors therein (Brent & John Mann, 2005).

3.4 | Relevance of prior history of suicidality

Of all the risk factors for suicide, the most consistent and precarious is a history of prior suicide attempts (Gonda et al., 2012). At least half of completed suicides in the BD population were carried out by individuals with a history of attempted suicide (Miller & Black, 2020). In the same

vein, having previously attempted suicide "increases the risk of suicide by 37-fold in bipolar patients" (Miller & Black, 2020, 4). Moreover, "the lifetime rate of prior suicide attempts was found to be significantly higher in bipolar patients compared to unipolar [depression] patients" (Gonda et al., 2012, 18). Prior suicide attempts can raise the threshold and habituation to pain, which in effect serve as "cognitive rehearsal" (O'Connor & Kirtley, 2018, 4) or preparation for subsequent suicide attempts that may have a greater likelihood of pain and lethality (Malhi et al., 2018). From a cognitive perspective, it is also believed that "[e]ach time a suicidal mode becomes activated, it becomes increasingly accessible in memory and requires less triggering stimuli to become activated the next time" (van Heeringen, 2012, 118).

4 | MODELLING SUICIDALITY IN BD

Although there is a substantial corpus of literature documenting the quantitative aspects of suicidality in persons with BD, far less is known about *why* people take their own lives (Jamison, 1999). There is still much to be learned about the mechanisms and processes over which implicated factors interact to generate suicidality. Issues that have been addressed yet remain incompletely answered include how suicidal ideation leads to suicidal action, why suicidality and suicide are not uniform outcomes of being faced with the same risk and predisposing factors and how internal (e.g., neurobiological, physiological and genetic features) and external factors (e.g., environmental stressors, quality of life and relationships) mediate or aggravate suicidality across individuals. Furthermore, to comprehensively understand the causality of suicidality, the *reasons* for suicide must be explored. This involves examining the cognitive dimensions of suicidality, which are extensively intertwined with psychological, social and environmental factors. A number of models (Malhi et al., 2018; 2013) exist that aim to explain why suicidality in persons with BD (as well as in those without BD) occurs. Significantly, these models account for suicidality in terms of the interplay between cognitive, psychological, social and physiological factors, thereby highlighting the effectiveness of multidimensional explanatory frameworks. Some of these models are briefly reviewed in what follows.

The *stress-diathesis* model (Mann & Rizk, 2020) proposes that suicidality depends on interactions between the individual's threshold for stress and the presence of internal and external predisposing factors. This threshold is influenced by the interactions between pre-existing risk factors (such as psychiatric history, genetic predisposition to suicidality or psychiatric illness, previous trauma and other factors that affect neural and physiological systems responsible for regulating stress and emotional responses) and presently or recently experienced stressors in the environment (such as difficult life circumstances or poor quality of relationships). Importantly, this model holds that "the development of suicidal behavior involves a vulnerability or diathesis as a distal risk factor, which predisposes individuals to such behavior when stress is encountered" (van Heeringen, 2012, 114). In BD, symptomatic periods, substrates of the disorder and their effects on physiology and lived experience act as a diathesis, as they can increase vulnerability to suicidality, in particular through difficulty regulating affect, restricting thought patterns, causing psychic pain, increasing impulsivity and/or aggression, decreased resilience to stress, frequent or prolonged exposure to depressive periods or that may be accompanied by suicidality.

The *cry of pain (CoP)* model identifies three cognitive components of suicidality (van Heeringen, 2012; Williams & G., 2002). The first is *sensitivity to signals of defeat*, wherein "an involuntary hypersensitivity to stimuli signalling 'loser' status increases the risk that the defeat response will be triggered" (van Heeringen, 2012, 118). Of the three, feelings of defeat appear to be the most influential in generating suicidal behaviour (Malhi et al., 2013). The second, *perceived "no escape,"* is the outcome of a restricted capacity for problem-solving that leads to the perception that one cannot escape from problems or difficult circumstances. Finally, *perceived "no rescue"* refers to the inability or difficulty in imagining that the future can have in store positive events and experiences. A "biologically mediated *mental helplessness script"* (Malhi et al., 2013, 560) can arise when these states are experienced. Depending on the individual's internal and external circumstances, this script may be acted on in the form of suicidal behaviour. Importantly, these cognitions tend to accompany depressed periods, and thus may be recurrent or frequent in persons with BD.

According to the *bipolar suicidality model (BSM)* (Malhi et al., 2013), the *appraisal system*, which assigns valence to information about one's circumstances or internal states, is likewise implicated in generating suicidality. When the appraisal system evaluates one's situation negatively, it is possible for feelings of defeat, entrapment and hopelessness to arise, which can thus give rise to a suicide script wherein suicide appears as a viable option for relief or escape. Importantly, in BD, the appraisal system is affected by the cognitive and emotional dysregulation engendered by symptomatic periods (Kelly et al., 2012; Malhi et al., 2013), so that appraisal of circumstances may be disproportionately negative or positive during depression and mania or hypomania, respectively.

The *interpersonal theory of suicide (IPTS)* (Joiner, 2005) argues that a sense of *thwarted belongingness* and *perceived burdensomeness*, combined with an *acquired capability for suicide* are responsible for suicidality (Malhi et al., 2018). Thwarted belongingness is defined as "feelings of isolation that emerge from actual or perceived rejection by peers/friends and/or family, and exclusion from social interactions and gatherings," while perceived burdensomeness refers to the "perception that one is implicitly or explicitly a burden on others" (Malhi et al., 2018, 342). While the degree to which these thoughts are experienced can change over time, especially during symptomatic periods, it is nevertheless possible for them to become deeply entrenched or relatively permanent in the construal of one's situation, at times to the point that one begins to view suicide as the only viable option. According to the model, this is how suicidal ideation *can* arise. However, transformation of ideation into action requires having the actual capacity for suicidal behaviour. This capacity may manifest as a tolerance for the level of pain involved in suicidal actions, or a diminished fear of death. These aspects of the capacity for suicide are dynamic and variable over time, and are susceptible to influence by the symptoms of BD (Malhi et al., 2018). It is when all these factors are present and sufficiently salient that suicidal actions are likely to be carried out.

The *integrated motivational and volitional (IMV) model* (O'Connor & Kirtley, 2018) is a biopsychosocial model that "delineates the final common pathway to suicidal ideation and behaviour" (p. 2). According to the IMV, suicidal ideation is engendered by defeat and entrapment, while the translation of suicidal ideation to suicidal behaviour is driven by *volitional moderators*. The model has three phases: *pre-motivational*, which elucidates the biopsychosocial context of individual predispositions toward suicidality, such as by "identifying vulnerability factors and triggering negative events" (O'Connor & Kirtley, 2018, 3); *motivational*, which refers to the emergence of suicidal ideation and formulation of suicidal intentions; and *volitional*, wherein suicidal actions are implemented. Among the constructs central to the model are *defeat/humiliation* and *entrapment*. Individuals who possess *vulnerability factors* are more likely to develop suicidal ideation when faced with adverse experiences (pre-motivational phase). Vulnerability factors can be biological, psychosocial, environmental or cognitive; BD and its symptoms act as a constellation of vulnerability factors that fall within these different domains. Vulnerability factors increase susceptibility to feelings of defeat or humiliation, which in turn can lead to a sense of entrapment. Depending on which *motivational moderators*, i.e., aggravating or protective factors, are present, suicidal ideation can naturally progress from entrapment (motivational phase). Importantly, these motivational moderators are largely cognitive or psychosocial, and include "reasons for living, attainable positive future thinking, adaptive goal pursuit, belongingness or connectedness", or "feeling a burden, having little or no social support, and depleted resilience" (O'Connor & Kirtley, 2018, 4). Finally, *volitional moderators* bring about the last, volitional phase of the model, by mediating the translation of suicidal cognitions into suicidal behaviour. Volitional moderators can be understood as factors that reinforce or facilitate the implementation of suicidal actions. Similar to the IPTS, volitional moderators encompass the "components of the acquired capability for suicide (fearlessness about death and increased physical pain tolerance)," as well as other internal and external factors like prior suicide attempts, availability of instruments for suicide, "exposure to the suicidal behaviour of others ..., [and] exposure to inappropriate representations of suicide" (O'Connor & Kirtley, 2018, 4).

Finally, the *three-step model (3ST)* (Klonsky & May, 2015) is explicitly described as an "ideation-to-action framework" by its proponents. These steps are 1) *the development of suicidal ideation*, 2) *strong* versus *moderate ideation* and 3) *progression from ideation to attempts*. The model has four concepts: "pain, hopelessness, connectedness, and suicide capacity" (Klonsky & May, 2015, 116). It is proposed that suicidal ideation is the outcome of the conjunction of pain—especially prolonged pain—*and* feelings of hopelessness. Both pain and hopelessness must be experienced, as neither on its own is sufficient to give rise to suicidal ideation. However, a sense of connectedness can act as a protective factor that can moderate or alleviate suicidal ideation. While connectedness is typically interpersonal or social, it can also "refer to one's attachment to a job, project, role, interest, or any sense of perceived purpose or meaning that keeps one interested in living" (Klonsky & May, 2015, 117). Finally, the translation of suicidal ideation into suicidal action depends on the capacity for suicide, the lack of which hinders the process from moving to the third step. Expanding Joiner's (2005) conceptualisation, the proponents distinguish between *dispositional, acquired* and *practical* contributors to the capacity for suicide. Dispositional factors refer to "relevant variables that are driven largely by genetics, such as pain sensitivity or blood phobia" (Klonsky & May, 2015, 119), and other physiological predispositions such as those associated with suicidality in BD (see Sec. 3). Acquired factors refer to "habituation to experiences associated with pain, injury, fear, and death," while practical factors consist of "concrete factors that make a suicide attempt easier" (Klonsky & May, 2015, 119).

Taken together, these models demonstrate how multidimensional frameworks clearly elucidate the complex causality of suicidality. While the models are not limited to suicidality in BD, they have provisions for constellations of predisposing factors such as the biological, cognitive and psychosocial features associated with BD. Although suicidality is not unique to BD, their intricate relationship forms a distinctive starting point for investigating the structure of suicidality. In the following section, two examples of multidimensional models will be discussed, to demonstrate more broadly how the influence of diverse factors on psychiatric conditions can be accounted for without invoking level-based reduction.

5 | MULTIDIMENSIONAL MODELS

The need to understand how heterogeneous factors contribute to a psychiatric phenomenon has long been recognised, and multidimensional models that address this concern are indeed present in the literature. Two of these, the classic *biopsychosocial model* (Engel, 1977) and a more recent *enactivist* framework (de Haan, 2020), will be discussed briefly. This will demonstrate how multiple dimensions and disciplines can be integrated to arrive at comprehensive accounts of psychiatric phenomena.

The biopsychosocial model, which was developed by George L. Engel, arose in response to a crisis about psychiatry's status as a branch of medicine, given that the disorders it treats are a combination of "natural ... [or] biological brain dysfunctions" and "problems of living ... produced primarily by psychosocial variables" (Engel, 1977, 129). While the former fall within the domain of medicine, whether the latter remained medical issues or were best addressed by the behavioural sciences was the subject of debate. However, Engel (Engel, 1977) points out that biological factors may be necessary but not sufficient for a disorder to arise, and that experience of a disorder is usually intertwined with one's behavioural and psychosocial circumstances. Significantly, he further notes that treatment directed solely at the biological components of a disorder "does not necessarily restore the patient to health even in the face of documented correction or major alleviation of the abnormality" (Engel, 1977, 132). The biopsychosocial model thus acknowledges that biological, psychological and sociological factors all contribute to a disorder, and that the clinician's task requires identifying how extensively they do so (see also Engel, 1981). Only then can the clinician develop effective treatment programmes: "It is the doctor's ... responsibility to establish the nature of the problem and to decide whether or not it is best handled in a medical framework" (Engel, 1977, 133).

Similarly, the enactivist model proposed by Sanneke de Haan is an "integrative account of how diverse aspects of psychiatric disorders relate" (de Haan, 2020, 4). According to enactivism (Varela et al., 1992), cognitive or mental phenomena are profoundly influenced and are inextricable from the dynamic interactions between the organism and the environment. As such, psychiatric disorders are best understood in light of the individual's context, which comprise *physiological, sociocultural, experiential* and *existential* dimensions. Importantly, these dimensions are not regarded as level-like, but are distinguished in terms of how *local* or *global* they are, i.e., the extent to which they incorporate processes internal or external to the individual. For instance, since the substrates of physiological processes are largely found within the individual, the physiological dimension is "more local than experiential processes" (de Haan, 2020, 20). In contrast, because the experiential dimension involves factors such as social circumstances, in addition to physiological ones (e.g., the presence of a mood disorder), it is more global.

Each dimension substantively impacts the others, such that they can only be understood in light of one another. While psychiatric symptoms may be caused predominantly by factors falling under one dimension, they can nevertheless affect the others. Thus, correct understanding of how a psychiatric condition presents itself in an individual depends on correctly understanding the directions of causality between the different dimensions. While causality should not be interpreted as "linear [and] sequential," it is vital to determine "what set [the experience] in motion" (de Haan, 2020, 14). She further writes that "it still makes a difference whether an experience (anxiety, annoyance) is caused by an event in someone's life world ..., or instead [physiologically] caused" (de Haan, 2020, 14).

Applied to suicidality in BD, these models yield the following insights. As discussed over the course of the previous sections, suicidality in BD can be attributed to heterogeneous but interrelated factors, some internal and others external. Although some individuals with BD have a biological predisposition towards it, suicidality may be precipitated by non-biological factors such as stressful situations. Likewise, the individual may be experiencing adverse living conditions, but suicidality is the outcome of biological factors such as symptomatic periods. Thus, the clinician must first identify the dimension that is the most salient in generating suicidality, in order to better trace the directions of causation in which other dimensions are subsequently affected. This way, the clinician gains more detailed information about the individual-specific context in which suicidality arises, and can thus design or adjust treatment programmes accordingly.

6 | SUICIDALITY AND MULTIDIMENSIONAL APPROACHES

The multidimensional nature of suicidality in BD demonstrates the importance of developing heterogeneous models that can bring together multiple disciplines, rather than continuing in the same vein as traditional reductionist frameworks. Multidimensional models are advantageous in several ways. To begin with, they take into consideration the influence of physiological, socio-cultural or environmental, experiential (i.e., lived experience) and existential factors on psychiatric phenomena, and elucidate how they relate to each other (de Haan, 2020). In doing so, they are capable of directing inquiry in the multiple disciplines studying the same phenomenon, as they serve as "an overarching framework [that] can provide orientation, treatment rationale, a shared language for communication with all those involved, and the means to explain treatment decisions" (de Haan, 2020, 3). A further advantage of multidimensional frameworks is their ability to accommodate unpredictability (Chang, 2012), such as individual presentations of BD and experience of suicidality. While there are patterns in the risk and predisposing factors, there is extensive variation in suicidality across individuals. Aspects of individual life experience such as culture, mores, norms, social circumstances, personal values or character traits act as differential factors with significant and not entirely predictable influences on suicidality. These factors affect how suicidal cognitions (e.g., "I want to end my suffering by killing myself") interact with other cognitions (e.g., "If I kill myself nobody will look after my dog"), as well as the courses of action they give rise to (e.g., "I won't kill myself because I'm worried about what will happen to my dog if I do"). A heterogenous framework can thus present a comprehensive picture of suicidality that accounts for physiological processes and their effects on lived experience, which is vital to understanding why suicidality occurs.

Suicidality is an exemplar of a phenomenon best understood and managed through a multidimensional approach since it arises from the interplay of diverse causal factors—from the biological through to the psychological and cognitive to the sociocultural (Jamison, 1999; Joiner, 2005). It can likewise be addressed through multidisciplinary methodologies, depending on its individual presentation. While suicidality is largely regarded as a phenomenon that must be prevented or alleviated, the type of intervention through which it can be addressed successfully varies across individuals (Jamison, 1999; Joiner, 2005). Some may be more responsive to a pharmaceutical approach that intervenes biologically (Miklowitz & Gitlin, 2014; Rihmer & Gonda, 2013; Wilkinson et al., 2022), while for others a psychological approach that addresses its cognitive aspects is more effective (Brown et al., 2006; Jobes et al., 2015). On the other hand, treatment based on one dimension may be less effective if suicidality is the outcome of factors from another: "Although psychotherapy is not a substitute for medications, there are things you can accomplish in therapy that won't be accomplished by medications. There are also things that medications can do for you that therapy won't" (Miklowitz, 2019, 121). For instance, medication may not sufficiently address suicidality arising from how one construes one's circumstances, whereas talk therapy may not successfully alleviate suicidality when it is caused largely by biological factors. An important component of treatment strategies is thus to identify which dimension—mental, physical or environmental—is more salient to suicidality in a particular case, and address it accordingly (see de Haan, 2020).

One step towards developing a stable multidimensional approach towards addressing suicidality is to establish points of contact regarding the "biological realization of [cognitive] structures" (Murphy, 2008, 128). An example of this task would be identifying neural correlates of typical types of suicidal cognitions—such as feelings or beliefs of "hopelessness ..., perceived burdensomeness ..., thwarted belongingness ..., defeat ..., and unbearability" (Bryan et al., 2022, 270)—or determining the physiological and neurological characteristics accompanying them. Another step is to use explanations from one dimension to formalise or describe cognitive concepts, while not dismissing the relevance of their content (Smith et al., 2022). The importance of cognitive content is underscored by BD, wherein the physiological effects of symptomatic periods can generate suicidal cognitions, which however may not always be responsive to physical interventions such as medication. It would be helpful to recognise which physiological processes contribute to realising the different types of suicidal cognitions (Bryan et al., 2022; Rudd & Bryan, 2021). This could then help trace their interactions with physical factors associated with other factors implicated in suicidality, such as the types of brain activity and physiological processes associated with BD's symptoms, thereby helping to understand how certain sets of physiological conditions contribute to certain types of cognitions.

7 | CONCLUDING REMARKS: MAKING THE CASE FOR LEVELLESS REDUCTION

So far, we have shown that in psychiatry, both psychological and neurobiological conceptualisations of mental illness are widely utilised alongside each other. This

multidimensional approach carries over into strategies for addressing psychiatric phenomena such as suicidality. For instance, in addition to clinical or therapeutic management, programmes for suicide prevention include environmental approaches such as restricting access to commonly used means for suicide (e.g., firearms or pharmaceuticals), raising public awareness and providing guidance on news reporting. Restricting access to bridges, tall buildings and railway tracks have proven to be among the most successful interventions for suicide prevention (Platt & Niederkrotenthaler, 2020). Suicidality is thus managed through programmes that address factors both internal and external to the individual.

The discussions throughout this paper, which demonstrate the explanatory strength of models that integrate diverse dimensions, support our endorsement of a levelless model of the psychoneural relation. We are not alone in this motion for abandoning the notion of levels in the conceptualisation of the psychoneural relation. Recently, philosopher John Bickle and neuroscientist collaborators André F. de Sousa and Alcino Silva (Bickle et al., 2022) have proposed a case study that exemplifies the inadequacy of the level-based reduction debates to capture the reality of contemporary scientific practice in the field of cellular and molecular cognition.

We suggest focusing on *multidisciplinary*/*multidimensional* rather than *multi-level* accounts of psychiatric phenomena. In our view, reduction may occur in psychiatry, but it is a reduction of boundaries between the disciplines employed in the study of psychiatric phenomena in which multiple disciplines blend for the purpose of providing multidimensional explanations. Consolidation, or reduction in number, occurs. However, it does not entail one discipline subsuming another. Thus, our approach could be considered as *interdisciplinary reduction* as opposed to the outdated view of *intertheoretic reduction*.

AUTHOR CONTRIBUTIONS

Sidney Carls-Diamante and Nina Atanasova contributed equally to the conceptualization, writing and editing of the manuscript.

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