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***Journal of Affective Disorders* Special Issue on Suicide-Related Research: Hopeful Progress but Much Research Urgently Needed**

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Suicide is a preventable cause of death, yet every 40 seconds someone dies by suicide resulting in about 800,000 suicide deaths each year across the globe (WHO, 2014). There are recent alarming increases in rates, that vary by age, gender, and geography, for reasons not well understood. Elucidation of the biological, psychological and social mechanisms that confer risk for suicide is urgently needed to generate novel prevention strategies that more effectively target the critical risk factors. This special edition of *JAD* brings together reviews and original articles that address pressing research questions on biopsychosocial mechanisms underlying suicide risk to improve understanding and thereby reduce stigma, and that suggest or evaluate novel interventions.

Progress in the field is reflected in the convergent findings among the cross-sectional neuroimaging studies in this special issue, in showing alterations in fronto-limbic activity and connectivity associated with suicidal thoughts and behaviors (STBs) across mental disorders (Fan et al., 2019; Schwartz et al., 2019; Segreti et al., 2019). As described in these studies, fronto-limbic systems subserve processes that have shown impairments in individuals with and at risk for STBs, including emotion regulation, decision-making, impulsivity and self-referential thoughts. This neurobehavioral convergence provides important leads for understanding STBs and generation of early detection and preventive strategies. This special issue also shows the hopeful movement towards the critical next steps for the field in performing longitudinal studies to identify biomarkers that predict attempts, as in Lippard et al. (2019) which provides new evidence that lower fronto-limbic gray matter and structural connectivity may predict future suicide attempts.

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Conflicts of interest

The authors declare no competing financial interests. HPB received an honorarium for a talk at Aetna.

This issue also reflects the movement in the field to deepened studies of the genetic and molecular pathways to STBs to identify novel mechanisms that can be targeted in intervention and prevention studies. These studies increasingly implicate inflammatory pathways to STBs. Dwivedi reviews the evidence that micro-rnas involved in stress-related inflammatory responses, such as cytokine tumor necrosis factor (TNF)-alpha, may play a role in suicidal ideation (Dwivedi, 2018). Chang et al. (2019) suggest peripheral TNF-alpha levels may be associated with features that can sometimes be seen in individuals with STBs, including impulsivity, poor sleep or aggression. In addition to these inflammatory mechanisms, research on oxytocin levels (Lebowitz et al., 2019) and oxytocin-related gene polymorphisms (Parris et al., 2018) implicates oxytocin-related mechanisms with STBs.

Studies of behavioral and psychological risk factors included in this special *JAD* issue demonstrate that they are robust contributors to STBs, highlighting their importance in early identification and prevention strategies, and suggesting them as targets for public health and policy efforts aimed to reduce STBs. Behavioral risk for future suicidal attempts includes prior actual attempts and prior suicidal ideation (Iorfino et al., 2018). While different phenotypic features and underlying mechanisms are implicated in non-suicidal self-injury (NSSI) compared to suicidal behavior, NSSI is still an important risk factor for suicidal ideation and attempts (de Beurs et al., 2018; Iorfino et al., 2018; Kiekens et al., 2018). Risk for STBs related to alcohol use and disorder (Chang et al., 2019; Iorfino et al., 2018), highlight the importance of alcohol use and abuse prevention methods for reducing STBs. With regard to psychological traits, studies link impulsivity to suicidal ideation and attempts (Chang et al., 2019; Wetherall et al., 2018). In their review, Orri et al. (2019) conclude that irritability may be a transdiagnostic risk factor for STBs. However, they also highlight the current heterogeneity in definitions and measures to study irritability and the need for strong methodological future studies. Finally, studies support the importance of social risk factors in STBs. STBs were found to be worsened by perceived negative social interactions in young people (Lebowitz et al., 2019), perceived burdensomeness (Wetherall et al., 2018) and perceived social problems (loneliness, rejection and trauma) in adults (de Beurs et al., 2018).

This *JAD* edition includes new evidence revealing the mechanisms through which the above factors may lead to risk for STBs, suggesting novel and more targeted preventive approaches. For example, Malhi et al. (2019) suggest that lithium treatment can reduce impulsivity associated with STBs, potentially through its fronto-limbic actions. They further suggest that the underlying molecular mechanism of lithium treatment may be a reduction in glycogen synthase kinase-3 β (GSK3 β), which regulates immune responses, including pro-inflammatory cytokines and interleukin production (Malhi et al., 2018). Inflammatory mechanisms are also implicated in ketamine's effects, as Ballard et al. (2018) show that higher baseline interleukin-5 levels predict remission from suicidal ideation after ketamine treatment. Non-pharmacological treatments targeting biological risk pathways also show promise. This includes the reduction of suicidal ideation in depressed youth with transcranial magnetic stimulation (TMS) of the left primary motor cortex (M1) (Lewis et al., 2019), potentially through GABA mediated cortical inhibition (Croarkin et al., 2018). In line with their demonstration as robust STB risk factors, there is increasing recognition that social factors can be important targets for interventions and modifiers of treatment effects. For example, Casale et al. (2019) show that increased social support via group interventions

lowered STBs in HIV positive youth. Finally, novel interventions are emerging that leverage the increased use of digital technology; Bailey et al. (2018) propose a novel social networking-based online intervention that targets high perceived burdensomeness in young people (Bailey et al., 2018), and Allen et al. (2019) discuss exciting technological advances in the form of digital phenotyping using smartphones, wearables and smart home technology for short-term STB risk prediction.

The studies included in this special issue represent research conducted by leading researchers from Australia, Canada, Europe, South-Africa and the United States. However, unfortunately, there is an underrepresentation of researchers from second and third world countries, which is where the majority of suicides occur (WHO, 2014). STB risk, and therefore the underlying mechanisms, vary for gender and age across the globe (Hedegaard et al., 2018; Naghavi, 2019). It is therefore important that future studies examine gender and age in research on STB risk and treatment response worldwide. The experimental studies included in this special issue include both adult samples (4 studies; mean age 37.6), as well as adolescent samples (10 studies: mean age 17.6). The study of youths is critical for the understanding of STB development and the generation of improved early risk identification and intervention. However, as older age is a strong risk factor for STB (Iorfino et al., 2018; Wetherall et al., 2018), and older aged individuals have the highest rate of suicides (WHO, 2014), it will be important for future studies to specifically examine risk for and prevention of STBs in older individuals.

Thus, this special *JAD* issue brings together research studies from across disciplines that represent important advances in improving our understanding of suicide risk and advancing prevention. We hope that this special issue fuels and guides further research on STBs in order to ultimately better prevent needless loss of life to suicide globally.

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References

- Allen NB, Nelson BW, Brent D, Auerbach RP, 2019 Short-term prediction of suicidal thoughts and behaviors in adolescents: Can recent developments in technology and computational science provide a breakthrough? *J. Affect. Disord* 250, 163–169. 10.1016/JJAD.2019.03.044 [PubMed: 30856493]
- Bailey E, Rice S, Robinson J, Nedeljkovic M, Alvarez-Jimenez M, 2018 Theoretical and empirical foundations of a novel online social networking intervention for youth suicide prevention: A conceptual review. *J. Affect. Disord* 238, 499–505. [PubMed: 29936387]
- Ballard ED, Yarrington JS, Farmer CA, Richards E, Machado-Vieira R, Kadriu B, Niciu MJ, Yuan P, Park L, Zarate CA, 2018 Characterizing the course of suicidal ideation response to ketamine. *J. Affect. Disord* 241, 86–93. [PubMed: 30099268]
- Casale M, Boyes M, Pantelic M, Toska E, Cluver L, 2019 Suicidal thoughts and behaviour among South African adolescents living with HIV: Can social support buffer the impact of stigma? *J. Affect. Disord* 245, 82–90. [PubMed: 30368074]

- Chang HB, Munroe S, Gray K, Porta G, Douaihy A, Marsland A, Brent D, Melhem NM, 2019 The role of substance use, smoking, and inflammation in risk for suicidal behavior. *J. Affect. Disord* 243, 33–41. [PubMed: 30223137]
- Croarkin PE, Nakonezny PA, Deng Z-D, Romanowicz M, Voort JL Vande, Camsari DD, Schak KM, Port JD, Lewis CP, 2018 High-frequency repetitive TMS for suicidal ideation in adolescents with depression. *J. Affect. Disord* 239, 282–290. [PubMed: 30031247]
- de Beurs D, Vancayseele N, van Borkulo C, Portzky G, van Heeringen K, 2018 The association between motives, perceived problems and current thoughts of self-harm following an episode of self-harm. A network analysis. *J. Affect. Disord* 240, 262–270. [PubMed: 30086470]
- Dwivedi Y, 2018 MicroRNAs in depression and suicide: Recent insights and future perspectives. *J. Affect. Disord* 240, 146–154. [PubMed: 30071418]
- Fan S, Lippard ETC, Sankar A, Wallace A, Johnston JAY, Wang F, Pittman B, Spencer L, Oquendo MA, Blumberg HP, 2019 Gray and white matter differences in adolescents and young adults with prior suicide attempts across bipolar and major depressive disorders. *J. Affect. Disord* 245, 1089–1097. [PubMed: 30699851]
- Hedegaard H, Curtin S, Warner M, 2018 Suicide Mortality in the United States, 1999–2017. *NCHS Data Brief* 330, 1–8.
- Iorfino F, Hermens DF, Cross SPM, Zmicerevska N, Nichles A, Groot J, Guastella AJ, Scott EM, Hickie IB, 2018 Prior suicide attempts predict worse clinical and functional outcomes in young people attending a mental health service. *J. Affect. Disord* 238, 563–569. [PubMed: 29940520]
- Kiekens G, Hasking P, Boyes M, Claes L, Mortier P, Auerbach RP, Cuijpers P, Demyttenaere K, Green JG, Kessler RC, Myin-Germeys I, Nock MK, Bruffaerts R, 2018 The associations between non-suicidal self-injury and first onset suicidal thoughts and behaviors. *J. Affect. Disord* 239, 171–179. [PubMed: 30014957]
- Lebowitz ER, Blumberg HP, Silverman WK, 2019 Negative peer social interactions and oxytocin levels linked to suicidal ideation in anxious youth. *J. Affect. Disord* 245, 806–811. [PubMed: 30699863]
- Lewis CP, Camsari DD, Sonmez AI, Nandakumar AL, Gresbrink MA, Daskalakis ZJ, Croarkin PE, 2019 Preliminary evidence of an association between increased cortical inhibition and reduced suicidal ideation in adolescents treated for major depression. *J. Affect. Disord* 244, 21–24. [PubMed: 30292987]
- Lippard ETC, Johnston JAY, Spencer L, Quatrano S, Fan S, Sankar A, Weathers J, Pittman B, Oquendo MA, Blumberg HP, 2019 Preliminary examination of gray and white matter structure and longitudinal structural changes in frontal systems associated with future suicide attempts in adolescents and young adults with mood disorders. *J. Affect. Disord* 245, 1139–1148. [PubMed: 30699858]
- Malhi GS, Das P, Outhred T, Irwin L, Morris G, Hamilton A, Lynch K, Mannie Z, 2018 Understanding suicide: Focusing on its mechanisms through a lithium lens. *J. Affect. Disord* 241, 338–347. [PubMed: 30142593]
- Naghavi M, 2019 Global, regional, and national burden of suicide mortality 1990 to 2016: systematic analysis for the Global Burden of Disease Study 2016. *Bmj* 194 10.1136/bmj.194
- Orri M, Perret LC, Turecki G, Geoffroy M-C, 2018 Association between irritability and suicide-related outcomes across the life-course. Systematic review of both community and clinical studies. *J. Affect. Disord* 239, 220–233. [PubMed: 30025311]
- Parris MS, Grunebaum MF, Galfalvy HC, Andronikashvili A, Burke AK, Yin H, Min E, Huang Y, Mann JJ, 2018 Attempted suicide and oxytocin-related gene polymorphisms. *J. Affect. Disord* 238, 62–68. [PubMed: 29860184]
- Schwartz J, Ordaz SJ, Ho TC, Gotlib IH, 2019 Longitudinal decreases in suicidal ideation are associated with increases in salience network coherence in depressed adolescents. *J. Affect. Disord* 245, 545–552. [PubMed: 30439679]
- Segreti AM, Chase HW, Just M, Brent D, Pan L, 2019 Cortical thickness and volume reductions in young adults with current suicidal ideation. *J. Affect. Disord* 245, 126–129. [PubMed: 30388554]

Wetherall K, Cleare S, Eschle S, Ferguson E, O'Connor DB, O'Carroll RE, O'Connor RC, 2018 From ideation to action: Differentiating between those who think about suicide and those who attempt suicide in a national study of young adults. *J. Affect. Disord* 241, 475–483. [PubMed: 30149335]
World Health Organization. Preventing suicide: a global imperative (2014).

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