

# HOT TOPICS Imaging suicidal thoughts and behavior: the promise of computational models

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Neuroimaging has advanced identification of brain circuitry of suicidal thoughts and behaviors (STBs), highlighting central roles for frontolimbic systems in STBs in adults and their altered trajectories in the development of STBs in adolescence when STBs often first emerge [1]. Critical next steps are to elucidate contributions of biopsychosocial factors and generate individualized prediction. Large-scale multimodal datasets combined with innovative computational approaches are required. Recently forged international consortia (e.g., Help Overcome and Prevent the Emergence of Suicide, HOPES, and Enhancing Neuro Imaging Genetics through Meta-Analysis, ENIGMA) bring new hope; their multimodal imaging and manifold potential risk factor data in large samples provide unprecedented opportunities. However, the numerous and potentially interacting polygenic and exposome factors present complex computational challenges and group level findings may not generalize to the individual [2]. For example, while the ventral prefrontal cortex is a brain region in which STB-related findings have converged, imaging findings have been in gray or white matter structure or function, and have shown varying influences of age, sex, genetic, and immunological factors and exposure to stressors such as child maltreatment [1, 2]. Furthermore, the emergence of large-scale longitudinal data through digital technologies provide unique opportunities for modeling dynamic changes over time, but these present additional computational challenges. Advanced multivariate statistical approaches, such as machine-learning and network-modeling methods, which have shown success in predicting STBs from complex albeit non-imaging data hold promise for addressing these challenges.

Supervised machine-learning techniques are well-suited to analyze multimodal data difficult to theoretically conceptualize and practically model, and can be used to make individualized predictions. Studies using large-scale datasets have started to identify multimodal predictors for future STBs [3]. For example, machine-learning approaches applied to psychological risk data in 3508 young adults (18–34 years) predicted both suicide ideation and suicide attempts at 1-year follow-up with an area under the curve up to 0.83 [4].

Theory-driven multivariate techniques are optimal when there are clear a priori assumptions about the underlying relationships among factors. These include structural equation modeling analyses as they integrate multidomain variables to examine hypothesized causal relations amongst variables based on existing theoretical models. For example, path modeling used to compare four causal models on relationships between social risk factors and self-harm in adolescence supported a cumulative risk model in which adverse social experiences accumulate to increase risk for self-harming behaviors [5]. Another promising technique, network modeling, allows quantification of complex interplays between many interacting variables and can either be theory-driven or data-driven. Recent use of this method, to analyze core risk factors postulated in the interpersonal psychological and integrated motivational-volitional theories of STBs, provided novel views on salient psychological risk factors such as perceived burdensomeness, internal entrapment, mental well-being and interpersonal needs and complex relationships among them [6].

The application of such multivariate computational methods to analyze emerging large-scale imaging and multi-risk factor longitudinal datasets has the potential to identify targets for early and personalized suicide risk detection and prevention strategies [2] to reduce this preventable cause of early mortality.

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# REFERENCES

- Schmaal L, van Harmelen AL, Chatzi V, Lippard ETC, Toenders YJ, Averill LA, et al. Imaging suicidal thoughts and behaviors: a comprehensive review of 2 decades of neuroimaging studies. Mol Psychiatry. 2020;25:408–27.
- Van Harmelen AL, Schmaal L, Blumberg HP. Journal of Affective Disorders Special Issue on Suicide-related Research: hopeful progress but much research urgently needed. J Affect Disord. 2019;251:39–41.
- Just MA, Pan L, Cherkassky VL, McMakin DL, Cha C, Nock MK, et al. Machine learning of neural representations of suicide and emotion concepts identifies suicidal youth. Nat Hum Behav. 2017;1:911–9.
- van Mens K, de Schepper C, Wijnen B, Koldijk SJ, Schnack H, de Looff P, et al. Predicting future suicidal behaviour in young adults, with different machine learning techniques: A population-based longitudinal study. J Affect Disord. 2020; 271:169–77.
- Cassels M, van Harmelen AL, Neufeld S, Goodyer I, Jones PB, Wilkinson P. Poor family functioning mediates the link between childhood adversity and adolescent nonsuicidal self-injury. J Child Psychol Psychiatry. 2018;59:881–7.
- De Beurs D, Fried El, Wetherall K, Cleare S, DB OC, Ferguson E, et al. Exploring the psychology of suicidal ideation: a theory driven network analysis. Behav Res Ther. 2019;120:103419.