Biological Psychiatry: CNNI

Can't Stop Remembering: Neural Decoding of Representations of the Deceased Predicts Subsequent Intrusive Thinking and Coping Strategies

Scott A. Langenecker, Alex Leow, and K. Luan Phan

Is there a neural signature for close loved ones after they die? Can that signature predict persistently intrusive thoughts of the loved one? Does knowledge of brain processes involved in thinking about the deceased allow us to better understand maladaptive grieving processes that may interfere with life functioning? Grief and complicated grief constitute one area that is dramatically understudied in the field (1,2), and the clues within study of grief may offer a window into understanding how to avoid complicated grief. Grieving is often elucidated by self-report, and different proxies are needed to better reflect deceased-related thinking.

While the topic of complicated grief is not new, it has long been understood that grief over loss/bereavement might be categorically different from major depressive disorder. Moreover, discussion of the concept of complicated grief has emerged in the DSM only recently, again, as distinct from major depressive disorder. Individuals who treat this condition as well as individuals who experience it acknowledge many of the same symptoms and feelings as observed in major depressive disorder, but they deny that it is the same process. Thus, we turn to the neural systems involved in loss and grief to potentially arbitrate between the idea that grief over a deceased loved one might have a unique neural signature and a corresponding unique impact on the affected individual.

The study by Schneck *et al.* (3) addresses this knowledge gap. They employed a number of innovative strategies to better elucidate how deceased-related thinking (thinking or thoughts or neural signature representative of the loved one) might be measured at the neural level and how this neural representation can discriminate and predict subsequent deceased-related thinking that emerges during a "mindless" sustained attention task sensitive to mind-wandering and reflects avoidance coping strategies. Briefly, Schneck *et al.* demonstrate 1) that they can decode a neural pattern of circuits engaged in thoughts about the deceased loved one, 2) that this machine-learned pattern of circuits can be modeled to identify the intrusion caused by thoughts of the loved one on a subsequent cognitive task, and 3) that such thinking is unique to the deceased and reflects extent of subject-specific avoidance. There are also some important methodological steps taken and related challenges that we will briefly highlight before discussing the implications and the possible next steps.

Functional magnetic resonance imaging relies on differences in relative measurements in blood flow, often based on subtraction techniques in which a condition of interest is compared with a "control" condition (4,5). Much has been described regarding the role of the concept of "cognitive insertion" for understanding differences between conditions of interest relative to control conditions, but often the importance of the control condition is underappreciated. Schneck *et al.* (3) employed several strategies to address this potential weakness in event-related functional magnetic resonance imaging. There are three active and three control events. They employed a conjunction analysis to hone in on regions that are relevant to the deceased in two of those three conditions. Schneck *et al.* further used multivariate pattern analysis with machine learning to model the neural signature of deceased-related thinking (6). This approach can help to control for the relative inaccuracy of activation in a given representational node by looking at many such nodes in tandem. Finally, they employed a comparison of two null regions to demonstrate the specificity of the machine-learning approach.

This neural-based circuit representation of the deceased was then employed in a second task to evaluate the ability to detect thinking about the deceased in normative, day-to-day contexts. More specifically, might the deceased-related thinking serve as a form of distraction (e.g., mind-wandering) in everyday life, and might this illustrate the severity of the response to the loss and the degree of potential dysfunction associated with such loss? The neural pattern elucidated from conjunction analyses was used to classify and detect deceased-related thinking during a sustained attention task. The model was successful in relating to the extent of self-reported thinking (or not, as in the case of avoidance) about the deceased but, more importantly, was indicative of the arousal and frequency of thinking about the deceased. The regions associated with the model are salience and valence regions as well as anterior default mode regions. While there are confounds of salience and valence associated with comparing the deceased with a living known analog person, it was difficult to avoid this particular confound. Schneck *et al.* (3) made an attempt by covarying by entering subjective ratings of arousal. However, we note that covariance with variables that are not equally distributed between groups can lead to inversion effects (7).

There are several compelling and interesting advances that might be inspired by this work. First, in the future, variance in arousal and salience might be modeled as a separate regressor within person and as a feature encoding individual differences (8). Such individual difference features might have great specificity in defining individuals at risk for adverse

SEE CORRESPONDING ARTICLE ON PAGE 421

  http://dx.doi.org/10.1016/j.bpsc.2017.05.003
Biological Psychiatry: Cognitive Neuroscience and Neuroimaging July 2017; 2:384–385 www.sobp.org/BPCNNI ISSN: 2451-9022

outcomes and in identifying the persistence of deceased-related thinking at the individual level. Second, the idea that neural "thought" processes can be accurately modeled, and in particular related to a person, a disorder, or even an emotional state, is emerging as a novel and critically important way to understand individual differences (or even in-the-moment mind-wandering of the same individual) and risk for or expression of disease (9). Such approaches may lead to probabilistic and perhaps revolutionary approaches to risk and prevention strategies in mood and related disorders. Third, the representation of loss can be further stratified based on whether such a loss is sudden, whether the relationship was conflictual or supportive, and whether the method of loss was violent (e.g., homicide or suicide) as well as whether the loss was recent or remote.

Lastly, one could use the neural model from this sample to predict deceased-related thinking in a new sample. It could be contrasted with models in which subjective arousal and valence are better matched. How much and how often one is unable to "let go" of memories of the deceased could depend on how the individual perceives the loss in terms of intensity and meaning, the recency of the loss, the degree of conflict in the relationship, the degree of closure, and the unexpectedness of the loss. For example, individuals who have lost a child to a sudden, unexpected suicide could be compared with individuals who have lost a parent to a long-lasting and anticipated cancer, as each loss could have a differential emotional impact. Elucidating individualized neural patterns that reflect behavior could promote new therapeutic strategies, including prevention. For example, subject-specific neural patterns could be targeted in real time by neuromodulation (e.g., transcranial magnetic stimulation), cognitive training (e.g., distraction, reappraisal), and brain-based biofeedback (10). Such patterns could also be expanded further for use in electroencephalography and/or event-related potential designs, whereby any successful modeling could be more readily translated in remote clinical settings. The study by Schneck *et al.* teaches us about how novel design and analytic strategies inform us about a neural index of the grieving process that is different across individuals and that could complicate maladaptive strategies to fight against grieving; as such, these neural profiles could be used as predictive biomarkers to detect individuals who would be susceptible to complicated grief so that prevention strategies could be deployed following a loss. Moreover, they elucidate brain-behavioral targets for existing and novel interventions in other related conditions.

Acknowledgments and Disclosures

This work was supported by the National Institute of Mental Health Grant Nos. MH101487 and MH101497 (to SAL and KLP).

The authors report no biomedical financial interests or potential conflicts of interest.

Article Information

From the Department of Psychiatry, University of Illinois at Chicago, Chicago, Illinois.

Address correspondence to Scott A. Langenecker, Ph.D., Department of Psychiatry, University of Illinois at Chicago, 1601 West Taylor Street, m/c 912, Chicago, IL 60612; E-mail: slangenecker@psych.uic.edu.

Received May 23, 2017; accepted May 24, 2017.

References

1. Gundel H, O'Connor M-F, Littrell L, Fort C, Lane RD (2003): Functional neuroanatomy of grief: An fMRI study. Am J Psychiatry 160: 1946–1953.
2. Kersting A, Ohrmann P, Pedersen A, Kroker K, Samberg D, Bauer J, *et al*. (2009): Neural activation underlying acute grief in women after the loss of an unborn child. Am J Psychiatry 166:1402–1410.
3. Schneck N, Haufe S, Tu T, Bonanno GA, Ochsner KN, Sajda P, Mann JJ (2017): Tracking deceased-related thinking with neural pattern decoding of a cortical-basal ganglia circuit. Biol Psychiatry Cogn Neurosci Neuroimaging 2:421–429.
4. D'Esposito M, Zarahn E, Aguirre GK (1999): Event-related functional MRI: Implications for cognitive psychology. Psychol Bull 125:155–164.
5. Logothetis NK (2008): What we can do and what we cannot do with fMRI. Nature 453:869–878.
6. Haynes J-D, Rees G (2006): Decoding mental states from brain activity in humans. Nat Neurosci 7:523–534.
7. Stevens J (1996): Applied Multivariate Statistics for the Social Sciences. Mahwah, NJ: Lawrence Ehrlbaum Associates.
8. Phan KL, Taylor SF, Welsh RC, Ho SH, Britton JC, Liberzon I (2004): Neural correlates of individual ratings of emotional salience: A trial-related fMRI study. Neuroimage 21:768–780.
9. Xing M, Ajilore O, Wolfson OE, Abbott C, MacNamara A, Tadayonnejad R, *et al*. (2016): Thought chart: Tracking dynamic EEG brain connectivity with unsupervised manifold learning. In: Ascoli G, Hawrylycz M, Ali H, Khazanchi D, Shi Y, editors. Brain Informatics and Health. BIH 2016. Lecture Notes in Computer Science, vol 9919. Cham: Springer.
10. Lo M-C, Widge AS (2017): Closed-loop neuromodulation systems: Next-generation treatments for psychiatric illness. Int Rev Psychiatry 29:191–204.