Commentary

Changing Views on the Salience Network in Response to Data on Exposure to Assault

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The salience network (SN) is an intrinsically connected network anchored in the dorsal anterior cingulate cortex (dACC) and the anterior insula cortex (aIC) (1). Major subcortical nodes of the SN include the amygdala, ventral striatum, and ventral tegmental area. Models of attention have long pointed to the importance of the dACC/aIC in orienting attention (2). However, more recently there have been suggestions that these systems serve saliency detection; i.e., that the SN identifies the most relevant endogenous and external stimuli so that behavior can be guided adaptively (1). Atypical functioning of the SN has been implicated in a variety of psychiatric conditions, including posttraumatic stress disorder. It has been suggested that posttraumatic stress disorder might reflect hyperactivity of the larger SN (3).

In a study by Cisler *et al.* (4) in this issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, neural responses within the SN anchor regions of the dACC and the bilateral aIC were examined in 30 adolescent girls who had previously been physically or sexually assaulted and 30 healthy controls in the context of three tasks. One was an expression processing task: fearful and neutral expressions that were either overtly (500 ms in duration) or covertly (33 ms in duration) presented. The other two were three-arm bandit reinforcement-based decision-making paradigms where participants chose between either three faces or three houses to gain money. Strikingly, within the dACC and aIC anchor regions, the girls who had previously been assaulted, relative to the healthy controls, showed 1) greater activity to faces with particularly overt fearful expressions but 2) reduced activity to negative prediction errors, particularly in the reinforcement-based decision-making paradigms involving face stimuli.

There are several important implications of this study. The first is methodological. It is notable that if Cisler *et al.* (4) had written an article on either the face expression task or the reinforcement-based decision-making tasks (or probably the results of a resting-state functional magnetic resonance imaging study), they would have ended up with misleading results. An article focusing on the face data would have suggested that the experience of assault leads to hyperactivity of the SN. An article focusing on the reinforcement data would have suggested that experience of assault leads to hypoactivity of the SN. By combining the data from more than one task from the same participants, we are forced to more complex conclusions than simply that experience with assault leads to hyperactivity (or hypoactivity) of the SN.

The second implication concerns how we understand the impact of maltreatment, or at least exposure to assault, on neural functioning. Before these data, we might have held the position that exposure to assault induces heightened (or reduced) SN activity. It would not have been unreasonable to consider that exposure to assault leads to a state where the brain is particularly primed to identify significant external stimuli so that behavioral responses to avoid threats can be rapidly engaged. But Cisler *et al.*'s data (4) suggest that such a position is incorrect. These data, however, also clearly indicate that there is an impact of exposure to assault on SN activity; effects for both tasks were significant—just in opposite directions. As such, the current data suggest the possibility that exposure to assault has specific, but opposite, impacts on other, different components of the SN (or other neural systems that feed activity to the SN) that, when overstimulated (by faces) or understimulated (by negative prediction errors), propagate into the SN anchor regions (the dACC and bilateral aIC). Notable in this regard are the subcortical nodes of the SN: the amygdala and the ventral striatum. Considerable previous work has indicated that maltreatment increases amygdala responsiveness to threat stimuli (5). Moreover, work has begun to suggest that striatal responses to reward are compromised by maltreatment (6,7). As such, activity within the anchor regions of the SN (the dACC and the bilateral aIC) may reflect the impact of exposure to assault on subcortical nodes of the SN, increasing amygdala responsiveness to threat and decreasing striatal responsiveness to reward. Assuming that these data are robust, exposure to assault may not impact the SN, but only components of this network, which then propagate this impact through the network because of their interconnectivity with the other structures.

The third implication concerns how we understand the function of the SN itself. As noted above, there have long been suggestions of the importance of the dACC/aIC in orienting attention (2), but more recently there have been suggestions that the SN detects salient stimuli—that it identifies relevant endogenous and external stimuli (1). However, the current data indicate, at the very least, that the anchor regions of the SN (the dACC and the bilateral aIC) do not detect salient stimuli (or at least do not detect the types of salient stimuli examined in the current paradigms). A group of individuals should not exhibit a saliency "detector" that is more responsive to one class of salient stimuli but less responsive to another class of salient stimuli. Of course, it could be argued that the salience detection function is driven by subcortical nodes of the SN, such as the amygdala and the ventral striatum. But the salient stimuli the amygdala responds to—e.g., unconditioned, conditioned, and novel stimuli—are all important for its critical

role in stimulus reinforcement learning. As such, one might better understand the functional roles of the anchor regions of the SN (the dACC and the bilateral aIC) as orienting attention to stimuli important for emotional learning (either in response to facial expressions or monetary reinforcement information), at least with respect to the current paradigms.

In conclusion, the article by Cisler *et al.* (4) is of interest for several reasons. The results stress the importance of multitask approaches for the same participants; it is useful to examine replicability across tasks as well as across laboratories when considering functional accounts of a disorder. The results of a single paradigm, even in a resting state, might provide a conclusive biomarker of a disease state but probably cannot reveal a full functional account. Hyperresponsiveness of the SN to emotional stimuli or hyporesponsiveness of the SN to negative prediction errors might be identified in future work as biomarkers of exposure to assault. However, level of responsiveness of the SN per se, at least according to these data, is not the basis of a functional account of the impact of exposure to assault on the brain.

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References

1. Menon V (2015): Salience network. In: Toga AW, editor. Brain Mapping: An Encyclopedic Reference. New York: Academic Press, 597–611.
2. Corbetta M, Patel G, Shulman GL (2008): The reorienting system of the human brain: From environment to theory of mind. Neuron 58:306–324.
3. Patel R, Spreng RN, Shin LM, Girard TA (2012): Neurocircuitry models of posttraumatic stress disorder and beyond: A meta-analysis of functional neuroimaging studies. Neurosci Biobehav Rev 36:2130–2142.
4. Cisler JM, Esbensen K, Sellnow K, Ross M, Weaver S, Sartin-Tarm A, et al. (2019): Differential roles of the salience network during prediction error encoding and facial emotion processing among female adolescent assault victims. Biol Psychiatry Cogn Neurosci Neuroimaging 4:371–380.
5. McCrory EJ, Gerin MI, Viding E (2017): Annual Research Review: Childhood maltreatment, latent vulnerability and the shift to preventative psychiatry—the contribution of functional brain imaging. J Child Psychol Psychiatry 58:338–357.
6. Gerin MI, Puetz VB, Blair RJR, White S, Sethi A, Hoffmann F, et al. (2017): A neurocomputational investigation of reinforcement-based decision making as a candidate latent vulnerability mechanism in maltreated children. Dev Psychopathol 29:1689–1705.
7. Mehta MA, Gore-Langton E, Golembo N, Colvert E, Williams SC, Sonuga-Barke E (2010): Hyporesponsive reward anticipation in the basal ganglia following severe institutional deprivation early in life. J Cogn Neurosci 22:2316–2325.