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The Reciprocity of Brain and Behavior

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The rise of neuroscience in our field has raised legitimate questions about the relative value of brain versus behavioral data to inform our understanding of the etiology and treatment of childhood mental disorders. There is no doubt that data on brain function and structure has wielded unique power and influence in mental health research over the last two decades. This may be based in part on its inherent objective and quantitative features in a field that has searched for, and thus far generally failed to find, clearly measurable markers of psychopathology for clinical use. However, it may also be based on a reductionist philosophy that posits that the brain is the source and driver of all human emotions and behavior and therefore should be of central importance. Contrasting this view, recent neuroscience perspectives have emphasized that detailed studies of behavior are essential to inform neuroscience¹. While the brain basis of behavior is clear, this reductionist approach also fails to take into account the more reciprocal nature of brain behavior relationships in which emotions, behavior and life experience can also influence and change the brain^{2,3}.

In the article “Preschool and School-Age Irritability Predict Reward-Related Brain Function” by Dougherty *et al*, the authors demonstrate a relationship between early life irritability and functional connectivity within reward networks measured at school age.⁴ The article provides an excellent illustration of this issue and the need to account for signals from both brain and behavior. Irritability, measured behaviorally during the preschool period and again at school age, was related to functional connectivity of reward networks (measured during a reward task performed in the scanner), even after controlling for the effects of prior or concurrent measures of irritability. Also notable and important, was that irritability at preschool and school age was only very weakly correlated. Notwithstanding design limitations such as the lack of availability of neuroimaging during the preschool period, this study suggests is that irritability displayed behaviorally early in life left a detectable mark on brain function later in childhood which remained significant even after accounting for concurrent irritable behavior. Importantly, this detectable alteration in brain function was specific to the core of the behavioral abnormality in that irritability, which is often operationalized as “frustrative non-reward”⁵ was associated with alteration in brain function

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most strongly during experiences of non-reward during the task. Findings suggest a relationship between early behavior and later brain function in the same core domain even when the behavioral abnormality may no longer be obvious.

There is increasing evidence from multiple empirical studies that measures of brain function may provide greater power to detect abnormalities when they are not yet observable, or manifest as symptom states. Consistent with this principle, the findings from the Dougherty *et al* paper suggest that brain function abnormalities can be detected related to earlier experiences of symptoms when symptoms may no longer be manifest.⁴ This should not be interpreted to suggest that brain imaging should be conducted on our patients as a more powerful means of detecting abnormalities. This would be neither pragmatic nor cost effective and there is no evidence of its utility in individual patients. However, the use of brain imaging may be useful towards the goal of guiding more refined behavioral assessments by providing clues from alterations in underlying neural correlates of specific emotional and behavioral processes. Such information gleaned from studies targeting brain function might then lead to the identification of more subtle and specific symptom manifestations and observable developmental processes to enhance early detection and guide more targeted prevention prior to clinical symptom manifestation.

Another advantage that measures of brain function may offer are evidenced by the finding in the Dougherty *et al* study that children with high preschool irritability showed alterations in connectivity during both receipt and non-receipt of reward.⁴ This suggests that reactions to achieving success and failing to achieve success are both heightened in irritable children, a finding that is less evident based on behavioral observations alone which have emphasized abnormal response to frustration and non-reward. Along the line of the above, these findings suggest further behavioral study of irritable children's reactions to successful receipt of reward should also be the focus of future study and potentially clinical attention.

Another area that the article does not investigate but could in the future, is how behavior might better inform our understanding of brain function. Currently, the interpretation of connectivity and what it means for emotional and behavioral function remains highly ambiguous with studies suggesting that increased connectivity may be associated with better regulatory function and other studies suggesting it is associated with higher need and less efficient regulation. The current study could potentially inform this issue by using concurrent behavior to inform the interpretation of findings of higher or lower connectivity. This could be achieved by rating the child's objective ability and subjective experience of emotion regulation during these tasks.

Overall, the current study provides new insights into the nature and later developmental consequences of irritability in childhood. Brain measures elucidated alterations in reward processing related to early irritability and suggest possible new dimensions of abnormality in reward processing less evident by observation. Alternatively, these data could also be useful to give more meaning and clinical interpretation of the alterations in brain function regularly reported but poorly understood from a behavioral perspective. This study provides a salient example of how measures of brain function enhanced our understanding of behavior and

provides further evidence for how behavior may be changing the brain underscoring the need for careful measurement in both domains to advance the public health.

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