

Behavioral Inhibition Linked to Anxiety in Adolescents

BOSTON—The neural links between behavioral inhibition in adolescence and anxiety were explored at the 54th Annual Meeting of the American Academy of Child and Adolescent Psychiatry. Koraly Pérez-Edgar, PhD, Assistant Professor in the Department of Psychology at George Mason University in Fairfax, Virginia, explained that temperament is a biologically based construct that can be seen as young as 4 months, and hypothesized that behavioral inhibition—a common temperamental trait—is associated with an enhanced sensitivity in multiple neural regions to processing salient stimuli.

“The first thing you have to do before you process information in your environment is pick what you’re going to process,” Dr. Pérez-Edgar said. “The argument is that [behaviorally inhibited] children are more likely to pick things they think are threatening, so they have a bias to threat. But coloring that is the fact they find more things threatening than other kids do. So not only are they biased to threat, but they see more threat out there.”

Dr. Pérez-Edgar explained that the tendency of certain children to be more reactive to novel stimuli in their environment is linked to a more reactive amygdala, which results in more visceral feedback to the limbic sites of the brain. As such, these children have a special preparedness to detect subtle differences in their environment, which Dr. Pérez-Edgar believes is linked to a sensitivity in the attention system for detecting threat, novelty, or salience in the environment. This creates a cascading effect that is visible to others as a construct of behavior known as behavioral inhibition. One way to ascertain evidence of this process is by observing peripheral markers of amygdala activity.

In prior work, Nathan A. Fox, PhD, of the University of Maryland, Dr. Pérez-Edgar, and other researchers selected 4-month-old infants and presented them with novel auditory and visual stimuli to examine such markers as arching of the back, vigorous limb movements, and negative vocalization. The infants were then separated into three groups: those with negative responses to novel stimuli (higher risk of behavioral inhibition), those who had neutral responses (lower risk of behavioral inhibition), and infants who had positive responses (lowest risk of behavioral inhibition). These infants were also seen at 9, 14, and 24 months, as well as at 4, 7, and 15 years. In early childhood, participants were then reclassified based on whether they went on to

display behavioral inhibition. They were examined at age 9 months for fear-potentiated startle reflex, a negative reaction that Dr. Pérez-Edgar and colleagues found among infants at risk for behavioral inhibition. At age 7, the researchers found increased heart rate during anxiety and decreased heart rate variability in behaviorally inhibited children. This provided evidence that a similar pattern of behavior was present from infancy into childhood and that this behavior pattern paralleled that seen in children with anxiety disorders.

At age 15, the children were screened for psychiatric disorders meeting clinical cutoffs on the Kiddie Schedule for Affective Disorders and Schizophrenia. Results showed that children who were behaviorally inhibited at earlier time points had more diagnoses than those who were not behaviorally inhibited. When the diagnoses were limited to just anxiety disorders, a more statistically significant gap was observed between children with and without behavioral inhibition, and this gap widened further when the diagnoses were limited to only social anxiety disorder. These data were confirmed by a parent-reported measure and a self-reported measure, as both the parents and the behaviorally inhibited participants themselves agreed that they were exhibiting more anxiety, particularly social anxiety, than were children who were not behaviorally inhibited.

“So we’re seeing some specificity from the clinical point of view, the parent report, and the child’s own presentation of what he or she is feeling,” Dr. Pérez-Edgar explained. “It’s social anxiety that’s bearing the burden of diagnoses within the behaviorally inhibited children.”

Empirical Testing of Neural Model

Schwartz et al had previously found that children who were behaviorally inhibited at age 2 and then examined at age 20 showed increased amygdala activity to novel stimuli. Dr. Pérez-Edgar, with Dr. Fox and Daniel S. Pine, MD, of the NIMH, followed up on this work by examining a subset of their cohort. These 44 children between ages 10 and 15 were separated into either a behaviorally inhibited or a non-behaviorally inhibited group and were administered a face-rating task and a monetary incentive delay task.

In the first task, the participants were presented with four types of faces: neutral, happy, angry, and fearful. Each face presentation was accompanied by four requests: Look at the face, judge how hostile

the face is, judge how afraid of the face you are, and determine how wide the nose is (control). The researchers found that behaviorally inhibited children showed deactivation of amygdala reactivity when asked to simply look at the faces, and there was no difference between behaviorally inhibited and non-behaviorally inhibited children when they were asked to judge hostility or compare nose width. When asked to judge how afraid they were of a fearful face, behaviorally inhibited children showed significantly more bilateral amygdala activation than did non-behaviorally inhibited children. However, amygdala reactivity was also greater among behaviorally inhibited children when they were asked how afraid they were of a happy face, which Dr. Pérez-Edgar theorized could mean they showed a generalized response to stimuli or that they were responding to the novelty of the question, “How afraid are you of a happy face?”

Next, a reward task was administered by Amanda E. Guyer, PhD, of the NIMH, in which 15-year-olds attempted to avoid monetary loss and increase monetary gain by exhibiting rewarding behavior. Instead of seeing less activation to reward among behaviorally inhibited children than among non-behaviorally inhibited children, the researchers found that behaviorally inhibited children were acutely sensitive to the amount of risk and reward that they were being subjected to. Their “neural systems were titrating to the amount of risk and reward that they were experiencing,” Dr. Pérez-Edgar said.

“What I’m arguing is that behavioral inhibition is associated with an enhanced sensitivity in multiple neural regions to processing salient stimuli, such as threat cues within the context of particular attentional states and incentive cues,” Dr. Pérez-Edgar summarized. “This extends across both social and non-social stimuli, going right back to the original way in which these children were selected at 4 months of age. The risk for psychopathology may be manifest as functional anomalies in neural processing and could reflect an underlying, but not yet fully characterized, gene-by-environment interaction. [This hypothesis could account for] that small percentage of the overall population that persists in temperamental shyness and that shows a clinical anxiety disorder.”

—John Merriman

SUGGESTED READING

Pérez-Edgar K, Roberson-Nay R, Hardin MG, et al. Attention alters neural responses to evocative faces in behaviorally inhibited adolescents. *Neuroimage*. 2007;35(4):1538-1546.