

## WHY DO SOME CHILDREN BECOME VERY ANXIOUS?

**Rachel Bernstein<sup>1†</sup>, Jordan Galbraith<sup>1†</sup>, Devi Lakhani<sup>1†</sup>, Isaac Morales<sup>1†</sup>, George A. Buzzell<sup>2</sup>, Ranjan Debnath<sup>3</sup>, Ellen Leibenluft<sup>1</sup>, Daniel S. Pine<sup>1</sup>, Nathan A. Fox<sup>4</sup> and Anita Harrewijn<sup>1,5\*</sup>**

<sup>1</sup>Emotion and Development Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, United States

<sup>2</sup>Department of Psychology, Center for Children and Families, Florida International University, Miami, FL, United States

<sup>3</sup>Leibniz Institute for Neurobiology, Magdeburg, Germany

<sup>4</sup>Department of Human Development and Quantitative Methodology, University of Maryland, College Park, MD, United States

<sup>5</sup>Department of Psychology, Education and Child Studies, Erasmus University Rotterdam, Rotterdam, Netherlands

### YOUNG REVIEWERS:



**ANAND**

AGE: 14



**SPANDANA**

AGE: 14

While it is normal to be scared of things, some children are so scared that it disrupts their lives. This is called an anxiety disorder. To help children with anxiety disorders, we need to know how anxiety disorders start. From other research we knew that toddlers who avoid new situations are more likely to become anxious later in life. They are *more likely*, which does not mean they all become more anxious, just some of them. We wanted to know if brain activity could predict which children would become anxious. We studied avoidance in toddlers and invited them back as preteens. We studied their brains while they were resting and while they were making mistakes in front of somebody else. We found that brain responses to mistakes predicted which avoidant toddlers became very anxious as preteens. This helps us understand who might develop anxiety, so that we can help!

## ANXIETY

An overwhelming sense of worry, uneasiness, or fear (for example, of spiders, snakes, or public speaking). Sometimes anxiety is felt in the body as tension, sweating, or increased heart rate.

## ANXIETY DISORDER

Anxiety so severe that it disrupts daily life. Children with anxiety disorders may not be able to go to school or leave their homes because they are too scared.

## AVOIDANT

Moving or turning away from something. Avoidant toddlers do not want to play with new toys or do not want to approach a stranger that enters the room.

## WHY DO SOME CHILDREN GET ANXIETY DISORDERS?

Everybody is scared from time to time. Some children are scared of spiders, some fear snakes, and others are nervous about saying something in front of the class. Some children are so anxious they cannot go outside or go to school. This extreme level of **anxiety** is called an **anxiety disorder** [1].

We want to know why some children develop anxiety disorders and others do not. This will help us prevent children from getting anxiety disorders. Studies have shown that some toddlers avoid new situations a lot more than others do. For example, some toddlers stay very close to their mothers if somebody enters the room, and they will not play with unfamiliar toys. These toddlers are called **avoidant**, and they are more likely than others to be anxious when they are older [2]. But not *all* avoidant toddlers will become anxious when they grow up. So, we wanted to find out why some of these avoidant toddlers become anxious.

## DOES THE BRAIN PLAY A ROLE?

To learn why some avoidant toddlers become anxious, we studied their brains [3]. We wanted to know if the activity of the brain can predict which avoidant toddlers are more likely to become anxious as preteens. We measured brain activity in two situations: while the preteens were resting and while they were making mistakes. To measure brain activity during rest, preteens just had to sit still and do nothing. To measure brain activity when they were making mistakes, the preteens were asked to do a difficult task very quickly. Usually, your brain gives a “warning signal” when you make a mistake. This signal is even bigger if somebody else sees your mistake [4]. We wanted to know if brain activity during rest and during mistakes could show which preteens have become very anxious.

In our study, we asked two research questions. First, does the brain activity of preteens during rest show us which avoidant toddlers have become very anxious? Our hypothesis was that brain waves at rest will show which avoidant toddlers will become very anxious as preteens. Second, does the brain’s response to making mistakes in front of somebody else show which avoidant toddlers have become very anxious as preteens? Our hypothesis here was that avoidant toddlers who have bigger warning signals when making mistakes in front of somebody else as preteens will be more anxious than those with smaller warning signals.

## HOW DID WE STUDY THE ROLE OF THE BRAIN IN ANXIETY?

To study whether the brain can show which avoidant toddlers become very anxious as preteens, we needed to wait until they grew up.

## LONGITUDINAL RESEARCH

A study that gathers information about an individual or a group multiple times over a long period.

### Figure 1

Toddlers were placed in three situations to test how avoidant they were. They were placed in a room with a grown-up stranger, given a loud robot toy, and presented with a dark, mysterious tunnel. We measured how long it took them to play in these situations [5].

After they became preteens, we could look at how their brains might be different. This is called **longitudinal research**: we studied the same children several times over 10 years. Children first came to the University of Maryland when they were 2 and 3 years old. Then, they came back when they were 13 years old!

We looked at how 268 toddlers (2–3 years old) behaved in three new situations (Figure 1). In the first situation, they were in a room with a grown-up stranger. In the second situation, they were given a loud robot toy. In the third situation, they were near a dark and mysterious tunnel. All these situations could be scary for a toddler. We wanted to put them in scary situations to see how they reacted. Some toddlers took longer to go to these new and scary things. Some toddlers stayed close to their parents. Others played with the robot right away. We used these situations to see which toddlers were more avoidant.

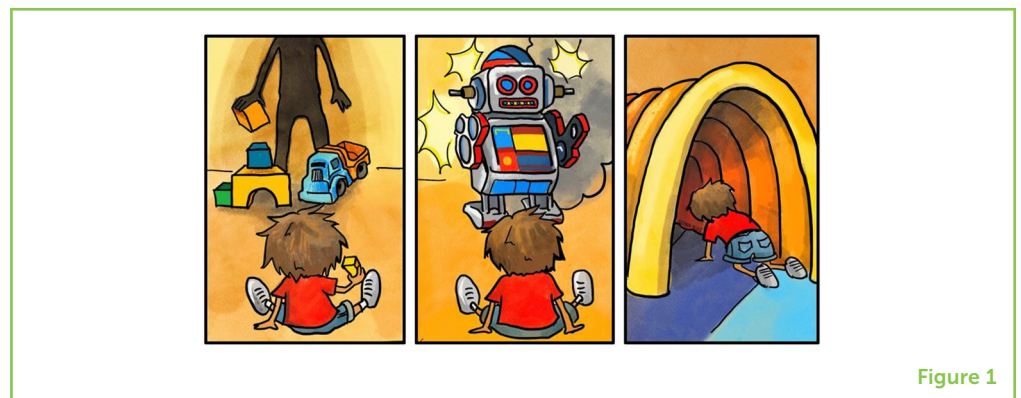


Figure 1

## ELECTRO-ENCEPHALOGRAM (EEG)

A recording of the electrical activity of the brain. It is recorded using a cap with sensors that is worn on the head.

## SOCIAL FLANKER TASK

Computer task in which preteens indicate the direction of an arrow. In the social condition, they thought they were being watched by another preteen—but this was not the case.

Some of the same children came back when they were 13 years old. During this visit, 123 preteens filled out a questionnaire about how anxious they are in different situations. Their parents filled out the same questionnaire about their children [6]. We also studied the children's brain activity using an **electroencephalogram** (EEG), which is a recording of the electrical activity of the brain. Brain activity consists of little bursts of electricity that happen when the brain is doing something. These bursts of electrical activity can be big or small, and fast or slow, depending on what the brain is doing. To record brain activity with an EEG, the preteens wore a cap with sensors while they either rested or performed a task on the computer.

We first measured brain activity during rest, when the preteens were sitting still and doing nothing. An experimenter in the room asked the preteens to keep their eyes closed for 30 s and then open their eyes for 30 s. This happened 6 times in total. Then, we measured brain activity when the preteens were making mistakes. To make sure the preteens would make mistakes, they all played the same computer task called the **social flanker task** [4]. During this task, the preteens saw 5 arrows on a screen and had to indicate whether the middle arrow pointed to the left or right (Figure 2A). Sometimes, the middle arrow was different

from the arrows around it, which made the task difficult and caused preteens to make mistakes—that is exactly what we wanted! If the preteens did not make enough mistakes, the computer asked them to go faster, to make sure that they made some mistakes.

### Figure 2

We used the Social flanker task measure brain activity when preteens were making mistakes. **(A)** In this task, preteens had to indicate if the arrow in the middle was pointing to the left or right. That is easy if all arrows are pointing in the same direction (top), but difficult if the middle arrow is different (bottom). **(B)** In the social condition, preteens thought that another preteen would watch and evaluate them. However, this was not the case. **(C)** In the alone condition, preteens were told that the computer would give them feedback, and not another preteen.

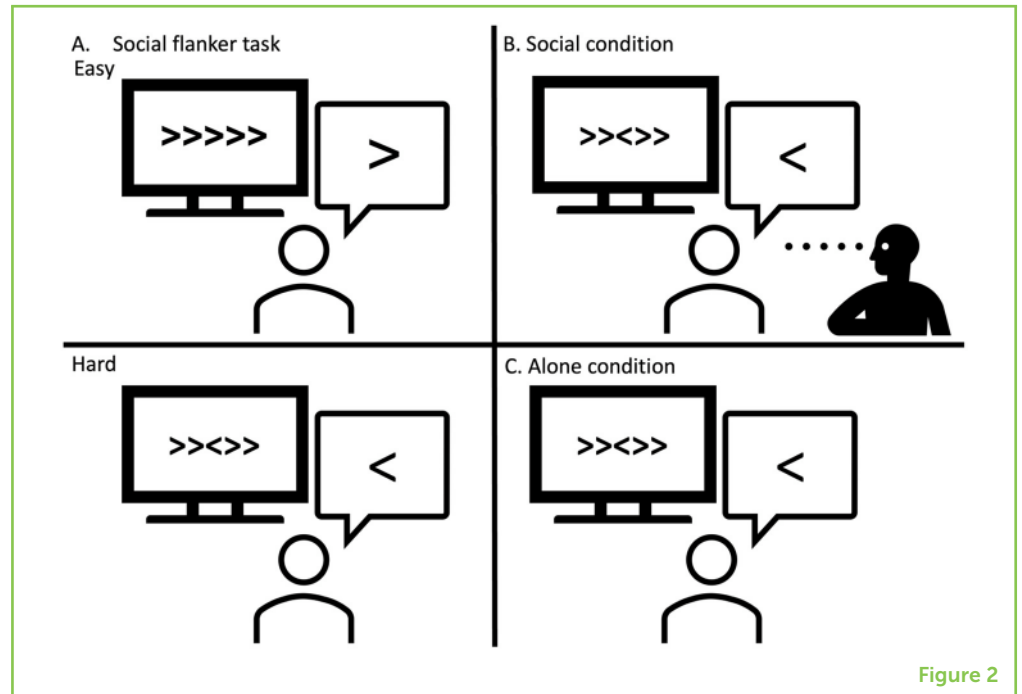


Figure 2

As you can see in Figure 2, there were two versions of the task: a social condition and an alone condition. During the social condition, preteens were told that another preteen would watch and evaluate them through a webcam. In reality, nobody was watching them! During the alone condition, the preteens received feedback from the computer instead of an imaginary preteen. We wanted to see if preteens would react differently to mistakes if there was somebody watching them.

### WHAT DID WE FIND?

To remind you of our research question, we wanted to know if brain activity could tell us which avoidant toddlers actually become more anxious as preteens. If brain activity can tell us something about anxiety, we can use this information to help find and treat preteens who struggle with anxiety.

First of all, we found that brain activity when preteens were at rest did not tell us which of the avoidant toddlers were more anxious as preteens [7]. However, when preteens made mistakes, their brains responded with a “warning signal.” This signal was bigger when they thought that they were being watched by somebody else. Preteens who showed this bigger warning signal when being watched and who

were avoidant as toddlers were more anxious than those with smaller warning signals [8].

## SUMMARY

In our study, we wanted to know why some children develop anxiety disorders. We also wanted to find out if the brain plays a role. Some toddlers avoid new situations, for example, they do not want to play with a new and noisy toy. Some want to stay close to their mothers if a stranger comes into the room. These avoidant toddlers have a greater risk of developing an anxiety disorder later in life, compared to toddlers that do not avoid new things. We wanted to figure out why only *some* avoidant toddlers become more anxious as they grow up. To answer this question, we studied how their brains responded to various situations.

We now know that brain activity when a preteen is at rest does *not* show which avoidant toddlers have become very anxious as preteens. Before our study, we thought that resting brain activity *would* help us to predict anxiety. Even though our initial prediction was wrong, this finding is still important because it will help other scientists who might think of the same question when they try to help anxious kids. Now, those scientists can ask *new* questions about anxiety in the brain. We also learned that avoidant toddlers whose brains had a bigger warning signal as preteens were more likely to be anxious. This finding gave us an idea of which toddlers might develop anxiety. If we know which toddlers are more likely to be anxious, we might be able to help those kids before their anxiety becomes too severe.

Studying the brain and behavior can help us to understand why some children develop anxiety while other children do not. As we learn more about the brain, we can come up with new ways to help children feel less anxious. We want to find new ways to help anxious children, so that every child can feel happy, even when they are in new or scary situations.

## FUNDING

This work was supported by the National Institute of Mental Health, USA (R37HD17899 and U01MH093349) to NAF and the Intramural Research Program at the National Institute of Mental Health, USA (ZIAMH002782 and NCT00018057) to DSP.

## ORIGINAL SOURCE ARTICLE

Harrewijn, A., Buzzell, G. A., Debnath, R., Leibenluft, E., Pine, D. S., and Fox, N. A. 2019. Frontal alpha asymmetry moderates the relations between behavioral inhibition and social-effect ERN. *Biol. Psychol.* 141:10–16. doi: 10.1016/j.biopsycho.2018.12.014

## REFERENCES

1. Strawn, J. R., Lu, L., Peris, T. S., Levine, A., and Walkup, J. T. 2020. Research review: pediatric anxiety disorders—what have we learnt in the last 10 years? *J. Child Psychol. Psychiatry* 62:114–39. doi: 10.1111/jcpp.13262
2. Fox, N. A., Henderson, H. A., Marshall, P. J., Nichols, K. E., and Ghera, M. M. 2005. Behavioral inhibition: linking biology and behavior within a developmental framework. *Ann. Rev. Psychol.* 56:235–62. doi: 10.1146/annurev.psych.55.090902.141532
3. Halladay, L. R. 2019. Look out! how teams of brain cells help keep us safe from harm. *Front. Young Minds.* 7:63. doi: 10.3389/frym.2019.00063
4. Barker, T. V., Troller-Renfree, S. V., Bowman, L. C., Pine, D. S., and Fox, N. A. 2018. Social influences of error monitoring in adolescent girls. *Psychophysiology* 55:e13089. doi: 10.1111/psyp.13089
5. Ruiz, S. R. 2021. *Behavioral Inhibition Tasks* [Digital]. Available online at: <https://sruizdesign.wordpress.com/>
6. Birmaher, B., Khetarpal, S., Brent, D., Cully, M., Balach, L., Kaufman, J., et al. 1997. The screen for child anxiety related emotional disorders (SCARED): scale construction and psychometric characteristics. *J. Am. Acad. Child Adolescent Psychiatry* 36:545–53. doi: 10.1097/00004583-199704000-00018.
7. Harrewijn, A., Buzzell, G. A., Debnath, R., Leibenluft, E., Pine, D. S., and Fox, N. A. 2019. Frontal alpha asymmetry moderates the relations between behavioral inhibition and social-effect ERN. *Biol. Psychology* 141:10–16. doi: 10.1016/j.biopsycho.2018.12.014
8. Buzzell, G. A., Troller-Renfree, S. V., Barker, T. V., Bowman, L. C., Chronis-Tuscano, A., Henderson, H. A., et al. 2017. A neurobehavioral mechanism linking behaviorally inhibited temperament and later adolescent social anxiety. *J. Am. Acad. Child Adolescent Psychiatry* 56:1097–105. doi: 10.1016/j.jaac.2017.10.007

**SUBMITTED:** 05 April 2021; **ACCEPTED:** 22 June 2022;

**PUBLISHED ONLINE:** 12 July 2022.

**EDITOR:** Ryan E. B. Mruczek, College of the Holy Cross, United States

**SCIENCE MENTORS:** Vishal Shah and Elizabeth S. Lorenc

**CITATION:** Bernstein R, Galbraith J, Lakhlani D, Morales I, Buzzell GA, Debnath R, Leibenluft E, Pine DS, Fox NA and Harrewijn A (2022) Why Do Some Children Become Very Anxious? *Front. Young Minds* 10:691084. doi: 10.3389/frym.2022.691084

**CONFLICT OF INTEREST:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**COPYRIGHT** © 2022 Bernstein, Galbraith, Lakhlani, Morales, Buzzell, Debnath, Leibenluft, Pine, Fox and Harrewijn. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution

or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

## YOUNG REVIEWERS



### ANAND, AGE: 14

An avid learner of science and history, Anand enjoys biology and health science. His specific areas of interest are neuroscience and neurosurgery. Outside of academics, Anand's hobbies include participating in academic competitions and learning more about roller coasters. He is a black belt in Tang So Do karate.



### SPANDANA, AGE: 14

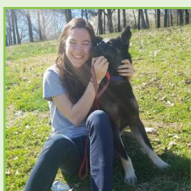
Hello, my name is Spandana! I like to read sci-fi and play volleyball. I find science interesting and love to learn about psychology and space. Some of my hobbies are drawing, listening to music, and playing my guitar.

## AUTHORS



### RACHEL BERNSTEIN

I am a research assistant at the National Institute of Mental Health in Bethesda, Maryland. In our research group, we work to understand more about anxiety disorders in children. I am especially interested in understanding more about how certain relationships, like parents and peers, impact the way children develop. Eventually, I hope to go back to school to become a clinical psychologist, so I can do more research and work as a therapist to help children and teenagers work through difficult times in their lives.



### JORDAN GALBRAITH

I am a research assistant at the National Institute of Mental Health in Bethesda, Maryland. Our lab focuses on children with anxiety disorders, and it is my job to help run research tasks with the children, like the ones in this article. In this way, we can learn more about anxiety and how to treat it. My goal is to go to medical school and to continue researching mental health issues like bipolar disorder and schizophrenia. I am most interested in how the various parts of the brain are connected to the behaviors we see in patients with these disorders.



### DEVI LAKHLANI

I am a research assistant at the National Institute of Mental Health in Bethesda, Maryland. Our group studies the development of anxiety disorders in children and adolescents. I am particularly interested in investigating neural processes and behaviors that differ between people with and without anxiety disorders. I plan to go to medical school and 1 day help people with mental health illnesses. I also hope to

continue researching mental health disorders to inform the scientific and medical communities about promising therapies and treatments.



### **ISAAC MORALES**

I am a research assistant at the National Institute of Mental Health in Bethesda, Maryland. Our lab focuses on pediatric anxiety, what it looks like in the brain, and how to treat it. My goal is to pursue a Ph.D. in clinical psychology, so I can research how to provide effective treatments to communities with fewer resources. I am particularly interested in behavioral parent training, community-level interventions, and building interdisciplinary partnerships. Through my future research and hands-on clinical experience, I hope to make mental health care more accessible for everybody.



### **GEORGE A. BUZZELL**

I am an assistant professor at Florida International University in Miami, Florida. My research focuses on how individuals self-regulate their behavior. For example, when we make mistakes, we must recognize such failures and then hopefully adapt our behavior to reduce future mistakes. I am interested in how these abilities develop across childhood and adolescence, as well as how they relate to social behavior and social anxiety. Ultimately, I hope that my work can help to improve the lives of children and their families.



### **RANJAN DEBNATH**

I am a researcher at the Leibniz Institute for Neurobiology, Magdeburg, Germany. I did my Ph.D. in Psychology at the University of Otago and worked as a postdoctoral fellow at the University of Maryland, College Park. In our lab, we study attention development throughout childhood. I am particularly interested in the development of auditory attention and related learning and memory processes. I use EEG to study attention development at the behavioral and brain level. In our group, we also investigate attention in children suffering from attention disorders, which happen frequently and are associated with learning disorders.



### **ELLEN LEIBENLUFT**

I am a senior investigator and chief of the Section on Mood Dysregulation and Neuroscience at the Intramural Research Program of the National Institute of Mental Health. My research uses cognitive neuroscience techniques and neuroimaging modalities to study brain mechanisms mediating severe irritability in youth.



### **DANIEL S. PINE**

I am the chief of the Emotion and Development Branch at the Intramural Research Program of the National Institute of Mental Health. I moved to this position in 2000, after 10 years of training, teaching, and research at Columbia University. Since graduating from medical school at the University of Chicago, I have been researching pediatric mental disorders. Currently, my group examines the degree to which mood and anxiety disorders in children are associated with brain function.



### **NATHAN A. FOX**

I am a professor at the University of Maryland, College Park. For many years, I have been studying how infants and young children differ from one another in their reactions to novelty and uncertainty. I have done longitudinal studies following infants until they are adults. My lab uses multiple approaches to study these individual



differences, including measuring brain electrical activity, observing and coding behavior, and asking questions via questionnaires and interviews. Come visit my lab website at [www.cdl.umd.edu](http://www.cdl.umd.edu).

**ANITA HARREWIJN**

I am a post-doctoral researcher in the Clinical Psychology Department of the Erasmus University Rotterdam in The Netherlands. I am interested in why some children get anxiety disorders while other children do not. I study various processes that may play a role in this, such as responding to stressful situations (such as giving a speech) and focusing attention on scary things. In my research, I measure anxiety by looking at brain activity, heart rate, sweat responses, and behavior. \*[anitaharrewijn@gmail.com](mailto:anitaharrewijn@gmail.com)

†These authors have contributed equally to this work