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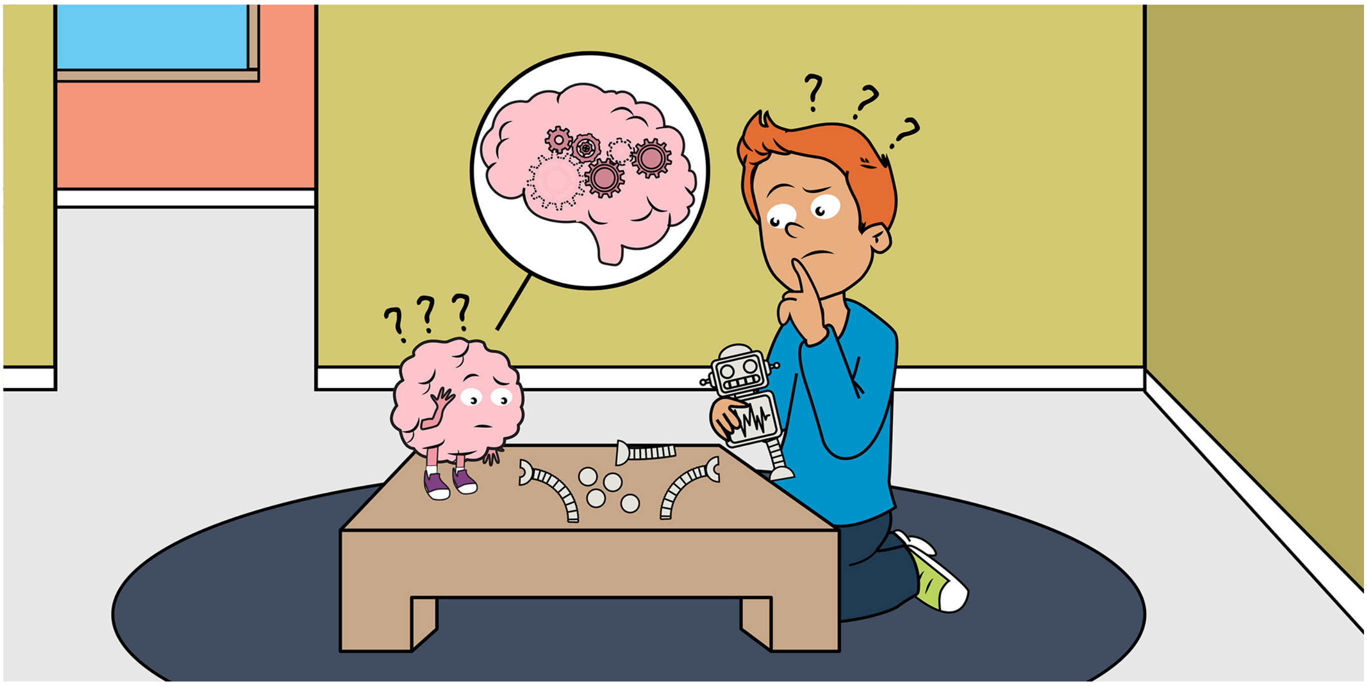

INTEGRATING BRAIN IMAGING RESULTS TO BETTER UNDERSTAND AUTISM

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YOUNG REVIEWER:

ELIZA

AGE: 11

In this article, we will describe a big summary (called a meta-analysis) of 16 brain mapping studies in people with autism spectrum disorder. People with autism often have difficulty with activities like decision-making, planning, and switching between tasks, which are called executive function (EF) activities. We found that certain parts of the brain become more activated when EF activities are being performed. In people with autism, these brain regions do not seem to communicate as well during EF activities as they do in people without autism. It is possible that these differences in the patterns of brain activity might be a big reason why individuals with autism tend to have trouble with executive function tasks.

BIG SCIENTIFIC QUESTIONS REQUIRE THE WORK OF MANY SCIENTISTS

Scientific research is a race for knowledge. As scientists, we ask important questions that we think will help people if we can find the answers. Every day, thousands of scientists all over the world wake up and conduct research to answer these big questions. Scientists publish the results of their studies in scientific journals so that other scientists can understand what was discovered. Because of the sheer volume of published studies, it can be hard to keep track of all the scientific discoveries on any given topic. It is incredibly important for scientists to keep up with scientific discoveries and the latest developments in knowledge. By understanding what is already known, we can be inspired to ask novel questions, create new solutions to existing problems, and answer the bigger, more difficult research questions.

When a research question is complex, it takes a team of scientists running lots of research studies to arrive at an answer. How do we draw conclusions from the data of a large number of scientific groups doing similar research studies? One way is to combine all the findings from the individual studies into one big answer, using a method called **meta-analysis**. Imagine if you were trying to lift something heavy. Is it easier to do this with one person, or a group of people? It is easier to lift with a team of people! Similarly, pooling the work of many scientists in a meta-analysis can significantly increase the amount of data available to answer the question, making the answer more reliable and applicable to more people. This is especially important for neuroimaging studies. In our study, we combined the work of many scientists to help do the "heavy lifting" of answering a big question about what is going on in the brains of people with autism when completing EF tasks.

META-ANALYSIS

A large-scale analysis of data from many studies pooled together. This method can significantly help make the answer to scientific questions more reliable and applicable to more people.

AUTISM SPECTRUM DISORDER (AUTISM)

A disorder affecting brain development. Autistic people sometimes have trouble understanding the world around them; they may perform repetitive actions or movements or have trouble with social experiences.

EXECUTIVE FUNCTIONS

A set of brain skills that work together to help us achieve our goals. They include planning, task-switching, stopping an impulsive thought or behavior.

AUTISM AND THE BRAIN

You might already know that **autism spectrum disorder**, also called autism, is a difference in how a child's brain develops that often affects how a person interacts socially [1]. While symptoms of autism vary, many children with this disorder have trouble using what are called the brain's **executive functions** [2, 3], which are a set of cognitive processes important for control of behavior and thought processes. The brain has a network of areas that work together to help us perform these functions. You can think of the brain's EF network as the principal of a school. The EF network tells other brain systems (the teachers) about their duties and assignments and monitors their performance to help the brain succeed in performing a task or executing a behavior by telling brain systems when to work, stop, or slow down. EF helps the school run properly so that each student performs well, and the school as a whole is successful. Differences in EF network functioning has been suggested as a reason for the difficulty some autistic individuals experience with decision-making, planning, switching tasks, and stopping an ongoing activity.

But not everybody with autism has trouble with EF, and sometimes people have trouble with *some* EF skills, like planning, but do well in others, like switching from one activity to another. To make things even more complicated, not all scientists agree on what is happening in the brains of autistic children when they engage in EF tasks. For example, some studies show that the anterior part of the brain, called the **prefrontal cortex** (PFC), is too active in autistic children during EF tasks. Others find that it is not active enough! As you can see, this is a big question. The mixed findings make it difficult to know whether EF differences really *are* an important component of autism.

PREFRONTAL CORTEX

The very front part of the brain, which is very important for performing executive function tasks.

HOW DO WE STUDY THE BRAIN IN AUTISM?

To study the activity of the brain (firing of neurons) in living humans, scientists use a technique called **functional magnetic resonance imaging** (fMRI). An MRI is a giant magnet that takes pictures of the brain and maps brain activity under various conditions [4]. Functional MRI detects changes in blood flow to specific regions of the brain, to determine which brain regions are activated during a specific mental state (for example, while at rest or not performing a task) or during active tasks that involve processing new information, which are called **cognitive tasks**. Many scientists use fMRI to look at what the brain does during cognitive tasks, so there are hundreds of published fMRI studies. Since MRI is an expensive procedure, each study usually has only a few participants (maybe 15–30 per study). Sometimes having a small number of participants makes it difficult to draw reliable conclusions that apply to most people. In addition, fMRI studies differ substantially in the types of MRI scanners used, how strong the scanners are, and the tasks participants complete during the study. These differences make it hard to identify patterns in the data and arrive at meaningful conclusions. This is where meta-analysis comes in! By using a meta-analysis of many fMRI studies, we created a summary of what scientists currently know about what is going on in the brains of autistic people as they perform EF tasks.

FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI)

A technique to take pictures of the brain while it is performing specific activities.

COGNITIVE TASK

Tasks that require mental processing or thinking and use of new information.

OUR BIG SUMMARY STUDY

We did an extensive online search and located 16 fMRI studies of EF in autism. We used a special type of meta-analysis to determine the most common brain areas found to be active across these studies. This special meta-analysis is called an **Activation Likelihood Estimation** (ALE). Using ALE allowed us to find overall patterns in the location of brain activity when participants engaged in EF tasks. The common location of brain activity was estimated in 739 people (a huge number!)

ACTIVATION LIKELIHOOD ESTIMATION

A special type of meta-analysis to determine the most common brain areas found to be active during a certain task or behavior

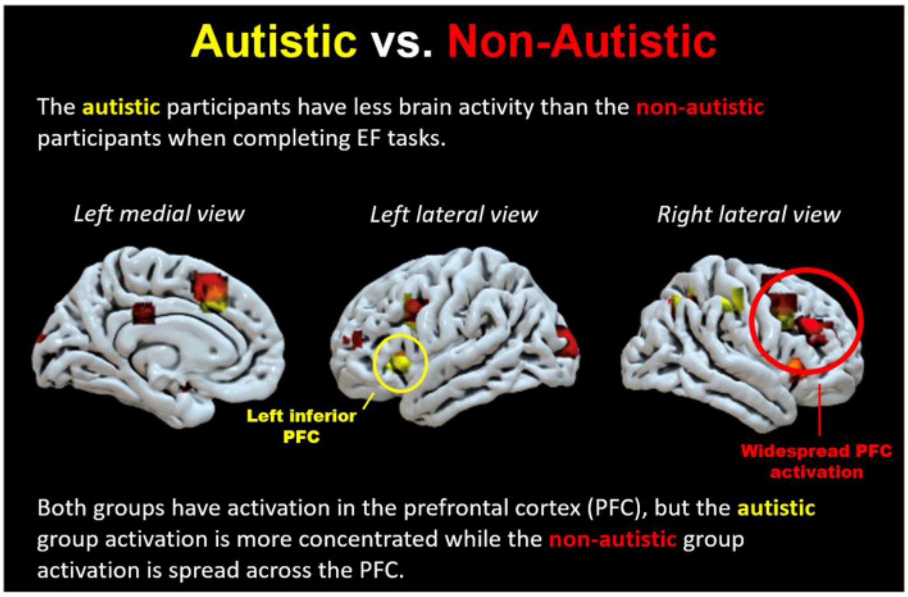

Figure 1

Figure 1

Brain activation in autistic and non-autistic people during EF tasks, as measured by fMRI. Brain areas activated in the autistic group are shown in yellow and those activated in the non-autistic group are in red. Orange indicates areas that were activated in both groups. The autistic participants had less brain activity than the non-autistic participants during EF tasks. You can see that both groups had activation in the PFC, but activation was more concentrated in the autistic group, while activation in the non-autistic group was spread across the PFC.

between the ages of 7 and 52 years. 356 participants were autistic and 383 were not autistic.

We looked at which brain areas were active in autistic and non-autistic study participants as they performed EF tasks (Figure 1). At first glance, the activation of the PFC, which is known to be extremely important for EF functions, looked similar in both groups. But a closer look showed that PFC activation in the autistic group was occurring at slightly different spots than it was in the people without autism. We also found that the autistic participants' PFC activation was confined to a limited area compared to the more widespread PFC activation seen in non-autistic participants. In non-autistic adults, the connections between the PFC and a different brain region called the posterior parietal cortex (toward the back of the brain) are critical for completing EF tasks. It may be that the lack of widespread PFC activation in the autistic participants reflects trouble with getting multiple brain areas to work together properly to accomplish EF tasks. In other words, in autism, regions of the brain may be poorly connected and not communicating with each other effectively.

When we grouped research studies by age of participants, and compared groups of people under or equal to 25 to those over 25, we saw a different pattern (Figure 2). While both autistic and non-autistic groups showed changes in activation with age, we saw no significant brain activity in important EF areas in autistic people under age 25 during EF tasks. This was very different from the non-autistic participants who showed PFC activation in both age ranges. In autistic participants older than 25 years, brain activity was seen in areas that are not usually associated with EF!

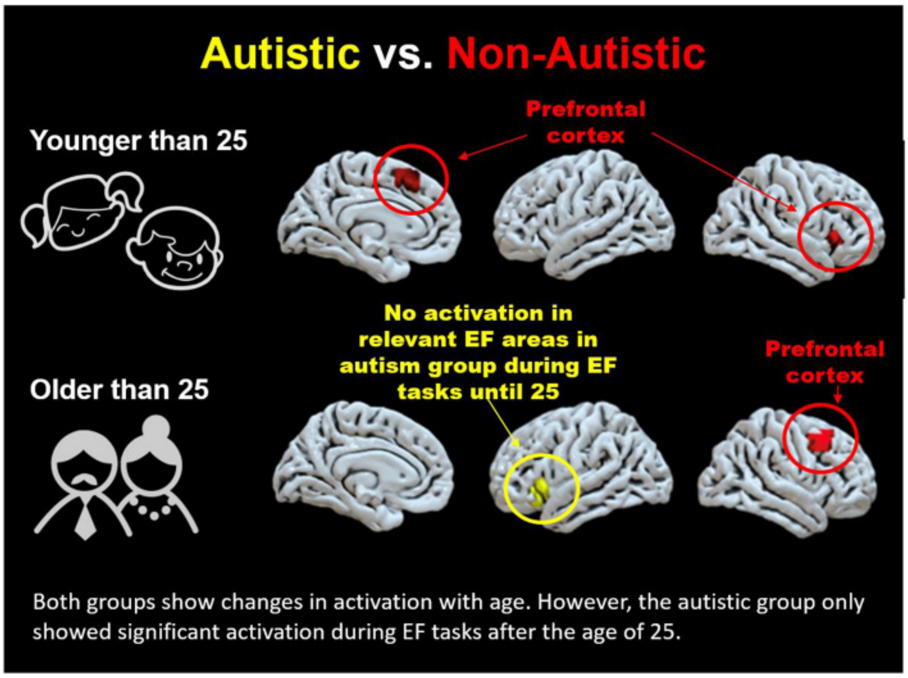

Figure 2

Figure 2

Brain activation differs by age. Meta-analysis was used to compare brain activity of autistic (yellow) and non-autistic (red) participants who are younger than 25 to those who are older than 25. While both autistic and non-autistic groups showed changes in activation with age, autistic participants under 25 did not show activation in the PFC while performing EF tasks (top row). After the age of 25, there was some PFC activation in the brains of autistic participants (bottom row). Therefore, there was less brain activity in important EF areas in people with autism under the age of 25 during EF tasks. In comparison, the non-autistic group showed PFC activation in both age ranges.

SO WHAT?

This study is important for two reasons. First, it gives us a detailed picture of what the EF network looks like in the autistic brain. The results demonstrate that differences in the levels and patterns of EF network function may cause some of the difficulty autistic individuals experience in their daily lives, particularly with tasks like problem-solving and decision-making. Specifically, decreased activity of the brain's PFC might be a big reason why people with autism have trouble with EF tasks.

Second, this study shows the importance of meta-analyses as tools for answering big scientific questions. Meta-analyses can increase the power of a research study by combining data on many participants, so that the conclusions of the study are more reliable and generalizable. Meta-analyses can also help identify the gaps in research and new questions that still need to be answered. Our hope is that our meta-analysis will help other scientists create new research that can further improve the understanding of the brain in autism. More research must be done to determine whether the brain activation patterns we found are common in autism. If they *are* common, the results of this study could be used to design training to help autistic people to improve their EF functions, such as planning or switching between tasks. Hopefully, by pooling the hard work of many scientists, we can help autistic people to successfully engage in social activities and cognitive tasks that were previously difficult for them.

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ORIGINAL SOURCE ARTICLE

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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.

YOUNG REVIEWER

ELIZA, AGE: 11

Hi! My name is Eliza. I love to read and bake muffins. I have two dogs, named Arnie and Benji. I also like to do math with my dad. My mom has a Ph.D. in neuroscience, which I think is really interesting.

AUTHORS

KAITLYN E. MAY

I am a doctoral student at the University of Alabama, studying to be an educational neuroscientist. I am interested in how the brain enables children to be successful in school and in life. I am especially interested in how children's higher-level thinking helps them socially. To study this, I use behavioral experiments and brain mapping. I am also very interested in making science exciting and understandable, especially for kids like you! *kmay3@crimson.ua.edu

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I am a cognitive neuroscientist. I am interested in how the brains of people with autism are different. I am especially interested in how the similarities and differences in brain functioning in people with autism affect the ways that they think, act, and relate to others. I use brain mapping methods like magnetic resonance imaging (MRI) to study the structure, functions, and connections of the brain. I am a professor at the University of Alabama.