Investigating altered connectivity in the depressed adolescent brain

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INTERVIEWS | NEUROSCIENCE

Depression is a common mental disorder among adolescents, yet the underlying biology is not well understood.

In this interview from the 2023 meeting of the Society for Neuroscience (SfN) (11–15 November; Washington DC, USA), Margot Wagner (left), a postdoctoral researcher at the University of California, San Diego and the Salk Institute (both CA, USA), discusses her results from a project using deep learning techniques to obtain biomarkers from MRI scans from the Adolescent Brain Cognitive Development (ABCD) study.

Could you tell us about the study you presented at SfN?

We looked at functional connectivity in depressed adolescents. Functional connectivity is different from structural connectivity, as there is no physical connection between the

have been implicated in various mood disorders, not just depression. They are the central executive network, the default mode network and the salience network. The central executive network is primarily active during cognitive tasks and the default mode network is primarily active when you're at rest, ruminating or self-reflecting, but not actively doing any task. The salience network is in charge of switching between these and maintaining some kind of balance. We found that there is increased connectivity in the salience, in the default mode, and interestingly, in the connection from the salience to the default mode network. So, we found this preference in depressed adolescents towards the default mode network, which is theorized to be causing the symptoms of rumination or internalizing that you see in depressed adolescents as well as adults.

What techniques did you use in this project?

We used a couple of new and exciting techniques. We used deep learning models for automatic segmentation of the neuroimaging data. This is usually a very slow step in processing, but this alternative method has been trained on synthetic images that were created with generative AI to help be more robust to different heterogeneous conditions, for example. Because the ABCD study is such a big study, there are multiple different scanner types, and this method helps to get more consistent results in the segmentation between scanner types.

We also used a novel method of obtaining connectivity that allows us to have directed functional connectivity. The old methods could just tell us that region A and region B were connected, but we didn't know if A was going into B or vice versa. Now, with this new method, we can establish the connection from A to B and the separate connection from B to A.

What challenges did you face in this project?

Lots. I think with big data, there's a lot of inherent challenges. I think the biggest challenge, which I mentioned before, is the differences in how these images are obtained between sites – there are 21 different collection sites – so you have to account for that somehow. I think something to keep in mind with big data in general is being aware of what might come across as a false correlation and correcting for those things.

It could have a huge impact. Basically, we're on a mission to get rid of the Diagnostic and Statistical Manual of Mental Illnesses (DSM). If we can completely oust it from the field, that would be the goal. This research helps drill down on these very real biomarkers, which will help better diagnose people. It'll also help with treatment because it gives a lot more insight into where these differences are actually occurring and how we can help. Additionally, it's been shown in other literature that these kinds of alterations in functional connectivity may even show up before some of the behavioral symptoms that are assessed with the DSM, so earlier intervention will help prevent serious mental health outcomes.

What's next for this project?

There are tons of directions for this project. We'd really like to integrate this with some of the other measures that are included in ABCD. What's great about the ABCD study is it's not just biological measures, there are cultural and environmental measures too. So, we'd like to see if connectivity is the most important difference or where it ranks along those things. So, accounting for sex differences, regional differences, income and other demographics. Also, now that we have these connectivity maps of the subjects, can we use deep learning to automatically classify the individuals as having depression or not? Then, because ABCD is longitudinal, we can actually use the exact same methods that we have used in this project to look at the follow-up years as well and see how these trajectories of connectivity change over the course of the disease.

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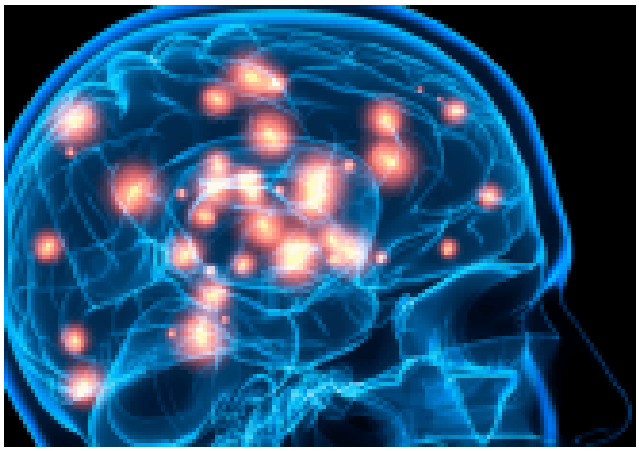

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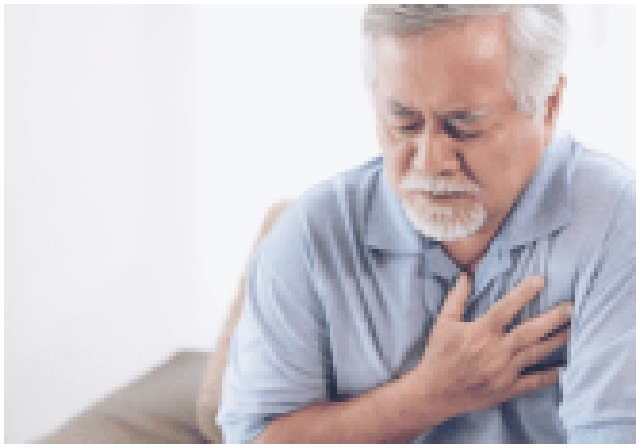

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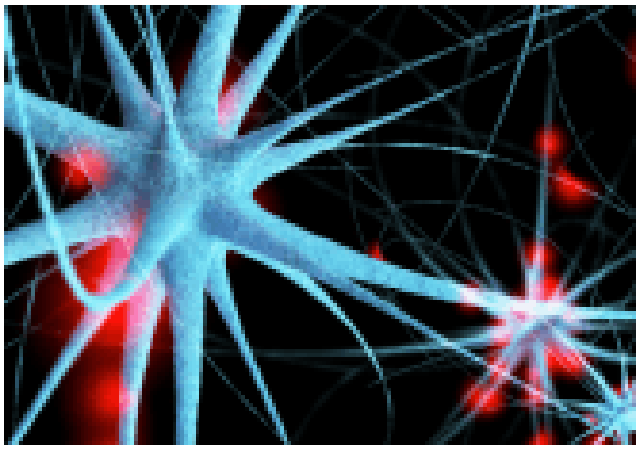

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