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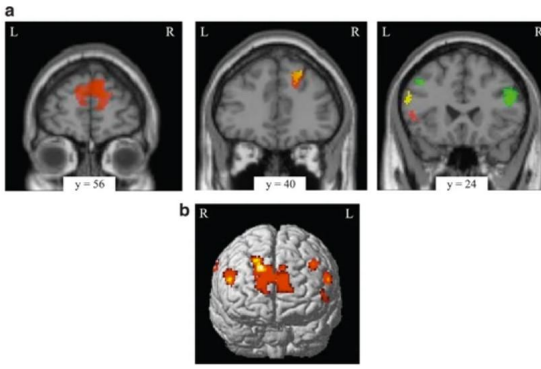
Markers for Anxiety analyzed in Brain Scans of Parents and their Children

Introduction

Anxiety is a common mental disorder that 19.1% of adults in America suffer with an anxiety disorder ("Anxiety"). This high prevalence of anxiety in America is concerning. Anxiety can significantly decrease one's quality of life as they may be more likely to avoid certain situations out of fear. People with an anxiety disorder can experience a racing heart rate, sweating, headaches, feelings of apprehension or dread, and irritability. These symptoms can have debilitating negative impacts on everyday life and lead to depression. Learning more about the neurobiological factors behind anxiety disorders through brain scans will help discover the causes of anxiety, identify new anxiety medications, and provide powerful information on how to prevent the onset of anxiety. This could be life changing for many, enabling them to live happier, more productive, and more social lives.

Anxiety disorders have been shown to correlate to direct distinguishable changes to one's brain. These effects are able to be seen through different brain imaging methods. These methods include fMRI (functional magnetic resonance imaging) in which brains are scanned live to analyze different activities and activation of different parts in the brain. A study done at the University of Rochester medical center has used fMRI in a study to view participants' brains (some of these participants who report having anxiety) while playing a virtual reality game where there were known safe areas and danger areas. Those suffering with anxiety showed brain activity that indicated they were associating safe areas as danger areas (Smith). fMRI scans have also shown that those with an anxiety disorder display a decreased connection of pathways in the amygdala of the brain (Paradiso). fMRI imaging employs the principle of using radiofrequency pulses and a magnetic field; the energy of protons released in the patient as they realign with the magnetic field is measured. A benefit of this imaging technique is that it does not use harmful ionizing radiation. A constraint of this type of imaging is that the magnetic field needed is very strong so one needs to be careful what they bring into the detector. Additionally the radiofrequency energy can heat the body so it is best to not have prolonged imaging (Center).

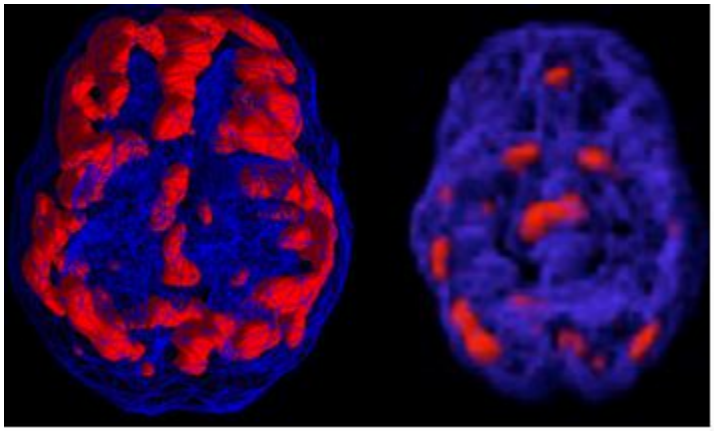
The image to the right is from fMRI scans of people with anxiety and non anxious control (Price). The red shows areas in the prefrontal cortex where the anxious participants had greater levels of activation from negative words than the non-anxious controls (Price). This study shows how fMRI imaging can be



(Price)

utilized to show brain differences in those with and without an anxiety disorder because the participants with anxiety disorder showed greater brain activation reacting to negative words than their non-anxious counterparts. This makes sense, because those with anxiety tend to be more worried about negative thoughts than those without anxiety.

Another imaging technique that has been used to see anxiety within the brain is known as a single-photon emission computerized tomography (SPECT) scan. This scan utilizes a radioactive tracer (probe) which emits gamma rays seen by a camera detected by a CT scanner. This scan is used to create a 3D map of blood flow in the brain (Spine). By seeing where blood flow is in the brain one can see what parts of their brain are most active; this helps to indicate how people are thinking and the emotions they are experiencing.



(Spine)

SPECT scans done of people with anxiety disorders have been associated with increased blood flow in the prefrontal cortex (Maron). As shown in the image above (Edwards), the overactive brain flow is depicted in the left image from a brain of someone with an anxiety disorder and the right brain is the image of a healthy brain from someone without an anxiety disorder (Edwards).

Specific Aim 1: Find if there is a positive correlation regarding which scenarios induce the most anxiety in the brain between a child and their parent by rank-ordering FMRI scans

Anxiety is a complex mental disorder that has a large variety of contributing factors. However, there have been studies that have shown that a parents' prevalence of having anxiety can greatly increase their child's chance by a factor of four of also developing an anxiety disorder (Kalin). Using these SPECT and fMRI scans, I intend to analyze anxiety markers in the brain scans of both a parent and their child who both identify as suffering from an anxiety disorder. I want to devise a test using a virtual reality game. This test would introduce different possible anxiety-inducing situations such as hearing negative comments, walking down a dark hallway, standing on a stage in front of people, and more. As controls I would need to also run the test on parents and their children who both do not have an anxiety disorder. I would be testing to see if children and their parents who both have an anxiety disorder have similar brain activity during the virtual reality game. I would specifically be trying to see if the children and parents' brain scans are positively correlated regarding which specific situations induced the

most and least anxiety. Like in the study done by Price, I would utilize fMRI imaging. Per participant, I would rank-order the anxiety inducing situations in the video game from causing the highest levels of activation to lowest levels of activation. I would then see if there is a positive correlation between the rank-ordered list of a child and to the rank-ordered list of their parent. The significance of finding the similarity of brain scans between children and parents with anxiety will further provide evidence for the genetic link of anxiety as well as provide information that specific types of anxiety are inheritable (i.e. find correlation that the same types of situations that makes a parent anxious also makes their child anxious). This information could help adults identify their own anxiety and use this information to predict what situations could make their children anxious. By having this information parents could make sure to introduce these potential anxiety inducing situations in healthy ways so that their child does not develop the same anxiety as they did. Being able to prevent the onset of an anxiety disorder could eliminate the need for future medication and therapy while also improving people's quality of life.

Limitations and Solutions

A limitation is the strong magnetic field from the fMRI machine (Center). To overcome this issue it is necessary to be hyper vigilant regarding what is let into the imaging area. All safety precautions need to be taken as far as making sure no one wearing jewelry, zippers, taking painkillers, having a pacemaker, and pregnant women partake in the study and undergo imaging (FMRI Safety). Another risk is the fact that anxiety levels may be higher due to the fact that participants are undergoing a study and are nervous to see their results. To combat this participants will have their blood pressure and heart rate measured before they begin the test to make sure they are relaxed before they undergo scanning.

Specific Aim 2: Study the differences in how anxiety presents itself in children versus adults using SPECT scans to find the magnitude of fluorescence within the "fear network

My second specific aim is to compare the level of activation of the brain's fear network between the groups with anxiety and the control groups without an anxiety disorder. Past studies have shown that those with anxiety disorders areas of the brain known as the "fear network" (the anterior cingulate cortex and the insula) within the brain demonstrate increased activation when provoked with stressful scenarios (Holzschneider). I would compare these levels of activations between 4 key groups: adults with anxiety, adults without, children with anxiety disorders, and children without anxiety disorders. Specifically how I would do this would be using the SPECT scan shown above. Looking specifically at the areas of the brain associated with anxiety (amygdala,prefrontal cortex, insula) I would measure the surface area and level of brightness that it is lit up. Higher surface area and fluorescence levels would indicate higher anxiety levels. By comparing the levels of activation within these four groups I would be aiming to see which

scenarios cause more anxiety in children versus adults. By studying which situations seem to be anxiety inducing between children and adults. I would be able to present information key for the differences between children and adults in treating anxiety.

Limitations and Solutions

The limitation of using the SPECT scan for this second aim is that it can produce inaccurate results due to potential risks from participants moving during the scan and if the SPECT scan is improperly spatially aligned (Livieratos). To account for these potential risks controls will need to be used as tests before the test is run on the participant. Furthermore, making sure effective training of how to do an accurate SPECT scan will need to be done before scans can be performed.

Training Needed

To conduct this study extensive training would be required. One must be trained in using SPECT and fMRI imaging. Additionally, one must be trained in how to interpret the images of these scans in order to make comparisons between the scans. Furthermore, one should be trained in speaking to the participants in the study to make sure they are comfortable with the tests. Considering that the tests are measuring anxiety in the brain, it is especially important that they feel as relaxed as possible before the test in order to produce the most accurate results in the scans.

Additionally, there are many classes that could be used to help with the training for this project. These classes are found on the UCSD graduate degree programs site and include: BENG 141: Introduces students to a wide array of biomedical imaging techniques and BENG 280: Graduate level class which goes over the principle of bioimaging (Graduate Degree Programs).

Due to this project's focus on anxiety,which is mental health related, graduate level psychology classes would also be valuable training in order to complete this project. These include: PSYC 231: Tools for Experimental Analysis and NEU: 200C: Basic Neuroscience (Graduate Degree Programs).

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