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Anxiety, Depression, and Their Effect on the Limbic System in Autistic and Neurotypical Adolescents

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Abstract

This study explores various effects of stress-induced anxiety and depression on neurotypical and autistic adolescents within the limbic system. Through the outcome of the study, the groundwork was laid to effectively bridge the gap of required stress treatment for autistic adolescents. The research utilized the methods and procedures of a systematic review. There were several major differences in how the autistic and neurotypical brains respond to anxiety and depression disorders such as generalized anxiety disorder and major depressive disorder. These included levels of cortisol secretion, amygdalar structure and activity, and hippocampal volume. In individuals suffering from depression with autism spectrum disorder (ASD), amygdalar structure decreased in volume while encountering blunted activity in neurotypical individuals. Looking at cortisol activity, its levels were found to be inconsistent and dysregulated. On the other hand, in neurotypical individuals, hippocampal volume decreased as well as a decrease in gray matter volume in this region. While the components of the limbic system affected are similar, their structural, volumetric, and/or functional changes are variable, which caters to the fact that ASD varies individually. Along with this, the study brings light to the severity of depression and anxiety in adolescents with ASD compared to neurotypical adolescents.

Keywords: Behavioral and social sciences, Sociology and social psychology, Autism spectrum disorder (ASD), Depression, Anxiety, Adolescents, Limbic system

1. Introduction

This study investigated how stress-induced anxiety and depression affect both neurotypical and autistic adolescents at the level of the limbic system. Autism spectrum disorder (ASD) is a neurodevelopmental disorder that enhances certain components of the brain but consequently inhibits other areas. It can be defined by repetitive behaviors, social deficits, and language abnormalities. Autism is also characterized by its heightened comorbidity with other mental health diagnoses, such as attention deficit hyperactivity disorder (ADHD), generalized anxiety disorder, and major depressive disorder (Redlich et al., 2017). The disorder itself varies for each individual and not all neurological changes and symptoms cannot be coined as umbrella terms for ASD; some individuals may have heightened visual sense while others exhibit specialization in a subject of interest. From childhood to adolescence, autism displays itself neurologically through size changes in the hippocampus and overall accelerated brain growth to halted growth and possible degeneration of areas like the amygdala and hippocampus (Courchesne et al., 1997). The degeneration of these components leads to deficits in emotional input processing and episodic memory.

Regarding the cause of these, it could be speculated that it may be associated with anxiety and depression that many neurotypical adolescents face. Adolescent-onset major depressive disorder (MDD) is one of the most prevalent

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conditions in modern adolescents. This condition is characterized by symptoms of depression, whether from anxiety and stress or suicidal behavior. Little literature exists of neuroimaging adolescent-onset MDD but the few that exist provide evidence of increased amygdala activity as a result of negative stimuli along with decreased hippocampal volume and increased sensitivity of the limbic system.

Researching the differences in brain response to anxiety and depression in neurotypical and autistic teens is vital in understanding future medical therapies that can positively impact society. Analyzing these differences can also help future diagnoses because the symptoms of autism will be present in brain responses under stressful and anxious circumstances. Adolescents are the ideal group to examine due to the fact that teenage brains are still developing and that they are typically under the most stress and anxiety at that age. This review examines the different responses in the limbic system, the part of the brain responsible for emotions, between neurotypical and autistic individuals with a specific focus on the amygdala's response to positive and negative stimuli. The activity of the amygdala specifically, in response to positive and negative stimuli, will also be looked at. It was observed that cortical dysgenesis and white matter abnormalities in autistic cases, including thickened cortices, high neuronal density, irregular laminar patterns, and poor gray–white matter boundaries. Cortisol is a hormone produced by adrenal glands above the kidneys. It helps the body use glucose, protein & fats. It is often called the body's main stress hormone. Abnormal cortisol activity and differences in the hippocampus and prefrontal cortex will be analyzed throughout this paper. The study compares the different responses in the limbic system in autistic and neurotypical adolescents when under stressful conditions, anxiety, or a depressive state.

2. Literature Review

Autism is a neurodevelopmental disorder that causes drastic neurological changes in certain areas of the brain, which can lead to affected sensory or visual input processing. Symptoms of autism generally include social deficits, language implications, and repetitive behaviors/actions that are seen as "unnatural". However, symptoms vary individually in autism resulting in the disorder being dubbed ASD, or autism spectrum disorder, where there is a spectrum of disorders ranging from Asperger syndrome to pervasive developmental disorder. ASD has a high comorbidity rate (Palmen et al., 2004) with mental health disorders such as generalized anxiety disorder or major depressive disorder, both of which are also present in neurotypical adolescents. Due to the comorbidity, it was speculated as to what neurological changes would occur in autistic adolescents, specifically in the limbic system: a composition of brain structures responsible for creating emotional and behavioral responses. If these alterations in the limbic system were attributed to anxiety or depression, then by using MRIs, radiologists would be able to determine the presence of anxiety or depression in adolescents with ASD. This study focuses on examining the neurological effects of stress-induced anxiety and depression on the limbic system in adolescents with ASD.

In the studies analyzed, there was a specific focus on the amygdala: a component of the limbic system responsible for emotion processing. The amygdala in neurotypical adolescents is generally more active, and activity has been seen to spike when exposed to negative emotional stimuli (Redlich et al., 2017). In teens with ASD, however, the amygdala has shown rapid development in childhood, followed by a deceleration point where null volume differences are exhibited (Herrington et al., 2017). Another component of focus in the limbic system affected by ASD is cortisol release. With a cortisol serum test, the paper by Spratt et al. (2011) found increased cortisol and salivary levels 20 to 40 minutes after blood was drawn. Methods of data collection and visualization included but were not restricted to MRIs, fMRIs, anxiety questionnaires (eg. GAD-7), and depression questionnaires (eg. PHQ-9). Across the reviewed literature, the results showed a general consensus of decreased amygdala volume and activity in adolescents with autism and higher cortisol levels.

2.1 Brain Characteristics of Autistic Individuals

Regarding its effect on the limbic system, anxiety, and depression can result in functional and volumetric changes in components of the limbic system, such as increased cortisol levels and/or heightened activity of the amygdala. There are also similar changes in the limbic system in individuals with autism. For example, people with autism have

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shown abnormal levels of hormones and neuroactive substances, including cortisol, which plays a role in the stress response, leading to higher levels of anxiety and depression.. In autistic people with anxiety or depression, the amygdala can exhibit hyperactivity or increased responsiveness. Understanding the implications of anxiety and depression on the limbic system is vital to discern the divergent patterns of brain response between autistic and neurotypical adolescents, shedding light on the distinctive challenges encountered by individuals with autism in relation to their mental well-being.

The Amygdala

The Amygdala Theory of Autism (Baron-Cohen et al., 2000) explores the role of the amygdala in social intelligence and how it is one of the main brain regions that is abnormal in an autistic individual. This research utilized structural MRIs and found that in individuals with autism, there is evidence of an amygdalar activity deficit and reduced amygdalar volume. Patients with ASD exhibited reduced temporal lobe blood flow and decreased amygdala activation during mentalizing tasks, providing direct evidence of a deficit of amygdala function in autism. This research study was good because it analyzes how the structure and functionality of the amygdala varied in autistic individuals.

Altered Development of Amygdala-Connected Brain Regions in Males and Females with Autism (Lee, et al., 2022) explains how the amygdala-connected network undergoes significant developmental changes in early to middle childhood of autism. These changes were exclusive to sex and age with differences in sebgenual volume and gyri between men and women. They obtained these results by taking brain scans of neurotypical and autistic individuals of both genders while also conducting MDMR analyses on gray matter for volumetric comparisons.

The study, In a study by Seguin et al., (2022) they examined amygdala volumes for children and teens with anxiety and ASD, attention deficit hyperactivity disorder, or obsessive-compulsive disorder (Seguin, et al., 2022) and explored if the potential alterations in the volume of the amygdala are associated with anxiety in adolescents with autism. While conducting their study, the majority of their participants were under 21, and mainly adolescents with neurodevelopmental disorders (ADHD, ASD, OCD) were selected. They found that children and adolescents with ASD had larger anterior amygdaloid areas in relation to higher anxiety scores.

Herrington et al. (2017) explore if individuals with ASD and occurring anxiety disorders can be differentiated from individuals with ASD alone by only looking at the amygdalar volume. Tests were conducted with a neurotypical group of men and women and an autistic group of men and women, further subdivided into smaller groups of individuals with and without anxiety disorders. Utilizing Post Hoc regression analysis, the results of this study found that anxiety in ASD has been shown to decrease the volume of the right amygdala in an area corresponding to the lateral nucleus. This study is significant because it looks specifically at the parts of the amygdala that are different in autistic individuals with anxiety present.

Cortisol Levels

Enhanced Cortisol Response to Stress in Children in Autism (Spratt, et al., 2012) explores the hypothalamic–pituitary–adrenal (HPA) axis stress response in children with autism spectrum disorder compared to that of developing children. The study utilized a group of 20 individuals with autism and 28 healthy neurotypical adolescents and found that the serum cortisol levels obtained during the blood draw were significantly higher in the autism group compared to the control group. Children with autism showed a greater peak cortisol response 20 minutes after the blood draw compared to those without autism, and their salivary cortisol levels remained above the baseline even at 40 minutes. Based on these finding, a pattern can be seen of literature reinforcing the differences between those with and without autism through differences in hormonal production.

2.2 Brain Characteristics in Neurotypical Individuals

Adolescent-onset major depressive disorder (MDD) is one of the most prevalent conditions in modern adolescents. One of the biggest changes that occur neurologically in the adolescent mind involves one of the brain's most significant networks and nerves called the limbic system. The limbic system is responsible for behavioral and emotional response, the focus will be on the response of the limbic system as a result of depression or anxiety. As

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adolescents are undergoing neurological changes, they are more prone to encounter MDD. Their limbic system itself is still developing. As far as the effect on the limbic system is concerned, MDD and anxiety are responsible for increasing cortisol levels and heightening amygdala activity in the limbic system (Redlich et al., 2017) as will be discussed in the studies that follow. These effects will be compared to those of an autistic individual as discussed in the previous section.

The Amygdala

In the study, Blunted Amygdala Activity is Associated with Depression Severity in Treatment-Resistant Depression, by Ferri et al. (2018), the researchers examined amygdala activity in individuals with treatment-resistant depression (TRD) compared to healthy controls (HCs). Through fMRI tasks involving emotion and gender labeling, they found that TRD patients exhibited reduced amygdala activation during affect labeling, which correlated with higher depression severity. This blunted amygdala activity during emotional processing was associated with the worsening of depression symptoms, including in cases of TRD.

The study by Roozendaal et al., (2009) investigates the impact of stress on the amygdala's role in memory. The research identifies neural changes induced by stress in the amygdala, affecting cognitive performance, anxiety in affective disorders, and interactions with memory-related brain regions like the hippocampus and prefrontal cortex. These stress-induced alterations can disrupt memory consolidation, recall processes, and the formation of aversive memories.

Cortisol Levels

The paper by Dedovic *et al*., (2009) examines the regulation of stress-induced cortisol secretion in the limbic system. Utilizing the Montreal Imaging Stress Task (MIST) and serial subtraction paradigm in fMRI environments, the study reveals reduced limbic system activity, particularly in the hippocampus, when exposed to stress. Moreover, a correlation is observed between increased cortisol secretion and decreased activity in the orbitofrontal prefrontal cortex during psychological stress tasks.

2.3 Summary

The previously described literature gave an in-depth review of the different effects that anxiety and depression have on the adolescent autistic and neurotypical limbic systems. More specifically, the studies had shown a focus on certain components but not restricted to the amygdala, the amygdala-connected network, the hippocampus, and cortisol levels in response to stress. The literature surrounding the amygdala has all used functional or structural MRIs and several forms of analyses to gather results which, as a general consensus, showed volume differences in separate areas of the amygdala. Overall, the studies had very thorough methods for data collection and analysis but in relation to the research question, the papers by Lee et al. (2022) and Herrington et al. (2017) did not have an adolescent population, therefore it would be false to assume that all the changes in the amygdala apply to adolescents with ASD. In the future, it would be optimal to have a population consisting of a wide range of ages so the results would not only show brain changes at a specific age group but possibly create a timeline as to how the brain changes in response to anxiety or depression in ASD throughout a lifetime. The ASD population also showed an increase in cortisol response. From the source, Enhanced Cortisol Response to Stress in Children in Autism (Spratt et al., 2012), the group of autistic individuals that were being tested was found to be significantly older, but the two groups were similar in terms of race and gender. So similar to other literature, results cannot be applied to adolescents.

Literature having a neurotypical adolescent population with either depression or anxiety has shown similar components of the limbic system affected. The amygdala, for example, has exhibited heightened activity, structural alterations, and functional alterations in response to depression and stress. Both studies utilized functional or structural MRIs (and their tasks) to gather information, along with several forms of analyses. The studies had in-depth results and gave insight into other areas affected by stress, such as the hippocampus and prefrontal cortex.

Both the neurotypical and ASD populations showed volumetric, structural, and/or functional changes to the amygdala, along with increased cortisol secretion in response to stress. Through a systematic review, this paper will

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evaluate the current research on the effects of stress-induced anxiety and depression on the limbic system between autistic and neurotypical individuals.

3. Methodology

To conduct a thorough literature search for the research paper, a systematic approach was implemented using a variety of academic databases and libraries. A systematic review was conducted of four academic databases and libraries. the search spanned a specific timeframe, encompassing publications from as early as 1997 to the present day. This created the ability to gather relevant and up-to-date information pertinent to the research. To ensure a focused and targeted search, suitable search terms were employed regarding the target population (adolescents), specific conditions (autism, anxiety, stress, depression), and relevant neurobiological factors (limbic system, cortisol levels, amygdala). By incorporating these terms, twenty-seven studies were retrieved that explored the relationship between these factors in adolescents.

In devising the inclusion and exclusion criteria, both theoretical and empirical factors were thoroughly considered. The following inclusion criteria were decided to be incorporated: a specific focus on studies involving individuals within the age range of 13 to 19. This parameter created the ability to concentrate more effectively on the pertinent developmental phase. Moreover, studies concerning both neurotypical and autistic individuals were also included, intending to make a comparative analysis of anxiety and depression within the brain between these two groups.

Conversely, the approach to the exclusion criteria aimed to refine the search and ensure the utmost relevance of the selected studies. Studies that significantly deviated from the specified age range (13-19 years) were excluded to maintain a targeted emphasis on the adolescent population and avoid any potential confounding factors stemming from varying developmental stages. Additionally, studies that focused on individuals with brain conditions other than autism, anxiety, and depression were excluded as such conditions could potentially interfere with investigating the limbic system. This criterion aimed to maintain a sample group with greater homogeneity and reduced confounding factors unrelated to the specific research inquiry.

The literature that was analyzed implemented various techniques to investigate the activity of the limbic system in response to stress-induced depression, specifically MDD. One of these techniques included a variety of fMRI tasks that were conducted with treatment-resistant depression (TRD) patients, as well as with healthy controls (HCs). These tasks included the identification of emotion on faces (affect labeling) and gender on faces (gender labeling), as well as passively viewing faces. These tasks were associated with analyzing amygdalic response and activity. The amygdalic activity was also compared with depression severity which could be assessed from these. Two other methods were also implemented in studies looking at analyzing cortisol levels. These include the Montreal Imaging Stress Task (MIST) and serial subtraction paradigm in fMRI environments. These techniques helped reveal reduced limbic system activity, particularly in the hippocampus, when exposed to stress. It was also useful in looking at activity levels in the orbitofrontal prefrontal cortex.

In the analyzed literature, any functional, structural, volumetric, or size differences in components of the limbic system between neurotypical and autistic individual after exposure to a form of anxiety and depression were focused on. Specific focus was placed on the amygdala, hippocampus, and cortisol release in the limbic system. For baseline statistics on these limbic system components, articles with individuals with just ASD and not anxiety or depression as a comorbidity were utilized. In addition to this, certain descriptive statistics were integrated as well, such as the autism comorbidity rates and neurotypical depression/anxiety rates, as introductory information. In order to gain the results and give necessary background information, these were the employed expectations that were used.

4. Results & Analysis

Over the analysis of literature pertaining to limbic system activity during depression or anxiety in individuals with and without ASD, it was found that similar components of the limbic system are affected in individuals with ASD, such as the amygdala, hippocampus, cortisol levels, and others.. Literature regarding the amygdala, its subnuclei, and its connected network has shown variable results in autistic adolescents, such as stress-induced anxiety and

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depression being associated with decreased right amygdala volume, central nucleus volume, cognitive functioning, poorer executive functioning, and/or activation of error-related negativity. Neurotypical individuals showed similar but less severe neurological reactions to anxiety along with increased blunted amygdalar activity in response to depression severity. In regards to cortisol levels, the ASD group had shown a higher peak of cortisol secretion after salivary extraction compared to neurotypical individuals in response to stress. The average number of participants in each study who had ASD was about 55 per study. On the other hand, the average number of participants in each study who were neurotypical was about 90 per study. The general ages of individuals in the studies range from 10 to 19 with and without autism. Throughout these studies, some common technologies and analyses used include fMRIs, MRIs, SPSS, MIST, ADIS IV, 3 Tesla MRI, and Serial Subtraction Paradigm. Studies that were systematic reviews as well as had a subject pool of individuals with and without ASD but the numerical amount of each was undefined were also utilized.

Throughout the analysis of the literature that was conducted, patterns and similar findings in each source were detected. These correlations were seen with each of the main components of the limbic system that was studied. Starting off the amygdala, a general consensus was found that pointed towards a decrease in amygdalar volume in individuals with ASD who suffered from depression and anxiety. However, in neurotypical individuals, amygdalar volume stayed consistent during depression but resulted in blunted activity. Moving onto cortisol levels, individuals suffering from depression with ASD were not seen with significant differences in their cortisol activity but did have inconsistent cortisol dysregulation. Contrary to ASD individuals, neurotypical individuals did see any significant changes in cortisol regulation. Cortisol levels were seen to correlate with hippocampal volume in neurotypical individuals, as an inverse relationship was found between hippocampal volume and cortisol levels during stress. There was also an association seen between hippocampal volume and self-esteem. Hippocampal volume was seen to decrease in neurotypical individuals with depression, and there was also a reduction in gray matter volume in the bilateral hippocampal formation. These individuals also saw a decreased gray matter volume in the right hippocampus. Decreased gray matter volume was also seen in the left anterior cingulate cortex. Broadening out, there was a significant association between poorer executive functioning and higher anxiety levels, but not depression in individuals with ASD. Individuals with ASD also experienced more episodic disorder while encountering MDD. Error-related negativity, an event-related potential, was also seen to be associated with social anxiety symptoms. The analyzed results do show relevance and significance to the current question as they give a clear answer as to which areas of the limbic system experience neurological changes.

5. Discussion & Conclusions

This paper reviewed studies regarding the effects of stress-induced anxiety and depression on the limbic system. the study focused on cortisol levels, the amygdala, the hippocampus, and general types of functioning(executive functioning, social cognition, etc.) in the limbic system. Between neurotypical and autistic adolescents, there were variable results across the components such as the amygdala showing decreased volume in autistic adolescents while neurotypical individuals experienced increased blunted activity and consistent volume (Ferri et al., 2017), both of which as a result of depression. While this does confirm the hypothesis that there are different effects between the two populations, they should be interpreted with caution. For example, many studies had a small sample size. This might affect the accuracy of the results such as the amygdalar volume differences and changes in cortisol levels. These results along with others focusing on different areas of the limbic system will be critiqued in this discussion.

The distinctions in response in the amygdala to anxiety and depression between autistic and neurotypical people are notable. Autistic individuals demonstrate altered connectivity in some subregions of the amygdala that are important to social symptoms, which may have implications for social processing (Kleinhans et al., 2015). Additionally, amygdalar activity is affected by stress in individuals with autism, leading to less activation of the frontal components and the amygdala. This increases reliance on the temporal lobe (Baron-Cohen et al., 2000). In contrast, when responding to negative stimuli, the amygdala in neurotypical individuals' activity is heightened, indicating higher emotional responsiveness. The different responses from the amygdala between the autistic and neurotypical populations offer insights into the neurobiological aspects of anxiety and depression from these populations. The

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findings from some of these studies could vary due to the fact that the age group is slightly younger than desired. In a medical setting, this data can be employed to improve the comprehension and management of anxiety and depression in both autistic and neurotypical individuals. The amygdala responses in autism can help guide clinicians in creating therapeutic interventions for specific neurobiological characteristics and social processing challenges associated with anxiety in autistic patients. Understanding the heightened amygdala activity in neurotypical individuals when faced with negative stimuli may assist in devising targeted interventions to effectively regulate emotional responsiveness and mood in this population.

There were several different responses in the hippocampus in relation to stress-induced anxiety and depression between autistic and neurotypical adolescents. In neurotypical individuals, in instances related to depression, there was diminished hippocampal volume and gray matter in the bilateral hippocampal formation (Chen et al., 2018). In contrast, autistic individuals displayed irregular cortisol regulation implying differences in stress response compared to neurotypical counterparts. This implies an irregular structure and volume of the hippocampus due to irregular cortisol regulation (Dedovic et al., 2009). The majority of the studies underscore the importance of understanding hippocampal alterations in both groups and their implications for mental health interventions among adolescents suffering from anxiety and depression. These insights can contribute to the development of certain therapies that can be applied in the medical field to treat specific hippocampal alterations in each group. Furthermore, this knowledge can potentially aid in early detection and diagnosis of anxiety and depression in adolescents, allowing effective treatment options to be applied early on. While the sources produce adequate information on the hippocampus, some of the findings come from systematic reviews, which can be subject to different biases rather than getting information directly from the research studies. Overall, however, the information gathered was beneficial and can have a positive contribution to the medical field and social science research.

There is a significant difference in the regulation of levels and secretion of cortisol in the brain as a result of depression and anxiety between autistic and neurotypical individuals. Regarding autistic individuals, it was seen that they possessed higher serum cortisol levels, a greater peak response, and a prolonged duration of salivary cortisol levels (Spratt et al., 2012). Additionally, inconsistent cortisol dysregulation was also seen in these individuals (Makris et al., 2022). However, in neurotypical individuals, high depressive symptoms and impulsivity were associated with decreased cortical thickness in the ventromedial prefrontal cortex and medial orbitofrontal cortex (Merz et al., 2018). Though these sources display significant differences between cortisol activity in times of depression, there is a contradiction in a source stating that there was no significant difference in cortisol levels in response to stress (Corbett et al., 2006). The distinct responses through cortisol levels between autistic and neurotypical individuals can help researchers understand how to combat the neurological changes that occur when individuals with ASD encounter depression, as the symptoms in autistic individuals are different from the neurological changes that occur in neurotypical individuals. While autistic individuals encountered cortisol dysregulation, neurotypical individuals experienced decreased cortical thickness.

Though the amygdala, hippocampus, and levels of cortisol make significant changes in response to depression and anxiety in autistic and neurotypical individuals, there are various miscellaneous parts of the limbic system as well as overall social cognition that have significantly different responses in individuals with ASD versus neurotypical individuals. Starting off with the gyrus of the limbic system, neurotypical individuals showed decreased gray matter volume (GMV) in the left anterior cingulate cortex as well as the left superior frontal gyrus (Chen, et al., 2018). As for autistic individuals, they were seen to encounter a local increase in cortical thickness of the fusiform gyrus as well as there being an anatomical covariance between amygdala volume and the increase in fusiform gyrus local thickness was significantly smaller in the group with ASD (Dziobek et al., 2010). As for social cognition and executive functioning, patients with ASD showed a significant association between poorer executive functioning and higher levels of anxiety, but not depression. In contrast, neurotypical individuals showed a more stable correlation and activity. These differences in cognition between these two groups of adolescents explain how individuals with ASD versus neurotypical individuals face and deal with depression and anxiety differently. These correlations and changes elaborate on why these two groups of individuals need to be treated differently to suit their own personal behaviors to ensure they receive the care they need.

Several limitations can be identified when it comes to the implementation of the methods mentioned above. The

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basic fact that further developments could be made in new research that is not accounted for in this paper is a huge limitation. The conclusions drawn off the basis of the research that has been done to date and published in literature is what is presented in this paper and any new developments could potentially contradict these conclusions. Information from different pieces of literature could contradict with one another which can cause discrepancies when attempting to reach conclusions on certain questions. There is also potential for misinterpretation of the conclusions that are written in the literature that is analyzed. The conclusions could also be susceptible to bias.

While the findings of this paper confirm the hypothesis and show that multiple components of the limbic system undergo structural changes, there were other kinds of data that could have been analyzed. One of these sources is MRI imaging which was presented in the sources. Many of the articles used structural or functional MRIs and presented their imaging, most of them being MRIs of autistic participants post-trial. This paper used techniques from a systematic review, a common component of systematic reviews is meta-analysis where statistics from two or more papers are combined into a single interpretation of data. For example, graphed information from literature on amygdalar volume could be combined into a single graph that shows volume changes of the entire amygdala rather than just nuclei or subnuclei of the amygdala. These and other limitations were responsible for preventing this paper from providing other forms of evidence that would support the results. Thus, while the hypothesis has been proved, more research on this subject would be required in order for this research to be further confirmed.

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