Neuroanatomy of Autism and Mental health

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Autism Spectrum Disorder (ASD) and Mental Health Disorders, such as depression and anxiety, are both neurological illnesses that influence our social behavior and well-being. There are roughly 1 in 100 children diagnosed with ASD and roughly 300 million people who suffer from major depressive disorders in today's global population (Zeidan et al., 2022; Chodavadia et al., 2023). However, these two conditions are not frequently linked together, despite the multiple relations between them.

A few parallels between the two disorders are in their symptoms. In both ASD and depression, for instance, their social interactions are different from a neurotypical person. In depression, patients frequently report their social interactions as negative which impacts their sense of belonging to certain social groups or their likelihood of engaging in social experiences (Steger & Kashdan, 2009). These sorts of social differences are also seen in ASD patients but it is more of a core symptom. The most characteristic symptom of ASD is a deficiency in social communication skills. (Frye, 2018).

A common anxiety disorder, OCD, is habitually associated with the patient's compulsions, which are defined as repetitive behaviors a patient feels urged to perform to reduce stress and anxiety (Brock & Hany, 2023). In ASD patients, repetitive actions/interests are a key diagnostic symptom and are a core feature among patients (Richler et al., 2010).

I will explore comorbidities, in symptoms and brain areas, between Autism Spectrum Disorder and mental health disorders such as depression and anxiety. Then, I will conclude with a neuroscientific overview of both conditions and a discussion of the advancements that could be made in the diagnosis and treatment of ASD, taking into consideration these parallels.

Overview of Mental Health :

Mental health is an umbrella term used to describe psychological wellness. Recent advances in neurology and psychiatry are often related to advances in neuroscience. As a result, our contemporary understanding of the neural basis of mental health is a rapidly changing field. The most recent advances are primarily focused on the therapeutic areas of depression and anxiety. Depression is a mental disorder that exists on a wide and diverse spectrum and is majorly characterized by an individual's behavioral patterns. These can include symptoms like irritable mood, loss of interest in normally enjoyable things, a sense of worthlessness, and intense guilt (American Psychiatric Association, 2013). However, even with all these general characterizations, depression still looks vastly different in different people, ranging from mild, moderate and severe depressive episodes, depending on the number and types of symptoms (National Collaborating Centre for Mental Health (UK), 2010).

The treatments of depression rely on either, or a combination of, traditional psychotherapy or pharmacology. The initial form of treatment, especially for mild depression, is psychological treatment, which includes cognitive behavioral therapy. Cognitive behavioral therapy combines

two different methods: Behavioral therapy, which is a process that aims at breaking unhealthy patterns (such as constant negative thoughts or feelings of guilt) or Cognitive therapy, which changes the value people place on certain things(such as people or situations). This form of treatment is used first because sometimes the initial symptoms get better without medication, thereby potentially avoiding some of the side effects of medication. Even though medication is not the initial treatment option that doesn't mean it is not effective. Pharmaceutical medications like antidepressants, such as SSRIs and Tricyclics, and herbal products are meant to lift mood and increase motivation (InformedHealth.org [Internet], 2020).

Anxiety disorder is not a specific disorder but rather a general term for a disorder that has many distinct illnesses associated with it, such as social anxiety disorder, panic disorder and generalized anxiety disorder (GAD) (National Institute of Mental Health, 2023b). The most common of these 3 is GAD; patients do not experience this anxiety in waves, but they carry this constant weight on their shoulders for years of their lives. Symptoms of this include being irritable, difficulty concentrating, and struggles with falling or staying asleep. Similarly to depression, anxiety can be treated with types of therapies or with medications.

There is a lot of overlap between anxiety and depression. People with either or both of these illnesses are at a higher risk of having other physical comorbidities like cardiovascular illnesses. In general, living with these illnesses lowers the quality of life (Hohls et al., 2021). So, despite the name, mental illnesses affect life both physically and mentally. Conversely, depression and

anxiety can be secondary illnesses that could be produced by the presence of a different underlying illness of the brain, such as Alzheimer's disease, immune-modulated inflammatory diseases (Botto et al., 2022; Whitehouse et al., 2019) and autism spectrum disorders. As a result of high comorbidity between depression and anxiety disorders with other neurological conditions, treatment and clinical management of the symptoms can be challenging.

Overview of ASD:

Autism spectrum disorder (ASD) is a developmental disability that influences social interactions and behavior. Autism is a developmental disorder not because it is only diagnosed in younger children, but because most of the symptoms usually show up within the first 2 years of life (National Institute of Mental Health, 2023a). ASD is a disorder that exists differently in every person, hence, the word spectrum in the name. According to the DSM-5, ASD can be diagnosed by multiple symptoms including, but not limited to, deficits in social communication and social interaction and restricted, repetitive patterns of behavior, interests, or activities (American Psychiatric Association, 2013). However, due to the diversity of autism, these symptoms can exist in multiple ways. One patient who has been diagnosed with ASD could have a few of these symptoms, while another patient could have all of them. In the context of social interaction and communication, some indicators are inconsistent eye contact, difficulties in back-and-forth conversation, and displaying facial expressions that do not match what is being said. Some of the more common symptoms related to restrictive and repetitive behavior are having a lasting

and intense interest in particular topics and becoming upset with changes in routine. Another symptom that is often observed is hyper- and hyposensitivity to sensory input like light, sound, etc. These symptoms of ASD are very few of a long list, which is growing with medical development, of what determines if a patient is on the spectrum or not. These symptoms have led to the diagnosis of over 75 million people.

After being diagnosed, patients are recommended to begin treatment as soon as possible. The most common treatments are interventions and medications. Different interventions exist for different reasons, including behavioral, psychological, educational and skill-building. These interventions help the patient improve their quality of life while living with ASD. These programs typically include the patient's family members and close friends so that the people closest to the patient can learn, understand and accept the patient. The interventions help teach social, communication, and language skills, reduce behaviors that interfere with daily functioning, increase or build upon strengths and ultimately teach life skills for living independently. This is just one of the suggested treatments and the patient must decide which works best for them.

The medications used for ASD are not curative but rather help to treat certain symptoms associated with ASD (Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH, HHS, 2021). One type of medication used is SSRIs, which are a group of antidepressants used to treat symptoms/disorders caused by chemical imbalances in the brain,

like anxiety and aggressive behaviors. Another medication is called tricyclics, which is another group of antidepressants that have been used to treat depression and obsessive-compulsive disorders. A third category of medication is stimulants, which increase focus and decrease hyperactivity. And lastly, anti-anxiety medications, which help relieve anxiety and panic disorders.

The use of antidepressants to treat ASD can show us that there is a potential relationship between ASD and depression. The rate of comorbidity of depression and ASD is 54.1% and the prevalence of depression in ASD seems to coincide with higher functioning forms of ASD and increasing age. This link could be explained by the fact that ASD affects social skills and is most evident in youth and adolescents because social interaction is a vital skill used at that age, and the lack of such skills may result in deteriorating mental health. Despite the obvious correspondence between the two conditions, efficient and safe modes of treatment are lacking in these areas resulting in patients only getting treatment that has been tested within patients with typical development (DeFilippis, 2018).

Clinicians often overlook mental health comorbidities associated with ASD for a variety of reasons, including clinician specialty. Most ASD patients see pediatricians or neurologists, and not psychiatrists and other mental health professionals, thus the detection and diagnosis of mood disorders in this patient population may be underreported. The issues of diagnosis are

compounded by the unique communication challenges of the ASD population. Significant portions of the ASD population are non-verbal and have communication impairments, which limits the detection of mood disorders given that diagnoses are often made informed by patient descriptions of their symptoms.

Overview of neuro similarities of ASD and mental health:

The comorbidity between depression and ASD is not only due to the circumstance of the patient but should be expected when you factor in the neuro-similarities between the two conditions. ASD is a disorder that primarily impairs the patient's social skills, which is why it affects the four main 'social' areas of the brain: the amygdala, orbitofrontal cortex (OFC), temporoparietal cortex (TPC), and to a lesser extent the insula(Weston, 2019). These same regions of the brain are affected by depression. These four sectors of the brain all have functions that have direct correlations to both depression and ASD (Pandya et al., 2012).

The amygdala is a deep structure within each temporal lobe, which resides on the sides of the brain, at and below the level of the eyes. The amygdala is a part of the limbic system that regulates our emotions, and motivation, and also plays a significant role in combining our memories and emotions (AbuHasan et al., 2023). There has been a reported volumetric decrease in the amygdala in unmedicated depressed patients and elevated activity has been connected with the severity of symptoms. This change has been observed to return to normal

after successful pharmacological therapy (Hamilton et al., 2008). In ASD, the amygdala is seen to be larger than typical due to a faster growth rate in youth and linked with greater social deficits in the future. (Shen et al., 2022).

The orbitofrontal cortex (OFC) is a section of the prefrontal cortex, located in the frontal lobe. The OFC is critical for separating emotional connections to situations while making decisions and therefore making more rational than impulsive decisions (Premkumar et al., 2015). The PFC is especially important for a range of social and behavioral responses (Nelson & Guyer, 2011). OFC dysfunction leads to anxiety disorders and post-traumatic stress disorder (Milad & Rauch, 2007). The OFC has increased connectivity to other areas in the brain in depression, which explains the difficulties in making decisions (Rolls et al., 2020). The OFC is subdivided into lateral and medial sections. The lateral OFC is more concerned with the rewards assigned to options while the medial OFC is more concerned with the choosing of options (Noonan et al., 2017). In ASD, there have been reports of decreased size of the right lateral prefrontal cortex compared to neurotypical patients, which results in symptoms like social unconcern and reward processing deficits (Janouschek et al., 2021). Since the OFC is responsible for processing rewards and punishments, the decreased volume of the region leads to the patient having less value of these rewards and less inclination to engage in social stimulation, especially during developmental years.

The temporoparietal cortex (TPC) is a region that functions mainly in social situations, for example in social awareness and episodic memory retrieval (Igelström et al., 2016). The TPC has been seen to be hypofunctional, especially in depression patients, which results in lower emotional response (Moratti et al., 2008). This provides a framework to understand why patients with depression often report finding less joy in things they once enjoyed and a generally lower quality of life. The TPC has been known to have direct links to social stimulation and interaction and as a result, is involved in ASD (Krall et al., 2015). The TPC is thought to be hypoactive in ASD patients. One study stimulated the rTPC (right temporoparietal cortex) and found that the patient's social function improved and other symptoms of ASD, such as unwarranted anger and frustration, lessened (Wilson et al., 2018).

In a recent clinical study, a patient who had been diagnosed with ASD had undergone sessions of stimulation to his rTPJ. During the treatment and post-treatment, the patient reported increased interest in social interactions and a generally higher awareness of the emotions of the people around him. This suggests that prior to this experiment, the TPC may have been hypoactive in this patient and could potentially be reflective of similar TPC phenotypes in other ASD patients (Wilson et al., 2018). Further research is needed to evaluate the generalizability of this finding and therapeutic approach. If the TPC is found to be abnormally inactive in ASD patients and its activity can be rescued by rTPJ stimulation, this could be a new treatment modality for ASD patients.

The links between ASD and mental health disorders are proven to be seen in multiple aspects of the patient's lives, the activity in certain sections of their brains, the similarities in the manner by which they are treated separately and the similarities in their everyday behavior. These comorbidities have provided multiple avenues to developments in the treatment and care of ASD patients. As this link has been established, steps that could be carried out to consider it are more specific and innovative treatments, especially regarding the stimulation of certain parts of the brain such as the rTPJ. Also, due to the similarities in social symptoms, the family and friends close to the patients may attempt to alleviate the symptoms they report by being intentional with their social interactions and doing exercises with them to develop their skills to treat the mental illness they are experiencing to help their ability to live with both conditions simultaneously. Further research in both of these areas can build a foundation that could potentially lead to new drugs and forms of diagnosis for the patients. Although these steps may not be as effective for all patients in all situations, they could be seen as stepping stones in a path of future advancements for patients living with these conditions to achieve a better quality of life. The exploration of multiple relationships between two seemingly unrelated conditions can lead us to question where else we can uncover connections between conditions such as these; these questions are not only important to making advances in the scientific world but could also quickly become linked to practical applications that would positively impact millions of people around the world.

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