Autism From a Neurobiological Perspective: A Disorder, Not A Disease

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Abstract

Many scientific manuals such as the DSM-5 (Diagnostic and Statistical Manual) define autism spectrum disorder (ASD) as a lifelong condition that impairs both social skills and autonomy [44]. For years, scientific definitions of autism mention the impaired abilities individuals have, without identifying a known origin. Consequently, this leads to the understanding of autism to be treated like a disease with no known cure, rather than a condition. Although there is not one specific origin, many studies commonly indicate that autism is the result of an intersection of genetic and environmental factors [49]. While autism does impair certain abilities of individuals, it also enhances various other abilities.Therefore, it is important to understand that ASD is a highly variant disorder.

In this paper, research studies have been analyzed on the prevalence of neurobiological factors of autism, and how that impacts the behavior of autistic individuals to provide a clear understanding of ASD. Given this context, this paper mainly focuses on why we should eradicate the perception of autism spectrum disorder (ASD) as a disease. By providing insight into what treatments have been used to address behaviors related to ASD, we can re-evaluate them to provide safe and accurate support and intervention for individuals with ASD.

Introduction

The definition of Autism spectrum disorder (ASD) is a neurodevelopmental disorder with difficulties in social skills, communication, and restrictive and repetitive behaviors (RRBs) [19]. Experts divide RRBs into four main categories, which include stereotyped or repetitive motor movements (e.g., the repetitive use of objects or speech), insistence (e.g., verbal and non-verbal behavior); this can include repetitive speech or not being able to comprehend nonverbal social cues such as when one may be uncomfortable [42] and fixed interests in which interest is given a higher focus and intensity [49]. Other behaviors can be aggressive, self-injurious, anxious, or can include a short attention span and specific phobias [39]. However, while behaviors such as fixed interests may seem like a negative outcome and indicate that ASD impairs the abilities of individuals; these interests are related to positive outcomes for individuals with ASD. Many surveys of adults with autism showed that these interests included but were not limited to computers, music, and gardening [21]. Having strong interests in subjects like these sheds light on the concept that individuals with ASD may have a high level of intelligence that may get overshadowed by perceptions of disability; which may fuel the misconception of ASD being conceptualized as similar to a disease.

Given this context, scientists and experts need to stop analyzing autism as a disease to be cured and change the ways they evaluate and consider this neurological condition. Understanding basic information on the role biological mechanisms of ASD play on the behavior, and assessing current methods used to diagnose and treat autism, can support interpreting autism through a different lens.

Neurobiological Factors and Behavior

Many of the neurobiological mechanisms of ASD consist of but are not limited to, genetics, brain structures, and synaptic proteins found in the brain neurons [19].

When identifying ASD, many genetic alterations have been found. Many experts have found that a prevalent example of these genetic mutations is a disease called Fragile X Syndrome. Fragile X Syndrome is an inherited genetic disorder that causes physical abnormalities, behavioral issues, and other health defects. It is detected by the appearance of the X chromosome looking loose, giving it a “fragile” or “broken structure” [7]. Fragile X Syndrome is noted to be a leading cause of high rates of ASD, especially if the individual’s parents or siblings have Fragile X Syndrome there is an increased probability of having ASD [43]. The inheritance of Fragile X syndrome has many behavioral impacts as well and increases poor sleep and high aggression [7]. This is notable given that many experts consider sleep as a behavioral and emotional regulator, especially in individuals with ASD. Any sleep deprivation worsens behavior in children with ASD and promotes disruptive or inflexible behavior and anxiety [56].

Genetic mutations do not only impact the inheritance of ASD, but they also affect the development of neurons in the brain. For instance, genetic and epigenetic mutations (i.e., mutations by behavior and environment) and remodeling processes of the chromatin proteins occur within specific neurons [30]. These proteins impact the brain’s morphology, and when seen in mice, some proteins that impact brain morphology include the Neuroglin-3 (NL3) and the Methyl CPG binding (MECP2) proteins. The NL3 protein is a cell adhesive and forms synapses in the brain [20]. Mutation of this protein disrupts neural circuits in the areas of the brain striatum which can contribute to the prevalence of repetitive and stereotypical behaviors exhibited by individuals with ASD [50].

Additionally, The MECP2 protein attaches to the DNA and affects transcription. Although it is unclear what biological functions it targets, research suggests that mutations in the MECP2 are associated with Rett’s syndrome [48]. This neurodevelopmental disorder includes a loss of mobility, slow brain growth, as well as cognitive issues, and seizures. The mutation for Rett’s syndrome is carried on the X chromosome and mostly affects females [29][41]. However, current diagnostic technologies do not classify ASD and Rett’s syndrome to be comorbid [58], the impacts of the mutations in genes linking both can be seen in other conditions related to ASD, such as obsessive-compulsive disorder (OCD) [39].

The mutations of certain genes also impact the inheritance of ASD. Some common examples are SHANK3, CNTNAP2, and CHD8. The SHANK3 gene specifically is noted to be involved in social and communication activities. The CNTNAP2 gene is linked to regulating behavior and developing ASD [2]. The Chromatin Helicase DNA-binding (CHD8) protein regulates gene transcription, has a high behavioral association with intellectual developmental disorder and promotes facial dysmorphia. It also plays a role in ASD development, as well as macrocephaly (i.e., enlarged head size) along with showing early growth in children [11]. Although it is uncertain which genes control which traits in autism, knowing the genetic basis for how autism is inherited throughout populations is crucial before knowing the impacted cognitive features [17]. Additionally, from these descriptions it is clear that genetic mutations play a clear

role in disruptive behaviors related to ASD; however, it is important to note that while certain abilities may be impaired the condition does not need to be cured. ASD, like many neurodevelopmental disorders, pertains to individuals who display atypical behaviors due to a difference in neurological activity [53].

Several neuroanatomical structures have been implicated in autism and influence many of its behaviors. These structures can range from granular structures such as the neurons, and gray and white matter to major structures such as the striatum, cerebellum, and amygdala [29]. Neuroanatomical abnormalities begin with understanding the mutations in the tiniest unit of the brain: neurons. Within neurons, some synapses consist of specific interactions of neurons with glial cells that are also effective as early detectors of autism [29]. These interactions are seen through protein synthesis within the dendrites and promote gene transcription. This results in activity-dependent signaling which regulates synapse development and increases the neuroplasticity (i.e., the ability to form neural connections) within the brain [15]. This is explained by microscopic structures called glial cells which are considered the “glue” between neurons. They are vital for brain functioning for the brain to form neurons, and synapses as well as inflammation in certain brain areas and myelinating neurons. However, in ASD there is not as much data known about glial cells, which may explain hypotheses of why individuals with ASD have less developed brains [18]. The complexity of this development suggests that brains with ASD operate with rapid neural firing. However, the understanding of ASD being treated as a disease makes individuals underestimate how complex autistic individuals’ brains are. The size of the brain is also important when understanding ASD. Between 2 and 4 years of age, many autistic individuals tend to have larger brains than their non-ASD counterparts. However, this difference is more difficult to identify in older kids who are diagnosed with ASD. A common explanation for this situation is that at an older age, those with autism show a decrease in the volume of the brain as well as the number of neurons [9].

Children with ASD also tend to have higher amounts of gray matter content and abnormal distributions of white matter [4]. Gray matter contains the neuronal cell bodies, dendrites, synapses, and glial cells. It is critical for muscle control, sensory perception, memory emotion, and decision-making. White matter, on the other hand, consists of myelinated or insulated axons that coordinate communication of the brain’s different regions [19]. The increased gray matter, however, affects the social cognition-related brain regions and is seen as a biomarker of ASD [4]. The arrangement of these structures shows that more connectivity in gray matter and less white matter connecting across brain conditions manifests in some of the typical behaviors associated with ASD. These symptoms, especially seizure activity, can be explained by the differences in white and gray matter present in individuals with ASD [54].

Additionally, many other major brain regions display signs of mutations. Mutations found in specific brain structures can promote ASD comorbidity with conditions such as OCD, anxiety, and schizophrenia [39]. Many of these commonly recognized structures have abnormal functions that include the striatum and cerebellum. For instance, damage to the striatal circuit could make it hard for autistic individuals to prioritize sensory cues. Dysfunctionality in the striatum could cause interruptions to learning underlaid with motor control difficulties and inflexible repetitive movements, making it difficult for them to distinguish between important and unimportant sensory information. It also contributes to their social impairment making it difficult to adapt and change to social cues in environments [24]. For many autistic individuals, during

their early childhood, the inflammation in brain structures prevents specific neurons in the cerebellum from maturing completely. The cerebellum is a brain region responsible for motor control and higher cognitive functions in language, social skills, and emotional regulation [50]. Inflammation specifically of these brain structures can impact the transmission of neurochemicals such as GABA, serotonin, dopamine, and melatonin [37]. Some of the variations in these vitamins are also mutations in the neurotransmitter systems, including those involving serotonin and dopamine, and have been linked to the repetitive behaviors and restricted interests often seen in autism [1].

Furthermore, Serotonin is a neurotransmitter that regulates mood and sleep [5]. The levels of serotonin in individuals with ASD are higher than others [1]. These high levels can also be related to deficits in serotonin receptors, which can give rise to an autoimmune reaction in the brain [1]. Dopamine is a neurotransmitter that regulates social play and behavior and social cognition and movement. While many papers do not specify how high or low dopamine levels in autistic individuals are, dopamine levels have different behavioral effects on individuals with ASD such as an increase in social play behavior. Their potentially lower levels are also said to explain the reduced motivation for social interaction [34].

The abnormalities in many of the biological structures in autistic individuals provide high relevance and reasoning behind their atypical behavior. The variations in the brain structure and function are linked to the unique behavioral patterns observed in autistic individuals. For instance, differences in the size and connectivity of certain brain regions, such as the amygdala and the prefrontal cortex, have been associated with the social and communication challenges characteristic of autism [19]. Moreover, studies have identified atypical development in the mirror neuron system, which is thought to play a crucial role in understanding and imitating the actions of others (Kilner et al., 2013). This could explain the difficulties many autistic individuals face with empathy and social interaction [19]. In addition, the mirror neuron system in autistic individuals is observed to have a greater sense of connectivity between various brain regions which may or may not contribute to the social cognitive function in ASD [14].

While there are a multitude of specific behaviors that may differ in ASD, these biological differences offer a substantial basis for understanding why these behaviors manifest. For example, sensory processing differences can lead to heightened or diminished responses to sensory stimuli, affecting how individuals interact with their environment and others [36]. Understanding the connection between biological abnormalities and behaviors, is crucial for developing targeted interventions and supports that address the specific needs of autistic individuals. It also emphasizes the understanding that those who have ASD's brains work differently, and it is perhaps not something that needs to have a specific cure, as multiple factors and mechanisms shape the condition for what it is.

Psychometric Tests and Standards of Care

Compared to other conditions, diagnosing and treating ASD can be a gray area. While scientifically classified as a disorder, there are different types of intelligence individuals possess that can be amplified in this condition. These types of intelligence can include but are not limited to visual, auditory, reading, and kinesthetic (by action) [12]. When it comes to finding out which standards of care should be taken for ASD, one should keep in mind the diagnosis technologies as well as the treatment: medications and therapies.

Many identification methods of ASD and therapeutic approaches have varying scales as to how functional they may be. For instance, some methods include the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) [33]. and the Modified Checklist for Autism in Toddlers, Revised (M-CHAT-R) [33]. These methods are not diagnostic tests but rather, they each list criteria that can help diagnose ASD. Both of these methods assess social interaction difficulties, as well as restrictive and repetitive behaviors. They also assess different areas of development to conclude an appropriate diagnosis [33]

The DSM-5 includes the diagnostic criteria to be assessed to determine if a child has ASD; they must meet the following three criteria by showing social deficits in emotional reciprocation, understanding relationships, and non-verbal cues. The individual must also show two out of the four behaviors: difficulty showing flexibility in routine change, restrictive interests with hyper-focus, hyperactivity or hypoactivity to sensory input, as well as repetitive behaviors, movements, or speech. ASD is comorbid with other conditions such as attention-deficit/hyperactivity disorder (ADHD), schizophrenia, and anxiety [33]. While the DSM-5 can go beyond assessing if an individual has ASD, with the comorbidity in multiple conditions, it may be confusing to determine which conditions may be present for the individual. If more conditions are detected in a patient, it may lead others to think that the patient needs extensive treatment which may not be necessary and could lead to further misconceptions of the child's diagnosis. Typically, ASD diagnosis needs extensive training, and usually, the DSM-5 is handled by mental health professionals and some of them may lack training in using the DSM-5 to diagnose ASD; because it is seen as a more complex method to receive mentorship on how to conduct. The DSM-5 is also less sensitive to individuals with higher IQs meaning more cases could get missed leading to diagnosis error [52].

The M-CHAT (Modified Checklist of Autism in Toddlers) is a screening for ASD in Toddlers that is considered universal for children at this stage, and low-cost. The M-CHAT-R is a revised version of this screening, and it is more suggested to use than the M-CHAT because it is a more recent updated version of the screening and reduces the number of follow-up screenings needed to make sure the previous M-CHAT findings were accurate [46]. The M-CHAT-R is also known for providing an increasingly earlier detection of ASD by 2 years earlier [8]. It is also less expensive and more accessible as it can be used in multiple languages, unlike the DSM-5. With 23 yes-or-no questions and a follow-up parental interview, there are less likely to be false positives of an ASD diagnosis [33]. However, the downside of the M-CHAT could be that it is designed to assess individuals of a younger demographic. The M-CHAT screening is given for children aged 16 to 30 months, and a follow-up screening is given when the children have reached 42 to 54 months of age to confirm consistency in ASD diagnosis [24]. While the M-CHAT provides a consistent measure of detecting ASD over time in younger children; this may not apply to finding ASD in relatively older individuals. Currently, there are some tests, but they have limitations that cannot accurately conclude an ASD diagnosis in adults [10]. The other factors that may also contribute to why ASD is difficult to detect in older patients can be explained by differences in brain size. As mentioned earlier, there tends to be shrinkage in the brain with older ASD patients, which can make behaviors such as RRBs less obvious as the individual may grow out of it. However, it is also important to understand that in some cases it may be difficult to find ASD in younger individuals because while the brain tends to be growing for demographics as young as toddlers, development patterns may not be apparent simply because they are not at the age to adapt to or portray abnormal behavior; or they may be portraying behavior similar to another disorder. For example, in many ASD cases, parents

generally found out that children had sensory processing issues before the age of 2, however until the child is placed in a schooling environment or a social situation; they are not given a diagnosis of ASD. A mother found out her child had sensory processing at 2 years old, but received an ASD diagnosis at age 4. In individuals who were diagnosed with ASD that also had ADHD sensory processing was a symptom that overlapped between both conditions. As a result, many parents and professionals do not look into further diagnosis for ASD and get treatments for conditions like ADHD, limiting their opportunity to get necessary therapies for ASD [6]. As shown by these cases, many behaviors that are related to ASD not being apparent from a younger age often lead to mistreatment of the condition; which is an issue needed to be addressed by families and professionals.

Additionally, it was also reported that the M-CHAT is not as accurate for children who were born prenatal or with hearing and vision loss [26]. The M-CHAT assesses whether individuals with ASD see or hear something when pointed to or referenced. Regardless of whether a child has ASD or not, if the M-CHAT test is used with individuals who are visually impaired or have hearing loss, they are more likely to be diagnosed with ASD based on these question types, which can lead to more false positives as well as false negatives [26].

While both criteria have pros and cons, they have limitations for different people. This includes those who may be visually impaired, adults, or have comorbid disorders. To be able to accurately detect ASD, and clear up the perception of it being medically treated like a disease instead of a disorder, there is a need to investigate more representative yet accurate methods of testing ASD. This can be done by mainly using the fact that most ASD testing focuses on outward behaviors; if researchers take the time to focus more on the internal mechanisms such as brain size, or neural activity when conducting ASD testing, they will be able to find a more distinctive and accurate diagnosis for patients. However, brain scans showing abnormalities in both gray matter, and white matter as well as accelerated growth leads to the notion that ASD is a disease [27]. This is because structural abnormalities are mistaken to indicate pathological abnormalities but ultimately there are no known outcomes of the structural abnormalities of ASD that suggest it is a disease; rather they show variation in behaviors.

ASD has no singular treatment, but rather there are multiple treatments for different cases. Treatments come in two forms: therapies and medication. If an individual exhibits destructive behavior toward those around them or themselves, medication needs to be used for treatment. Some medications can treat symptoms such as irritability and aggression, atypical social behavior as well as insomnia. For example, risperidone is an antipsychotic drug used on individuals aged 5 or older, to reduce irritability. Individuals did show less social withdrawal and hyperactivity, but there was weight gain, anxiety, and increased appetite as well [33]. For abnormal social behavior, it is common to use oxytocin, a hormone related to forming social relationships in humans and animals. By using intranasal oxytocin, individuals found more socially meaningful stimuli and improved emotional recognition [33]. To treat insomnia, some examples include melatonin and Mirtazapine. Melatonin, like oxytocin, is a hormone that impacts sleep and decreases sleep latency (i.e., difficulty in falling asleep) by less than 30 minutes in 85% of ASD patients [33]. Mirtazapine is an oral drug that promotes noradrenergic activity (norepinephrine) and serotonergic activity (serotonin). It helps insomnia by promoting less irritable behaviors such as aggression and self-injury [33]. However, since it is an antidepressant, some consequences to be aware of include suicidal behavior and thinking and major depressive disorder. It is important to note that these medications are just a few that can help ASD and considering the additional physiological or behavioral consequences that may

occur; one with ASD should proceed with caution before taking them. To eradicate the stigmas around ASD being treated like a disease, physicians should stop using medication as an immediate treatment of ASD as there are many consequences and it may not be necessary. It can also lead others to believe that medications can cure ASD, when in reality it is a treatment to use only when behaviors cannot be controlled by other interventions such as therapy.

Therapies are usually used for regulating behaviors in ASD; some examples can be Applied Behavior Analysis (ABA), Occupational therapy (OT), and speech therapy. ABA is a behavioral therapy and is based on analyzing environmental variables to find what influences the various social behaviors in ASD. Each therapy plan intends to be individualized and practical. This therapy focuses on teaching the skill sets needed for individuals to communicate, play, and interact with those around them. Some ABA interventions include picture exchange and communication systems (PECS), where individuals rely on visual icons to communicate their needs. The outcomes of ABA therapy have shown improvements in intelligence scores, language development, and social functioning for individuals with ASD [51]. However, some cases with individuals who had lower IQs below 50, did not find this therapy effective which may contribute to why this therapy is not higher ranked than most ASD interventions [51]. The nature of ABA can be intensive. Many ABA sessions can be up to 40 hours a week which is difficult for children with ASD to manage and can be too intense. Many interventions are also deemed formulaic which can be repetitive and frustrating at times for individuals with ASD, due to the repertoire placed in certain training programs to reinforce desired behavior [31]. To avoid this repetitive manner, utilizing a naturalistic teaching approach to ABA therapy provides instruction that applies to multiple environments beyond the household the client is raised in; such as daycares and integrated education environments rather than having a focus on only a specific few areas in general ABA. The skills focused on general ABA tend to be more related to academic environments. Skills taught using a naturalistic approach to ABA are in events for play or recurring events [32]. While ABA is effective in fixing behavioral issues, it may not target specific skills that some with ASD may face, that others may not. Many researchers can overcome this ethical concern with ABA by finding specific training programs that are more accommodative and efficient. Like naturalistic teaching approaches, they should find similar interventions that are less focused on restricting stereotypical behavior.

Occupational therapy (OT) is used with individuals with ASD to target physical, sensory, and issues related to cognition, and overall it is meant to promote independence and allow individuals to do daily activities [16]. The skill sets targeted in this therapy include social, communicative, and motor skills. Some examples of motor skills are basic skills such as cutting, folding clothes, holding pencils, and writing and drawing. The way OT is administered is flexible, as there is no standard method on how it should be done. However, this may make it difficult to find consistent results of progress in improving upon skill sets that may be lacking in ASD [22]. Another possible concern is that ASD has a 50-70% comorbidity with ADHD [22]. A common perception is that to manage behaviors such as hyperactivity, they may use OT to relieve it by burning off all this energy through more physical activity. However, this can be a sensory overload which can be a point of overstimulation and can lead to a sense of discomfort. At the same time, many experts, such as Board Certified Behavior Analysts (BCBAs) who deliver and supervise ABA therapy, also question the use of OT as they believe there is no research evidence explaining the reasoning behind the interventions used in the therapy [16]. In other words, many ABA therapists feel that OT does not have as effective of practices, which may construe perceptions of it to be less reliable.

Speech therapy is used in ASD to promote communication and interaction with others. This therapy focuses on increasing verbal skills such as correctly labeling people and things, emotions, sentence formation, and speech pacing. Speech therapy is also used to help non-verbal communication such as promoting the use of hand signals as well as sign language and using PECS. It is also used to build social skills by encouraging skills such as eye contact [45]. Although speech therapy can benefit those who are verbal and nonverbal, some modern-day interventions include the use of speech apps also known as iPads to allow children with ASD to communicate. The devices these apps are on are called augmentative and alternative communication devices (AAC) enabling individuals with ASD to communicate through technology [15]. Devices that are considered AAC include smartphones, smartwatches, and tablets [27]. Common examples of apps that allow communication include Proloquo2go, which has press icons in an “I want” request format, My Choice Board, and GoTalk NOW. The My Choice board has an audio-visual display where the icons express their needs [38]. The GoTalk NOW app has customizable pages that can include symbols for communication based on what activities that child requests [3]. With many advancements in speech therapy, a positive is that the communication methods encouraged in speech therapy are not too strenuous and allow convenient alternatives, especially for those with ASD who are non-verbal. However, the use of digital technologies may not benefit the treatment of ASD symptoms as one may become overly reliant on these communication technologies and may struggle to communicate without them. Even if a child with ASD is taught to use digital technologies to communicate, experts should also look into teaching them other methods to communicate as well that do not require a device. This can include teaching sign language, or if possible, trying to use vocal exercises to teach and repeat sounds for simple words.

ABA, OT, and speech therapy are a few of the many therapies used to treat ASD. While all of them have their pros and cons, these therapies can focus on areas that are less likely to allow ASD to be viewed as a condition than a disease. Although ASD is labeled a disorder by scientists, many therapies fail to address specific behavioral and emotional aspects of individuals. As a result, this can lead to ineffective treatment and a distorted understanding of the condition; reinforcing the idea that certain behaviors may need to be treated when it isn't necessary. If professionals understand where these therapies fall short, and try to change them by changing their criteria for how these standards of care are administered, both children and adults with ASD can see significant progress with their treatment.

Conclusion

Understanding structural and behavioral differences in autism, as well as re-evaluating therapies are crucial to helping kids with autism. Although it is classified as a spectrum, many analyses and treatments medically treat ASD as a disease which makes them less efficient.

Society confuses their understanding of ASD as a disease where they think it is a condition that has a particular cause and cure; however, in reality, there is not a single factor that causes ASD. Because ASD is a spectrum disorder, individuals may not exhibit the same symptoms as others because of how varied they can be. Being a disorder, this means there is a group of symptoms that may disrupt functions related to the brain such as social interaction. However, one should keep in mind that individuals with ASD may outperform others in niche interests, which could show enhanced intelligence.

From understanding the current therapies and technologies used today, physicians and scientists consider the factors of how ASD affects the brain, external behavior, and current

treatments. It will help eradicate the perception that it is being treated as a disease and will create better futures for individuals on the ASD spectrum and those surrounding them, as there will be more accurate data and solutions.

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