Exercise and Autism Spectrum Disorder: A Neuroscience Perspective

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Introduction:

Autism spectrum disorder (ASD) is a developmental disorder that permeates throughout all aspects of an individual's life.[1] It is characterized by disordered and/or delayed development of language, restricted or repetitive patterns of behavior, and qualitative impairments in social reciprocity[1,2,3,4] ASD affects each individual in a different manner, with different physical and psychological characteristics.[1,5] Physical and psychological characteristics include self-stimulatory behaviors, infrequent eye contact, lack of verbal initiations, and erratic mood. People with ASD may also experience motor discoordination, hypo- or hypersensitivity to specific sensations, or restrictive interests.[1,6] Also noted are difficulties in playing imaginatively, participating in social games, sharing/turn taking, holding conversations, and making friends.[7] While the exact cause is highly debated, these characteristics of ASD can have a major effect on the integration of the individual into the mainstream community.

Evidence suggests that children with ASD may also lack participation in regular physical activity (at least 60 minutes a day) as part of their lifestyle.[5,6] This may be due to social and behavioral deficits and poor motor coordination. To assist with the prevention in decline of cognitive function, physical activity is needed continuously throughout one's lifespan.[7] Physical activity may also assist a child in maintaining sustained cognitive tasks that require selective attention and suppressing distractions.[8] Studies have shown a decrease in aggressive, unproductive, disruptive, stereotyped and self-injurious behaviors through the use of moderate to intensive aerobic exercise.[4,6] An increase was observed in concentration, attention span, work performance, and on-task behavior.[4,6] Studies demonstrated that a decrease occurred in specific disruptive behaviors, but not in general to all behaviors; fatigue factor was a major concern for the decrease in these behaviors.[1,6] The exact effects of moderate to vigorous exercise on the core symptoms of ASD are still being researched and could depend on several factors such as duration, setting, and characteristics of the individual.[1,9]

The aim of this review is to examine the correlation between exercise and ASD, and explore how exercise may have a positive influence on the social functioning of a child with ASD.

Key Characteristics of Autism:

ASD is diagnosed on the basis of a two-domain model: social-communication and repetitive and restricted behaviors (RRB) behaviors.[10,11,12,13,14] Each individual is affected differently, exhibiting diverse core and non-core deficits. Individuals vary greatly in cognitive ability, language proficiency, onset of patterns, and sensory response to environment, with most obvious behavioral symptoms appearing late in the second year of life.[9,10]

RRBs include rocking, hand flapping, and spinning, with more severe self-harming behaviors presenting only rarely.[1,6,14] Overall, repetitive behaviors are observed in a large portion of children with ASD, and are distracting to the child with ASD as well as the mainstream community.[1,15,16]

Impaired modulation of eye contact for social purposes is one of the most critical characteristics used in diagnosis.[1,3,4,14] Children with ASD show less frequent and shorter fixation on the eyes in various experimental settings.[17] Shorter gaze may interfere with the facilitation of behavioral mimicry. Gaze behavior may serve as an important social function for understanding another individual's mental state and coordinating attention and activities. Processing this direct gaze is not as rapid in individuals with ASD, as compared to typically developing individuals.[18] There is a limitation of visual reciprocity, which suggests neglect in the importance of the eyes as a social information source.[18] Children with ASD show an atypical response to mutual gaze or eye contact; atypical mutual gaze is the individual's inability to mimic expression during passive viewing but the ability to mimic when instructed to do so.[17]

Another important diagnostic factor is impaired verbal communication.[1,13,4] Language development is often atypical and may include an extended period echolalia--repeating other's vocalizations with or without understanding.[19] Children with ASD often have challenges processing auditory or verbal information.[19] Difficulties in perceiving small auditory changes may lead to deficits in communication development, including lack of age-appropriate language growth.[19]

Individuals with ASD often prefer solitary activities and spend significantly less time making eye contact; however they do focus longer on a speaker's mouth or body.[4,19] Face processing has been associated with early potential for sensory processing, and later cognitive function.[19] Deficits in visual motion processing may impact the ability to process social cues, such as emotional expressions, eye gaze shifts, gesture, and learning and responding to the dynamic environment.[9] More natural and powerful cues come from dynamic facial expressions than static expressions.[22] These behaviors often interfere with positive behavior and provide greater difficulty with integration into the mainstream population.[1]

A child with ASD may suffer from a mood that is erratic with poor sitting tolerance and temper tantrums.[1,3] Social motivation deficit theories suggest children with ASD do not properly recognize or value the pleasures of a social stimulus.[20] There may be difficulty in identifying and explaining inappropriate social behaviors, violating social rules, showing increased levels of interpersonal aggression, poor emotional regulation (e.g. tantrums), and reduced positive interaction behaviors.[21] The individual may poorly distinguish appropriate social behaviors and classify normal behaviors as strange compared to typically developing children.[21]

Social Implication of Autism Spectrum Disorder:

Deficits in social interaction may be expressed in a variety of ways, such as the inability to recognize that others have a point of view, slower reaction times socially, and deficient understanding of emotional facial expressions.[19,22] Recent models show lower behavioral responsiveness to social incentives, such as competition, which could account for reduced social motivation. This deprives children of crucial social-emotional input thereby hindering the later development of communication skills.[20]

Children with ASD showed similar benefits from social reward to typically developed children, which can predict the growth of social communication through reward learning.[5]

Autism and the Brain:

Roughly 90% of toddlers with ASD have 5% to 10% – and as high as ~20%– abnormal enlargement in brain volume by the second or third year of life, which will then shift to abnormally slow growth.[9,12,13,24] The enlarged areas of the brain that are most affected include the frontal, temporal, and parietal lobes, with increased gray matter in the inferior and middle temporal gyri.[25] These abnormal developments of the brain are expected to have an impact on auditory development, and visual motion perception, which may lead to conduction delays that affect functional and structural long-range under-connectivity.[9,13] Long-range under-connectivity within the brain may affect language acquisition.[9] During abnormal development, smaller brain size favors long-distance connections, and conversely large brain size favors short-distance connections.[10] Under-connectivity is observed in older children, adolescents, and adults with ASD.[26] Abnormal hyperplasia within the brain is also observed in the cerebellar vermis, and cerebral cortex.[12] Children may develop normally for 18-30 months showing subtle symptoms but then fail to progress further or even regress.[9] Abnormalities in the connections may become more prevalent as the child ages.[26] Regression may occur in as many as 20-50% of children with ASD, when observed to have a significant digression in language and nonverbal communication skills.[9] The timing of the onset of brain development shown through modeling could explain the variety of the disorder's presentations.[9]

Several studies propose that ASD is associated with altered functional and structural connectivity between brain regions, as opposed to deficits in a specific region. Under-connectivity is observed between frontal-parietal or temporolimbic regions, the limbic system and the cerebellum.[19,25] Also observed are low levels of brain-derived neurotrophic factor (BDNF).[18,25] BDNF not only protects nerves but also encourages the growth of new neurons.

The following regions have been explored for responsibility for differential encoding and are deficient in ASD: anterior superior temporal sulcus (aSTS), posterior STS (pSTS), intraparietal sulcus (IPS), inferior parietal cortex, fusiform gyrus (FFG), amygdala (AMY), and the dorsal medial prefrontal cortex (dmPFC).[18,19,22,26] Brain regions involved in social perception and cognition include the AMY, orbitofrontal cortex, and FFG.[19] The FFG, pSTS, dmPFC and AMY deal with direct gaze.[18]

The anterior cingulate, dorsolateral prefrontal cortex, the caudate, and the dorsal striatum are engaged during repetitive behavior. The amygdala-hippocampus complex is key in social perception and detects threats and elicits an appropriate behavioral response.[19] The AMY also assists with recognition of social emotions of faces, and the integration of visual and auditory information.[9,19] Hyperarousal of the AMY during social stimuli could contribute to the social deficits of a child with autism, overall hypoactivation within the AMY is observed in individuals with ASD outside incidents of social stimuli.[19,22] Difficulty in disengaging from previous tasks may be associated with cognitive inflexibility and is thought to be caused by poor disconnection of the inhibition network in the frontal-parietal process.[19] Hyperactivation is sometimes observed in the frontal cortex and inferior parietal cortex.[19] The anterior cingulate cortex is an important brain region in social orientation involving emotional self-control, focused problem-solving, and error recognition.[19] The cerebellum is associated with the core symptoms of ASD and cerebellar activation is significantly reduced during attention tasks.[12] Purkinje cell loss is consistently observed in the cerebellum for individuals with ASD, possibly affecting impulsivity.[25]

Studies have reported a reduction in theory of mind for individuals with ASD.[21] Theory of mind (ToM) is the ability to attribute mental states to oneself or others and is believed to rely on the medial prefrontal cortex (mPFC), posterior superior temporal sulcus (pSTS), temporoparietal junction (TPJ), and temporal poles.[21] The medial frontal cortex (MFC) has shown unusual activity in individuals with ASD during tasks in adults and irony comprehension (which is related to ToM) in children.[21] The MFC contains the mPFC and is responsible for understanding violations of social norms, morality, appropriateness of facial expressions, and person perception and monitoring.[21] Further, Carter suggests that regional cerebral blood flow is abnormal in the mPFC and that temporal pole activity is found to be abnormal in adults with ASD.[21] The temporal poles are suggested as a key component in the neural circuitry that is impaired in ASD, and it appears to never deactivate after resting state.[21]

Neural deficiencies have also been observed in the anterior cingulate cortex during monetary reward achievement, and ventral striatum in response to both monetary and social reward.[20] These deficits suggest developmental abnormalities in reward circuitry in the frontostriatal and limbic regions, leading to the basis of atypical reward functioning.[20] During direct gaze, a lack of context-dependent activity in the STS was observed and showed no difference in activation compared to typically developed individuals and no change between direct gaze and gaze shifts.[27] The right anterior insula (AI) – important for regulation of emotion – was not activated, while the left lateral occipital complex (LOC) – important for object identification – was active.[27] This shows that some individuals with ASD recruit regions of the brain for processing gaze that a typically developing individual does not.[27] TPJ affects individuals with ASD in opposition to typically developing individuals by being activated during averted gaze in ASD versus direct gaze in typical individuals. Additionally, left dorsolateral prefrontal cortex is diminished during direct gaze similar to the processing of averted gaze in typical individuals.[21]

Brain waves are also affected by ASD including the P300 and N170.[19,20] Children with ASD generally have a smaller amplitude in the P300 leading to delayed information transmission with no change to diminished response in social reward anticipation.[19,20] Social deficits correspond with weaker P300 activity in response to reward anticipation, which may have resulted from a deficit in the intervening reward circuitry.[20] Individuals with ASD also show longer N170 latencies when distinguishing faces, but normal latencies when distinguishing objects.[19]

Children with high functioning ASD have smaller grey matter (GM) volume in the fronto-pallidal region.[24] Thinning in the inferior frontal gyrus is correlated with social difficulties while age-appropriate growth does not occur in the GM volume of right inferior parietal lobule, which is important in social perception and posterior cingulate important in social cognition.[24] Slowing to stopping of white matter tracts in brain regions associated with social cognition has also been observed.[12] Abnormalities which may result in early overgrowth, followed by slow growth, were predominantly observed in the right inferior parietal lobule and posterior cingulate.[24]

Characteristics of Exercise:

Higher levels of fitness are associated with higher brain function over a lifespan.[24] Physical activity is important for the development of the brain and cognition at childhood.[24] During physical activity, a greater level of cognition is required – with more active children outperforming inactive children in cognitive activities.[24,28] Still it is unclear whether duration of physical activity plays a role in brain changes; children did perform at a higher levels of cognitive function when participating in a 40-minute daily dose of exercise in comparison to a 20-minute dose.[29]

Physical activity and exercise can provide opportunities for social interaction. Coordinative movements and motor learning play an important role in cognitive function and development, especially attention and the ability to handle visual and spatial information.[29,30] Improvements in task performance were found after nine months for physically active children; high aerobic capacity helped cognitive function.[8,28] Low intense physical activity such as resistance training may also improve cognitive function.[7] Combining physical activity with speech and language stimulation has shown to increase recall, imitation skills, verbal receptive skills, and expression.[3] Physical activity can provide sensory feedback and physiological arousal in a manner similar to self-stimulation.[1] It may also assist with the flexibility of adaptations of behaviors toward specific goals and maintenance of these goals and for teenagers it assists with cognitive development into late adulthood.[8,29]

Exercise and the Brain:

Single bouts of exercise have been shown to improve cognitive function and neuroplasticity with stimulation after the exercise.[7,28] Exercise plays a crucial function in hormonal regulation, influencing brain circuits involving various neurotransmitters.[28] Physically active individuals show reduced frontal activation after training in areas that were previously active, while increased activation was seen in the frontal, temporal, and parietal lobes.[29] Exercise helps assist with enhancing learning ability and memory function, and protects cognitive decline related to aging and neurodegeneration.[31] Increases in neuroplasticity-related proteins such as BDNF have been observed after bouts of exercise.[32]

The frontal cortex plays a major role in cognitive function and development, including attentional selection, working memory, task switching, and inhibitory control.[8,29] Physically fit children have shown reduced activation of the frontal cortex with a maintenance of attention levels.[8,29] The frontal region involved in task management are shown to be more hypoactive in physically active children.[8] The frontal lobe in children is more susceptible to change than that of a mature individual due to the late development of this region.[7]

The right anterior prefrontal region shows a decrease in activation on fMRI scans from pretest to posttest.[8] Cardiovascular fitness shows higher recruitment of prefrontal and parietal cortex during high cognitive tasks.[29] Studies have demonstrated that physical activity positively affects the anterior prefrontal brain function for goal maintenance throughout one's lifetime, which may lead to a child's participation in physical activity presenting more adult-like recruitment of the anterior prefrontal cortex.[8] Increased brain activation was shown in the frontal and parietal lobes, while a decrease in activation was shown in the anterior cingulate cortex.[7,29] The anterior cingulate cortex works with the anterior prefrontal cortex in cognitive control.[8] Coordination training showed decreased activation of the prefrontal region with stretching shown to increase connectivity between the frontal and parietal regions.[8] This increased connectivity may be beneficial to cognitive function.[8]

Exercise has shown restorative effects and resurgence of the hippocampus improving cognition, and increased volume of the hippocampus as well as improved connectivity between the hippocampus and the anterior cingulate cortex.[29,33] Regional central blood flow improved in various brain structures in response to cognitive tasks leading to better task performance.[7,29,34] Specifically, central blood flow to the hippocampus increased, showing better vascularization of the tissue and increased gray matter.[7,29,34]

After exercise, cerebral blood flow was shown to improve immediately and longer term improvements were seen in cerebrovasculature.[16] Rats undergoing exercise showed an increased number of Purkinje cells and an increased number of synapses of parallel fibers in the cerebellum and the cerebellar cortex – particularly after thirty consecutive days of training.[35] Research has also shown that exercise in adolescent male mice lead to significant changes in the expression of genes associated with synaptic plasticity and signaling pathways.[36]

Exercise and Autism Spectrum Disorder:

Children with ASD spend less time in moderate physical activity than typically developing children. They do not meet the *Healthy People 2010* standard for adolescents 6-17 years of age, which is sixty-minutes of moderate physical activity every day and twenty-minutes of vigorous activity three days a week.[37] One of the limiting factors for not meeting this standard is opportunity, as peers and family play an important role in influencing physical activity regardless of social impairments.[5,30,37] Avoidance of activity may also be a limiting factor and may be due to difficulties with required skills needed for participation.[30]Participation in moderate to vigorous physical activity further declines as the child ages, leading to health concerns associated with inactivity, such as obesity.[1,37,38,39]

Aerobic exercise has been shown to increase positive behaviors and decrease repetitive behaviors, with the greatest decreases occurring right after exercising.[6,11,16,39] There is little evidence, however, of the long-term effects of exercise on repetitive motor behaviors. Special education teachers reported better attentiveness and cooperation after physical activity with individuals with ASD.[1,6,16,39] The physical activity must be of a sufficient length and durability to decrease the repetitive behaviors. However, the length of that change is uncertain. Some have reported an increase in as little as 10 minutes.[1,6] Intensity has also been shown to play an effect, with more vigorous activity amplifying positive behaviors more than light to moderate physical activity.[11,39]

More intense aerobic exercise (i.e., increase of heart rate above 130 bpm) showed a decrease in negative social aspects of ASD such as hyperactivity and aggression. Moderate activity corresponds with an increase in attention span, on-task behavior, and social play.[1,4] In rodent models of ASD, treadmill exercise has shown alleviation of aggressive tendency and improved correct decision making in spatial learning memory.[31] Contingent exercise was also observed to consistently decrease both aggressive actions and comments in individuals with ASD.[15] Following bouts of physical activity; a decrease in negative behaviors was observed along with an increase in positive behaviors such as time on task.[31,39]

Another form of exercise that has shown a positive impact on ASD is yoga; parents have reported an improvement in the ability of the child to interact with others.[3] In addition, there have been observed changes in communication, language, play, and joint attention, as well as eye contact improvement and increased alertness through yoga intervention.[3]

Discussion:

Some evidence supports the notion that early intervention is beneficial to a child with ASD.[14] Interventions should include behavioral, social, and communication skills associated with the disorder.[2] More clinicians are recognizing the importance of healthy sleep, nutrition and exercise as part of an early intervention program. The following section is intended to provide some insight and pose several important questions in regards to exercise and its impact on ASD.

Does exercise assist with the activation of the amygdala during rest? Hypoactivation is observed in the amygdala (AMY).[19] The AMY assists with facial recognition, direct gaze, and integration of visual and auditory stimuli.[9,18,19] When physical activity is combined with speech and language stimulation, improvements are observed in recall, imitation skills, verbal receptive skills, and expression.[3] Occupational therapy has similar sensory feedback as moderate physical activity, and has shown an increase in language use and social interaction.[1] When exercised, rats with ASD showed improved decision making in spatial learning memory.[31]

Could exercise impact the activation of the anterior cingulate cortex (ACC) and alter the repetitive behaviors of ASD? Repetitive behaviors may inhibit the individual's ability to integrate into the mainstream community.[1,16] The ACC is engaged during repetitive behaviors, emotional self-control, and error recognition, and is deficient during monetary reward achievement.[19,20] Physical activity provides stimulation similar to self-stimulatory behaviors, and decreases the activation of the ACC.[1,7,29] With decreased activation of the ACC, bouts of exercise have shown a reduction in self-stimulatory behaviors, hyperactivity, and aggression with an increase in positive behaviors.[1,4,6,11,16,39] The restorative effects of exercise have also improved the connectivity between the hippocampus and the ACC.[29]

Could increasing BDNF encourage the growth of new neurons and assist with improved connectivity? Increased brain size is present in the frontal, temporal, and parietal lobes.[25] It has been hypothesized that this increased size may lead to conduction delays, specifically in long-range under-connectivity.[13] Studies have also reported that ASD is associated with altered functional and structural connectivity.[19] Lower levels of BDNF have been observed.[18,25] Exercise has been shown to increase BDNF and similar neuroplasticity related proteins.[8,32] When combined with coordination training, connectivity between the frontal and parietal lobes improves.[8,32]

If regular physical activity is maintained, could the hyperactivation of the frontal cortex experienced in children with ASD diminish over time?[19] With later development in life, the frontal lobe is more susceptible to change in younger individuals.[7] The frontal cortex is vital in cognitive function and development, reduced activation is observed with exercise.[8,29] Exercise has also been shown to increase attention span and on task behaviors.[1] A reduced activation after training was observed in the frontal areas that were previously active.[29]

A limitation of this review was the lack of open access to research that looked at the long-term effects of exercise on ASD. Also, limited research has been performed on the overall effects of exercise on ASD, while specific studies are needed to break down each known individual mechanic of ASD and how it relates to exercise and development. Further studies are required to determine the potential roles of exercise in the development of individuals with ASD including looking at duration, intensity, and type of exercise.

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