

Abnormalities In Autistic Brains and Behavioral Consequences

Bahar Afsahi¹ and Avi-Yona Israel[#]

¹Canyon Crest Academy

[#]Advisor

ABSTRACT

Autism is a neurological disorder known to manifest in certain classical behaviors. These behaviors include difficulty with social interaction, repetitive behaviors, communication difficulties, sensory issues and obsessive interests. Human behaviors are not only determined by the interactions *within* certain sections of the brain; rather, they are a result of complex interactions of neurons and chemical changes *throughout* the brain. This combinatory quality of the brain makes it difficult to pinpoint the exact areas that cause autistic behaviors. This paper reviews recently published studies on genetics, neuropsychology, brain imaging, and pathology of the autistic brain, in order to summarize the state of the literature on the specific differences in autistic brains. There is scientific consensus that the amygdala, frontal and temporal lobes, cerebellum, prefrontal cortex, synaptic plasticity and cortical organization have significant abnormalities in the autistic brain. These differences contribute to the manifestation of the classical symptoms of autism. Further research should focus on treatment and provision of new therapies for autistic individuals.

Cognitive Aspects of Autism, Generally

Autism spectrum disorder (ASD) is diagnosed in adults and children. Many people believe that autism translates to a learning disability or that an individual diagnosed with autism has a lower IQ however, autism diagnoses exist on a wide spectrum of behaviors and IQ levels. There are certain cognitive deficits and behaviors that all autistic individuals present on some level. The areas of abnormal behavior are known to be in a group of social, communicative and sensory/cognitive behaviors (Baron-Cohen, 2004). This selection of behaviors includes language development, social cues, repetitive behaviors and obsessive interests.

Socially, individuals with ASD often have difficulty receiving and presenting social cues. In Fulvia Castelli et al. (2002), autistic groups gave few and inaccurate descriptions of an emotional interaction of animated triangles while the neurotypical group was able to easily identify the implied interaction. Additionally, individuals with ASD struggle with eye contact and understanding emotions through eyes. In a recent study, a group with ASD and a typical group were tested on the perception of social cues through different images of fearful gazes; the autistic group showed atypical activation in the brain suggesting a shortfall in grasping social cues through gazes (Zürcher et al., 2013). People with ASD experience a general lack of empathy which causes them to have difficulty understanding other mental states beside their own and displaying appropriate behavior for certain situations (Baron-Cohen., 2004). The inability to easily empathize further affects social connections and friendships. Autistic individuals do make close connections and meaningful friendships, but it is more likely for someone with ASD to be socially isolated compared to a neurotypical person. In a public school classroom, autistic children have a higher rate of experiencing exclusion from peers and isolation in social activities (Chan et al., 2023).

Beyond social deficits, communicative issues in autism include language and verbal limitations. Children born with ASD often don't develop verbal language until past two years of age. Some people with high functioning autism are completely non-verbal, meaning they do not communicate with spoken language. The connection of social

and communicative deficits in autism involves the inability to skew from the path of literal language. Autistic individuals have a harder time understanding figurative language, sarcasm and idioms, even if in their first language. A specific indicator of autism is the display of repetitive behavior, such as hand-flapping, echolalia, rocking, routines, and fixated interests. Repetitive behaviors are part of the motor, sensory, and cognitive behaviors featured in autism. These behaviors can actually be seen as deficits or strengths. As well as a triad of deficits in autism, there exists a triad of strengths, by which autistic individuals have great attention to detail, pattern recognition and understanding of input/output systems (Baron-Cohen S 2004). Repetitive behaviors that include obsessions with systems or routines are included as part of this triad.

In many children who are diagnosed with ASD early on, systemizing is an indicating factor. Young children may become intently focused on a simple system such as a light switch (Baron-Cohen, 2008); when presented with a light switch, an autistic child can spend a great amount of time understanding specifically how the light switch works and the result of pressing it. Along with a gift for systemizing, autistic people may have incredibly precise attention to detail. In some individuals, attention to detail can be evident in the way that they speak, such as when they refer to an object with its exact name rather than its generic name. For example, one might refer to their car as a “blue car” while an autistic individual may say “a Blue Honda Civic 2004”. These characteristics allow people with ASD to deeply pursue topics they are passionate about and have an advantage in the sciences, due to the abundance of patterns involved in such disciplines.

Some repetitive behaviors such as hand-flapping and rocking can be results of sensory needs. Sensory issues in autism can range from hypersensitivity to sensory underresponsivity to sensory seeking behaviors (Hazen et al., 2014). To illustrate, a hypersensitive response can manifest as increased anxiety and negative responses to small stimuli, such as a clothing tag. In under-responsive behaviors, individuals can have delayed responses to pain, such as leaving their hand on a hot stove. Sensory seeking behaviors can include the previously-mentioned rocking, resulting from a craving for certain physical stimuli.

Autism and the Amygdala

The *amygdala* is among the vital parts of the brain responsible for regulating emotions, social behavior, and sensory responses towards emotional or fearful objects. As a result of its importance in emotional recognition and social processing, the amygdala has been considered an area of abnormality in autistic brains. Multiple experiments have found a slight abnormality in the development of the amygdala (Salmond et al., 2003). Research has shown us that, in general, there is a rapid amygdalar growth in autistic children, followed by an abnormally slow development as they reach adolescence and adulthood. Another experiment found that, in a group of three high functioning autistic individuals and eleven individuals with Aspergers, half of this group had significant abnormalities in their amygdala compared to a neurotypical group (Salmond et al., 2003). General differences in the amygdala don't explain much about the behavioral changes such a difference causes. More recent studies have shown that, initially, prenatal amygdala growth is normal. However, as the brain continues to develop after birth, the amygdala experiences a prolonged period of growth, due to the migration and maturation of immature neurons, which extends into at least late adolescence (Avinoia et al., 2018). In adults, this growth slows down so that when we compare neurons in the amygdala of normal adults to adults with ASD, we see 20% fewer neurons in the amygdala than in neurotypical adults (Avinoia et al., 2018).

These differences in the amygdala contribute to atypical processing, due to differences in connections and neurons. Specifically, this early maturation and migration contributes to an overactive amygdala. Further, this abnormality in the growth and migration of neurons contributes to the impairment of the amygdala circuit. Kamila Markram et al. (2007) used an animal model of autism to further understand the effects of the abnormally developed amygdala. Using a model of autism in rats, they tested the results of fear conditioning, social interaction, repetitive behaviors, nociception, anxiety, and spatial memory, compared to normal rats. The results in fear conditioning showed that they had enhanced fear memories and an impaired fear extinction rate. This is evidence for the hyperactivity and increased

neuronal density in the amygdala in autistic individuals. The amygdala plays a key role in processing emotional information, and abnormalities in its structure or function can lead to difficulties in recognizing and responding to social cues, as well as general increased anxiety, due to the hyper-sensitivity of an autistically-developed amygdala.

Autism and the Frontal and Temporal Lobes

The frontal and temporal lobes are areas of abnormality in autism which result in sensory issues, “sticky” attention to detail, and difficulty with social cues. The frontal and temporal lobes are highly interconnected regions of the brain. Together, they are significant areas required for language processing, meaning they process speech and body language, as well as responding to a certain context. Next, the two lobes work together in order to regulate emotion. The frontal lobe regulates emotion by controlling impulsive behaviors. The temporal lobes are crucial in processing emotions because of the special region that recognizes and responds to emotional stimuli. Together, the frontal and temporal lobes are able to allow an individual to plan and make decisions that benefit them in the long-term. Lastly, the frontal and temporal lobes are one of the areas that are responsible in the process of social cognition. The temporal lobes are involved in recognizing facial language and understanding social cues that include body language and tone. The frontal lobe is known for controlling an individual's ability to empathize (understand another person's mental state and beliefs). Since the areas that the temporal and frontal lobes are responsible for are areas where autistic individuals have drawbacks, it is an area thought to develop differently in autism.

As seen in Scott-Van Zeeland et. al (2010), there exists a dysfunction of long range connections and an abnormality of white matter fibers (Catani et al., 2016) within the frontal lobe in autistic individuals. Because the frontal lobe is responsible for integrating and sending information to and from multiple areas of the brain, frontal lobe dysfunction can cause difficulty in cognitive and social function, as seen in autism. Additionally, there is hyperconnectivity between the temporal and parietal lobe (Mottron et al., 2014). Because the temporal lobe is involved in the processing of auditory and visual information, while the parietal lobe supports spatial and body awareness, this hyperconnectivity could result in the atypical responses to sensory stimuli (when compared to neurotypical individuals). Not only does this relationship contribute to atypical responses, but hyperconnectivity between these two regions also is a cause of hypersensitivity to sensory inputs, such as sound, textures and visuals.

For non-social tasks, studies have found greater activity in the *middle frontal cortex* (MFC) compared to that of non-autistic individuals (Mottron et al., 2014). The increased activity in the MFC is yet to be explored. According to executive dysfunction theory, the increased activity in the MFC is to compensate for deficits in attention, planning, and cognitive control. Autistic individuals struggle with higher order cognitive processes known as executive behaviors (Christ et al., year). ED theory is based on the idea that an overactive MFC is a compensatory mechanism that allows autistic individuals to perform non-social tasks. Even though the neural processing of a certain task is different in autistic and neurodivergent individuals, the compensatory mechanism allows for this task to be performed at the same level as that of an autistic individual's non-autistic peers (Christ et al., 2010). Overactivity in the MFC may explain the difficulties in shifting attention experienced by autistic individuals (Shafritz et al., 2008).

One of the most active areas of the frontal lobe is the *prefrontal cortex* (PFC). The PFC is crucial in cognitive processes such as planning, working memory, attention, and goal directed behavior. In autistic brains, there is underconnectivity between the PFC and certain regions of the brain that are responsible for global perception of information and information processing (Martínez-Sanchis, 2014). This abnormal connection results in the increased focus on attention and sensory detail. Because the PFC is also related to language processing, autistic individuals have a difficult time understanding body language, using language, and interpreting general social cues (Martínez-Sanchis, 2014).

Autism and the Cerebellum

The *cerebellum* is known for its role in motor coordination, language, emotion, and attention. The main function of the cerebellum is to regulate one's movement, posture, and motor responses. The cerebellum will receive sensory input from multiple areas of the brain (such as the thalamus, brainstem, and cerebral cortex) and process this information in order to produce a motor response. The cerebellum is also involved in higher-order cognitive processes. Like the frontal lobe described earlier, the cerebellum is also responsible for attention and executive functions, such as those that help an individual stay focused on a task. Lastly, the cerebellum contributes to language processing such as comprehension and grammar and also in the regulation of emotions, especially fear.

Autism researchers have frequently investigated the role of the cerebellum, as many autistic individuals present deficits in motor responses, coordination, planning, and comprehension of grammar and syntax. A study made up of 18 neurotypical and 14 autistic individuals was created in order to test the individual brains of the control and autistic group. According to VBM analyses, 11 of the 14 autistic individuals had a significant abnormality in their cerebellum (Salmond et al., 2003). Because this study was not specific to the cerebellum and only proved a general abnormality, its findings with respect to the cerebellum are inconclusive. An abnormality can cause a range of deficits from motor to cognitive and social. Studies have found that, in autistic individuals, there is a reduction in the number of Purkinje cells, and the general volume of their cerebellum is less than that of a neurotypical brain.

Many disorders that are included within the autism spectrum are associated with abnormalities in the cerebellum. (McKelvey et al., 1995; Hallahan et al., 2009; Yu et al., 2011). Imaging of the cerebellar pathways in children with ASD has suggested that there is abnormal connectivity between the cerebellum and cerebellar projections (Sivaswamy et al., 2010). The abnormalities in the cerebellar pathways present themselves through motor and social deficits (Gowen & Hamilton, 2013). Many people on the autism spectrum have difficulty in gross motor skills, such as handwriting, eye-to-body coordination, and repetitive hand movement (Fournier et al., 2010). Since the cerebellum is a vital area for social cognition and language, this cerebellar abnormality causes difficulties in both areas. For example, many people on the autism spectrum have a hard time with eye contact, understanding body language, maintaining conversation, and receiving non-verbal cues. In terms of verbal language, the most common symptoms of cerebellar abnormality are the delayed development of language in children, difficulty with syntax, and confusion in a social context. Lastly, one of the observed results of the difference in cerebellar connectivity is the way it presents itself as a deficit of reward processing, specifically, to social rewards (Dichter & Adolphs, 2012). Autistic individuals have a reduced sensitivity to social stimuli, such as a smiling face (Rogers et al., 2013). In a mouse model of autism, where there was a general or specific abnormality to their cerebellums, the mice showed behaviors such as reduced social interaction, repetitive behaviors, and abnormal responses to their environments (Testa-Silva et al., 2012).

Autism and Cortical Organization

In addition to general abnormalities in the cerebellum, the structure of the cerebral cortex in an autistic individual is quite significant as well. Presently, it is believed that the cortex is divided into regions that are responsible for different functions such as vision, hearing, motor skills, memory, and language. These regions are organized in a way that is crucial for transmission of information through the brain. The cortex is made of many neurons and specialized cells that are organized in six different layers (Casanova, 2010). Each layer is different in shape and organization of neurons. Each layer also receives different inputs and is responsible for certain outputs. One of the most common neurons found in the cortex is the *pyramidal neuron*. These neurons are responsible for executive and sensory functions, such as perception, planning, memory, and decision-making. The way that each layer is organized is based on the type of input it will receive. For example, the visual cortex is responsible for processing perceptive inputs and creating a visual map of an individual's surroundings. The neurons in the visual cortex are packed closely together and are near regions of visual fields.

One of the most vital purposes of cortical organization is the ability for neurons to easily communicate with each other. The communication of neurons can depend on the activity of adjacent neurons and the excess of neurotransmitters. The organization of the cortex can facilitate transmission of information to different areas/layers which is important for producing appropriate cognitive responses (Casanova, 2010). Cortical organization and the general organization of neurons in the brain has been of particular interest to studies of autistic brains, due to the fact that it is responsible for the functions of perception, social behavior, language, and perception. Multiple studies have concluded that there is an abnormality in the neuronal patterning and cortical connectivity of the autistic brain (Pardo et al., 2007). One of the main reasons for the altered neuronal pathways and organization is the atypical growth of the brain (Courchesne et al., 2004). This increased growth rate followed by a decreased growth results in irregular patterns of growth in specific regions of the brain, such as the cerebellar cortex, which is related to the abnormalities in cortical organization.

Further, localized white matter enlargement found in autistic children causes interhemispheric and cortico-cortical connections (Herbert et al., 2004). One of the main results of this difference in autistic brains compared to neurotypical brains is the language delay that many children with ASD experience (Ziegler et al., 2003). Alongside language delay, a study with 18 high functioning autistic individuals and 18 neurotypical individuals found that autistic individuals had lower connectivity among brain regions necessary for executive dysfunction (Just et al., 2007). This study illustrates that the cortical underconnectivity in autistic brains can cause the executive dysfunction symptom that is commonly seen in autism. Overall, the weaker connections between regions of the brain leads to abnormal processing of information which results in social deficits, underdeveloped language processing, issues with sensory processing and executive dysfunction.

Possible Treatments

Currently, there is no complete treatment of autism. However, there are a multitude of ways that individuals decrease the intensities of autistic symptoms. These methods include nutritional treatment, medications and psychological therapies. In terms of nutritional interventions, studies have found that having a gluten-free and casein-free diet can have a very slight effect on autistic symptoms (Whitley et al., 2010). Additionally, supplementing Omega-3 fatty acids has shown a potential benefit in the social aspects of children with autism (Van De Sande et al., 2014). Both of these nutritional changes are based on the hypothesis that autistic individuals have impaired gastrointestinal function which leads to inflammation. Omega 3 fatty acids and a gluten-free diet can help reduce gastrointestinal inflammation. Specifically, Omega-3 fatty acids are thought to possibly reduce inflammation in the brain (Bent et al., 2011). Omega-3 fatty acid has been shown to possibly affect neurotransmitter functions in the brain and overall brain development, which can be important for mood stability, behavior control and cognitive function.

Medical treatments and interventions include medications such as risperidone, methylphenidate, and fluoxetine; these are the three common medications used in autism. Risperidone is an antipsychotic medication that blocks dopamine and serotonin receptors in the brain. This blockage results in a decrease in irritability, aggression and disruptive behavior. According to Maneeton et al. (year), risperidone leads to a decrease in symptoms of autism such as aggression and self-injurious behavior. Methylphenidate is a stimulant medication that works by increasing levels of dopamine and norepinephrine in the brain. These increased levels contribute to increased focus, attention and control over impulsive behavior. This medication is used for attention deficit hyperactivity disorder (ADHD), which is an attention disorder that commonly manifests alongside autism. As a result, methylphenidate is used to improve attention in children with ASD (Struman et al., 2017). Fluoxetine is the other commonly-used medication to improve autistic symptoms. Fluoxetine is classified as a selective serotonin reuptake inhibitor (SSRI). An SSRI increases serotonin levels in the brain by preventing the reuptake of serotonin. This allows for more serotonin to remain between spaces of nerve cells, which can result in more efficient communication between cells because serotonin is a neurotransmitter. Fluoxetine can treat depression, anxiety and obsessive-compulsive disorder (OCD) by moderating mood and increasing serotonin. In individuals with ASD, fluoxetine has improved both repetitive and social behaviors (Todd 1991).

Alongside physical treatments, psychological therapies play a role in the treatment of autistic symptoms. There are multiple different therapies to help improve the symptoms of autism. However, three that are the most common therapies for the treatment of autism are applied behavior analysis (ABA), cognitive behavioral therapy (CBT), and social skills training (SST). Applied behavior therapy is a psychological therapy that focuses on creating skills that reduce problematic behaviors, such as self-injurious behaviors, ignoring social cues, and behaving aggressively with peers. ABA pinpoints problem areas by breaking down large goals into smaller steps. A therapist will usually start with an assessment and devise a behavior plan that can include visual aids, charts, and pictures, to pinpoint a goal for the individual. One of the most crucial components of ABA is positive reinforcement in which desired behavior is rewarded to encourage that specific behavior. Once the patient has made significant progress by acquiring goal behaviors, the ABA therapist will help the individual practice their behavior in different environments, so that they can utilize them in the future and remain independent. Through observation, it has been noted that not only does ABA significantly produce positive behavior in the patient, but it also increases the knowledge and understanding of autism for the family members of the patient (Howlin 2010).

Cognitive behavioral therapy is a therapy targeted at decreasing anxiety, negative mindsets, and improving social skills in autism. When a therapist has analyzed an autistic patient and targets specific skills, such as social, communication, emotional, and problem solving skills, the therapist will begin reconstructing negative thoughts that could be contributing to skill difficulties. Using consistent therapy, positive reinforcement and routines for home, an individual will learn to challenge their negative thoughts that may contribute to anxiety and to base their behavior off of realistic views. However, because CBT utilizes a more abstract approach, it can be difficult for autistic individuals to benefit from it. Further, CBT has shown improvement in anxiety-related issues rather than other autistic behaviors (Howlin, 2010).

Lastly, due to the difficulty autistic people have with social skills and communication, social skills training is often used for treatment in ASD. Therapists will build a plan based on their assessment of a patient to target problem areas. Those problem areas most commonly seen in ASD are understanding nonverbal cues, maintaining conversations, and making eye contact. Therapists use example stories of social situations, videos, and scenarios to help the patient understand how others behave in different types of social situations. After this understanding is acquired, the individual will practice these skills consistently over a period of time at home and in session to feel comfortable. One of the most crucial parts of SST is practicing these skills in multiple environments and situations, as it promotes independence in the future. According to a 2006 review, simply using social scenarios or stories hasn't contributed a significant change in autistic individuals (Ali et al.), which is why it is used in combination with other strategies. Generally, SST has led to a significant improvement in the social skills of autistic individuals, especially when addressed at a young age (Howlin, 2010). The optimal way to treat autism is to identify specific difficulties in an autistic person early in their childhood. Alongside identifying difficulties, one must categorize the functionality of autism in the individual and determine if they are higher functioning (HF) or lower functioning (LF). Once this assessment has been completed, investing in psychological, psychiatric and possibly nutritional pathways together can show the greatest improvement and allow independence, especially for LF individuals.

Summary

Autism spectrum disorder is a neurodevelopmental disorder that affects an individual through social, cognitive, sensory, and, occasionally, motor deficits. It is evident that these classical symptoms are a result of abnormalities in specific regions of the brain and its development. The amygdala, prefrontal cortex, cortical organization and the cerebellum are all partly responsible for the social deficits that people with ASD experience. Multiple brain regions affect one task because segments of the brain work together to produce certain behaviors, and, if a certain region is lesioned or damaged, there is a significant effect on the ability to complete such a task. Sensory issues are present due to abnormalities of cortical organization, frontal lobes, and the cerebellum. General cognitive issues in autism range through all the abnormal regions of the brain, but they are largely caused by atypical cortical organization because it

is responsible for the effective transmission of neuron signals. To augment the results of treatment in autism, it is essential to address the symptoms at a young age and to fully utilize behavioral, psychiatric, and nutritional therapies.

References

- Avino, T. A., Barger, N., Vargas, M. V., Carlson, E. L., Amaral, D. G., Bauman, M. D., & Schumann, C. M. (2018). Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism. *Proceedings of the National Academy of Sciences*, *115*(14), 3710–3715. <https://doi.org/10.1073/pnas.1801912115>
- Baron-Cohen, S. (2004). The Cognitive Neuroscience of Autism. *Journal of Neurology, Neurosurgery & Psychiatry*, *75*(7), 945–948. <https://doi.org/10.1136/jnnp.2003.018713>
- Bent, S., Bertoglio, K., Ashwood, P., Bostrom, A., & Hendren, R. L. (2010). A pilot randomized controlled trial of omega-3 fatty acids for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *41*(5), 545–554. <https://doi.org/10.1007/s10803-010-1078-8>
- Casanova, M. (2010). Cortical organization. *Translational Neuroscience*, *1*(1), 62–71. <https://doi.org/10.2478/v10134-010-0002-2>
- Castelli, F. (2002). Autism, asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain*, *125*(8), 1839–1849. <https://doi.org/10.1093/brain/awf189>
- Catani, M., Dell'Acqua, F., Budisavljevic, S., Howells, H., Thiebaut de Schotten, M., Froudust-Walsh, S., D'Anna, L., Thompson, A., Sandrone, S., Bullmore, E. T., Suckling, J., Baron-Cohen, S., Lombardo, M. V., Wheelwright, S. J., Chakrabarti, B., Lai, M.-C., Ruigrok, A. N., Leemans, A., Ecker, C., ... Murphy, D. G. (2016). Frontal networks in adults with autism spectrum disorder. *Brain*, *139*(2), 616–630. <https://doi.org/10.1093/brain/awv351>
- Chan, D. V., Doran, J. D., & Galobardi, O. D. (2022). Beyond friendship: The spectrum of social participation of autistic adults. *Journal of Autism and Developmental Disorders*, *53*(1), 424–437. <https://doi.org/10.1007/s10803-022-05441-1>
- Chevallier, C., Kohls, G., Troiani, V., Brodtkin, E. S., & Schultz, R. T. (2012). The Social Motivation Theory of Autism. *Trends in Cognitive Sciences*, *16*(4), 231–239. <https://doi.org/10.1016/j.tics.2012.02.007>
- Christ, S. E., Kanne, S. M., & Reiersen, A. M. (2010). Executive function in individuals with subthreshold autism traits. *Neuropsychology*, *24*(5), 590–598. <https://doi.org/10.1037/a0019176>
- Dawson, G., Meltzoff, A. N., Osterling, J., & Rinaldi, J. (1998). Neuropsychological correlates of early symptoms of autism. *Child Development*, *69*(5), 1276. <https://doi.org/10.2307/1132265>
- Fluoxetine in autism. (1991). *American Journal of Psychiatry*, *148*(8). <https://doi.org/10.1176/ajp.148.8.1089b>
- Fournier, K. A., Hass, C. J., Naik, S. K., Lodha, N., & Cauraugh, J. H. (2010). Motor coordination in autism spectrum disorders: A synthesis and meta-analysis. *Journal of Autism and Developmental Disorders*, *40*(10), 1227–1240. <https://doi.org/10.1007/s10803-010-0981-3>
- Groen, W. B., Tesink, C., Petersson, K. M., van Berkum, J., van der Gaag, R. J., Hagoort, P., & Buitelaar, J. K. (2009). Semantic, factual, and social language comprehension in adolescents with autism: An fMRI study. *Cerebral Cortex*, *20*(8), 1937–1945. <https://doi.org/10.1093/cercor/bhp264>
- Happe, F., & Frith, U. (1996). The neuropsychology of autism. *Brain*, *119*(4), 1377–1400. <https://doi.org/10.1093/brain/119.4.1377>
- Hazlett, H. C., Gu, H., McKinstry, R. C., Shaw, D. W. W., Botteron, K. N., Dager, S. R., Styner, M., Vachet, C., Gerig, G., Paterson, S. J., Schultz, R. T., Estes, A. M., Evans, A. C., & Piven, J. (2012). Brain volume findings in 6-month-old infants at high familial risk for autism. *American Journal of Psychiatry*, *169*(6), 601–608. <https://doi.org/10.1176/appi.ajp.2012.11091425>

- Howlin, P. (2010). Evaluating psychological treatments for children with autism-spectrum disorders. *Advances in Psychiatric Treatment, 16*(2), 133–140. <https://doi.org/10.1192/apt.bp.109.006684>
- Just, M. A., Cherkassky, V. L., Keller, T. A., Kana, R. K., & Minshew, N. J. (2006). Functional and anatomical cortical underconnectivity in autism: Evidence from an fmri study of an executive function task and corpus callosum morphometry. *Cerebral Cortex, 17*(4), 951–961. <https://doi.org/10.1093/cercor/bhl006>
- Maneeton, N. (2017). Risperidone versus placebo in the treatment of children and adolescents with autism spectrum disorders: A meta-analysis and systematic review. <https://doi.org/10.26226/morressier.5971be87d462b80290b534c5>
- Markram, K., Rinaldi, T., Mendola, D. L., Sandi, C., & Markram, H. (2007). Abnormal fear conditioning and amygdala processing in an animal model of autism. *Neuropsychopharmacology, 33*(4), 901–912. <https://doi.org/10.1038/sj.npp.1301453>
- MartÃ-nez-Sanchis, S. (2014). Neurobiological foundations of multisensory integration in people with autism spectrum disorders: The role of the medial prefrontal cortex. *Frontiers in Human Neuroscience, 8*. <https://doi.org/10.3389/fnhum.2014.00970>
- McPartland, J. C., Crowley, M. J., Perszyk, D. R., Mukerji, C. E., Naples, A. J., Wu, J., & Mayes, L. C. (2012). Preserved reward outcome processing in ASD as revealed by event-related potentials. *Journal of Neurodevelopmental Disorders, 4*(1). <https://doi.org/10.1186/1866-1955-4-16>
- McPartland, J. C., Crowley, M. J., Perszyk, D. R., Mukerji, C. E., Naples, A. J., Wu, J., & Mayes, L. C. (2012). Preserved reward outcome processing in ASD as revealed by event-related potentials. *Journal of Neurodevelopmental Disorders, 4*(1). <https://doi.org/10.1186/1866-1955-4-16>
- Minshew, N. J., & Williams, D. L. (2007). The New Neurobiology of Autism. *Archives of Neurology, 64*(7), 945. <https://doi.org/10.1001/archneur.64.7.945>
- Mottron, L., Belleville, S., Rouleau, G. A., & Collignon, O. (2014). Linking neocortical, cognitive, and genetic variability in autism with alterations of brain plasticity: The trigger-threshold-target model. *Neuroscience & Biobehavioral Reviews, 47*, 735–752. <https://doi.org/10.1016/j.neubiorev.2014.07.012>
- Pardo, C. A., & Eberhart, C. G. (2007). The Neurobiology of Autism. *Brain Pathology, 17*(4), 434–447. <https://doi.org/10.1111/j.1750-3639.2007.00102.x>
- Rogers, T. D., McKimm, E., Dickson, P. E., Goldowitz, D., Blaha, C. D., & Mittleman, G. (2013). Is autism a disease of the cerebellum? an integration of clinical and pre-clinical research. *Frontiers in Systems Neuroscience, 7*. <https://doi.org/10.3389/fnsys.2013.00015>
- Salmond, C. H., de Haan, M., Friston, K. J., Gadian, D. G., & Vargha-Khadem, F. (2003). Investigating individual differences in brain abnormalities in autism. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 358*(1430), 405–413. <https://doi.org/10.1098/rstb.2002.1210>
- Scott-Van Zeeland, A. A., Abrahams, B. S., Alvarez-Retuerto, A. I., Sonnenblick, L. I., Rudie, J. D., Ghahremani, D., Mumford, J. A., Poldrack, R. A., Dapretto, M., Geschwind, D. H., & Bookheimer, S. Y. (2010). Altered functional connectivity in frontal lobe circuits is associated with variation in the autism risk gene *cntnap2*. *Science Translational Medicine, 2*(56). <https://doi.org/10.1126/scitranslmed.3001344>
- Shafritz, K. M., Dichter, G. S., Baranek, G. T., & Belger, A. (2008). The neural circuitry mediating shifts in behavioral response and cognitive set in autism. *Biological Psychiatry, 63*(10), 974–980. <https://doi.org/10.1016/j.biopsych.2007.06.028>
- Solomon, M., Ozonoff, S. J., Ursu, S., Ravizza, S., Cummings, N., Ly, S., & Carter, C. S. (2009). The neural substrates of cognitive control deficits in autism spectrum disorders. *Neuropsychologia, 47*(12), 2515–2526. <https://doi.org/10.1016/j.neuropsychologia.2009.04.019>
- Sturman, N., Deckx, L., & van Driel, M. L. (2017). Methylphenidate for children and adolescents with autism spectrum disorder. *Cochrane Database of Systematic Reviews, 2017*(11). <https://doi.org/10.1002/14651858.cd011144.pub2>

- Testa-Silva, G., Loebel, A., Giugliano, M., de Kock, C. P. J., Mansvelder, H. D., & Meredith, R. M. (2012). Hyperconnectivity and slow synapses during early development of medial prefrontal cortex in a mouse model for mental retardation and autism. *Cerebral Cortex*, 22(6), 1333–1342. <https://doi.org/10.1093/cercor/bhr224>
- van De Sande, M. M., van Buul, V. J., & Brouns, F. J. (2014). Autism and nutrition: The role of the Gut–Brain Axis. *Nutrition Research Reviews*, 27(2), 199–214. <https://doi.org/10.1017/s0954422414000110>
- Walsh, C. A., Morrow, E. M., & Rubenstein, J. L. R. (2008). Autism and brain development. *Cell*, 135(3), 396–400. <https://doi.org/10.1016/j.cell.2008.10.015>
- Whiteley, P., Haracopos, D., Knivsberg, A.-M., Reichelt, K. L., Parlar, S., Jacobsen, J., Seim, A., Pedersen, L., Schondel, M., & Shattock, P. (2010). The SCANBRIT randomised, controlled, single-blind study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders. *Nutritional Neuroscience*, 13(2), 87–100. <https://doi.org/10.1179/147683010x12611460763922>