Physical Areas of the Brain Affected by Autism Spectrum Disorders

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Abstract

Autism Spectrum Disorders (ASD) are multifaceted developmental disorder of the brain associated with wide ranging cognitive deficits. Typically diagnosed before age three, ASD is behaviorally defined but patients are thought to have protracted alterations in how their brains develop and eventually reach maturity (Hua 2013). This paper explores and explains the physical areas of the brain that are affected in the brains of individuals with Autism Spectrum Disorders. A brief description of this disorder is provided and some basic anatomy of the brain will be explained. Subsequent sections then address some of the physical differences in the brain of individuals with ASD by reviewing historical research, highlighting a few interesting aspects of current research and potential future trends that view development as a comprehensive ecosystem.

Defining Autism Spectrum Disorders (ASD)

Autism Spectrum Disorders (ASD) are complex neurodevelopmental conditions that usually manifest in children before the age of three and are characterized by deficits in social skills and communication ability along with the presence of stereotyped repetitive behavior. Motor skill anomalies and distinct recognizable patterns and styles of movement are also frequently associated with ASD. The study of ASD has intensified recently as the global prevalence of autism has increased more than twentyfold since the earliest epidemiologic studies were conducted in the late 1960's and early 1970's (CDC 2010). There has been a great deal of research into the causes and underlying physical or medical differences that may be neurological in nature. The effort to identify physical differences in the brain and to explain brain-behavior relationships has yet to deliver the results that researchers are seeking, especially in children and teens. According to Xiao (2014), "the literature is still quite limited with regard to information about the neurobiology of ASD in the early age of life."

Autism and Asperger syndrome are both part of the spectrum of autistic disorders. When considering this entire spectrum, it is sometimes helpful to distinguish between low-functioning autism, high-functioning autism, and Asperger Syndrome to allow consideration of them as distinct biological conditions as indicated by measurable neuroanatomical differences, and to test for differences in the particular areas of the brain showing physical differences (Lotspeich 2004). This view of autism as a wide spectrum has triggered considerable debate as to whether children diagnosed with Asperger Syndrome should be looked at as a separate population distinct from high-functioning children with autism. Fueling this debate is the fact that individuals with Asperger Syndrome usually reach normal language milestones, while those described as high-functioning typically display delayed development of language capabilities (McAlonan 2008). Further complicating the efforts to achieve a single definition of ASD is that many patients are not tested specifically for language development to allow detailed analysis of the combined population of all those on the spectrum of autistic disorders.

Asperger Syndrome is a relative newcomer to the lexicon of autism but its sudden rise to prominence in the 1990's was one of the driving forces in the change to describing autism as a spectrum. Asperger Syndrome was not added to the definitive Diagnostic and Statistical Manual of Mental Disorders until the publication of its fourth edition in 1994. The research of Lotspeich (2004) suggests that Asperger Syndrome is on the mild end of the autism spectrum. However, experimental study of brain-IQ relationships has revealed differences between high functioning autism and Asperger Syndrome, indicating that these conditions may be neuro-developmentally different. This distinction surfaces when the various patterns evident in multiple different measures are examined. Further investigations of brain-behavior relationships need to be conducted to validate these findings.

Basic Anatomy of the Brain

In order to describe physical differences in the brain and discuss their impact it is first essential to have a basic understanding of the anatomy of the brain. This knowledge provides a foundation to comprehend the specific descriptions contained in the research findings and understand some of the comparative differences that are found in the brains of someone with ASD. The brain is recognized by medical professionals as the most complex organ in the human body. Weighing only about three-pounds, this organ is responsible for thought, decision-making, interpreting sensory input, memory, judgment, and controlling behavior (Purves 2011). Despite its small size relative to the entire body, the brain consumes twenty percent of all the energy used by the body. Because of its critical and central role, the brain can be viewed as the nexus of all the qualities that define us as human beings.

When individuals view an image of the human brain, it is usually the cerebrum that stands out as the part they notice first. The cerebrum is at the top of the brain and is associated with the most essential of its capabilities: intellect and overall mental capacity. It is the cerebrum where memories are stored, and it is the cerebrum that gives us the human ability to plan ahead, and to use our imagination. The cerebrum is what makes it possible to recognize people in a crowd, to read this paper or a book, and to engage in play. To put it simply, it is the cerebrum that makes it possible for us to think.

The cerebrum is divided by a deep fissure into two seemingly identical halves called hemispheres. Despite this division, the two halves of the cerebrum function as interconnected parts and exchange signals through a thick bundle of nerve fibers called the corpus callosum located at the base of the physical rift that divides the two hemispheres. Although they appear at first to be mirror images of each other, the right and left hemispheres are in fact different. Amaral (2008) provides an example of these differences when he reports that "the ability to form words seems to lie primarily in the left hemisphere, while the right hemisphere seems to control many abstract reasoning skills."

Analyzing the structure of the brain more closely reveals that each half of the cerebrum actually contains multiple distinct sections, known as lobes (see Figure 1). Each of these lobes specializes in different functions. Two **frontal lobes** can be found directly behind the forehead. This part of the brain lets you plan your daily schedule, imagine what the future may be like, or make use of reason and logic to argue your position. The frontal lobes also seem to act as short-term information storage devices, allowing one idea to be retained in the mind and not forgotten even while other ideas are considered.

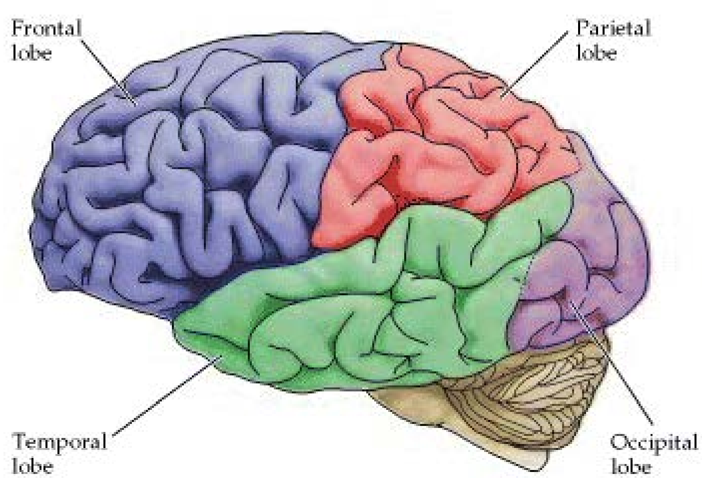

Figure 1: Major functional areas of the brain.
http://www.ncbi.nlm.nih.gov/books/NBK11138/bin/ch1f12.jpg

Toward the rear of each frontal lobe is a **motor area** which enables us to regulate voluntary movement. On the left frontal lobe is **Broca's area** which is where thoughts can be transformed into words. These areas are of particular interest in the study of ASD since the condition is typically associated with impairment of verbal skills, deficits in motor skills, and patterns of repetitive movement (Purves 2011).

Two **parietal lobes** are located behind the frontal lobes and are the areas that help process certain aspects of sensory input of the type that would be involved in appreciating a tasty meal—that is they help to perceive and experience taste, aroma, and the texture of the food. Toward the front of the parietal lobes are **sensory areas** which as their name indicates are primarily responsible for the human senses. These areas receive information through the nervous system from the rest of the body and process the information regarding temperature, taste, touch, and movement. As an example of the intriguing complexity of the brain, these same parietal lobes that handle physical sensations are also responsible for mathematical skills which represent a much more complex and abstract task. The sensory areas of the parietal lobes are of particular interest in the study of ASD since the condition is frequently associated with hypersensitivity to touch and an extremely limited palate of preferred tastes and textures in food (Alexander-Bloch 2013).

Toward the back of the brain are two areas called the **occipital lobes** which make it possible to read the words on this page. This area of the brain processes images from the eyes and can also link that information with images stored in memory. In front of these visual-processing areas, and located underneath the parietal lobes, are the **temporal lobes** which permit the human mind to appreciate music. Not surprisingly, these lobes also receive neural input from the ears and handle auditory processing. The lower portion of the temporal lobe plays a critical role in the formation and subsequent retrieval of memories, including those connected in some way with music. There is no shortage of examples in the literature that support the important connection between music and brain function in those with ASD with several studies exploring the therapeutic use of music as a treatment for problematic behaviors typically associated with ASD (Allen 2010). The temporal lobes have also been found to be involved in a large number of other diverse brain functions and the temporal lobes seem to help integrate memories and sensations of taste, sound, sight, and touch (Alexander-Bloch 2013).

In addition to understanding the primary sections of the brain, it helps to realize that there are different kinds of tissue found in various places of the brain. The outer surface of the cerebrum and the cerebellum is coated with a layer of tissue less than an eighth of an inch thick called the **cortex**. The word cortex derives from the word in Latin for the bark of a tree. This unique structure with its specialized tissue is where much of the information processing activity in the brain takes place. The highly convoluted shape of the tissue in this area results in an increased surface area which supports the processing of great amounts of information.

The term "gray matter" is frequently used to describe this area of the brain and its thin coating or wrapper. The cortex appears to be gray because the nerves in this area do not have an insulating layer of fat cells, and it is this insulating layer of lipids that makes most other parts of the brain appear white rather than gray. Several parts of the brain contain this type of “white matter” such as a large section of the frontal lobes called the basal ganglia which is a collection of nuclei that organize motor behavior. White matter is also found also in spinal cord and is related to carrying motor information between the brain and major muscle groups of the body.

History of Brain Studies

When studying the brains of patients diagnosed with ASD, much attention has been paid to the total volume of material found in major sections of the brain as well as the relative amount of specific types of material in particular sections of the brain. As early as 2002, Stigler reported that “children with ASD were found to have significantly increased cerebral volumes compared with typically developing children and developmentally delayed children." Brain imaging studies were conducted which showed an increase in total brain volume (see Table 1) and the increased volumes were associated with early acceleration in brain growth (Hazlett et al., 2005).

Tissue & Hemisphere	ASD Group	Control Group	Difference
Left Gray	325.4	301.6	23.8
Left White	213.3	197.6	15.7
Right Gray	317.8	308.9	8.9
Left Gray	235.0	218.4	16.6

Table 1: Tissue volumes by hemisphere (Hazlett, et al. 2005)

Despite the intriguing patterns found in such research studies, there is still no consensus regarding the specific correlation of brain volumes with the presence or severity of ASD. Different studies yielded different results and no single pattern of physical differences in the anatomy of the brain emerged (Brun 2009). In addition to variations found in the magnitude of the measurements themselves, differences were also noted in the timing of when these physical changes became noticeable and at what age they could be measured (Verhoeven 2010). Some studies also found variations that did not appear until adulthood (Nicolson & Szatmari 2003). Beyond these differences in studies that measured increases in overall volume, other attempts to identify the specific part of the brain where the volume increase occurred were also inconsistent in their findings (Bonilha et al., 2008).

Just as variations were found across studies of changes in brain volume, there have been inconsistent results reported by those attempting to correlate ASD with the relative prevalence or absolute amounts of gray and white matter. Some studies of patients with ASD found only differences in white matter, some found variations in only gray matter, and yet other studies found increases in the amount of both types (Nicolson & Szatmari 2003). Early MRI studies were also inconclusive in efforts to make the connection between volume differences or tissue type variations in the brain and ASD.

ASD and Brain Studies Today

Most traditional attempts to measure sections of the brain took measurements by volume and focused on specific region of interest (Yushkevich et al., 2006). These attempts to measure the volume of major sections of the brain were not designed to detect subtle differences or highly localized differences and may have overlooked such variations. Increasingly researchers have embraced the use of advanced mapping methods to accurately examine brain structure. Unlike the earlier studies that considered only volume differences, the statistical charts and images produced by these new mapping techniques can detect highly localized differences without the need to specify in advance where to look (Thompson et al., 2004).

New studies are also making better use of magnetic resonance imaging which allows researchers to virtually see inside tissue that is still alive to provide detailed pictures of internal brain structures without the need for dangerous invasive procedures. A number of these specialized and adapted techniques now allow scientists to clearly visualize blood flow, observe fluid and tissue movement, and detect the presence and concentration of various organic molecules. One of the main techniques investigators use to visualize neural activity in the brain is functional magnetic resonance imaging (fMRI). This type of MRI technique uses the magnetic fields generated by the machine to record images of brain activity in real-time as the people being observed perform experimental tasks (Booker 2013). The equipment that is most commonly used in this type of experiment is specifically designed to detect changes in blood flow within specific areas of the brain.

When sections of the brain become active, blood flow to those sections is increased to bring needed oxygen to these busy cells. Oxygen-rich blood has been found to have different magnetic properties than oxygen-poor blood. These differences in what is known as the "blood oxygen-level-dependent" signal can be measured and mapped by fMRI technology. These image maps provide a dramatic picture of brain activity (Booker 2013 see Figure 2).

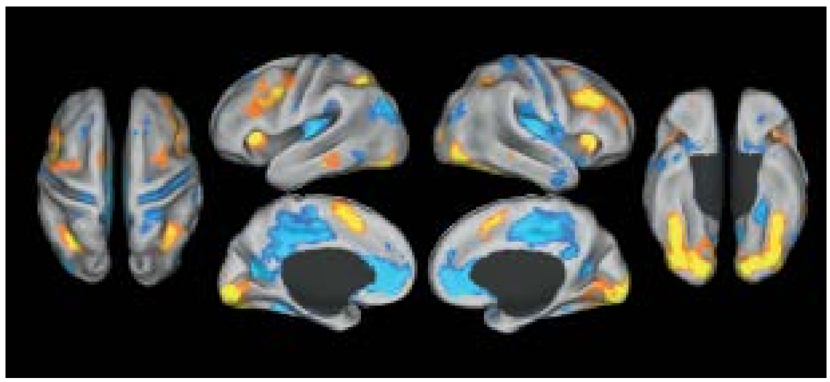

Figure 2: Results from the first cognitive neuroscience fMRI study at the Cornell MRI Facility, which required participants to match pictures of faces during a working memory task. Brain activity is shown in gold, and deactivated regions are in blue (Booker, 2013).

The resulting high resolution images are very large files but researchers are now able to leverage powerful computers to process the images and use the latest methods of statistical analyses to extract meaningful data. These methods have detected thinning of the tissue in very specific localized regions of the brain and subtle volume reductions in other defined areas in the brains of patients with ASD, even when there was no significant reduction in the overall volume of the brain (Verhoeven 2010).

The term “voxel” is used to describe a tiny and specific area within the brain. The word is a combination volume and pixel, and can be understood as the three-dimensional analogue of a pixel. A voxel is a volume element representing some specific numerical quantity of medical data. The smallest brain area that can be measured by the type of MRI used in brain studies is usually a 3mm to 5mm three-dimensional volume (Ashburner 2000). For comparison purposes this would be a cube of matter barely one eighth of an inch long on each side.

Researchers have also studied variations in the thickness of the membrane that divides the two hemispheres of the cerebrum and considered how those variances might be responsible for increases in overall brain volume in those with ASD (Hardan et al. 2009). Since the membrane being studied, the corpus callosum, serves to connect the two hemispheres, researchers also studied the possibility that changes in connectivity, rather than volume alone, might be the significant correlating factor in the brains of those with ASD. Hardan conducted other research (2008) which focused on a different area of the brain, the thalamus, using an advanced voxel-based imaging technology called multi-voxel, short echo-time proton magnetic resonance spectroscopy (H MRS). In this study he demonstrated again that volume alone did not show significant differences, but the relative amount of tissue types and differences in connectivity surfaced as topics worthy of further study. In yet another voxel-based mapping study, McAlonan (2005) reported that in some cases overall volume of the brain was normal in patients with ASD but the ratio of white matter to gray matter was significantly higher suggesting a lack of one critical material and an excess of another.

Another new direction for researchers is the rapidly evolving field of 3-D imaging and modeling. These new approaches combine existing MRI techniques with precise three dimensional mapping of the locations in each image down to the resolution of a single voxel. This allows overlays to be made showing very precise locations in multiple different brains. One such approach is called Tensor-Based Morphometry (TBM) which leverages the improved resolution now possible in brain scans along with the latest image processing techniques. This automated image analysis technique allows researchers to identify and characterize the structural differences in brain measurements among different populations (Hua 2013).

One factor that influences the validity of the findings in some patients studied by researchers is that patients were taking psychotropic medications. By design, these medications affect brain function and can, in some cases, impair the normal physical development of the brain (Williamson 2012). Although such medications are not usually prescribed for the diagnosis of ASD alone, the potential to negatively affect the validity of results is significant because ASD is often accompanied by other co-morbid conditions for which such medications are indicated (Bearden et al., 2007).

Impacts of Brain Studies on Understanding ASD

A number of studies have found excesses and deficits in adjacent regions of the brain which may indicate impaired connectivity of the nerve structures that serve to connect the different regions of the brain. This may result from inflammation in the area or from improper development of the fatty layer around the nerves, a process known as myelination. This pattern may also help to explain the divergent findings from earlier studies that showed inconsistent differences within specific brain sections of patients with ASD (Brun 2009).

Historical evidence clearly shows that ASD occurs with far greater frequency in boys than girls. In 2010 the Centers for Disease Control reported the ratio as almost five to one which translates into 80% of those diagnosed with ASD being boys (CDC 2010). It is not surprising to find that much of the research done to date has been studying boys. However, in those girls who were diagnosed with ASD, all of the same variations in brain volume and size were found (Bloss 2007). Some new areas not previously noticed in the study of the brains of boys were found to have unusual volumes and variations in the girls. Variations were also found in the amount and specific location of white and gray matter. The study of girls also revealed a strong correlation between patient age and increased volumes while no such relationship between age and brain volume had been found in the brains of boys (Bloss 2007).

Future Trends

One of the most promising areas of study now receiving focus and attention from researchers is the study of the brain from an ecosystem perspective. This approach is based on the premise that a dynamic interdependency exists among perception, cognition, and motor activity. According to Brandwein (2014), "individuals with ASD are impaired in their ability to integrate socially relevant audiovisual (AV) information, and it has been suggested that this contributes to the higher-order social and cognitive deficits observed in ASD." For practical reasons, many researchers have so far shied away from this complex view and comprehensive perspective.

Much research to date has been compartmentalized and focused on singular and specific differences in one area at a time. This narrow focus on only one area downplays the importance of the relationship between the three functions. By taking the combined view, future research can operate in the context that a human being is more than just the sum of the parts of the individual systems and functions. This approach will also support the inclusion of the sensory environment and experiential context as critical elements of study in analyzing the relevance of measured physical differences in the brains of those with ASD. Adopting the paradigm of an ecosystem takes into consideration the importance of context with regard to cognition and encourages the exploration of the intriguing relationship between perception and motor skills (Zachor 2013).

Conclusion

Research has led us to a point where we can definitively identify specific physical differences in the brains of patients with ASD. These differences frequently manifest as changes in volume or in the relative amount of brain matter of different types. Differences have also been identified in the connectivity between sections within the brain. Correlation has been demonstrated, but the research has not yet been able to establish causal relationships between physical changes in particular areas of the brain and specific aspects of behavior or capacity in patients with ASD.

New techniques are refining the precision with which physical differences in the brain can be found, mapped, tracked over time and compared between groups. Imaging technology and computer analytics become more accurate and more powerful with each passing year. These enhancements are enabling more precise studies of the physical differences found in different sections of the brain and the neural connectivity between them (Bons 2013). The establishment of ASD as a true spectrum of disorders has helped make it possible to conduct more research and to organize and present results more effectively.

The key to finding causal relationships may lie in the new approach which takes an ecosystem perspective and studies the full canvas of human behavior in context. This approach goes beyond simple biology and behavior to integrate motion, perception and cognition. One of the most promising aspects of this new research involves the use of specific sensory tests that can be administered at very young ages. Preliminary findings indicate a strong correlation between the results of these tests and the severity of impairment displayed years later in the same group of subjects (Brandwein 2014).

Given the rapid increase in ASD diagnoses, this new theme of integrated research and its view of the ecosystem of existence for those with ASD may be of critical importance. This comprehensive point of view may lead to better understanding of the physical differences in the brains of individuals with ASD, and may even lead to treatments and interventions that influence the mental processes and functions within the brain. Researchers are seeking ways to reduce the impairments of ASD and raise the probability that patients diagnosed with ASD can look forward to improved quality of life and realize their full potential as contributing members of society.

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