

## Exploring Brain Imaging Measures and Autism Spectrum Disorder Phenotypes Between Males and Females

---

Oluwatofunmi Love Afolabi

### Abstract

Neuroimaging techniques such as MRI scans can help determine several factors when it comes to assessing the severity of Autism Spectrum Disorder and tailoring interventions and management strategies for individuals with ASD. The purpose of this study was to explore the relationship between neuroimaging data quality and the manifestation of various cognitive measures in individuals with ASD, with a particular focus on sex as a moderating factor. The data from this study was obtained from the Preprocessed Connectomes Project, which systematically preprocessed the data from the 1000 Functional Connectomes Project (FCP) and International Neuroimaging Data-sharing Initiative (INDI) and openly shared the results. 1112 Participants were involved in data collection, ages ranged between (6 - 64) with a vast majority of them (19 or younger). Factors such as verbal intelligence, Foreground to Background Energy Ratio, Signal to Noise Ratio, Autism Diagnostic Observation Schedule total score (ADOS\_TOTAL), Full-Scale IQ, etc were all collected. After analyzing data, there is a significant positive relationship between age and anat\_snr in males, indicating that older males tend to have higher signal-to-noise ratios. In contrast, in females it is absent, indicating that older females tend to have lower signal-to-noise ratios. However, in both males and females, the severity of autism symptoms measured by ADOS\_TOTAL has no significant impact on the quality of anatomical MRI scans (anat\_snr). Improving MRI data quality and understanding its relationship with cognitive and behavioral measures can lead to more accurate and reliable diagnostic criteria and assessments for ASD.

### 1. Introduction

Autism Spectrum disorder (ASD) is a neurodevelopmental disability often caused by deviations from healthy brain development in humans. Once considered a rare diagnosis, improvements have revealed this condition as a prominent neurodevelopmental disorder. ASD is now characterized by challenges in social communication, repetitive, restricted behavior patterns, and atypical responses to sensory stimuli, as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The severity of symptoms of ASD patients is on a broad spectrum, ranging from severe intellectual disability to forms of the disorder that permit individuals to live independent lives. However, the neurobiological causes of this disorder

remain largely unknown. Much rarer is how neuroanatomical features of patients with ASD differ between sexes. Here, we use a correlational approach to determine the presence of sex differences across a variety of brain imaging measures that reveal some subtleties of how this condition impacts males and females.

The brain is divided into two right and left hemispheres. The left hemisphere is largely thought to control the right side of the human body whereas the right hemisphere controls the left side of the human body. Although they have separate functions, they work cohesively to ensure the body functions properly. However, researchers have found that individuals diagnosed with ASD may experience difficulty in communication between the two hemispheres due to weaker connections between them (Belmonte et al., 2004). Furthermore, according to researchers (Lord et al., 2012), differences in brain structure extend to the functional lobes of the brain, including regions that are key for decision-making and verbal abilities. Brains from ASD patients exhibit variations in the folding patterns of the cerebral cortex, particularly in the parietal, temporal, and frontal regions. These variations are associated with changes in neuronal network connectivity, which are thought to reflect deficits in executive functioning in these patients. Another consequence of ASD is weak connectivity within the sulci, that is, the shallow grooves and furrows on the surface of the brain. Deeper sulcal pits are linked to greater impacts on language production, as seen in autistic individuals (Im et al., 2011). Despite this information, there are still many more mysteries to uncover in the neurobiology of the brain impacted by ASD in the context of sex differences. Uncovering these mysteries will aid our understanding of treatment approaches that are more appropriate for one sex or the other.

Indeed, ASD is more prevalent in males than females (Schuck et al., 2019). According to the most recent report from the United States Center for Disease Control and Prevention, one in 38 boys and one in 152 girls aged eight years were diagnosed with ASD (Baio et al. 2018). The same report revealed that, although the average prevalence of males to females with a diagnosis is 4:1. The discrepancy in prevalence rates may indicate a distinct phenotypic difference between males and females with ASD, which may overall be reflected in the aforementioned structural measures of the brain.

In this research paper, I will explore various neurobiological measures from a brain imaging study and investigate their correlation with ASD symptoms, such as cognitive abilities, while shedding light on potential gender differences.

## 2. Methods

Data was collected from the Preprocessed Connectomes Project, which systematically preprocessed the data from the 1000 Functional Connectomes Project (FCP) and International Neuroimaging Data-sharing Initiative (INDI) and openly shared the results. The data encompassing individuals (mostly children) with Autism Spectrum Disorder was analyzed. Participants consisted of 1112 individuals, 165 were females and 947 were males.

## 2.1. Verbal IQ in ASD

Verbal Intelligence is the ability to understand, use, and manipulate language effectively, including skills such as comprehension, expression, and articulation of words and ideas. VIQ (Verbal Intelligence Quotient) is a numerical measurement of an individual's ability to reason out and understand others through spoken words. It measures a person's verbal and linguistic abilities and assesses comprehension, reasoning, expression, acquired knowledge, and attention to verbal information. Autism is a spectrum disorder, meaning it manifests differently in each person. Some individuals with autism might have low VIQ while others excel in this area and thus VIQ will be one of our key variables.

## 2.2. Foreground to Background Energy Ratio (*anat\_fber*) in ASD

*Anat\_fber* is our variable for a metric used in neuroimaging studies to assess the quality of brain images, particularly in diffusion MRI scans. It measures the contrast between the images' foreground (signal) and background (noise). In studies involving Autism Spectrum Disorder (ASD), researchers use this information to ensure the reliability and accuracy of the imaging data collected from individuals with ASD. High-quality images are crucial for accurately studying brain structure and connectivity differences associated with ASD.

## 2.3. Signal to Noise Ratio (*anat\_snr*)

In Neuroimaging research, *anat\_snr* is used to assess the quality of anatomical images from MRI scans. It is used to measure how much useful information (signal) can be separated from the contaminating background noise. A higher SNR indicates a more reliable, clear, and useful image allowing for more accurate readings when analyzing data. Several factors can affect the outcome of the SNR value, such as participant movement. For example, movement during scanning can create noise and reduce SNR. Therefore, it is crucial to account for movement in analyzing imaging data, especially in populations like children with ASD, who may have difficulty staying still. Researchers may use SNR to develop biomarkers for ASD, thereby leading to better diagnostic tools and therapeutic targets.

## 2.4. Mean Distance to Median Volume (*func\_quality*)

This is a control metric used in functional MRI (fMRI) scans to detect the consistency of the image's volume over time. It is used to evaluate the reliability of fMRI images, which is especially crucial when dealing with studies involving individuals with ASD. The median volume is the image volume that is the middle value when all volumes are sorted by a particular feature such as intensity or some other characteristic. The mean distance is calculated by taking the

average of the differences between each volume in the series and the median volume. A lower mean distance to the median volume shows that the volumes are more consistent with each other, suggesting that the data is of higher quality and reliability. Children and individuals sometimes struggle with being still during the scanning process, thus this metric helps in quantifying and managing these discrepancies which lead to more reliable and consistent conclusions.

## **2.5. ADOS\_TOTAL**

It is the total score derived from the Autism Diagnostic Observation Schedule (ADOS), a standardized diagnostic tool used to assess and diagnose ASD. The ADOS is a series of structured tasks and assessments that allow clinicians to effectively analyze the social interaction, communication, and play in individuals suspected of having ASD. The ADOS is divided into different modules based on a person's age and language abilities. Each module includes a variety of activities designed to elicit behaviors pertinent to ASD. Scores from various items are combined to generate the total score, referred to as *ADOS\_TOTAL*. The *ADOS\_TOTAL* score is used to determine the severity of ASD-related symptoms and behaviors. Higher *ADOS\_TOTAL* scores indicate a greater severity of autism-related symptoms. It helps facilitate both clinical decision-making and research into the treatment of ASD.

## **2.6. Full-Scale IQ (FSIQ)**

This is a measure of an individual's overall cognitive ability. It can be derived from standardized intelligence tests, such as the Wechsler Intelligence Scale for Children (WISC) or the Wechsler Adult Intelligence Scale (WAIS). In Autism Spectrum Disorder (ASD), *FSIQ* is used to assess the cognitive capacity such as verbal comprehension, perceptual reasoning, working memory, and processing speed of individuals with ASD. Some individuals with ASD may have intellectual disabilities (*FSIQ* below 70), while others may have average or above-average intelligence, thus making it a key variable for diagnostic purposes and for planning personalized interventions. It is important to note that *FSIQ* is only one aspect of cognitive functioning and may not fully capture the diverse abilities and challenges faced by individuals with ASD. It is important to note that factors such as anxiety, attention difficulties, and sensory sensitivities can affect test performance, and thus the *FSIQ* score, in individuals with ASD.

## **2.9. Fraction of Outlier Voxels (*func\_outlier*)**

This is a metric used in fMRI to assess the quality of images. It represents the proportion of brain voxels with unusually high or low signal intensities, indicating potential artifacts or noise in the data. High *func\_outlier* values can indicate the need for additional preprocessing steps,

such as motion correction, spatial normalization, or artifact removal, to improve data quality. Func\_outlier helps with the reliability of the data, making sure it is consistent and comparable. Outlier voxels can disrupt measures of functional connectivity, leading to inaccurate interpretations of the brain network activity.

## 2.10. Data Analysis

After organizing the data by sex, linear regression plots were created to compare various variables across this segmented patient population. Here we report  $R^2$  of simple linear regressions used to test whether each of our variables of interest could explain the variance of another. Our threshold for statistical significance was set at  $\alpha = 0.05$ .

## 3. Results

### 3.1. Association between VIQ and anat\_fber covariates

First, we wanted to compare verbal IQ (VIQ) and the Foreground to Background Energy Ratio (anat\_fber) in anatomical MRI data among individuals with ASD, stratified by sex. This association will show whether there are gender-specific associations between verbal IQ and the energy distribution in the MRI images. It will explore potential differences in the neural correlates of verbal IQ between males and females with ASD. The aim is to understand if there is a relationship between verbal intelligence and the quality or characteristics of brain images in individuals with ASD. This data was stratified by sex because there might be sex-specific neural mechanisms underlying verbal IQ in ASD. For instance, males and females might rely on different brain regions or networks for verbal processing.

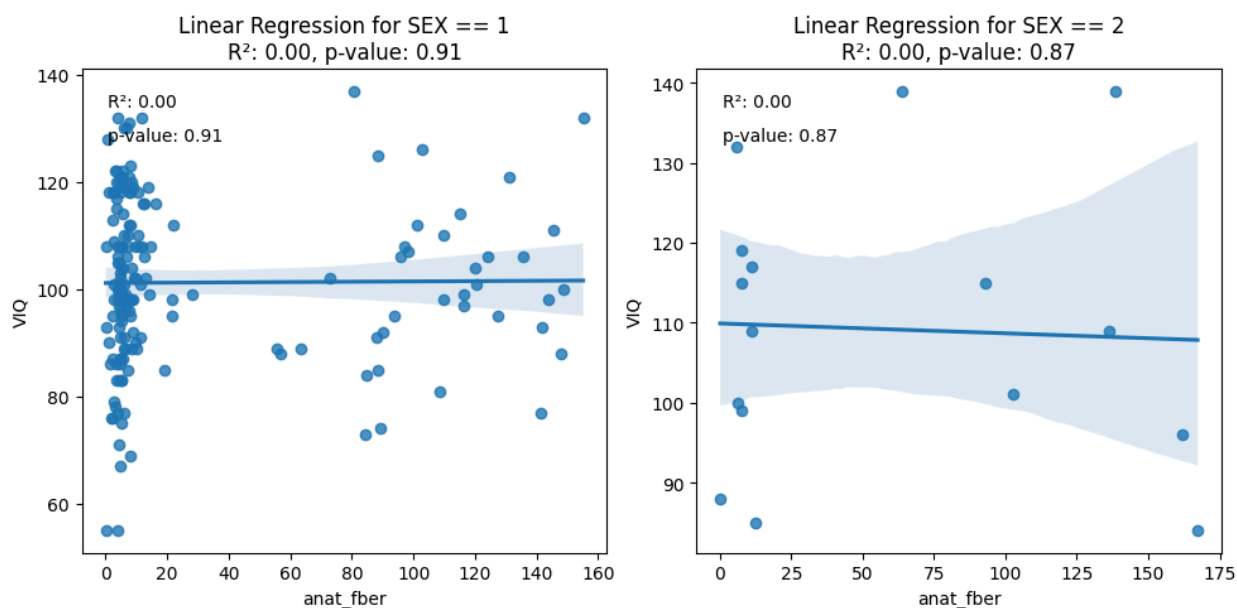


Figure 1: The image above represents a Linear Regression plot comparing *VIQ* to *anat\_fber*. SEX 1 indicates males, SEX 2 indicates females.

Simple linear regression analysis was used to test whether *VIQ* explained *anat\_fber* in SEX = 1, which indicates males (Fig. 1, left). The results of the regression indicated that one predictor *anat\_fber* explained a non-significant amount of the variation in *VIQ* [ $R^2 = 0.00$ ,  $p = 0.91$ ]. These results were not significant at the  $p > .05$  level. There is a 91% chance that the observed relationship (or lack of) between *VIQ* and *anat\_fber* occurred by random chance. This high p-value indicates that the relationship is not statistically significant, suggesting there is no meaningful association between the variables for males with ASD.

Simple linear regression analysis was also used to test whether *VIQ* explained *anat\_fber* in SEX = 2, which indicates females (Fig. 1, right). The results of the regression indicated that one predictor *anat\_fber* explained a non-significant amount of the variation in *VIQ* [ $R^2 = 0.00$ ,  $p = 0.87$ ]. These results were not significant at the  $p > .05$  level. There is an 87% chance that the observed relationship (or lack thereof) between *VIQ* and *anat\_fber* occurred by random chance. This high p-value suggests that the relationship is not statistically significant, suggesting that there is no meaningful association between the variables for females with ASD. In other words, knowing the *anat\_fber* value does not help in predicting *VIQ* at all for both males and females in this group.

### **3.2. Association between Age at scan and *anat\_snr* vs Age at scan and *func\_quality* covariates**

This research also compares age at scan (Age at Scan) with the relationship between the Signal to Noise Ratio (*anat\_snr*) in the anatomical MRI data and the Mean Distance to Median Volume (*func\_quality*) in the functional MRI data among individuals with ASD, stratified by sex. This association will show how age-related factors may influence the association between anatomical and functional MRI data quality. By examining the Age at Scan with the relationship between *anat\_snr* and *func\_quality*, this research aims to understand if and how age influences the quality of both anatomical and functional MRI data. Understanding how age impacts MRI data quality is vital because it can better optimize imaging protocols and data interpretation for different age groups. For example, younger children might have lower *anat\_snr* because of difficulties sitting still during the scan, while older age groups might show different patterns in *func\_quality* due to developmental changes.

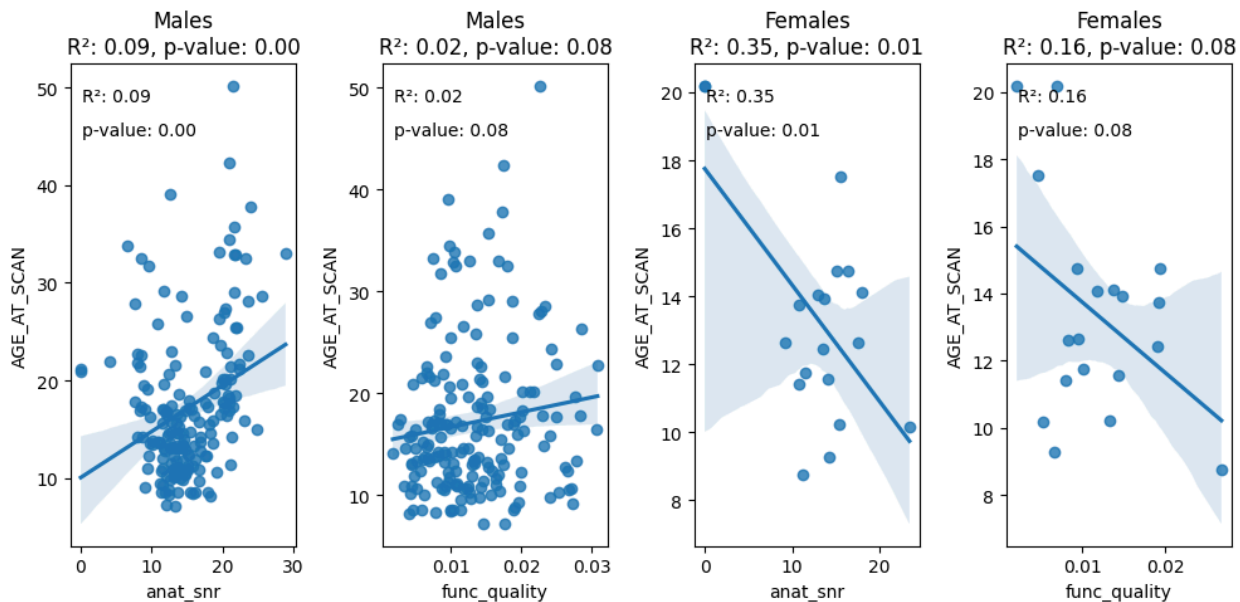


Figure 2. The image above represents a Linear Regression plot comparing age at scan vs. *anat\_snr* to age at scan vs. *func\_quality*. SEX 1 indicates males, SEX 2 indicates females.

Simple linear regression analysis was used to test whether *anat\_snr* explained age at scan in SEX = 1, which indicates male (Fig. 2, males, left panels). The results of the regression indicated that one predictor, *anat\_snr*, explained a significant amount of the variation in age at scan [ $R^2 = 0.09$ ,  $p = 0.00$ ]. These results were significant at  $p < .05$  level. This means only 9% of the variance in age at scan can be explained by *anat\_snr*. a relatively weak, but present, relationship between these variables. There is a very low probability (less than 1%) that this relationship is due to random chance. The positive correlation indicates that as age increases, *anat\_snr* tends to increase. This suggests an association between age and *anat\_snr* for males, meaning older males generally have higher *anat\_snr* values, potentially due to better compliance or reduced motion during scans.

Simple linear regression analysis was also used to test whether *anat\_snr* explained age at scan in SEX = 2, which indicates females (Fig. 2, females, left panels). The results of the regression indicated that one predictor, *anat\_snr*, explained a significant amount of the variation in age at scan [ $R^2 = 0.35$ ,  $p = 0.01$ ]. These results were significant at  $p < .05$  level. The negative correlation shows that older females tend to have lower *anat\_snr* values in their anatomical MRI scans, which could reflect age-related factors affecting image quality. There is a very low probability that this relationship is due to random chance. This result supports the finding that age influences *anat\_snr* in females, meaning older females generally have lower *anat\_snr* values, potentially due to different physiological changes compared to males.

Simple linear regression analysis was used to test whether *func\_quality* explained age at scan in SEX = 1, which indicates males (Fig. 2, males, right panels). The results of the regression indicated that one predictor, *func\_quality*, explained a non-significant amount of the

variation in age at scan [ $R^2 = 0.02$ ,  $p = 0.08$ ]. These results were not significant at  $p > .05$  level. This indicates a very weak relationship between these variables. The weak correlation suggests that age has little to no effect on the *func\_quality* metric for males with ASD. Thus, the observed relationship between age and *func\_quality* in males could likely be due to random chance.

Simple linear regression analysis was also used to test whether *func\_quality* explained age at scan in  $SEX = 2$ , which indicates females (Fig. 2, females, right panels). The results of the regression indicated that one predictor, *func\_quality*, explained a non-significant amount of the variation in age at scan [ $R^2 = 0.16$ ,  $p = 0.08$ ]. These results were not significant at  $p > .05$  level. This indicates a moderate relationship between these variables. The negative correlation indicates that older females tend to have worse *func\_quality*. Although the results show a potential trend in this correlation, more research is needed to definitively confirm this association.

In males, there is a significant positive relationship between age and *anat\_snr*, indicating that older males tend to have higher signal-to-noise ratios. However, there is no significant relationship between age and *func\_quality*. In females, there is a significant negative relationship between age and *anat\_snr*, indicating that older females tend to have lower signal-to-noise ratios. There is also a potential negative trend between age and *func\_quality*, although it is not statistically significant.

### 3.3. Association between *ADOS\_TOTAL* and *anat\_snr* covariates

The research goes on to compare the severity of autism symptoms (e.g., *ADOS\_TOTAL*) with the Signal to Noise Ratio, *anat\_snr*, in the anatomical MRI data among people with ASD, stratified by sex (males and females). This aims to show whether the severity of autism symptoms, measured by (*ADOS*), is associated with the quality of anatomical MRI scans of people with ASD. There could be potential links between the behaviors associated with ASD and anatomical neural images. This can help determine if certain autism symptoms are connected to specific features in brain scans. If a significant association is found, it could indicate that the severity of ASD symptoms is related to the quality of MRI scans. For instance, more severe symptoms could be linked to lower *anat\_snr*, potentially due to increased movement during scans or other factors. If symptom severities are associated with specific image qualities, we can improve the interpretation of MRI data in ASD research. Researchers can account for these factors when analyzing MRI scans, leading to more accurate and reliable results.



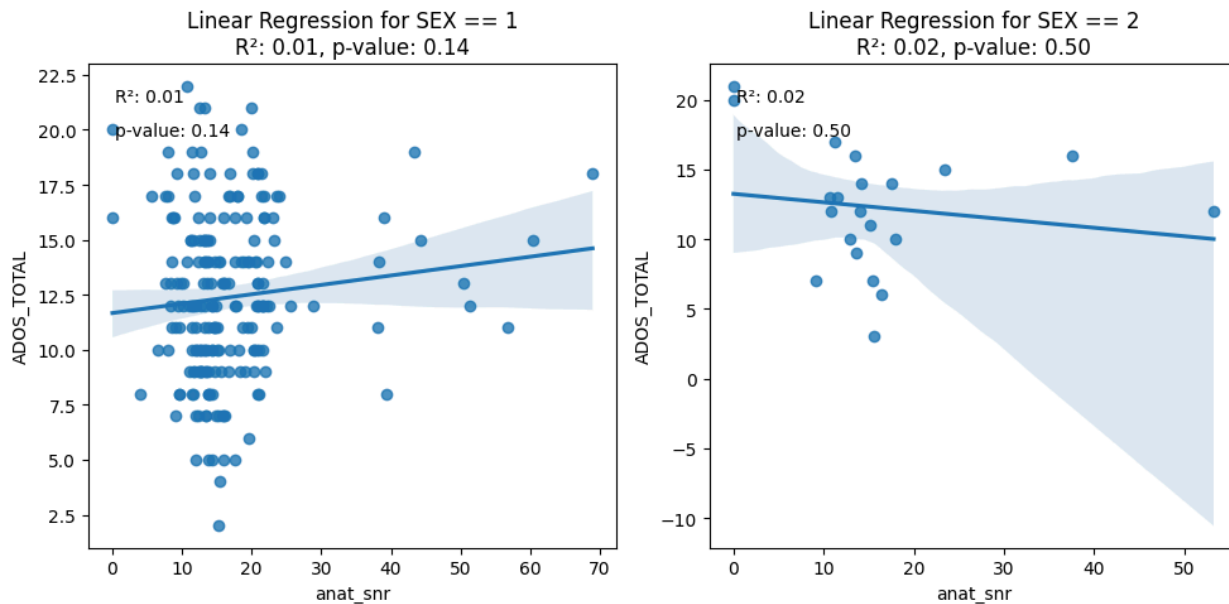


Figure 3: The image above represents a Linear Regression plot comparing *ADOS\_TOTAL* to *anat\_snr*.  
SEX 1 are the males, SEX 2 females.

Simple linear regression analysis was used to test whether *anat\_snr* explained *ADOS\_TOTAL* in SEX = 1 (Fig. 3, left), which indicates males. The results of the regression indicated that one predictor *anat\_snr* explained a non-significant amount of the variation in *ADOS\_TOTAL* [ $R^2 = 0.01$ ,  $p = 0.14$ ]. These results were not significant at the  $p > .05$  level. There is a very weak relationship between these variables. This weak correlation suggests that the quality of anatomical MRI scans (*anat\_snr*) does not significantly vary with the severity of autism symptoms (*ADOS\_TOTAL*) in males. This is an indication that any observed association between *ADOS\_TOTAL* and *anat\_snr* in males could likely be due to random chance rather than a true underlying relationship.

Simple linear regression analysis was also used to test whether *anat\_snr* explained *ADOS\_TOTAL* in SEX = 2 (Fig. 3, right), which indicates females. The results of the regression indicated that one predictor *anat\_snr* explained a non-significant amount of the variation in *ADOS\_TOTAL* [ $R^2 = 0.02$ ,  $p = 0.50$ ]. These results were not significant at the  $p > .05$  level. This is a very weak relationship between these variables. Similar to males, the weak correlation suggests that the quality of anatomical MRI scans (*anat\_snr*) does not significantly vary with the severity of autism symptoms (*ADOS\_TOTAL*) in females. This also implies that any observed association between *ADOS\_TOTAL* and *anat\_snr* in females is likely due to random chance rather than a true underlying relationship.

For both males and females, the severity of autism symptoms measured by *ADOS\_TOTAL* does not appear to have a significant impact on the quality of anatomical MRI

scans (*anat\_snr*). This suggests that the behavioral demonstrations of autism (measured by ADOS scores) do not correlate strongly with the technical quality of brain imaging in this sample. Other factors, not captured by *ADOS\_TOTAL*, might influence MRI scan quality. Future research could explore additional variables such as specific behaviors during scanning, overall compliance, or technical aspects of the MRI process.

### 3.4. Association between *FIQ* and *func\_outlier* covariates

Lastly, this research explores the association between cognitive abilities (e.g., Full-Scale IQ) and the Fraction of Outlier Voxels (*func\_outlier*) in functional MRI data among people with ASD, stratified by sex. This shows whether cognitive abilities, like IQ scores, are related to the outlier voxels in the MRI scans. It'll uncover potential connections between cognitive functioning and anatomical neural patterns. This can provide insights into whether individuals with higher or lower IQ scores have better or worse fMRI scan quality in terms of the prevalence of outlier voxels.

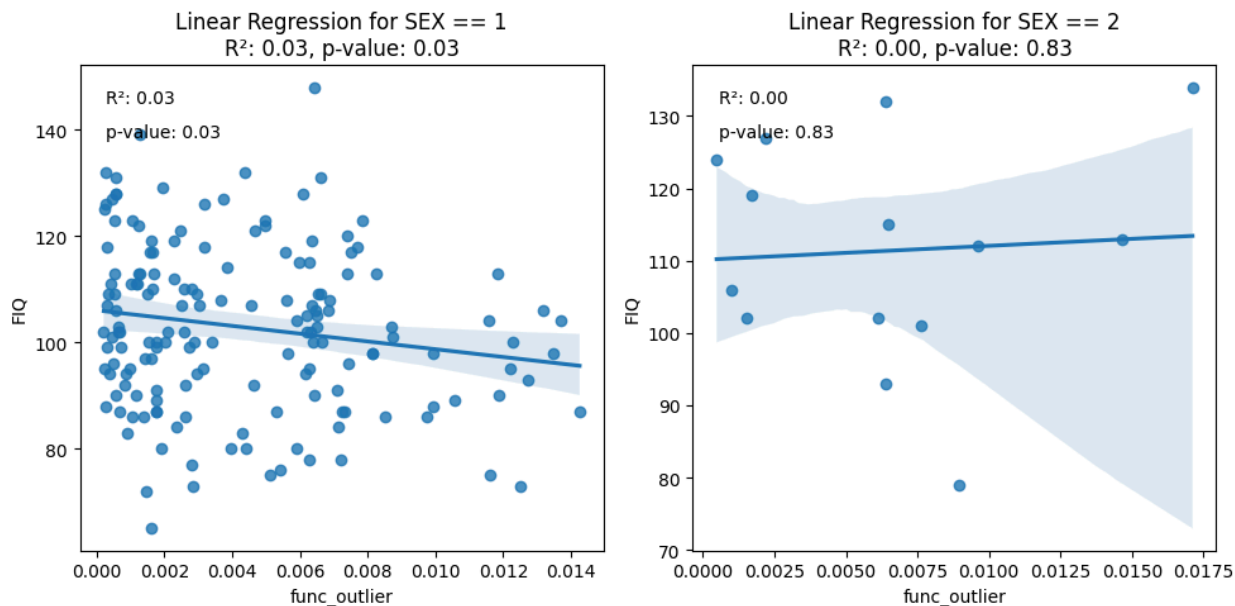


Figure 4: The image above represents a Linear Regression plot comparing *FIQ* to *func\_outlier*. SEX 1 are the males, SEX 2 females.

Simple linear regression analysis was used to test whether *func\_outlier* explained *FIQ* in SEX = 1, which indicates males (Fig. 4, left). The results of the regression indicated that one predictor *func\_outlier* explained a significant amount of the variation in *FIQ* [ $R^2 = 0.03$ ,  $p = 0.03$ ]. These results were significant at the  $p < .05$  level. This is a very weak relationship between these variables. The weak relationship suggests that *func\_outlier* is not a strong predictor of *FIQ* among males with ASD. Although the relationship is weak, it is unlikely to be due to random

chance. Thereby depicting that there is a small but real association between higher functional atypicality (*func\_outlier*) and lower *FIQ* in males. There is a very weak but statistically significant negative correlation between *func\_outlier* and *FIQ*. This might imply that as the measure of functional atypicality increases, the Full-Scale IQ slightly decreases.

Simple linear regression analysis was also used to test whether *func\_outlier* explained *FIQ* in *SEX* = 2 (Fig. 4, right), which indicates females. The results of the regression indicated that one predictor *func\_outlier* explained a non-significant amount of the variation in *FIQ* [ $R^2 = 0.00$ ,  $p = 0.83$ ]. These results were not significant at the  $p < .05$  level. There is no relationship between these variables. The slope of the regression line is nearly flat. The lack of relationship is likely not due to random chance, there is truly no significant association between *func\_outlier* and *FIQ* in this group. The flat slope and  $R^2$  value suggest that variations in functional MRI scan quality do not correspond to differences in cognitive abilities in this group.

#### 4. Discussion

Our analysis of the association/relationship between various brain- and cognitive-related variables, such as ADOS score and neuroimaging data, revealed several keynotes to consider when examining individuals with ASD and when considering sex in sampled populations. Specifically, we stratified all associated variables by sex to highlight the differences in cognitive abilities, symptom severity, and MRI data quality among males and females with ASD. We chose this approach to inform the tailoring of treatment interventions and imaging protocols to account for sex-specific differences that could enhance the accuracy and efficacy of clinical assessments.

Males displayed a weak but statistically significant relationship between the Fraction of Outlier Voxels (*func\_outlier*) and Full-Scale IQ (*FIQ*), suggesting that functional MRI data quality slightly impacts cognitive abilities. This implies that higher functional atypicality could be associated with lower IQ scores. In females, the lack of significant relationships in several analyses (e.g., *func\_outlier* vs. *FIQ*, *anat\_snr* vs. *ADOS\_TOTAL*) suggests different neural correlates of cognitive abilities and symptom severity compared to males.

The association between neuroimaging data quality (e.g. Signal to Noise Ratio (*anat\_snr*), Fraction of Outlier Voxels (*func\_outlier*), and cognitive abilities indicate that the image scan quality can influence the interpretation of cognitive abilities in an individual with ASD. Improved MRI scan quality is vital to accurately assess and understand cognitive abilities displayed by individuals with ASD. For instance, higher levels of outlier voxels, as explained in 4.4, could distort neuroimaging scans, thus leading researchers to inaccurate or misleading results (Power et al, 2012). Therefore, implementing strategies to minimize artifacts and enhance data quality during MRI scanning can improve the reliability of neuroimaging studies in ASD between males and females.

Additionally, there is a weak association between Autism symptom severity and these neural characteristics (e.g., *ADOS\_TOTAL*) and MRI data quality metrics (e.g., *anat\_snr*),

suggesting they are not linked linearly. This observation highlights the need for versatile, non-linear approaches to understand the neural basis for cognitive abilities between males and females in this patient population. In prior work, while some weak correlations exist, they do not provide a robust predictive model for symptom severity based on neuroimaging data alone (Gabrieli et al., 2015). A comprehensive, multivariate, and multimodal approach that combines neuroimaging with other biological, behavioral, and cognitive assessments is necessary to fully understand and address the diversity of ASD.

The age-related differences in the relationship between neuroimaging data quality and cognitive measures (e.g., *anat\_snr* vs. *func\_quality*) suggest that age factors should be considered when interpreting these associations. As explained in 4.2, Age at scan can impact the quality of MRI data and the manifestation of cognitive abilities and symptoms. Thus, understanding how age influences these relationships can help tailor interventions to different developmental stages in individuals with ASD. Longitudinal studies and age-specific analyses are crucial to capture the dynamic nature of ASD and its impact on neural and cognitive development (Van Dijk et al., 2010).

Ultimately, the observed disparities in the relationships between neuroimaging data quality and cognitive measures across different sexes and age groups could stem from inherent biological differences in sex at birth. Factors such as hormonal influences, brain maturation rates, and sex-specific neural connectivity patterns might contribute to these disparities. Further research is needed to explore these underlying mechanisms in detail. By recognizing the variability in neural and cognitive profiles based on sex, age, and symptom severity, interventions can be more effectively personalized to meet the unique needs of each individual with ASD. Improving MRI data quality and understanding its relationship with cognitive and behavioral measures can lead to more accurate and reliable diagnostic criteria and assessments for ASD, especially as symptoms may present differently in infant and teenage ASD patients compared to when they are adults. Combining neuroimaging data with comprehensive behavioral, cognitive, and biological assessments on a within-subject, longitudinal basis can provide a more holistic understanding of ASD, thus facilitating the development of targeted and effective treatments that may be more effective at specific developmental stages.

Further research should explore the underlying mechanisms driving these associations, consider additional factors influencing MRI data quality and cognitive functioning, and investigate the longitudinal impact of these relationships on developmental trajectories in ASD. Additionally, the study's sample size and demographic limitations may restrict the generalizability of the findings. There is also the potential for technical variability in MRI procedures that could affect data quality independently of the subjects' characteristics, as well as the potential of quality variability due to the type of MRI machine being used across different research institutions.

Future research should aim to address these limitations by including larger and more diverse samples across different institutions and parts of the world to enhance the

generalizability of the findings. Longitudinal studies that track changes in neuroimaging data quality and cognitive measures over time could provide deeper insights into the developmental trajectories of individuals with ASD and serve to predict when symptoms may improve or worsen. Furthermore, exploring additional variables that might influence MRI scan quality, such as specific behaviors during scanning and overall compliance, could improve the reliability of neuroimaging studies. Integrating neuroimaging data with comprehensive behavioral, cognitive, and biological assessments will be crucial for developing a holistic understanding of ASD and creating more effective diagnostic and treatment strategies by creating a more amenable MRI scanning environment that optimizes the minimization of image quality artifacts.

## 5. Conclusion

The current study delved into the intricate relationship between neuroimaging data quality and cognitive measures in individuals with Autism Spectrum Disorder (ASD), with a particular focus on age and sex as influential independent factors. Through linear regression analysis, our research underscores several critical insights that hold significant implications for the diagnosis, treatment, and management of ASD.

Firstly, the findings suggest that there is a weak but statistically significant correlation between functional MRI data quality and cognitive performance in males. However, this relationship does not hold for anatomical MRI data and autism symptom severity across both sexes. This indicates that while neuroimaging data can provide valuable information, it should not be solely relied upon for comprehensive diagnostic assessments or treatment planning. Instead, a multi-dimensional approach that integrates neuroimaging with behavioral and cognitive assessments is recommended.

The study also highlights the need for tailored management strategies that consider individual differences in age and sex. These factors appear to influence MRI data quality and cognitive outcomes, suggesting that personalized interventions could be more effective in addressing the unique needs of individuals with ASD. Perhaps testing and imaging environments that bring participants at ease differently for boys and girls in pediatric research should be considered when collecting MRI data in infant ASD populations.

However, the research is not without its limitations. The weak correlations observed and the potential for technical variability in MRI procedures indicate the necessity for further studies with larger, more diverse samples. Future research should also explore additional variables that might impact MRI data quality and investigate the developmental trajectories of neuroimaging and cognitive measures in ASD through longitudinal studies. There is also a clear disproportion in our sample size of males and females, with males comprising the vast majority of the data. Future work should do well to encourage the recruitment of female participants from families or those affected by ASD.

Ultimately, this study contributes to a deeper understanding of how neuroimaging data quality relates to cognitive functions in ASD, emphasizing the importance of personalized,

integrative approaches in diagnosis and treatment. By continuing to explore these relationships and addressing current limitations, future research can pave the way for more effective and individualized care for those with ASD.

## References

1. Martino, A. D., Yan, G., Li, Q., Denio, E., Castellanos, F. X., Alaerts, K., Anderson, J. S., Assaf, M., Bookheimer, S. Y., Dapretto, M., Deen, B., Delmonte, S., Dinstein, I., Ertl-Wagner, B., Fair, D. A., Gallagher, L., Kennedy, D. P., Keown, C. L., Keyzers, C., ... Milham, M. P. (2014). The Autism Brain Imaging Data Exchange: Towards Large-Scale Evaluation of the Intrinsic Brain Architecture in Autism. *Molecular Psychiatry*, 19(6), 659. <https://doi.org/10.1038/mp.2013.78>
2. Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, 59(3), 2142–2154. <https://doi.org/10.1016/j.neuroimage.2011.10.018>
3. Gabrieli, J. D. E., Ghosh, S. S., & Whitfield-Gabrieli, S. (2015). Prediction as a humanitarian and pragmatic contribution from human cognitive neuroscience. *Neuron*, 85(1), 11–26. <https://doi.org/10.1016/j.neuron.2014.10.047>
4. Van Dijk, K. R., Sabuncu, M. R., & Buckner, R. L. (2012). The influence of head motion on intrinsic functional connectivity MRI. *NeuroImage*, 59(1), 431–438. <https://doi.org/10.1016/j.neuroimage.2011.07.044>
5. Belmonte, M. K., Cook, E. H., Jr, Anderson, G. M., Rubenstein, J. L., Greenough, W. T., Beckel-Mitchener, A., Courchesne, E., Boulanger, L. M., Powell, S. B., Levitt, P. R., Perry, E. K., Jiang, Y. H., DeLorey, T. M., & Tierney, E. (2004). Autism as a disorder of neural information processing: directions for research and targets for therapy. *Molecular psychiatry*, 9(7), 646–663. <https://doi.org/10.1038/sj.mp.4001499>
6. Vasa, R. A., Mostofsky, S. H., & Ewen, J. B. (2016). The Disrupted Connectivity Hypothesis of Autism Spectrum Disorders: Time for the Next Phase in Research. *Biological psychiatry. Cognitive neuroscience and neuroimaging*, 1(3), 245–252. <https://doi.org/10.1016/j.bpsc.2016.02.003>
7. Im, K., Choi, Y. Y., Yang, J. J., Lee, K. H., Kim, S. I., Grant, P. E., & Lee, J. M. (2011). The relationship between the presence of sulcal pits and intelligence in human brains. *NeuroImage*, 55(4), 1490–1496. <https://doi.org/10.1016/j.neuroimage.2010.12.080>