

Acceptance date: 25/02/2025

DIFFICULTIES IN THE SOCIAL INTERACTION OF AUTISTIC INDIVIDUALS: A NEUROSCIENTIFIC PERSPECTIVE ON THE INTERPRETATION AND MANIPULATION OF EMOTIONS

Fabiano de Abreu Agrela Rodrigues

Post-PhD in Neurosciences, esp. Genomics
Heráclito Research and Analysis Center
(CPAH), Department of Neuroscience and
Genomics, Brazil & Portugal
<https://orcid.org/0000-0002-5487-5852>

Marco Aurélio Broccoli Lima

Graduated in Business Administration,
Specialist in Business Management, Business
Intelligence and Data Science and Artificial
Intelligence. Heráclito Research and
Analysis Center (CPAH), Department of
Neurobusiness, Brazil & Portugal
<http://lattes.cnpq.br/1129065074894512>

All content in this magazine is
licensed under a Creative Com-
mons Attribution License. Attri-
bution-Non-Commercial-Non-
Derivatives 4.0 International (CC
BY-NC-ND 4.0).



Abstract: Autism Spectrum Disorder (ASD) is characterized by significant challenges in social interaction, often associated with difficulties in interpreting and manipulating emotions. This article reviews the neurobiological basis of these difficulties, focusing on critical brain regions such as the amygdala, corpus callosum, insula, anterior cingulate cortex, basal ganglia, fusiform gyrus, superior temporal sulcus, dorsolateral prefrontal cortex and orbitofrontal cortex. The integration of neuroimaging data, neurochemical studies and brain connectivity analyses offers a comprehensive view of the dysfunctions that contribute to social difficulties in ASD. The implications of these findings for therapeutic interventions and future research are discussed.

Keywords: Autism Spectrum Disorder, Social Interaction, Neuroscience, Corpus Callosum, Amygdala, Insula, Anterior Cingulate Cortex, Superior Temporal Sulcus, Orbitofrontal Cortex, Fusiform Gyrus.

INTRODUCTION

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that affects millions of people globally and is characterized by a triad of behavioral difficulties: deficits in social communication, repetitive behaviors and restricted interests, and significant challenges in social interaction. Among these, difficulties in interpreting and handling emotions stand out as a critical factor underpinning compromised social interactions in individuals with ASD. ASD is characterized by a wide range of behavioral and cognitive challenges, among which difficulties in social interaction stand out as a central aspect. The neuroscientific understanding of these difficulties, especially regarding the interpretation and manipulation of emotions, is complex, involving a network of brain regions and neurochemical systems. This article aims to explore the neurobiological bases that underlie the social difficulties observed in individuals with

ASD, with a specific focus on the interpretation and manipulation of emotions.

Understanding the neurobiological basis of these difficulties has been a priority in recent research, with a growing emphasis on identifying the brain regions and neurochemical systems involved. Functional neuroimaging studies, brain connectivity analyses and neurochemical investigations have revealed a complex network of brain regions that, when dysfunctional, can contribute to the challenges observed in the perception of and response to social stimuli in individuals with ASD. Regions such as the amygdala, responsible for detecting emotional stimuli, and the corpus callosum, which facilitates inter-hemispheric communication, have often been implicated in research on ASD. In addition, areas such as the insula, the anterior cingulate cortex, the basal nuclei, and the dorsolateral prefrontal cortex play essential roles in integrating emotional information and regulating adaptive social behaviors. Understanding these neurobiological interactions is essential for developing more effective interventions and improving the quality of life of individuals with ASD.

This article aims to provide a detailed review of the neuroscientific evidence related to social interaction difficulties in ASD, with a focus on the neuroanatomical and neurochemical dysfunctions that contribute to these difficulties. In addition, we will discuss the implications of these findings for clinical interventions and future directions for research.

NEUROANATOMICAL AND FUNCTIONAL ASPECTS

Emotional interpretation in social interactions involves a brain network that includes the amygdala, the ventromedial prefrontal cortex (vmPFC), the anterior cingulate cortex (ACC), and the hippocampus. The amygdala, known for its central role in detecting and processing emotional stimuli, often shows functional alterations in individuals with ASD. Functional

neuroimaging studies suggest that hyperactivation or hypoactivation of the amygdala can lead to a distorted perception of emotional signals, such as facial expressions and vocal intonations, resulting in significant difficulties in reading emotional states in social contexts (Schultz et al., 2015).

In addition, the CPFvm, which is responsible for integrating emotional information with social decision-making processes, shows atypical connectivity in individuals with ASD. Dysfunction in this area may explain the difficulty in using emotions to guide appropriate behavior during social interactions, a feature often observed in the autistic spectrum (Kleckner et al., 2017). Altered connectivity between the CPFvm and the amygdala may impact the ability to regulate emotional responses and interpret emotions in real time, which contributes to pervasive social difficulties.

FUNCTIONAL IMPLICATIONS OF ALTERATIONS IN THE CORPUS CALLOSUM

Anomalies in the corpus callosum can result in inefficient inter-hemispheric communication, which can directly impact the ability of an individual with ASD to integrate social and emotional information in real time. For example, dysfunction in the transmission of information between the right hemisphere, which is often associated with the processing of emotional information, and the left hemisphere, which dominates linguistic and analytical processing, can result in difficulties in aligning emotional expressions with the verbal content of a social interaction (Alexander et al., 2007).

In addition, the inadequate integration of visual and emotional information between the hemispheres can lead to a fragmented perception of social situations, where the individual can correctly perceive the elements of an interaction, but fail to integrate them in a cohesive way. This phenomenon can contribute to difficulties in interpreting the intentions of others

or in adjusting their emotional behavior in accordance with social norms.

ROLE OF NEUROTRANSMITTERS AND NEUROMODULATORS

The functioning of this neural network is mediated by various neurotransmitters and neuromodulators. Serotonin (5-HT), for example, plays a crucial role in regulating mood and aggression, and has been associated with the modulation of social interactions. Studies indicate that altered serotonin levels in ASD may contribute to atypical social behaviors, including difficulty interpreting emotions in social contexts (Veenstra-VanderWeele et al., 2012).

Dopamine, a central neurotransmitter in the brain's reward system, particularly in the nucleus accumbens and ventral tegmental area (VTA), is also key to motivation social and the processing of social rewards. Alterations in dopaminergic signaling in individuals with ASD may explain the lower responsiveness to social stimuli, reducing motivation to engage in social interactions (Pavál, 2017).

The oxytocinergic system, which includes oxytocin and its receptors, has been extensively studied in the context of ASD. Oxytocin, known as the "social bonding hormone", is crucial for the facilitation of social behaviors and the perception of emotional signals. Studies show that altered levels of oxytocin or the dysfunction of its receptors may be involved in the social and emotional difficulties observed in ASD (Guastella et al., 2010).

OTHER NEUROANATOMICAL AND FUNCTIONAL ASPECTS

Insula: The insula is a cortical structure located deep within the lateral sulcus, and plays a central role in interoception, emotional perception and empathy. In individuals with ASD, the insula often has functional and structural abnormalities that can contribute to difficulties in interpreting emotions and responding empathically. The insula integrates emotional

and physiological signals, allowing an individual to perceive and respond appropriately to the emotions of others. Dysfunctions in this region can lead to an attenuated or distorted perception of social signals, which is common in ASD (Uddin & Menon, 2009).

Anterior Cingulate Cortex (ACC): The Anterior Cingulate Cortex (ACC) is a region involved in processing emotions, making decisions and regulating social behavior. The ACC plays a critical role in detecting errors and monitoring conflicts during social interactions, which is essential for adjusting behavior according to social norms. Alterations in the CCA in individuals with ASD can contribute to difficulties in adapting behavior according to social expectations, and also to inappropriate or inadequate emotional responses in social contexts (Di Martino et al., 2009).

Basal ganglia: The basal ganglia, which include structures such as the striatum and globus pallidus, are involved in regulating motor behavior and learning skills and habits, as well as playing important roles in motivation and social reward. In individuals with ASD, abnormalities in the basal ganglia may be associated with repetitive and stereotyped behaviors, as well as difficulties in developing and maintaining dynamic social interactions. Dopaminergic dysfunction in the basal ganglia can also impact motivation for social engagement, which is often observed in ASD (Turner et al., 2006).

Dorsolateral Prefrontal Cortex (DPC): The Dorsolateral Prefrontal Cortex (dPFC) is a key region for executive functions, including regulating social behavior and making decisions based on social rules. The DPCF is involved in planning, cognitive flexibility and inhibition of inappropriate responses, all skills necessary for effective social interactions. Individuals with ASD often show atypical connectivity and altered activity in this region, which can contribute to difficulties in adaptive social behaviors, such as initiating or main-

taining conversations, or following implicit social norms (D'Esposito & Postle, 2015).

Hypothalamus: Although generally associated with the control of autonomic and endocrine functions, the hypothalamus also influences social behavior through the regulation of hormones such as oxytocin and vasopressin. These substances are fundamental to social behavior and the formation of bonds. Anomalies in the hypothalamus or in the signaling of these neuropeptides may be associated with difficulties in forming social bonds and empathy in individuals with ASD (Insel, 2010).

Fusiform gyrus: The fusiform gyrus, located in the temporal lobe, is particularly relevant for face recognition, a crucial skill for social interaction. In individuals with ASD, the fusiform gyrus often shows reduced activity in response to faces, which can contribute to difficulties in recognizing facial identities and interpreting facial emotional expressions. This dysfunction can impair the ability of individuals with ASD to correctly interpret the emotions of others, an essential component for non-verbal communication (Schultz, 2005).

Superior Temporal Sulcus (STS): The superior temporal sulcus (STS) is a region of the brain involved in the perception of biological movements and the analysis of dynamic social signals, such as gaze direction, body movements and gestures. Alterations in STS activity in individuals with ASD may be associated with difficulties in interpreting these social signals, leading to challenges in understanding other people's behavior and responding appropriately to social interactions (Pelphrey et al., 2011).

Inferior Parietal Cortex: The inferior parietal cortex, which includes the angular gyrus and supramarginal gyrus, is involved in sensory integration and the perception of space, as well as aspects of social processing, such as theory of mind (the ability to infer the mental states of others). In individuals with ASD, dysfunctions in this area can contribute to di-

difficulties in understanding other people's intentions and beliefs, impacting the ability to engage in complex and understanding social interactions (Sowden et al., 2015).

Orbitofrontal Cortex: The orbitofrontal cortex, part of the prefrontal cortex, plays a critical role in evaluation and decision-making in social contexts, including the emotional valence of social interactions. Alterations in the orbitofrontal cortex in ASD can result in difficulties processing social rewards and assessing the value of different actions in social contexts, leading to social behavior that can be considered inappropriate or non-adaptive (Rolls, 2019).

Ventral striatum: The ventral striatum, which includes parts of the nucleus accumbens, is a key region of the brain's reward system and is involved in the motivation and pleasure associated with social interactions. In individuals with ASD, dysfunctions in the ventral striatum can lead to a reduced response to social stimuli, which can contribute to a lack of interest in social interactions and difficulties in forming social bonds (Chevallier et al., 2012).

Evidence and Clinical Implications: Evidence suggests that the interplay between neuroanatomical dysfunctions and neurochemical imbalances contributes substantially to the social challenges faced by individuals with ASD. Altered connectivity in emotional and social brain networks, combined with atypical levels of neurotransmitters such as serotonin, dopamine and oxytocin, offers a robust explanation for difficulties in interpreting and manipulating emotions.

These findings have significant implications for the development of therapeutic interventions. For example, approaches aimed at modulating dopaminergic or oxytocinergic signaling may offer new avenues for treating social difficulties in ASD. However, the efficacy of these interventions requires further research, with rigorous clinical studies assessing safety and potential long-term benefits.

BEHAVIOR SUSPICIOUS OF AUTISM: FICTITIOUS EXAMPLES AND THE IMPORTANCE OF PROFESSIONAL ASSESSMENT

João, a 16-year-old teenager, consistently avoids eye contact during conversations, preferring to stare at objects rather than the people he interacts with. In addition, he often has difficulty understanding jokes or sarcasm, interpreting them literally, which isolates him socially among his peers. Maria, an 8-year-old child, has an obsessive interest in dinosaurs, spending hours every day drawing and classifying different species, while showing no interest in other activities common among children her age. Carlos, a 35-year-old man, follows an extremely rigid daily routine and is deeply disturbed when something unexpected, such as unusual traffic or a change of schedule at work, disrupts his plans. He also finds it difficult to interpret facial expressions, often asking directly if someone is angry or sad, even when the emotions seem obvious to others. Laura, a 22-year-old, prefers to work alone on projects, avoiding social interactions, and often feels overwhelmed in noisy or busy environments, such as parties or shopping malls.

These fictitious examples illustrate behaviors that may suggest the presence of Autism Spectrum Disorder (ASD). However, it is essential to stress that these behaviors, although they may raise suspicions, are not diagnostic in themselves. Confirming a diagnosis of ASD requires a careful and comprehensive assessment by a qualified health professional, such as a psychiatrist or psychologist, who can consider the full range of symptoms and carry out the necessary tests. The content of this study aims to shed light on possibilities for more informed research, but should not be used as a definitive diagnostic tool.

FINAL CONSIDERATIONS

Difficulties in social interaction in individuals with Autism Spectrum Disorder are deeply rooted in a complex network of neurobiological dysfunctions that affect various brain regions and neurochemical systems. The review presented in this article highlights how alterations in areas such as the amygdala, corpus callosum, prefrontal cortex and other cortical and subcortical structures contribute to the challenges in interpreting and manipulating emotions, which are fundamental to social behavior. The integration of data from neuroimaging studies, brain connectivity analyses and neurochemical investigations provides a more comprehensive understanding of the

neurobiological basis of ASD. This understanding not only sheds light on the mechanisms underlying social difficulties, but also opens up new possibilities for specific therapeutic interventions, which may include neurochemical modulations or therapies based on neuroplasticity. Continued advances in neuroscientific research will be crucial to developing more precise and personalized approaches to the management of ASD, focusing on restoring or compensating for dysfunctions in the brain networks involved in social interaction. Ultimately, a deeper and more integrated understanding of these dysfunctions could lead to significant improvements in the quality of life of individuals with ASD, promoting better social inclusion and adaptation.

REFERENCES

- Schultz, R. T., Grelotti, D. J., Klin, A., Kleinman, J., Van der Gaag, C., Marois, R., & Skudlarski, P. (2015). The role of the fusiform face area in social cognition: Implications for the pathobiology of autism. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 358(1430), 415-427.
- Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., Quigley, K. S., & Barrett, L. F. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature Human Behaviour*, 1(5), 69.
- Veenstra-VanderWeele, J., Anderson, G. M., & Cook, E. H. (2012). Pharmacogenetics and the serotonin system: Initial studies and future directions. *European Journal of Pharmacology*, 667(1-3), 32-39.
- Pavál, D. (2017). A Dopamine Hypothesis of Autism Spectrum Disorder. *Developmental Neuroscience*, 39(5), 355-360.
- Guastella, A. J., Einfeld, S. L., Gray, K. M., Rinehart, N. J., Tonge, B. J., Lambert, T. J., & Hickie, I. B. (2010). Intranasal oxytocin improves emotion recognition for youth with autism spectrum disorders. *Biological Psychiatry*, 67(7), 692-694.
- Alexander, A. L., Lee, J. E., Lazar, M., Boudos, R., DuBray, M. B., Oakes, T. R., Miller, J. N., & Bigler, E. D. (2007). Diffusion tensor imaging of the corpus callosum in Autism. *NeuroImage*, 34(1), 61-73.
- Uddin, L. Q., & Menon, V. (2009). The anterior insula in autism: Under-connected and under-examined. *Neuroscience & Biobehavioral Reviews*, 33(8), 1198-1203.
- Di Martino, A., Ross, K., Uddin, L. Q., Sklar, A. B., Castellanos, F. X., & Milham, M. P. (2009). Functional brain correlates of social and nonsocial processes in autism spectrum disorders: An activation likelihood estimation meta-analysis. *Biological Psychiatry*, 65(1), 63-74.
- Turner, C. A., Presti, M. F., & Kalivas, P. W. (2006). Cognitive behavior in preclinical models: Involvement of basal ganglia. *Neurobiology of Learning and Memory*, 85(2), 202-206.
- D'Esposito, M., & Postle, B. R. (2015). The cognitive neuroscience of working memory. *Annual Review of Psychology*, 66, 115-142.

- Insel, T. R. (2010). The challenge of translation in social neuroscience: A review of oxytocin, vasopressin, and affiliative behavior. *Neuron*, 65(6), 768-779.

- Schultz, R. T. (2005). Developmental deficits in social perception in autism: The role of the amygdala and fusiform face area. *International Journal of Developmental Neuroscience*, 23(2-3), 125-141.

- Pelphrey, K. A., Shultz, S., Hudac, C. M., & Vander Wyk, B. C. (2011). Research review: Constraining heterogeneity: The social brain and its development in autism spectrum disorder. *Journal of Child Psychology and Psychiatry*, 52(6), 631-644.

- Sowden, S., Wright, G. R., Banissy, M. J., Catmur, C., & Bird, G. (2015). Transcranial current stimulation of the temporoparietal junction improves theory of mind in adults with autism spectrum disorder. *Brain*, 138(11), 3603-3612.

- Rolls, E. T. (2019). The orbitofrontal cortex and emotion in health and disease, including depression. *Neuropsychologia*, 128, 14-43.

- 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.