

Basic Neuroscience of Autism



With

Wale Oladipo

www.mindbodybreakthrough.net

Course Outline

- Basic understanding of autism



- Regions of the brain implicated in autism

Part 1

Basic Understanding: Autism

What is autism?

- Autism is a neuro-diverse condition, characterised by considerable challenges in understanding and navigating the **'social'** world. ⁽¹⁾
- Autism is a condition with a range of clinical presentations, from mild to severe, referred to as autism spectrum disorders (ASD). The most common clinical ASD sign is social-interaction impairment, which is associated with verbal and non-verbal communication deficits and stereotyped obsessive behaviours. ^(1a)
- While studies have shown that autism involves deficits in **'social'** intelligence or theory of mind, research shows that **social** intelligence might be independent of **'general'** intelligence, as many autistic people are capable of considerable understanding of the **'non-social'** world (e.g. computers, physics, maths, engineering, etc) while finding the **'social'** world confusing. ^(2, 3)
- Therefore, an autistic brain could be an opposite type of some non-autistic (**neurotypical**) brains who have no difficulty interacting with the **'social'** world but find **'non-social'** problem-solving confusing. ⁽⁴⁾

Famous People With Autism Spectrum Disorders include:

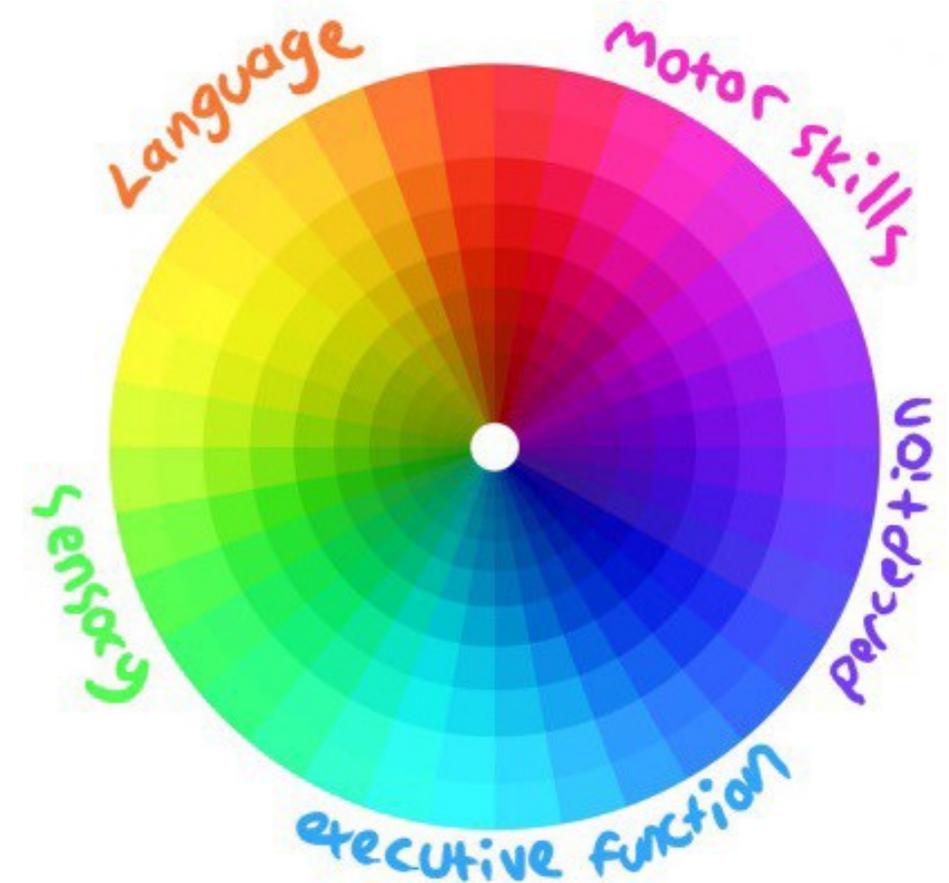
- Albert Einstein
- Wolfgang Amadeus Mozart
- Charles Darwin
- Michelangelo
- Abraham Lincoln
- Susan Boyle
- Elon Musk
- Steve Jobs
- Bill Gates



DSM-V & Autism Spectrum Disorder (ASD)

(American Psychiatric Association 2013)

According to the DSM-5, autism spectrum disorder is defined as “persistent difficulties with social communication and social interaction” and “restricted and repetitive patterns of behaviours, activities or interests” (this includes sensory behaviour), present since early childhood, to the extent that these limit and impair everyday functioning.



- In DSM-5, the terms ‘autistic disorder’, ‘Asperger disorder’, ‘childhood disintegrative disorder’ and ‘Pervasive Developmental Disorder - Not Otherwise Specified (PDD-NOS)’ have been replaced by the umbrella term ‘Autism Spectrum Disorder’.

- There is a variety of diagnostic tools, such as; the DISCO (Diagnostic Interview for Social and Communication Disorders), the ADI-R (Autism Diagnostic Interview - Revised), and the ADOS (Autism Diagnostic Observation Schedule) and 3Di (Developmental, Dimensional and Diagnostic Interview). The DSM V or ICD 11th criteria form the basis for the diagnosis, but the individual clinician’s judgement is important.

Symptoms Of Autism Spectrum Disorder (ASD)

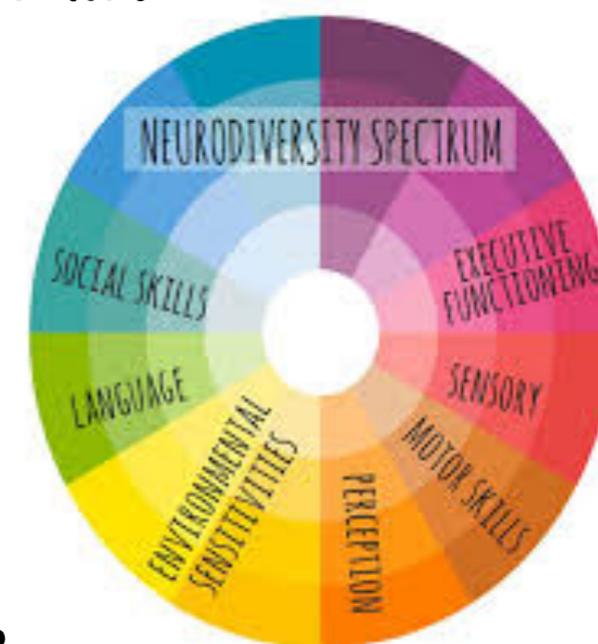
(American Psychiatric Association 2013)

The new diagnostic criteria have been rearranged into two areas: 1) social communication/interaction, and 2) restricted and repetitive behaviours.

Although symptoms must begin in early childhood, they may not be recognised fully until social demands exceed their internal resources for coping.

All of the following symptoms describing **persistent deficits in social communication/interaction** across contexts, not accounted for by general developmental delays, must be met:

- Problems reciprocating social or emotional interaction, including difficulty establishing or maintaining back-and-forth conversations and interactions, inability to initiate an interaction, and problems with shared attention or sharing of emotions and interests with others.
- Severe problems maintaining relationships — ranges from lack of interest in other people to difficulties in pretend play and engaging in age-appropriate social activities, and problems adjusting to different social expectations.
- Nonverbal communication problems such as abnormal eye contact, posture, facial expressions, tone of voice and gestures, as well as an inability to understand these.



Two of the four symptoms related to **restricted and repetitive behaviour** need to be present

- Stereotyped or repetitive speech, motor movements or use of objects.
- Excessive adherence to routines, ritualised patterns of verbal or nonverbal behaviour, or excessive resistance to change.
- Highly restricted interests that are abnormal in intensity or focus
- Hyper or hypo reactivity to sensory input or unusual interest in sensory aspects of the environment.

Causes Of & Contributors To ASD

Research suggests that ASD has a strong and complex genetic basis ⁽⁵⁾

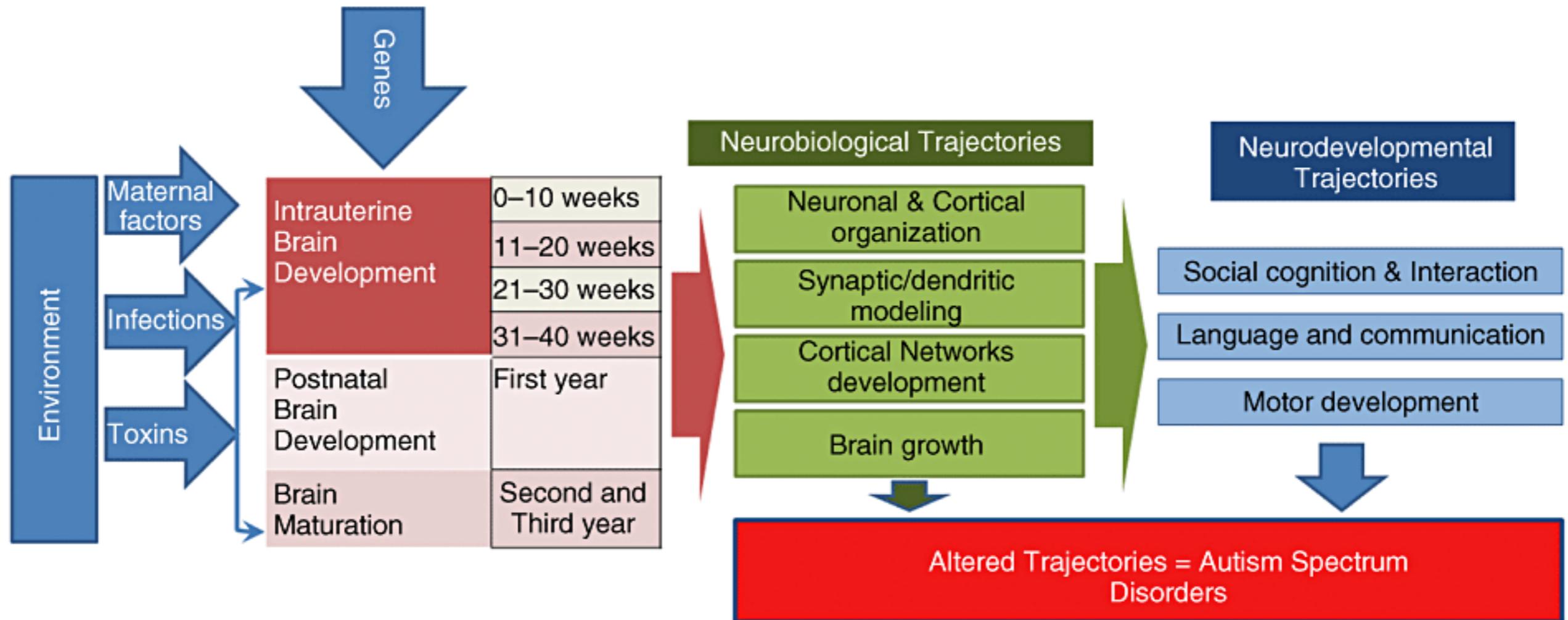
- Early studies of twins estimated the heritability of autism to be more than 90% ⁽⁶⁾
- When only one identical twin is autistic, the other often has some form of learning or social difficulties ⁽⁷⁾
- For adult siblings, the likelihood of having one or more features of the broader autism phenotype might be as high as 30%, much higher than the likelihood in controls. ^(8, 9)

Studies have also shown that some environmental factors may increase the risk of ASD:

- Poor growth of a fetus while in the mother's womb during pregnancy (Intrauterine growth restriction (IUGR)) have been linked to increased ASD risk factors in both term and preterm infants. For example, maternal nutrition and **inflammation** during preconception and pregnancy can influence fetal neurodevelopment. ⁽¹⁰⁾
- Maternal **inflammatory** and autoimmune diseases may affect fetal neural tissues or aggravate a genetic issue. ⁽¹¹⁾
- Exposure to air pollution during pregnancy, especially heavy metals and particulates, may also increase the risk of ASD. ^(12, 13)
- Environmental factors that have been argued (without much evidence) to contribute to or exacerbate autism include certain foods, infectious diseases, solvents, PCBs, phthalates and phenols used in plastic products, pesticides, brominated flame retardants, alcohol, smoking, illicit drugs, prenatal stress, and vaccines (such as MMR). ^(14, 15, 16, 17, 18)



The Neurobiology of Autism



Brain Pathology (2007). Volume: 17, Issue: 4, Pages: 434-447, DOI: (10.1111/j.1750-3639.2007.00102.x)

Genetic and environmental factors that influence intrauterine and early postnatal brain development likely alter neurobiological and neurodevelopmental trajectories that determine the clinical core of ASD.

Autism & Gender Bias

Studies have shown that ASD may be under-diagnosed in women and girls due to an assumption that it is primarily a male condition, as it is diagnosed four-to-five times more often in males than females. ⁽¹⁹⁾

Below are some theories that attempt to explain the social and communication symptoms/gender bias of ASD:

1. Empathising-systemising theory (E-S)

- This theory suggests that the male brain is shaped to engage more of a systematic thinking than empathic thinking (S>E), while a female brain engages more of an empathic thinking than systematic thinking (E>S). ⁽²⁰⁾
- For example, the E-S theory is argued to be a better predictor than gender regarding who chooses STEM subjects (Science, Technology, Engineering and Mathematics) which are more systemising than empathic, explaining why these subjects are dominated by males. ⁽²¹⁾
- Therefore, as ASD presentations are generally biased towards systematic thinking, this could be a reason why more males are diagnosed of ASD as their brains are already naturally wired for higher systemising thinking. ⁽²²⁾

2. Extreme male brain theory of autism

- Following his work on the E-S theory, Baron-Cohen developed the extreme male brain theory of autism that proposes that; "the male brain is programmed to systemise and the female brain to empathise ... therefore, ASD represents the extreme male brain." ⁽²³⁾

3. The fetal testosterone theory

- This theory hypothesises that higher levels of testosterone in the amniotic fluid of mothers push brain development towards improved ability to see patterns and analyse complex systems while diminishing communication and empathy, and males generally have higher levels of fetal testosterone, contributing to their systemic thinking bias. ^(24, 25, 26)



Part 2

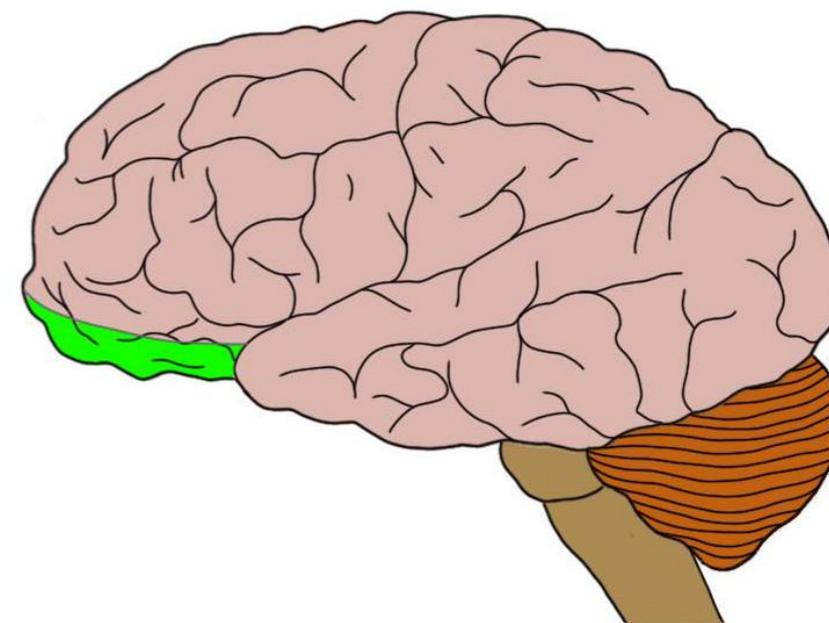
Brain Regions Implicated in Autism

Brain Regions Implicated in ASD

Studies have implicated a network of neural regions that are referred to as the “**social brain**,” which mediate ‘**social intelligence**.’ These brain regions include: **the orbito-frontal cortex (OFC), the amygdala, and the superior temporal sulcus (STS).** ⁽²⁷⁾

Orbito-Frontal Cortex:

- This is the area of the cerebral cortex located at the base of the frontal lobes and above the orbits (or eye sockets), involved especially in social and emotional cognition or what is known as ‘theory of mind’ or ‘mental state recognition’. ⁽²⁸⁾
- Theory of mind (ToM) is the ability to attribute mental states (beliefs, intents, desires, emotions, and knowledge) to others in order to predict and interpret their behaviours and non-verbal communications. ⁽²⁹⁾
- Studies have shown that **80%** of autistic children perform poorly in the false-belief task (such as, the ‘Sally-Ann’ task), which is the gold standard for measuring theory of mind capabilities. ^(30, 31)
- Neuro-imaging studies (SPECT) show decreased cerebral blood flow in the OFC of the autistic brain during the false-belief task. ⁽³²⁾ Lesions of the OFC impairs judgement of what is socially appropriate. ⁽³³⁾



ORBITOFRONTAL CORTEX (IN GREEN)

Sally-Ann’ task description: Children are shown two dolls, ‘Sally’ and ‘Ann’. Sally has a basket in which she places a marble. Then, she goes away leaving her basket behind. Ann takes Sally’s marble out of the basket and puts it in a box. Then Sally returns, and the children are asked: ‘where will Sally look for her marble? To pass the task, children must correctly predict that Sally will look in the basket where she believes the marble to be, as opposed to box where they know the marble is themselves. ^(34, 35)

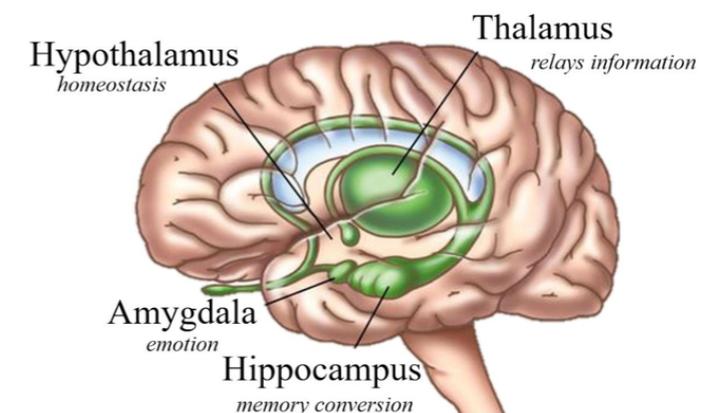
The Amygdala:

It is well known that the amygdala plays a significant role in the recognition of fear (fight/flight). (36,37,38)

The amygdala is not a single entity, but comprises a collection of 13 nuclei, divided into 3 subsets, that perform a variety of 'not well known' tasks: The Deep Nuclei, The Superficial Regions & Other Nuclei: (39)

- The deep nuclei have the greatest interaction with the **neocortex** and hippocampal formation, and the most connectivity with **sensory processing**.
- The amygdala receives a great deal of sensory input in a highly processed form, including somatosensory, visual, auditory, and all types of visceral inputs (40, 41). It also plays a role in the formation of conditioned fear responses to auditory stimuli. (42, 43)
- The amygdala is also activated in humans when decoding signals of social importance, such as gaze, expression-recognition (especially of fearful faces), and body movements. (44-49). The left amygdala is thought to be critically involved in identifying mental state/emotional processing from complex visual stimuli such as the eye region, providing strong evidence of the role of the amygdala in normal social intelligence, and abnormality of the amygdala in autism. (45, 47, 50)
- fMRI studies found significantly less amygdala activation in the autistic brain during a mentalising task (Judging the mind in the Eyes task), compared to controls (44). Imaging study of autism reported reduced amygdala volume. (51)
- The amygdala theory of autism also proposes that patients with amygdala lesions show impairments in social judgement (52, 53, 54) which have been likened to "acquired autism." (55, 56)
- Other studies have also found anomalous functioning in the cerebellum (57), hippocampal formation (58), medial frontal cortex (59) and fronto-limbic connections (60) in autism. Reduced neurone size and increased cell-packing density has also been found in the limbic system, specifically the hippocampus, entorhinal cortex (link btw cortex and hippocampus), and anterior cingulate in autism (61-65).

The Limbic System

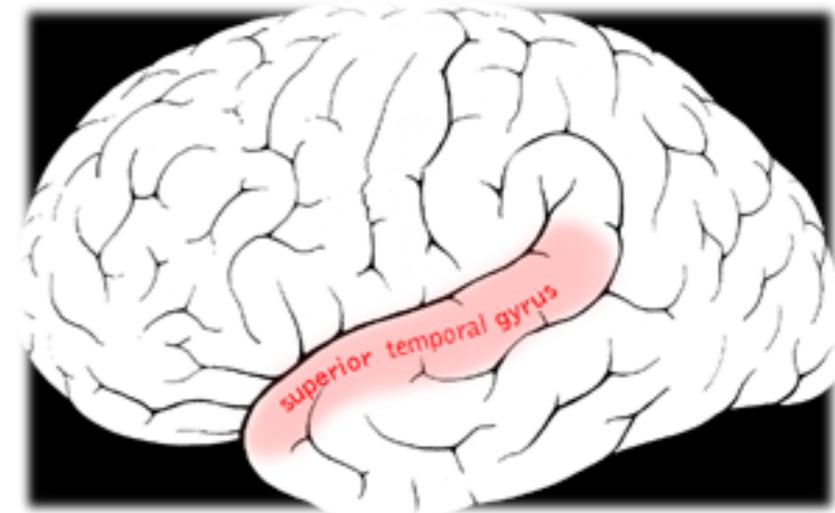


The superior temporal sulcus (STS):

The STS is the site for multi-sensory integration, auditory processing, spoken word recognition, and mirror neurones, necessary for social perception. ⁽⁶⁶⁾

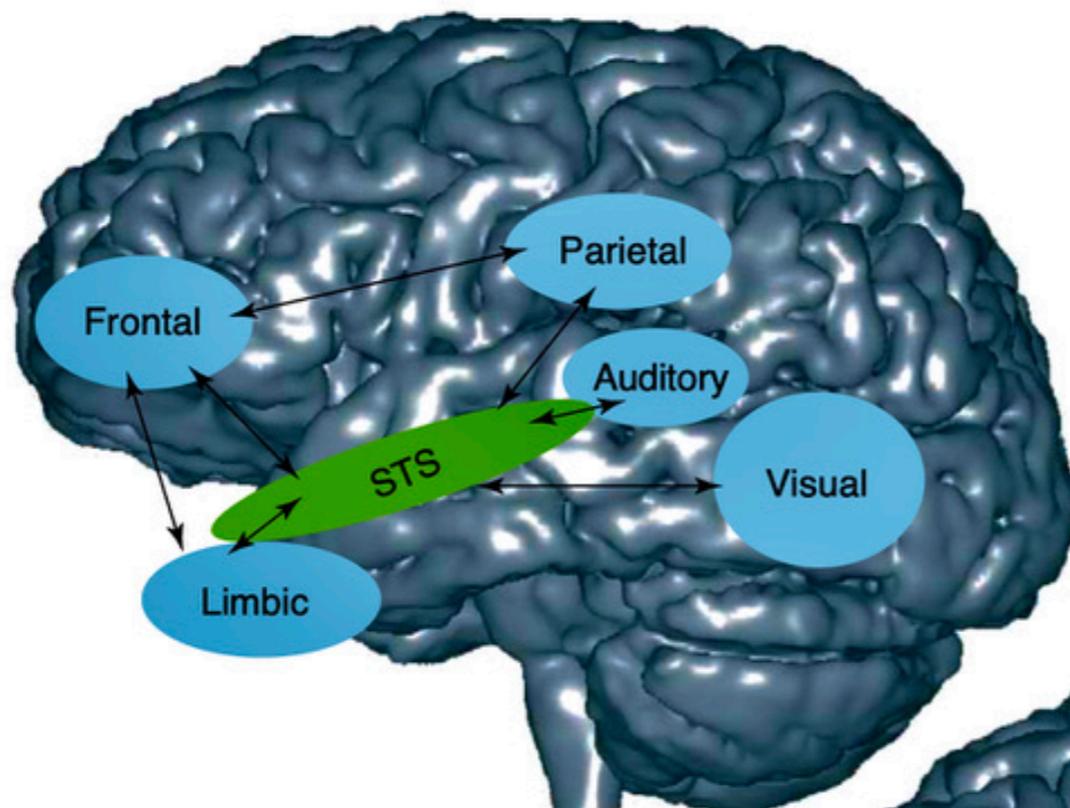
The STS is crucial for social cognition and is implicated in several steps of social interactions – in auditory and visual social perception (i.e. eye gazes, gestures, facial displays of emotions and voice perception) and in more complex social cognition (theory of mind and mentalising). ⁽⁶⁷⁾

- Brain-imaging studies have found local decreases of grey matter (cortical thinning) in ASD in areas belonging to the mirror neurone system (MNS) within the STS, argued to be the basis of empathic behaviours. Cortical thinning of the MNS was correlated with ASD symptom severity. ^(68, 69)
- In the non-autistic brains, listening to **voice** compared to **non-voice** sounds significantly activated a **voice-selective** area in the STS. In contrast, In the autistic group, listening to **voice** and to **non-voice** sounds does not activate the **voice-selective** area of the STS, indicating that autism involves difficulty in social perception in an auditory world. ⁽⁷⁰⁾

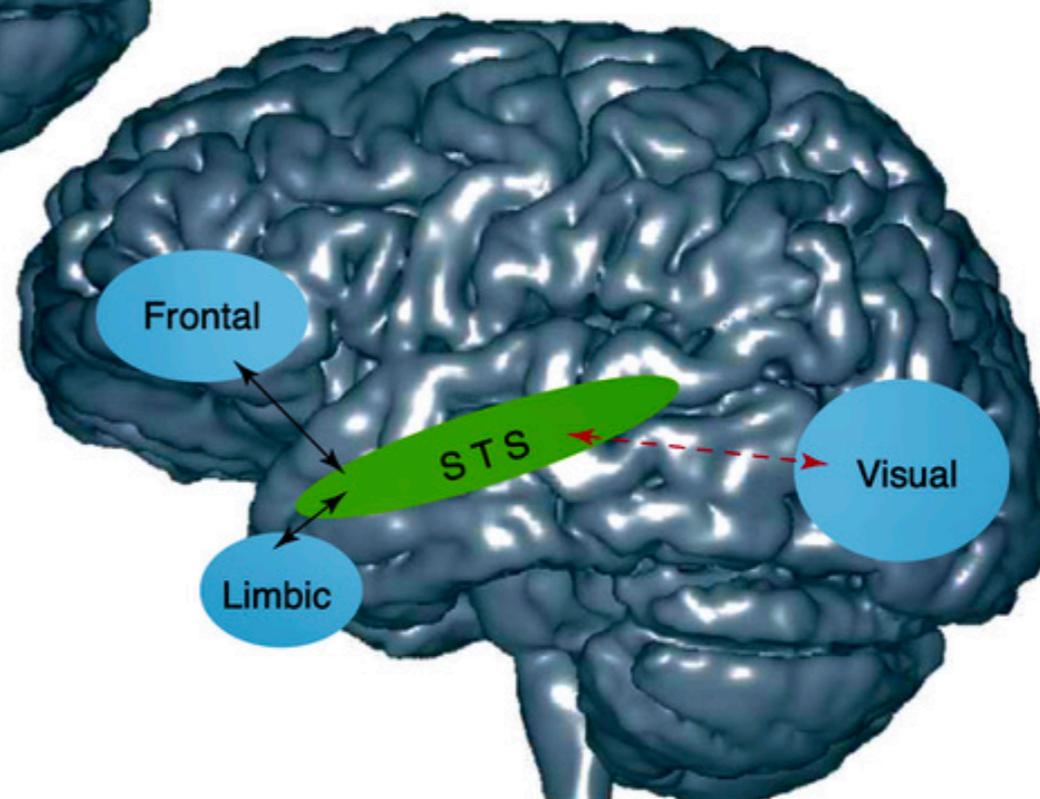


The STS & Social Cognition (71, 72)

(a) Main STS connections



(b) Abnormal functional STS connection during a visual social task in ASD



SPECT Scan Finding in ASD

Amen clinics SPECT studies on BRAIN PATTERNS in autism include:

- **HIGH ACTIVITY PATTERNS IN ASD:**

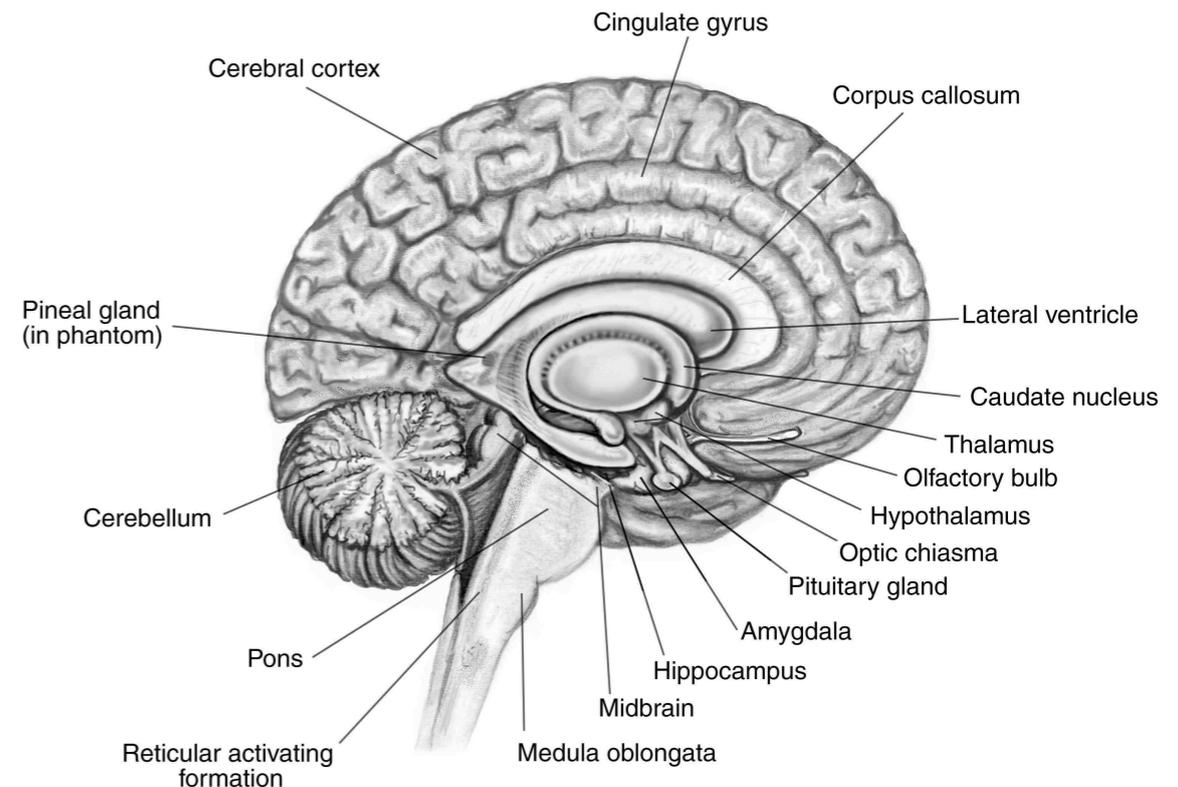
- Increased activity in the anterior cingulate gyrus and lateral prefrontal cortex, relating to symptoms such as: repetitious speech and behaviour, getting stuck on thoughts, problems with transitions and change

- Overall increased activity throughout the brain, which may be associated with inflammation and be related to: mood instability, emotional meltdowns, anxiety

- **LOW ACTIVITY PATTERNS IN ASD**

- Decreased cerebellum activity, which may contribute to: impeded or poor motor skills, problems with learning and thought coordination

- Decreased activity in the back portion of the brain, especially in the parietal and temporal lobes, contributing to: communication difficulties, learning problems, sensory processing issues (such as auditory, visual), problems with abstract thinking



Q&A Session