



Finding a Solution: Adapting Psychological Interventions to Autism and Asperger's Syndrome

Bachelor Degree Project in Cognitive Neuroscience

First Cycle 22.5 credits

HT22/VT23

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Abstract

Throughout my education I have found that the psychological interventions in use are largely tailored to the masses, and some may be ill suited for those from certain subpopulations such as Autism Spectrum Disorder (ASD) or Asperger's syndrome (AS). I investigated whether there are statistically significant neurological differences between those with high functioning ASD or Asperger's and those without, with the goal of using those differences to propose what aspects might be used to create new psychological interventions more suited to neurodivergent individuals. After a thorough literature search, I found that the areas seeming to be the common denominators marking out those with ASD or Asperger's were the amygdala and orbitofrontal cortex and hippocampus. My hypothesis that such neurological differences could be used to infer new psychological interventions for treating depression did not find support. The hope is that this review will nevertheless serve to inspire other researchers to create new interventions.

Finding a Solution: Adapting Psychological Interventions to Autism and Asperger's

Introduction

Autism Spectrum Disorder (ASD) and Asperger's Syndrome (AS) are topics I will address separately, and I will elucidate my reasons for this distinction later. It is likely that these and other neurodivergent conditions have existed since the emergence of modern humans. The term "neurodivergent" refers to neurological structures that diverge from what's considered typical or "neurotypical." While it would be inconsiderate to suggest that these conditions have only posed challenges, it's undeniable that they haven't always been advantageous. The breadth of research on this topic makes it challenging to derive clear conclusions without detailed scrutiny. This thesis aims to streamline this process through a systematic review. Specifically, it seeks to determine whether individuals diagnosed with high-functioning autism and AS exhibit a unique neural pattern, especially in areas like the amygdala, anterior cingulate cortex, orbitofrontal cortex, and hippocampus. If such a pattern exists, could this knowledge aid in developing more tailored interventions for clinical depression in these populations?

In this section, I will provide a concise overview of the autism spectrum and delineate why AS can be considered a distinct diagnosis within this spectrum. Subsequently, I will discuss the brain mechanisms linked to ASD. Additionally, I will touch upon a common issue associated with both ASD and AS: major depressive disorder. Following this, I will outline the conventional interventions for these conditions and highlight some of their limitations. Lastly, I will introduce the objective of this thesis.

The autism spectrum

Autism spectrum disorder (ASD) may be defined as a number of closely related conditions that affect the social and communicative capacities of diagnosed individuals. It can take the form of an inability to read social cues or read them correctly. It can render a person incapable of verbal

communication in its entirety, or to a significant degree limit it. It is ordered along a line of possibilities. Where one places along the line determines the severity of one's presumed disorder, with "low functioning" being more severe and "high functioning" less. The "spectrum" in "autism spectrum" evokes a range of severity of impairment from mild to severe, with cases found all along the continuum. Being a spectrum, it hampers some people more than others, and is commonly divided into levels.

First-level (high-functioning) autism requires the least care. Though high-functioning autists suffer from sensory sensitivity and social awkwardness, they typically cope better and can usually live independently. Second-level autism is more severe: those diagnosed require more care and support but can function somewhat independently; while third-level (low-functioning) autists require the most care and risk never being able to live independently. Low-functioning autism is characterized by apparently lower IQ, though this may be due to poor test-taking abilities; and by greater impairment, with many persons being partially or completely non-verbal.

Autism is not known to have any direct link to IQ or any physiological alterations to organs other than, arguably, the brain. Pennington et al. (2014) define it as a developmental disability significantly affecting verbal and nonverbal communication and social interaction, generally evident before the age of three. It can adversely affect a child's educational performance, but not necessarily. Those with high functioning autism can be very gifted, academically or otherwise. Other characteristics often associated with ASD are engagement in repetitive activities and stereotyped movement, resistance to environmental change or any change in daily routines, and unusual (to others) response to sensory experiences.

The APA Dictionary of Psychology (American Psychological Association, 2022a) describes autism spectrum disorder (ASD) as any of a group of disorders of which signs typically present themselves during the preschool years. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; American Psychiatric Association, 2013), ASD comprises classical autism, Asperger's disorder, and childhood disintegrative disorder.

Classical autism or Kanner's syndrome, commonly associated with low functioning-autism, is the type of autism most people think of when picturing autistic children. Its symptoms can include engaging in virtually no eye contact and being hypersensitive to stimuli. Those with Kanner's Syndrome display a profound need for routine and often show little to no interest in the world around them. They turn their attention inward rather than interacting with others.

Childhood disintegrative disorder is a developmental disorder wherein a child develops seemingly normally for the first 3-4 years only to suddenly degenerate and lose all skills she has accumulated such as walking, talking and relating socially. Currently there is no known cause, and the onset can be so rapid as to be noted by the affected, sometimes asking why they have suddenly lost a previously possessed skill.

Frazier et al. (2012) wanted to determine the validity of the new diagnostic criteria for ASD proposed for the DSM-V. They found the criteria accurate but proposed they be relaxed a bit as otherwise individuals appropriately assigned the diagnosis – in particular females – could risk going undiagnosed.

Classical autism, Asperger's syndrome, and childhood disintegrative disorder are no longer considered distinct diagnoses according to the DSM-V. That the DSM-V no longer distinguishes between autism and Asperger's is controversial (Devine, 2019). For purposes of this thesis, I will follow the arguments others have made and distinguish autism spectrum from Asperger's, as I believe there is enough evidence of significant differences between the two to cluster them together.

The APA dictionary goes on to describe ASD as a neurodevelopmental disorder characterized by repetitive behavior, sensory hypersensitivity and hyperfixation: seemingly obsessive behavior regarding a subject sometimes of the individual's choosing, sometimes not. Symptoms may include impaired sense of empathy or impaired empathic expression, preference for things remaining the same, trouble imitating others and distinct absence of social play or clear preference for self-play.

Difficulty diagnosing ASD varies with age (National Institute of Mental Health, 2022). It is considered much harder to diagnose in adulthood, in part because many symptoms overlap with other diagnoses such as anxiety disorder in a more nuanced way than in children. An evaluative discussion for adults may touch upon subjects like sensory issues, self-observed repetitive behavior and indications of restricted interests. Adolescents will often be noticed by teachers or other school staff, in which case an initial evaluation by school personnel may lead to recommendation for a specialist evaluation.

Pediatric diagnosis typically involves a developmental screening including (1) evaluation of cognitive skills, language and behavior and (2) assessment of age-appropriate skills the child should possess, like eating or using the toilet without assistance. Outside factors that could hinder development must also be taken into consideration, such as the home-life of the child: is it stable?

Asperger's Syndrome

One of the main arguments for the folding in of Asperger's into ASD was that the diagnostic criteria for Asperger's overlap to a large extent with those of high-functioning autism; nevertheless, some researchers and healthcare professionals feel that there are significant enough differences to continue to treat them as separate diagnoses. This sentiment was expressed by both Robert Naseef, clinical psychologist and advisor to the Autism society of America and Normand Giroux a clinical psychologist based in Canada (Corbyn, 2023). In particular, a distinction should be made based on motor skills, communicative skills and time of diagnosis (Macintosh & Dissanayake, 2004). Those with Asperger's rarely have issues developing language skills, compared with high-functioning autists who may experience initially stunted development. On the other hand, those with Asperger's have more difficulty with motor skills, which can manifest as clumsiness. Finally, one can be diagnosed with ASD earlier than one can be with Asperger's due to the mentioned language issue. As the symptoms of Asperger's can present similarly to ADHD (Rosenn, 2019) they are more likely to be misdiagnosed, with the diagnosis perhaps corrected later in life as other signs become more apparent.

In their review, Hosseini and Molla (2021) found that not everyone with a previous diagnosis of Asperger's fit the new criteria for ASD. Moreover, the diagnostic change carries with it potential social consequences: people previously diagnosed with Asperger's can feel that a part of their identity has been taken away and replaced with another, possibly more stigmatized diagnosis (Jones, 2020).

Asperger's syndrome can be defined as a condition that dampens social skills, but arguably to a lesser degree than high-functioning autism. Those with high-functioning autism and Asperger's appear to differ in their social approach: where high-functioning autists shy away from social interaction, those with Asperger's do not; rather, it is their clumsy approach that mars their interactions. Klin (2003, p.104) writes: "in some contrast to the social presentation in autism, individuals with AS find themselves socially isolated but are not usually withdrawn in the presence of other people, typically approaching others but in an inappropriate or eccentric fashion". Asperger's does not impair cognitive function in the way second- or third-level autism does.

The APA dictionary (American Psychological Association, 2022b) describes Asperger's as primarily social and not so much a communicative disorder. Those diagnosed have issues with conversational skills and social cues like body language. They often have trouble coping with changes in the environment, as well as issues separating out sound streams such as conversation from background noise. In contrast to autism, there is no significant delay in cognitive function, social skills aside. Obtaining motor skills is likewise not a problem; however, they are often less than graceful. As previously stated, those with high-functioning autism tend not to socialize by choice, whereas those with Asperger's seek socialization but have a difficult time due to their oftentimes socially tone-deaf approach. They have to learn the social rules intentionally and self-consciously rather than picking them up seemingly automatically. As they are strongly disinclined towards or simply having difficulty lying, they have a blunt form of honesty that can be misinterpreted as cruel.

Lorna Wing, arguably the person who most helped popularize autism and Asperger's research and who coined the term "Asperger's syndrome", described its main traits as "a lack of

empathy; naive, inappropriate, one-sided conversations; inability to form friendships; pedantic, repetitive speech; poor nonverbal communication; intense interest in certain subjects; and clumsy, ill-coordinated movements” (Wing, 1991, p. 105-107).

Persons diagnosed with Asperger's frequently call themselves “aspies”, a term that has been widely popularized within the Asperger's community. One group that has protested the diagnostic change and continues to use Asperger's to refer to a distinct diagnosis is the Asperger/Autism Network (2022), which feels that the diagnosis has become a part of people's identities.

The Asperger/Autism Network does not approve of the word “disorder” and prefers “profile”: i.e., “Asperger's profile”. It feels that “disorder” fails to acknowledge that many people with Asperger's have striking abilities, talents, and positive traits. While there are common traits among those with Asperger's, all are unique individuals. The belief is that traits are not fixed and, with education and support, people's brains, behaviors, and skills can change, as an individual learns to manage stress and lessen sensory sensitivities. “Disorder” implies that the fault is in the individual, when in the network's belief it is a failure of society to interact with those with Asperger's on equal terms. In other words, the problem is not in the individual but in the interaction between society and individual. What others see as disorder, the network views as diversity.

The network holds that diagnostic labels often disparage rather than aid. In the minds of its members, so-called *disorders* or *dysfunctions* are simply predictable differences in individual experiences, sensitivities, and perceptions. Finally, it argues that judgments about abilities are inherently subjective, and that what is a challenge in one environment may be an asset in another.

Brain diversity in Autism Spectrum Disorder and Asperger's Syndrome

Up until this point, not a lot of work has been done adapting interventions to clinical subpopulations, like those with Asperger's or other neurodivergent conditions. Aside from cognitive behavioral therapy, the field is very barren. Research on differences in brain structure and function between those with Asperger's or high-functioning autism and the neurotypical population began in the 1990s. Simon Baron-Cohen (1999) has posited that consciousness is split

into consciousness of what he calls the physical and mental world, and that those with autism have issues with the mental world insofar as it deals with emotion, wishes and intent. He is strongly associated with the claim that autists have significant empathic deficiency. This theory has been challenged by other researchers. Most notably, a theory has been proposed that runs directly counter to his argument: the Intense World Theory (Markram et al., 2007). It is not that those on the autistic spectrum have issues feeling and reading emotions; it's that they experience too much of them too strongly and, in response, try to block them out. It is the equivalent of someone yelling in your ear; the basic instinct is to cover one's ears. As a result of this sensory overload, those with Asperger's focus on only certain information, which leads to patterns they find manageable.

Silani et al. (2008) used alexithymia and empathy questionnaires to measure emotional introspection in people with autism and Asperger's as well as functional magnetic resonance imaging (fMRI: a brain-imaging technique that scans the brain using a strong magnetic field and a magnetic contrast injected into the bloodstream to produce images of the brain) to see what areas of the brain could be the root of the difficulties handling emotions. Although they were looking specifically at alexithymia, their focus was really on ASD/Asperger's more generally. Alexithymia is the inability to express, describe, or distinguish among one's emotions; it overlaps with ASD, but some consider it a disorder on its own; however, it is not classified as such in the DSM-V. Alexithymia is strongly correlated not only with a lack of empathy or empathy expression, but also low scores on empathic concern and perspective taking, as measured by questionnaires. Silani et al.'s results point to the importance of the anterior insula, involved in personal emotional awareness, which alexithymia is believed to inhibit. The anterior insula, a part of the brain that handles homeostatic maintenance of emotions like hunger and pain, is believed by some researchers to be a gateway to conscious access to sensory information (Huang et al., 2021).

Kikuchi et al. (2013a) using magnetoencephalography (MEG: a technique that measures the brain's magnetic field) were first to demonstrate a distinctive neurophysiological network – primarily along the right side of the brain – in young children (aged 3-7) diagnosed with ASD. This network is present in everyone but is used more and in different ways in children with ASD, where

it becomes more pronounced. The researchers prepared custom equipment and used noninvasive methods to obtain their results. They found altered gamma-band oscillations in those with ASD compared to the neurotypical population. They found rightward-lateralized connectivity via gamma oscillation unique to this age group and clinical population: i.e., it was not present in the neurotypical participants. The altered activity suggests that changes in the balance of excitation and inhibition may be a pervasive feature of brain dysfunction in ASD starting from a young age.

In a separate study the same year building upon the previous study and using the same methodology but a narrower age range, Kikuchi et al. (2013b) found that children with ASD aged 5-7 show rightward lateralization (specialization along one side of the brain) that neurotypical children of the same age do not. Specifically, they found that rightward lateralization of the right posterior brain contributes to visual-pattern reasoning in young children with ASD, but not in neurotypical children of the same age. Visual-pattern reasoning is the ability to analyze and mentally manipulate visual information to solve problems: for example, to identify what figure comes next in a pattern sequence or rotate a 3D image in one's mind.

Together with the previous study, this suggests that the properties of gamma oscillations are altered in ASD relative to information processing. That led the researchers to two possible conclusions regarding their results: either they were observing an ongoing deviant excitation/inhibition balance – an unusual ratio of excitation to inhibition of neuronal activation – which brought on the highly varied cognitive ability observed in young children with ASD; or an deviant excitation/inhibition balance during the fetal period results in aberrant prenatal and perinatal development that leads to lasting alterations in neural networks.

Neurological indications of ASD include enlarged total cerebral volume and unusual variations in ratio of gray to white matter in areas like the orbitofrontal cortex, which is involved in decision making; and the superior temporal sulcus, which helps handle theory of mind, for prediction of others' behavior (Hernandez et al., 2015). Indications of Asperger's are likewise unusual variations in ratio of gray and white matter, particularly in the amygdala (responsible for emotional responses, fear, anxiety, aggression etc.), hippocampus (responsible for short term

memory and spatial cognition) and anterior cingulate cortex (responsible for impulse control and emotion, including modulation of emotional reactivity) (Faridi & Khozrowabadi, 2017).

Major depressive disorder

Major depressive disorder, or clinical depression, is characterized by a period spanning a minimum of two weeks with pervasive low mood, low self-esteem and loss of interest or pleasure in things one would normally find enjoyment in. Lack of energy, weight gain or loss of appetite are possible symptoms. Due to the lowered sense of self-worth, thoughts of suicide are not uncommon. The DSM 5 (American Psychiatric Association, 2013, pp. 160-168) describes characteristics of major depressive disorder in addition to those previously mentioned as slowing down of thought, reduction of physical movement observable by others, fatigue or lack of energy on a nearly daily basis and diminished ability to concentrate or make decisions on a nearly daily basis. The number of cases has been rising. With a base prevalence of 7% in the US population (The Johnson Center, 2019) clinical depression is responsible for one of the largest economic impacts around, with a cost of US \$326.2 billion in 2018. The number of cases has been rising at the same time the number of people seeking treatment has remained the same (Greenberg et al., 2021).

Those with ASD or Asperger's are more susceptible to major depressive disorder and are three times more likely to have an acute depressive episode. This impedes their daily lives beyond what is normal for them and could cause a downwards spiral

Standard interventions and their shortcomings

Psychological interventions tend to have a common problem, which is their standardized nature: they are tailored towards the masses; whilst there are interventions for specific situations, there are few, if any, for specific types of individuals. A large part of cognitive neuroscience focuses on the similarities in the brain but fail to take into consideration that the individual variation can be staggering. This can lead to interventions being less effective or not effective at all. One such intervention is mindfulness training, which appears to have less effect on men (Rojiani et al., 2017; Bluth et al., 2017). Those with high-functioning autism or Asperger's are known to thrive on routines and to be more susceptible to depression including major depressive disorder when

deprived of those routines, significantly beyond the response of the neurotypical population to similar circumstances. To provide an intervention without proper consideration could disrupt the routines they are dependent on; handled correctly, the intervention could instead become part of the routines. The dependency on routines needs to be kept in mind as both a trigger to, and possible indicator of, depression. An intervention could be created to help establish new routines or recapture previous ones that have been lost.

Aim of the thesis

The thesis was inspired by two clients I encountered during my studies in applied positive psychology, as part of my study of motivational interviewing. I learned that some interventions are less effective depending on such circumstances as gender, age and culture, and I began to think about what other factors could render interventions less effective. Surely differences in brain chemistry based not on gender but on characteristics like having an Asperger's-type personality must alter the effectiveness of interventions as well. I have friends who fall under the ASD umbrella and I suspect I might, too, so I was naturally curious about what ways people differ in the effectiveness of interventions applied to them.

The aim of the thesis is to look for neurocognitive differences between persons with high-functioning autism or Asperger's and neurotypical persons of relevance to development of new interventions for clinical depression where standard interventions do not appear appropriate or fully effective for these communities. Far too little attention has been paid to developing interventions based on characteristics of those who fall outside the expected norm.

The research question posed by this thesis is, what are the measurably and statistically significant neurological differences – functional and structural (with focus on the amygdala, anterior cingulate cortex, orbitofrontal cortex and hippocampus) – between persons diagnosed with high-functioning autism or Asperger's vs. neurotypical people, and how can this knowledge be used in the development of specifically tailored interventions for major depressive disorder? The hypothesis is that the differences can be used to infer better interventions: perhaps an intervention

that gives tools to combat low self-worth or head off symptoms of major depressive disorder before they become too entrenched.

Methods

Search strategy

I searched PubMed, Medline Ovid and Medline EBSCO 28 July 2022 generating 44 papers. In this thesis the following search string was used: ((“high functioning” AND autis*) OR Asperger*) AND (fMRI OR MRI OR PET OR EEG) AND (correlate OR region)

After removing duplicates, 37 papers remained. Further screening based on titles and abstracts narrowed it down to 13 articles. Upon full-text review, seven more papers were excluded, four of which were due to the inclusion of participants under the age of 18.

Inclusion and exclusion criteria

To qualify for inclusion, papers had to be written in either English or Swedish. Pre-publication versions or drafts shared by esteemed researchers were also considered. The inclusion criteria stipulated:

1. Participants must be aged over 18 to ensure they could provide independent consent. This is also because the brains of children and adolescents differ significantly from adult brains.
2. Participants must be below the age of 65, as the risk of dementia, including potentially undiagnosed cases, increases with age.
3. The study should focus on individuals with a generally neurotypical brain, devoid of significant injuries, traumas, or any other deviations not directly relevant to a ASD or AS.
4. Participants must have been diagnosed with either high-functioning autism or Asperger's.

Studies were excluded if participants:

5. Had any psychological diagnoses indicating significantly altered brain chemistry.
6. Exhibited signs of dementia.

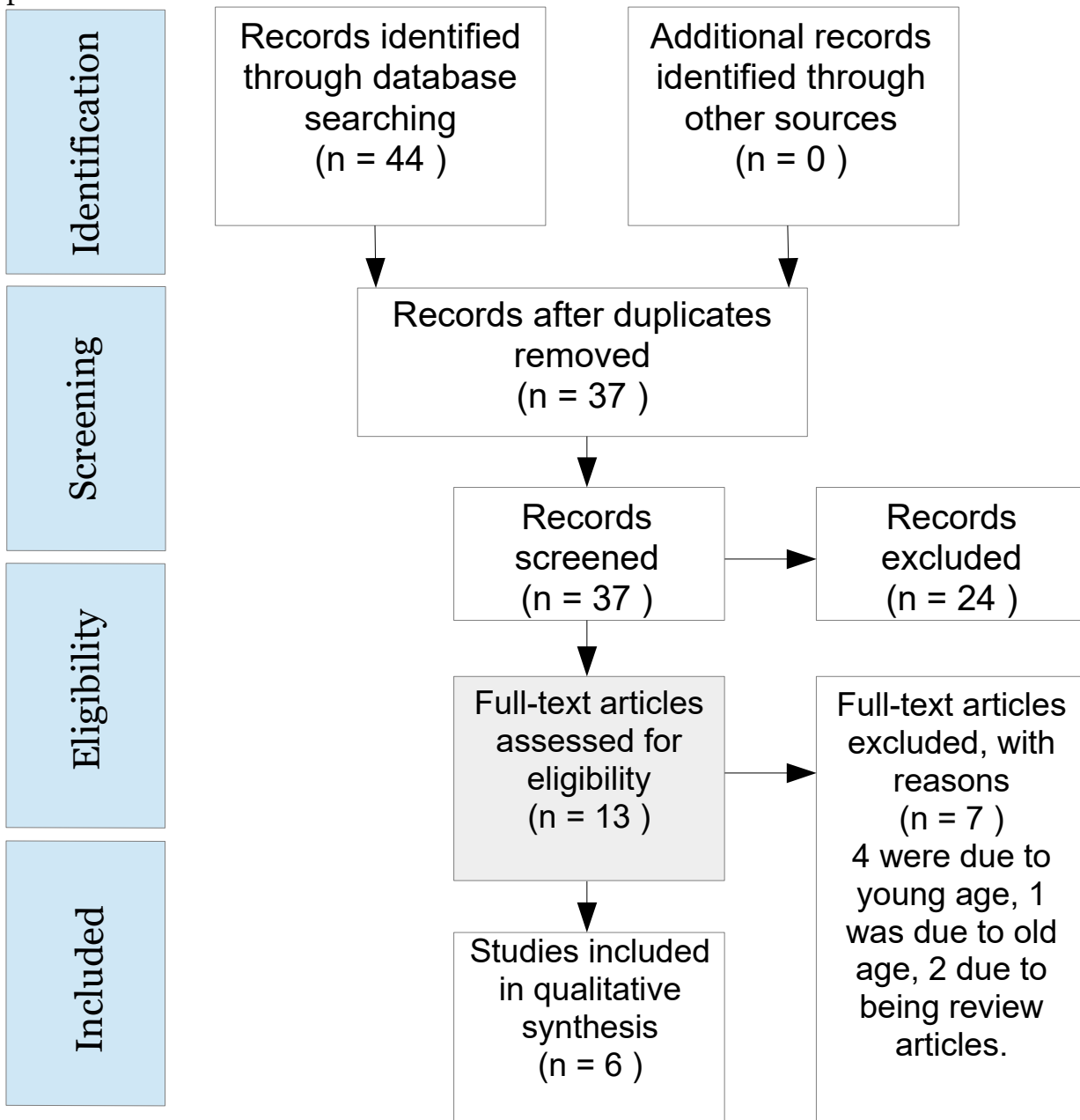
Data extraction

The relevant data categories for my analysis are (1) age, (2) diagnosis (high-functioning autism or Asperger's), (3) brain-scanning method, (4) task used (intervention), (5) brain areas scanned, (6) presence of a control group (yes or no), (7) any other within- or between-group comparisons made, (8) initial hypothesis, and (9) primary result(s). These were chosen using the PICO model (O'Sullivan et al., 2013). Problem/population accounts for 1, 2, 3 and 5; intervention is 4; control/comparison is 6 and 7; outcome is 8 and 9.

Figure 1

PRISMA 2009 Flow Diagram: standard flow diagram used to document the literature search

process.



Note: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *PLoS Med* 6(7):

e1000097. <https://doi.org/10.1371/journal.pmed.1000097>

Results

In two of the six studies (Studies 4 and 5) ASD symptoms were found to be related to irregularities in the amygdalohippocampal and cerebral areas, and in a further three (Studies 2, 3, 6) they were linked with disruptions of normal functions in one or all of the amygdala, orbito frontal cortex, temporo parietal cortex and insula. These disruptions could explain further ASD symptomatology, acting as triggers or catalysts for other disruptions. In two studies (Studies 4 and 6), researchers found that, to combat these disruptions, people with ASD compensated by using other parts of the brain (see Table 1).

Study 1 (Borowiak et al., 2018)

Aim

This study was prompted by a lack of research on the underlying networks behind visual-speech recognition deficit in people with ASD: a difficulty extracting speech information from facial movement.

Procedure

The study had a sample size of 34 with an even division of 17 neurotypical individuals and 17 with ASD. There was an identical division in each group of gender: 13 males and four females; as well as handedness: 14 right-handed and three left-handed.

Three participants were excluded. One participants could not be paired based on IQ; another moved too much in the MRI; and the third performed lower than two standard deviations in the speech-recognition experiment.

All included participants were high functioning as indicated by IQ at or above standard level of 85. All participants with ASD had a previous diagnosis of Asperger's or childhood autism. Control participants were screened for autistic traits; the results were either null or non-significant. No control participants reported a family history of psychiatric disorder or ASD. No participants reported a history of neurological disease.

Table 1: Summary of results

Study	Study 1	Study 2	Study 3	Study 4	Study 5	Study 6
Name	<u>Borowiak et al., 2018</u>	<u>Silani et al., 2008</u>	<u>Uono et al., 2022</u>	<u>Besseling et al., 2018</u>	<u>Critchley et al., 2000</u>	<u>Baron-Cohen et al., 1999</u>
Median age rounded	ASD 31, Control 32	ASD 36, Control 33	ASD 27, Control 29	N/A	ASD 37, Control 27	ASD 26, Control 25
Diagnosis	Currently ASD, previously Asperger's	High functioning ASD/Asperger's	ASD	ASD or Asperger's	ASD/Asperger's	High functioning ASD or Asperger's
Scanning method	mri, fMRI	fMRI	mri	fMRI	fMRI	fMRI
Task used	Visual-speech recognition, ROI localizer	Emotion stimuli task, Internal and external stimuli task	Emotion recognition task	Analysis using iCAPs	Explicit and implicit processing tasks	Gender recognition and mental state recognition
Brain areas scanned	Middle temporal visual area and the temporal visual speech area	Entire brain	Bilateral inferior frontal gyrus, superior temporal sulcus and amygdala	Entire brain	Entire brain	Orbitofrontal cortex, superior temporal gyrus and amygdala
Control group	Yes	Yes	Yes	Yes	Yes	Yes
Other comparisons between groups	Behavioral tests	Alexithymia and empathy questionnaires, behavioral study	N/A	N/A	Behavioral comparison, differences during explicit and implicit processing	N/A
Initial hypothesis/ aim of study	Lower response and/or connectivity in ASD compared to controls.	Reduced activity in those with ASD and high degrees of alexithymia.	Examine whether the correlation between the GM volume in the social brain regions and emotion recognition performance differed between ASD and control.	Find functional imaging biomarkers for ASD in resting-state fMRI data.	There are significant differences between ASD and controls in comparing explicit and implicit processing of facial expressions. That those with ASD would show less activity in brain areas associated with implicit processing of facial expressions.	Test Brothers' social brain theory as well as the validity of her neural model of social intelligence.
Primary results	Communication deficits in ASD might stem from atypical sensory processing.	Difficulties in emotional awareness are related to hypoactivity in anterior insula.	Those with ASD use different mechanisms for processing others facial expressions.	Findings align with known impairments in emotional processing and social interaction among the ASD population.	Findings suggest significant biological differences in those with ASD, in particular when shifting between explicit and implicit expression processing.	A confirmation of Brothers' theory that extracting socially relevant information from visual stimuli is normally associated with activation of the STG, areas of prefrontal cortex, and the amygdala.

Three experiments were performed, accompanied by eye-tracking and brain imaging. The first was a visual-speech recognition experiment paired with fMRI. Participants were instructed to memorize a syllable and identify whether or not it matched the syllable in videos shown, regardless of who pronounced it. Afterwards, they were instructed to memorize a face and identify if it matched the face in the videos independent of syllable spoken. Between videos, a white fixation cross was shown for 18 seconds as a form of mental reset.

The second experiment was an fMRI region of interest (ROI) localizer, extracting signals from a specified ROI – the middle temporal visual area and the temporal visual speech area – to functionally pinpoint them. It comprised four conditions: (i) static face (faces from different persons with different facial gestures while speaking), (ii) moving face (different facial gestures from the same person while speaking), (iii) static object (different objects from different views), and (iv) moving object (same object from different views). Participants were instructed to view blocks of pictures of objects and faces attentively. Each block lasted 25 seconds and every picture 500 milliseconds. After each block a fixation cross was presented for 18 seconds.

The third experiment was a behavioral test independent of fMRI. Participants were shown a word, after which they were shown a video without audio. In the video a person spoke either the word or an alteration of it, then the participant had to indicate whether it matched the written word.

Results

Results indicate that recognition of visual speech is impaired in those with ASD. There is reduced functional connectivity between visual-movement regions. Visual-speech recognition deficits were associated with divergent function already at the level of the visual areas required for perception of motion signals, while other speech regions appeared unaffected. Neurotypical participants and those with ASD shared similar gaze behavior

The researchers concluded that dysfunction perceiving visual movement hinders speech acquisition and comprehension in face-to-face interactions. This gives weight to investigating sensory deficits to understand communication difficulties.

Takeaway

The difficulties of impaired visual-speech recognition and therefore hindrance to communicative understanding could be a contributing factor in later stages of depression, exaggerating an already difficult situation. The uncertainty of reading a person's face accurately

could change the course of conversations entirely, leading to what was meant to be kind come off as mean-spirited, a joke that didn't fit there, a comment too far. Suddenly, feelings of regret, inadequacy and guilt compound the already strong depressive state.

Study 2 (Silani et al. 2008)

Aim

It is well-known that people with high-functioning autism or Asperger's syndrome appear to have difficulty grasping mental states like belief, desire or intention in others. Studies support the notion that they have poor self-introspection as well, but not a lot of research had been conducted. This study sought to increase the available literature on the matter.

Procedure

A total of 30 participants – 16 male, four female, exactly half of both groups having a diagnosis of ASD – were matched on age and IQ. They filled out the 20-item Toronto Alexithymia Scale (TAS-20; Bagby, Parker, & Taylor, 1994) and the BermondVorst Alexithymia Questionnaire (BVAQ-B; Vorst & Bermond, 2001). Individual differences in empathy were assessed with the Davis Interpersonal Reactivity Index (Davis, 1980). The Interpersonal Reactivity Index is a list of 28 items answered on a 5 point scale from “does not describe me very well” to does “describe me very well”. It contains four sub-scales: perspective taking, fantasy, empathic concern and personal distress. After this participants were presented with images viewed via a mirror from inside an MRI machine. The images were categorized into unpleasant, pleasant – designed to elicit emotional arousal, brain activity – and neutral.

Next, a behavioral study was performed outside the MRI apparatus to establish whether those with high-functioning autism understood the task in the same way and found it equally difficult compared to the control group. Using a 30-image set parallel to the experiment, participants rated them using five response categories and a five-button response pad. All other conditions were the same as in the scanner.

Finally, an fMRI study was done. There were two tasks, one internal task which focused on feelings evoked by the stimulus and one where participants rated aspects of an external stimulus, in this case the ratio of black to white pixels. Before testing, they were trained outside the scanner to familiarize them with the tasks. In the internal task, participants were instructed to rate the stimulus-evoked emotion on a visual analogue scale ranging from positive to negative. In the external task, they were asked to indicate the ratio of black to white pixels in a stimulus on another visual analogue scale ranging from white to black. The stimulus was shown for two seconds, with four seconds to respond by moving a pointer along a sliding scale before a fixation cross appeared for a second. This was repeated until there were no stimuli left.

Results

On the Toronto Alexithymia Scale, those with high-functioning autism had a significantly higher alexithymia score than neurotypical individuals, particularly when describing feelings. The BermondVorst alexithymia questionnaire found no significant difference on this point but did find poor insight and impaired cognition in the ASD group. The Interpersonal Reactivity Index found a significant link between empathy and alexithymia.

The two groups found the behavioral task equally difficult. Scores on the alexithymia and empathy questionnaires correlated with bilateral activity in the mid-anterior insula for both groups, with additional activity in the amygdala for the ASD group. The ASD group showed significantly less activity in MPFC, ACC, precuneus, left temporal pole and cerebellum when introspecting, and increased activity in more posterior regions such as the parietal and occipital cortex. When presented with unpleasant stimuli, the control group had greater activity in the inferior orbitofrontal cortex but not amygdala, suggesting a greater brain activity in response to emotional stimuli.

Findings are consistent with existing models of alexithymia, raising the possibility that alexithymic symptoms may vary depending on emotional state. A significant correlation was found between insular cortex activity, alexithymia scores, empathic

concern and perspective taking. The areas where activity correlated with alexithymia scores and the areas where activity correlated with empathy scores were one and the same. This leads to the hypothesis that the neural architecture underlying the conscious representation of emotion in self and others is also the same.

Takeaway

The study found increased amygdala activity when introspecting and decreased activity in the orbitofrontal cortex when presented with unpleasant stimuli in the ASD group. The amygdala and orbitofrontal cortex are areas implicated in clinical depression across various studies (Pandaya et al., 2012) and variations in functionality and performance in the amygdala could affect the prevalence and severity of clinical depression in people with ASD or Asperger's. It has been shown that the core size of the amygdala is decreased and the volume of the orbitofrontal cortex is lower in those with clinical depression.

Study 3 (Uono et al., 2022)

Aim

Previous studies have suggested that those with ASD are worse at recognizing facial expressions than neurotypical individuals. Research had been conducted on what areas of the brain might be responsible. This study sought to build upon previous research by pinpointing how neural correlates of emotion recognition differ between those with ASD and the background population.

Procedure

Twenty-seven participants with a diagnosis of ASD, six women and 21 men matched by an equal number of neurotypical individuals, performed an emotion-recognition task. The task consisted of looking at 48 photographs depicting six basic emotions (anger, disgust, fear, happiness, surprise and sadness) from four Caucasian and four Japanese models. Written labels of the basic emotions were presented around the photographs. Participants were instructed to

indicate which label best fit the face in the photograph. There was no time limit: the image was not removed until an answer had been given. MRI image acquisition was performed on another day than the emotion recognition task, with no task accompanying it. This data was used to assess correlations of gray-matter volume to accuracy in recognizing emotions using voxel-based morphology.

Results

The results from the emotion recognition task suggest that people with ASD are indeed less accurate identifying facial emotion – fearfulness in particular – than those without, and that they use different mechanisms – not identified in this study – for processing others' facial expressions. Grey-matter volume in the inferior frontal gyrus was positively correlated to accuracy of emotion recognition in controls but not in the ASD group. Instead, grey-matter volume was negatively correlated to total emotion recognition in the ASD group. On the other hand, in the ASD grey-matter volume in the left dorsomedial prefrontal cortex had a significant positive correlation to recognition of disgust.

Takeaway

This study demonstrated the low activation of ASD individuals' amygdala when processing facial information. It is a brain area implicated in clinical depression, as discussed in Silani et al.,2008.

Study 4 (Besseling et al., 2018)

Aim

While research on ASD has continued, findings have failed to keep pace with the need for early diagnosis, treatment options and prediction of outcomes. This study was a test of whether the *innovation-driven co-activation patterns* (iCAPs) model developed by Karahanoglu and Van De Ville (2015) can help identify neural biomarkers of ASD. The iCAPs model is a breakdown of fMRI data into sets of brain areas activating or deactivating together. Each iCAP is linked to a behavioral

profile in the Brainmap database (Research Imaging Institute, 2003), an online repository combining 10,000 activation maps from thousands of fMRI studies.

Procedure

Data was retrieved from the Autism Brain Imaging Data Exchange (*Autism Brain Imaging Data Exchange*, 2017). This is an open-access data-sharing initiative aggregating functional and structural brain-imaging data and processed using the iCAP model.

Due to each iCAPs being mapped to one of 50 behavioral profiles defined within Brainmap, researchers were able to derive combinations of iCAPs and behavioral interpretations. This way they could decode brain activity patterns and decipher the spontaneous fluctuations in functional network activity that could act as biomarkers for ASD and Asperger's.

Results

The results indicate an increase in activity in individuals with ASD in parts of the insula, thalamus, hippocampus and parahippocampus, superior and middle temporal gyrus and middle occipital gyrus. Those with ASD had significant activation in regions connected to emotion, memory and vision as well as upregulation – an increase in activity – in regions related to social cognition, explicit memory and emotion. These findings are in line with known patterns of emotion processing and social interaction among the ASD population. The findings were present in both the autism and Asperger's subgroups but was much more pronounced in the autism subgroup.

Takeaway

There is increased network activity in hippocampus in people with ASD or Asperger's. The hippocampus is another area implicated in clinical depression (Pandaya et al., 2012) and variations in the function of the hippocampus could be related to the prevalence of clinical depression in

people with ASD or Asperger's. Decrease hippocampal volume is common in those with clinical depression and even more common in those prone to relapse.

Study 5 (Critchley et al., 2000)

Aim

Some high-functioning adult autists report using explicit mechanisms like facial expressions to guide social behavior, even as they continue to display abnormal behavior. The hypothesis was that the researchers would find significant differences in neural structures related to explicit vs. implicit processing of facial expressions between people with a diagnosis of ASD and neurotypical individuals. Individuals with ASD should show less brain activity in areas associated with implicit processing of facial expressions.

Procedure

Eighteen adult male participants, half with a diagnosis of high-functioning ASD, were recruited for two experiments. Both experiments had the same conditions. Condition one presented a mix of happy and angry faces; condition two presented only neutral faces. Participants were shown a series of faces, each for three seconds with a 0.75 second interval between. While undergoing fMRI scan, they were asked to indicate via handheld response pad, whether (in the first experiment) the face was happy, angry or neutral; and (in the second) whether the face was male or female.

Results

Both groups reported no difficulties with the task; however, the ASD group made more errors than the neurotypical group, suggesting that they did not fully understand the task in spite of what they reported, and may have contributed to differences in brain activity. The ASD group showed greater activity in the left superior temporal gyrus and the left peristriate visual cortex compared to controls, whereas controls showed greater activation in the right fusiform cortex.

The hypothesis was supported: the control group showed activation in the left cerebellum and left hippocampal regions during the implicit task, but the ASD group did not. The control

group showed activation in the left middle temporal gyrus during the explicit task, but the ASD group did not.

Takeaway

This study shows no left increase in hippocampal activation in those with ASD during implicit expression processing. It is a brain area implicated in clinical depression, as discussed in Besseling et al., 2018.

Study 6 (Baron-Cohen et al., 1999)

Aim

The study had two separate aims, inspired by Brother's social-brain theory, which identifies the amygdala, orbitofrontal cortex and superior temporal gyrus as the *social brain*. The first was to test whether these brain regions activate jointly in subjects performing a simple social intelligence test. The second was to test the validity of Brother's neural model by comparing changes in cerebral blood oxygenation in neurotypical individuals to that of individuals with high-functioning autism or Asperger syndrome.

Procedure

A total of 18 subjects – 10 male, four with autism, and eight females, two with autism – were matched for IQ, age, handedness, socioeconomic status and educational level. They performed two tasks under fMRI in which they had to choose between two words displayed alongside a picture of a face. In the first task, the choice was “male” or “female”. In the second it was “concerned” vs. “unconcerned”, “sympathetic” or “unsympathetic”, or similar word pairs. There were 30 pairs of faces. The same set of stimuli was used for both tasks.

Results

The control group was more accurate both in identification of gender and mental state. It showed greater activation in the left amygdala, right insula and left inferior frontal gyrus, while the autism group showed greater activation in the bilateral superior temporal gyrus. These findings are consistent with Brothers' theory, which holds that extraction of socially relevant information from visual stimuli is associated with activation of the superior temporal gyrus, the amygdala, and areas of the prefrontal cortex. The ASD group did not appear to use the amygdala when identifying mental state or processing emotional information from visual stimuli, instead substituting the temporal lobe structures specializing in verbally labeling complex visual stimuli and processing eyes and faces, suggesting a use of facial memory and language to compensate for a divergent amygdala.

Takeaway

This study demonstrates a differently functioning amygdala in neurodivergent individuals. It is a brain area implicated in clinical depression, as discussed in Silani et al., 2008.

Discussion

The studies reveal several differences in neurological structures between the neurotypical population and those diagnosed with ASD or Asperger's (See Table 1), some relevant to this review. The brain areas I was looking for likely to be relevant were the amygdala, anterior cingulate cortex, orbitofrontal cortex and hippocampus. Out of these the studies bring up the amygdala and hippocampus and orbitofrontal cortex, but they are not discussed in any way that would aid in devising or revising interventions to suit the needs of those with ASD or Asperger's. The researchers did not look for the kind of differences useful to my purposes.

There is some relevance to science more broadly, as the various sub-populations affect other areas than just cognitive neuroscience, such as psychological and behavioral research.

There is value for psychiatry and psychology and relevance to society. Schools and jobs would benefit greatly from more focused and mentally healthy individuals. Society as a whole could benefit from a greater understanding and appreciation of diversity. Far too often is the initial reaction to not understanding something fear. Research could help stem the flow of misinformation and low understanding of ASD and Asperger's in society. If a person is able to hold down a stable job and contribute to society, being happy all the while, then what does it matter if they struggle with faces. So what if they need to work from home because they can't interact face to face; they contribute to society just the same.

Psychologists and psychiatrists would enjoy further information on the brain areas relevant to clinical depression in order to diagnose and prescribe medication more easily. They could find suitable interventions to go hand in hand with medication. Something not often considered is the interpersonal variability not only when choosing medicine, but also when choosing interventions, so trying to successfully find both an intervention and a medicine to work together can be quite the undertaking.

Ethical issues

All participants gave informed consent and had the experiment explained to them, but it was not guaranteed that they understood. As such all the studies have in common the problem of whether or not the participants fully understood what they were signing up for, something even neurotypical subjects can struggle with, the clearest example being Critchley et al. (2000). In Critchley's study researchers were made aware that some participants might not have had an accurate understanding of what was expected of them and what they consented to. Something else to take into consideration is that people with a diagnosis of ASD or Asperger's fall under the classification of vulnerable populations, populations that face prejudice and misunderstanding on a daily basis. As it is likely these individuals do have some trauma from society, it would be prudent to take their experiences into account and to apply extra caution when handling their briefings. Depending on the situation, a person with ASD or Asperger's could interpret the information differently, compromising their ability to give fully informed consent. Screening for

misinterpretations is not easy, but more care should be taken to make sure all participants have a clear understanding of the study as the researchers intended.

Limitations

The studies take great care to match participants according to a long list of criteria, though there is a consistent lack of female ASD participants. This is a problem: if results are to be properly generalized more female participants are a must. Historically it has been argued that ASD has a higher prevalence in men with a four to one ratio (Kirkovski et al., 2013). Researchers have recently argued the correct figure to be closer to three to one (Hag et al., 2018). Some argue that the difference in number of diagnosis is due to flaws in screening procedures (Belcher et al., 2022). Wigdor et al. (2022) argue it's due to the *female protective effect*, which posits that the genetic differences needed for autism to come about (presuming autism is genetically based) are less prevalent in females, who have extra genetic information from their second X-chromosome protecting them.

A concern that most if not all the studies raise is the small sample size. That is an understandable concern but, given the criteria for the studies being as restrictive as they are, a larger sample size might be hard to achieve. Not only has it been shown that increasing sample sizes can give diminishing returns, but that – depending on what populations you investigate – smaller samples might be better (Alexander, 2022b). Regardless of sample size studies often fail to take into account the great interpersonal variability in any population. With all this said, I believe the sample sizes are okay.

My own research has significant limitations. I did not include search terms like "intervention" or "clinical depression". "Intervention" was not included as I was unsure of how to include it. "Depression" was not included as the thesis originally wasn't looking at interventions for clinical depression in those with ASD and Asperger's but was broader. I did redo the search eventually, but had difficulty formulating the appropriate search string.

Future research

More in-depth research should be conducted on the needs of neurodivergent subpopulations, not just those with ASD and Asperger's. This would require different research projects for all the subpopulations. It would be good to have individuals with experience creating or adapting psychological interventions working in tandem with empirical researchers not only to devise new interventions but put them into practice. All subjects of such studies should be well-informed, but initial deception about the nature of the study might be needed to avoid problems like response bias. Afterwards the participants would need to be thoroughly debriefed on the true purpose of the study, taking extra care to make sure they understand. The problem is, now not only could there be issues with misunderstanding the purpose of the study and what is expected of the subjects, but also the false purpose and expectations could be misunderstood as well, along with the debriefing.

Were I given time and resources, I would like to continue the research I did in *gymnasium* where I investigated rhythm- and music-based interventions for those with a diagnosis of ADD or ADHD. Often their resources are limited to medicines that, while helping remedy their attention deficits, affect other parts of their lives. Interventions tailored to their individual needs would aid them while avoiding the side effects of medication.

I would focus my research on finding interventions for depression for ASD and Asperger's as the prevalence of clinical depression is so high in those populations. These could include interventions to aid in creating and maintaining the structure and routines that those with ASD and Asperger's thrive in. Their depression often stems from a lack of opportunities to flourish due to lack of resources, like schools incapable of addressing their needs. When employed in schools, these interventions could allow students that with ASD or Asperger's be afforded opportunities in education that might otherwise pass them over by increasing their focus and ability to learn.

Conclusion

My research question was, what are the measurably and statistically significant neurological differences – functional and structural – between persons diagnosed with high-functioning autism or Asperger's vs. neurotypical people, and how can this knowledge be used in the development of specifically tailored interventions for major depressive disorder?

I have only been able to answer the first part of that. The amygdala, orbitofrontal cortex and hippocampus are often less activated relative to the background population, and other times differing in their function – but not necessarily effectiveness – from their neurotypical counterparts. I was unable to find anything in the studies I reviewed that might be useful for informing new interventions for clinical depression, and I am unsure whether the approach I used even could have worked.

The results from my review are not usable for the purposes I had hoped, aside from further illustrating neurological differences, but I hope it inspires others to combat depression and design interventions for other mental health issues in those with a diagnosis of ASD or Asperger's.

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