Title:
A comparison of attention-deficit/hyperactivity disorder with autism spectrum disorder on cognitive, neural, and emotional estimates: a systematic review

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Conflict of interest. The authors declare no conflicts of interest

Abstract

Background: Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are two neurodevelopmental disorders that share common symptoms and frequently co-occur. We performed a systematic review of studies examining three main domains in ADHD vs ASD; executive functions, brain structures and functions, and emotional skills, in an effort to better understand their co-occurrence.
Methods: As ADHD and ASD frequently co-occur, we chose to focus on the relevant articles comparing ADHD (with no ASD) and ASD (with no ADHD) populations using appropriate measures. A systematic literature search was conducted using six electronic databases, up to May 18, 2022.
Results: A total of 19 articles were included. No significant differences were found in executive functioning between ADHD and ASD. For emotional skills, results were inconclusive, with greater theory of mind (ToM) and empathy skills in ADHD relative to ASD, but no significant differences in emotion recognition. Regarding brain structure and functions, there were inconsistent findings, with some studies reporting weaker brain connectivity in ASD, and reduced gray and white matter volumes in ADHD, while others reported no significant

differences.
Conclusions: Our review suggests a lack of studies directly examining ASD compared with ADHD. The existing literature does not suggest a unique association of either ASD/ADHD with executive dysfunction, emotional skills deficits, or brain structure/function abnormalities. Consequently, further research is necessary to develop a more comprehensive understanding of the overlaps and differences between these disorders and to address the existing gaps in knowledge.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are both neurodevelopmental disorders whose symptoms most often begin to manifest in childhood. ADHD is characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity which interfere with functioning in two or more life domains (American Psychiatric Association [APA], 2013). ASD is characterized by persistent deficits in social communication and interaction across multiple contexts, as well as restricted and repetitive patterns of behavior (APA, 2013). Until the publication of the DSM-5 in 2013, ADHD diagnosis was excluded if ASD was present. Therefore, ADHD and ASD could not formally co-occur, and symptoms of inattentiveness and hyperactivity among patients with ASD were considered an expression of the developmental disorder (APA, 1994). Since the publication of the DSM-5 and the exclusion of this criterion, increasing rates of co-occurrence of ADHD and ASD have been observed (Zablotsky et al., 2020). Studies examining children with ASD reported that over 75% of the children met DSM criteria for ADHD (Joshi et al., 2017; Brookman-Frazee et al., 2018). In a meta-analysis that examined the prevalence of co-occurring mental disorders in the autism population, ADHD was found to be the number one co-occurring disorder, with a prevalence of 28% (Lai et al., 2019). A later meta-analysis indicated that the prevalence of ADHD in the ASD population was 35% (Rong et al., 2021). In addition, studies have reported significant elevations of autistic traits in the ADHD population and vice versa (Goldstein & Schwebach, 2004; Sturm et al., 2004; Hattori et al., 2006). That is, literature has suggested a high level of comorbidity between ADHD and ASD, indicating that individuals diagnosed with one condition are at an increased risk of also having the other. It was found that the prevalence of ADHD in people with ASD is about 40% (Rong et al., 2021) and that the prevalence of ASD in youth diagnosed with ADHD is about 13% (Mohr Jensen & Steinhausen, 2015; Zablotsky et al., 2020). This overlap has led to questions about whether these two disorders are separate entities or if they share a common underlying pathophysiology. However, there is a lack of comprehensive research that directly compares and reviews the similarities and differences between ADHD and ASD.

Executive functions refer to a set of cognitive processes that are used to control and monitor one's behavior to achieve goals and adapt to changes (Diamond, 2013). Executive functions include basic cognitive skills such as attentional control, inhibitory control, working memory, and cognitive flexibility. Deficits in executive functions, among other cognitive abilities such as sustained attention and set-shifting, rooted in impaired inhibitory control, are considered a core aspect of ADHD (Barkley, 1997; Brown, 2002; T. E. Brown, 2009; Halleland et al., 2012). Studies reported an overall consistent and significant impairment in executive function performances among people with ADHD (Pennington & Ozonoff, 1996; Nigg et al., 2005). It seems that some features of autism are also related to deficits in executive functioning (Ozonoff et al., 1991; Demetriou et al., 2018). Autistic people often find it difficult to adapt to new situations and demonstrate behavioral flexibility, and also appear to be impulsive and have difficulty regulating their behavior and inhibiting their responses. A review paper that investigated executive functions in populations with different developmental psychopathologies, reported deficits in executive functions among people with autism (Pennington & Ozonoff, 1996). In a meta-analysis, Demetriou et al. showed consistent evidence that ASD populations have an overall impairment in executive function performance (Demetriou et al., 2018). In addition, other studies have found broad and significant executive function impairments in people with autistic spectrum disorders (Hill & Bird, 2006; Demetriou et al., 2019).

Another shared characteristic associated with both ASD and ADHD is reduced emotional skills in comparison to typically developing peers. In particular, ASD is characterized by impaired emotion perception and recognition abilities and by the ability to understand other people's mental states (also referred to as theory of mind) (Ozonoff et al., 1991). Also, studies have shown that individuals with ASD have difficulties in emotion recognition and regulation, compared to typically developing individuals (Kuusikko et al., 2009; Mazefsky et al., 2013; Uljarevic & Hamilton, 2013). In addition, studies have found significant impairments in emotional intelligence and empathy among individuals with ASD (Gillberg, 1992; Schulte-Rüther et al., 2011; Boily et al., 2017). Impaired emotional skills are also thought to be a prominent feature of ADHD. Studies have shown deficits in emotion recognition among people with ADHD (Cadesky et al., 2000; Miller et al., 2011). Furthermore, studies have demonstrated impaired theory of mind (ToM) abilities in individuals with ADHD, as well as deficits in empathetic skills (Groen et al., 2018; Maoz et al., 2019; Tatar & Cansız, 2022).

Research on ADHD and ASD has expanded to include a neuroscientific perspective, with studies demonstrating structural and functional changes in the brain among individuals with these disorders compared to typically developing individuals. Studies have reported changes in brain structures and functions among people with ADHD compared with typically developing people. In particular, findings showed an overall reduction in total brain volume and white matter volume, and decreased brain volumes in the cerebellum, frontal lobes, and corpus callosum, among individuals with ADHD compared to typically developing individuals (Krain & Castellanos, 2006; Qiu et al., 2011; Rubia et al., 2014; Bayard et al., 2020). A decrease was also found among ADHD in the functional connectivity in several areas in the cortex and the thalamus (Qiu et al., 2011; Rubia et al., 2014). In addition, studies have found brain structural abnormalities among individuals with ASD compared to typically developing individuals, including increased total brain volume, gray matter volume, and cerebral volumes, as well as enlargement in the amygdala, basal ganglia, and caudate nucleus (Sparks et al., 2002; Riddle et al., 2017). Moreover, Studies have observed atypical brain functional connectivity patterns in individuals with ASD, characterized by both hypo-connectivity and hyper-connectivity, with hypo-connectivity being more dominant and manifesting as whole-brain functional hypoconnectivity, frontal-posterior under-connectivity, as well as cortico-cortical and interhemispheric hypo-connectivity (Kana et al., 2014; Ha et al., 2015; Moseley et al., 2015; O'Reilly et al., 2017; Zhang & Roeyers, 2019).

This literature demonstrates the overlap between the two disorders, and the differences between these clinical populations and the typically developing population, hence raising the question of whether ADHD and ASD share similar underlying mechanisms and are part of the same continuum, or whether they are two distinct separate disorders. However, it mostly neglects to report a direct comparison between ADHD and ASD which is crucial to develop a deeper theoretical understanding regarding the unique and common basis of these disorders. For this aim, we performed a systematic literature review in which we examined the comparison between ADHD and ASD regarding three main aspects: executive functions; emotional skills; and brain structures and functions, by searching for relevant literature that compares the two disorders in the context of these three domains. Three questions are addressed: (1) Do ADHD and ASD differ in their underlying executive functions? (2) Do ADHD and ASD differ in emotional skills? (3) Do ADHD and ASD differ in brain structures or functions?

Based on previous studies described above, we expected to enhance our understanding regarding overlaps and differences in the executive functions, emotional skills, and brain structures and functions between ADHD and ASD. We believe that this systematic review would lead to a refinement of initial understandings that are mostly based on the comparison of each clinical group with its comparison typically developing group and lead to a deeper understanding of the similarities and differences between ADHD and ASD in these key areas.

Methods

Search Strategy. The literature was searched using 6 electronic databases: PubMed, Web of Science, Scopus, PsycNet, Education Source, and CINAHL. Relevant articles up to May 18, 2022, were included in the search. Three distinct queries were executed in each database, in line with the three key questions under examination as part of the research question. Each search included the search terms “ADHD” and “ASD”, alongside their corresponding synonyms, along with the terms "DSM", "ICD", and "diagnosis". In addition, a distinct group of search terms was applied to each of the three searches in each database, tailored to the particular research question. The first search included search terms related to executive functions and behavioral cognitive test measures, the second search included terms related to emotional skills, empathy, and ToM, and the third search focused on brain structures and brain imaging techniques. See supplementary information for exact search terms and queries.

Inclusion Criteria. Study inclusion criteria were as follows: (1) Studies examining populations with a validated clinical diagnosis of ADHD without ASD and vice versa. (2) Studies using appropriate measurement tools for the question at hand. For example, using behavioral tasks to test executive functions, or brain imaging tools to test brain structures and functions (see supplementary, Table 1). (3) Studies that conducted a direct comparison between the ADHD and ASD groups using relevant measures. (4) To exclude noise estimation of group differences, we focused on studies with samples >15 for each group. (5) We focused only on studies that examined participants with an (estimated) IQ of ≥70. Furthermore, review studies, pilot studies, or studies that were not published in peer-reviewed journals were excluded (see Figure 1).

Screening and Selection of Studies. The search yielded a total of 139 articles: 35 articles regarding executive functions; 41 articles regarding emotional skills; and 63 articles regarding brain structures and functions. Seventy-two duplicate articles were excluded: 12 of the articles on executive functions; 25 of the articles on emotional skills; and 35 of the articles on brain structures and functions. After reviewing the remaining articles, 43 were excluded because they failed to meet one or more of the inclusion criteria: 14 of the articles on executive functions; 10 of the articles on emotional skills; and 19 of the articles on brain structures and functions. In addition, 5 articles were not accessible in their full version and were therefore excluded: 1 of the articles on executive functions; and 4 of the articles on brain structures and functions. Finally, 19 articles were found relevant and were included in this review: 8 of the articles on executive functions; 6 of the articles on emotional skills; and 5 of the articles on brain structures and functions.

Figure 1: Flowchart of articles selection process

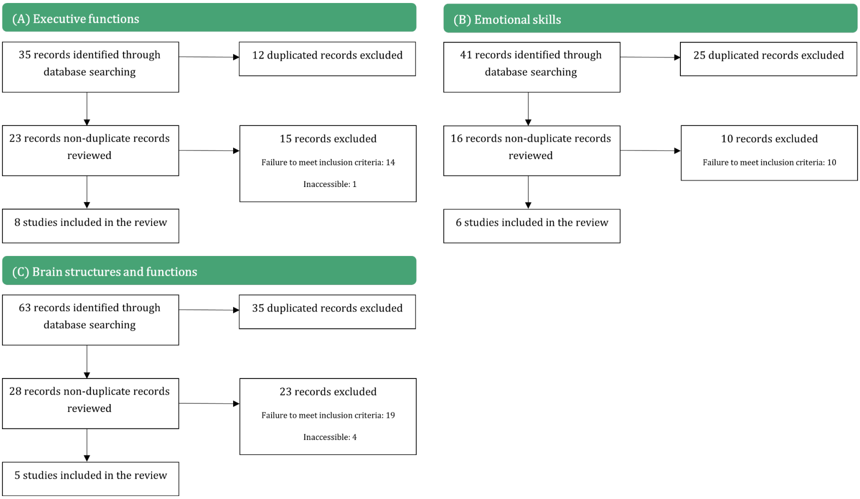

Figure 1. The article selection process included extracting relevant data from databases for each domain, excluding duplicate publications, and assessing the eligibility of the remaining articles based on the pre-determined inclusion criteria. Ultimately, articles that met the inclusion criteria were included in the review.

Results

A total of 19 studies met the inclusion criteria, were found relevant, and were reviewed across the three questions of interest (Table 1-3).

Executive functions. Eight studies were included in this section, with three reporting response-inhibition-related estimates, two reporting sustained-attention-related estimates, two reporting reward-related estimates, and one reporting working-memory-related estimates.

Xiao et al. (2012) examined response inhibition using a go/no-go task and a Stroop test. In the go/no-go task, participants were instructed to respond to the letters "A" and "B" as quickly as possible in Go blocks, and to respond to the letter "O" but withhold their response to the letter "X" in No-go blocks. In the Stroop test, participants were required to distinguish whether the meaning of the word represented was consistent with the color of the word, and to respond accurately, as quickly as possible. Results suggested no systematic differences between ADHD and ASD across estimates including behavior in no-go trials (commission errors), go trials (reaction time), and Stroop incongruent trials (accuracy rates and reaction times) (Xiao et al., 2012). Johnston et al. (2011) also used the Stroop task, as well as the Hayling Sentence Completion Test, to assess response inhibition. In the Hayling Sentence Completion Test, participants were required to complete sentences by adding a word that is at first connected and then unconnected (while inhibiting a connected word). In addition, they used the Matching Familiar Figures test, which involved identifying target pictures among five distractors. Across all three tasks, (Stroop, Hayling, and Matching Familiar Figures) ADHD demonstrated quicker reaction times coupled with lower accuracy rates compared with the ASD group which was slower to respond but showed higher accuracy overall (Johnston et al., 2011). Ishii-Takahashi et al. (2014) used a Stop Signal task to test the inhibition of prepotent responses and a Verbal Fluency task to stimulate cognitive activation involving the prefrontal cortex. The Stop Signal task included pre- and post-Stop Signal task periods, in which participants were instructed to indicate the direction of an image of a dog (left or right) by pressing a button as quickly as possible. During the stop signal trials (indicated by a short beep) participants were instructed to withhold their response. In the Verbal Fluency task participants were instructed to generate as many words beginning with a designated syllable. No statistically significant differences were observed among the ADHD and the ASD groups in any of the task-performance indices, including accuracy rates for stop and go trials in the stop signal task, and the total number of correct words generated in the verbal fluency task (Ishii-Takahashi et al., 2014).

Christakou et al. (2013) used a sustained attention task to assess participants' performance while performing a task under an increasingly difficult sustained attention load. Participants were asked to respond as quickly as possible to the appearance of a visual timer that appears after either predictable short delays of 0.5s, or after unpredictable long delays of 2, 5, or 8s, in random order. Results showed that the ADHD group had significantly higher intra-subject response variability across all delay times relative to the ASD group (Christakou et al., 2013). Vaidya et al. (2020) also used a sustained attention task that included two runs: a bottom-up and a top-down condition allowing to assess the participants' performance under low and high executive function demands, respectively. In the bottom-up run, participants were instructed to respond by pressing a key with their right hand when trials contained the central triangle target (25% of trials), but not when they contained peripheral distractors (50%) or did not contain the target nor the distractors (25%). In the top-down run, participants were required to do the same, but in addition, they were instructed to respond by pressing a key with their left hand when trials contained a peripheral distractor target of a red star. Results showed that the ADHD and ASD groups did not differ from each other in reaction time (Vaidya et al., 2020).

Chantiluke (2015) used the semi-self-paced reward reversal learning task to assess participants' ability to learn a stimulus-response association by reward and punishment and to reverse their response when the stimulus-reward contingency changes unexpectedly. This task requires the participants to choose between two stimuli, when the correct choice earns them a reward (an image of a 50 pence piece and a green happy smiley), and the incorrect choice, earns them a punishment (an image of a crossed-out 50 pence piece and a red unhappy smiley). After 4–6 consecutive correct responses there was a reversal so that the correct choice became incorrect and was accompanied by a punishment, while the incorrect choice became correct and earned a reward. No significant differences were found between the ADHD and ASD groups' performances, in means of the number of errors made (Chantiluke et al., 2015). Kohls et al. (2014) examined reward responsiveness using an incentive go/no-go task with monetary and social reward contingencies, in which participants were instructed to respond as quickly and accurately as possible upon seeing the target stimulus (black square) after a “go” cue and to refrain from responding upon seeing the target after a “no-go” cue. After a successful performance, participants could get a reward in accordance with a cue that was presented at the beginning of each block, signaling the reward type as per three different incentive conditions: non-reward, social reward, and monetary reward. Results showed that participants' reaction times and accuracy rates did not differ significantly between the ADHD and ASD groups in either of the reward conditions (Kohls et al., 2014).

Wang et al. (2018) used the Corsi Block Tapping Test to assess visuospatial working memory. In the test, participants were asked to point at squares in the same or reverse order as the examiner did, according to their color (red squares are used as forward cards and green squares are used as backward cards). Results showed that the ASD group showed significantly poorer performance compared to the ADHD group (Wang et al., 2018).

Emotional Skills. Six studies were included in this section, with three reporting emotion-recognition-related estimates, two reporting ToM-related estimates, and one reporting empathy-related estimates.

Waddington et al. (2018) examined visual and auditory emotion recognition using the Identification of Facial Emotions task and the Affective Prosody task, in two studies. In the Identification of Facial Emotions task, participants viewed individual photos of facial expressions and indicated if they saw or did not see the target emotion (happy, fearful, or angry) in these photos. In the Affective Prosody task, participants listened to sentences of neutral content that differed in prosody and had to verbally identify the emotion (happy, fearful, sad, or angry) of the voice they heard. Results showed that the ADHD and the ASD groups did not significantly differ in their performances on both tasks in regard to reaction time and accuracy. In addition, they did not differ in their speed-accuracy patterns, which suggests that impairments in emotion recognition were similarly frequent in ASD as in ADHD and that none of the impairments were particularly linked to ASD or ADHD (Waddington et al., 2018a; Waddington et al., 2018b). Greco et al. (2021) also examined facial affect recognition using an Emotion recognition morphing task, in which participants were presented with video clips of human and cartoon faces with neutral expressions, gradually developing basic emotions (sadness, anger, surprise, happiness, disgust, and fear). Results showed that in the human-face condition, the ADHD group exhibited significantly higher error frequency compared to the ASD group in identifying the emotion of surprise, while there were no significant differences between the two groups in identifying the emotion of disgust. The ADHD group tended to confuse the facial expressions of fear with sadness more frequently than the ASD group, while the ASD group more often confused fear with surprise compared to the ADHD group. For the facial expression of surprise, the ASD group responded slower than the ADHD group. In the cartoon-face condition, the ADHD group exhibited significantly higher error frequency compared to the ASD group in identifying the emotion of sadness. Concerning disgust, the ADHD group had a higher percentage of errors relative to the ASD group. In this condition, the ASD group showed overall slower response times compared to the ADHD group (Greco et al., 2021).

Ilzarbe (2020) examined ToM using the Frith-Happé task, in which during fMRI scanning participants were presented with clips involving two moving triangles, and then they were asked to identify their movement type by choosing one of three options: (1) ToM, e.g., persuading, (2) Goal-directed interaction, e.g., following, and (3) Random purposeless motions, e.g., floating. In addition, outside the fMRI scanning, participants were shown a subset of the clips (only ToM and Goal-directed interaction clips) and then they were asked what they thought was happening in the clip. Results showed that during the fMRI task, the ADHD group identified goal-directed motions more accurately than the ASD group. During the task outside of the fMRI scanner, No group differences were found in ratings of intention attributions and their appropriateness. However, it was found that the ASD group gave the shortest ToM descriptions, despite receiving more prompts than the ADHD group (Ilzarbe et al., 2020). Hutchins et al. (2016) used the Theory of Mind Task Battery to assess explicit ToM competence and the Theory of Mind Inventory to assess applied ToM competence. Both measures have three subscales that are intended to assess ToM abilities across three general levels of typical development: the Early Subscale intends to assess the earliest ToM abilities that emerge during infancy and toddlerhood; the Basic Subscale intends to assess ToM abilities of young school children; and the Advanced Subscale intends to assess more mature aspects of ToM that tend to emerge in later childhood. The Theory of Mind Task Battery consists of 15 test questions within nine tasks, arranged in order of ascending difficulty, that are presented as short vignettes in a story-book format with color illustrations and accompanying text. For all tasks, children were presented with ToM-related questions that have one correct response option and three plausible distractors. In The Theory of Mind Inventory, respondents were presented with 42 statements and were asked to rate them on a scale of 0-20 with higher values reflecting greater parental confidence that the child can perform particular ToM-relevant skills. Results showed that in the Theory of Mind Task Battery, the composite score of the ADHD group was significantly higher compared to the composite score of the ASD group. For the level of subscale scores, in the Early Subscale score, no differences between the ADHD and the ASD groups were found, apparently due to a ceiling effect. In the Basic and Advanced Subscales scores, the ASD group significantly underperformed the ADHD group. In the Theory of Mind Inventory, no difference was found between the composite scores of the ASD group and the ADHD group. In the Early and Basic Subscales scores, the ADHD group significantly outperformed the ASD group. In the Advanced Subscale score, the ASD group and the ADHD group did not differ from each other (Hutchins et al., 2016).

Aiello et al. (2021) assessed empathy using an Empathy Quotient questionnaire. The questionnaire measured the degree of empathy expressed in real-life situations; experiences; and interests. Results showed that the total score of the ADHD group was significantly higher compared to the ASD group (Aiello et al., 2021).

Brain structures and functions. Five studies were included in this section, with three reporting brain-connectivity-related estimates, and two reporting brain-structures-related estimates.

Connectivity analysis. Two DTI studies examined white matter organization in participants with ADHD and ASD. Aoki et al. (2017), found that participants with ASD had lower fractional anisotropy values in the genu, body, and splenium of the corpus callosum, compared to participants with ADHD. Also, participants with ASD had higher mean diffusivity, radial diffusivity, and axial diffusivity values in several portions of the corpus callosum, compared to participants with ADHD (Aoki et al., 2017). In contrast, Ohta et al. (2020), found no significant difference between the ADHD and the ASD groups regarding fractional anisotropy and radial diffusivity values in the corpus callosum (Ohta et al., 2020). In addition, Chiang et al. (2017), examined white matter alterations among participants with ADHD and ASD using both MRI and diffusion spectrum imaging (DSI) scans. Results showed that participants with ASD had lower mean generalized fractional anisotropy values in the right arcuate fasciculus, right cingulum hippocampal part, anterior commissure, and three callosal fibers (VLPFC part, precentral part, superior temporal part) compared with participants with ADHD (Chiang et al., 2017).

Structural analysis. Two MRI studies examined the structural gray matter and white matter volumes. Lim et al. (2015), examined brain volume for ADHD and ASD and showed that the ADHD group had significantly smaller total brain volume and total gray matter volume, and smaller gray matter volume in the left medial frontal region, right posterior cerebellum and left middle/superior temporal gyrus, compared to the ASD group. No significant group differences in gray matter volumes in the bilateral basal ganglia were observed between the two groups. Also, no significant group differences were observed in white matter volume (Lim et al., 2015). In a different study, Lim et al. (2013), used Gaussian process classification on gray matter volumetric data in an attempt to differentiate between participants with ADHD and participants with ASD. Results showed that a binary classifier trained to discriminate ADHD patients from ASD patients achieved a balanced accuracy of 85.2%, however, no theoretical report was provided for the type of differences that allowed such classification (Lim et al., 2013).

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Table 1. Studies examining the difference in executive functions between ADHD and ASD

Study	Participants	Age	Confounding variables	Tasks/ Measures	Outcome estimates	Results

Data-driven identification of subtypes of executive function across typical development, attention deficit hyperactivity disorder, and autism spectrum disorders	ADHD (N=307) ASD (N=240) TDC (N=465)	8-14 y	Age: ND Sex: SIG IQ: ND ODD/CD: missing	Sustained attention task (during fMRI scan) including two conditions: a 'bottom-up' run, and a 'top-down' run	Reaction time	The ADHD and the ASD groups did not differ from each other in reaction time
Differentiating neural reward responsiveness in autism versus ADHD	ADHD (N=16) ASD (N=15) TDC (N=17)	9-18 y	Age: matched Sex: ND IQ: matched ODD/CD: missing	Incentive go/no-go task with monetary and social reward contingencies	Reaction times for go hits Accuracy rates (% go hit rate; % no-go rejection rate)	Participants' reaction times and accuracy rates did not differ significantly between the ADHD and ASD groups in either of the reward conditions
Disorder-specific functional abnormalities during sustained attention in youth with Attention DeficitHyperactivity Disorder (ADHD) and with Autism	ADHD (N=20) ASD (N=20) TDC (N=20)	11-17 y	Age: matched Sex: ND IQ: matched ODD/CD: no	Sustained attention fMRI task	Intrasubject standard deviation of reaction time	The ADHD group had significantly higher intra-subject response variability across all delays relative to the ASD group
Executive Function Predicts the Visuospatial Working Memory in Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder	ADHD (N=22) ASD (N=21) TDC (N=28)	6-15 y	Age: controlled Sex: controlled IQ: controlled ODD/CD: no	Corsi Block Tapping Test test to assess visuospatial working memory	Total score (sum of forward and backward scores)	Significantly poorer performance in the ASD group compared to the ADHD group.
Inverse Effect of Fluoxetine on Medial Prefrontal Cortex Activation During Reward Reversal in ADHD and Autism	ADHD (N=15) ASD (N=18) TDC (N=21)	10-17 y	Age: matched Sex: ND IQ: SIG ODD/CD: no	The semi-self-paced reward reversal learning task	No. of perseverative errors made after a reversal trial	No significant difference was found between the ADHD and ASD groups under a placebo
Prefrontal activation during inhibitory control measured by near-infrared spectroscopy for differentiating between autism spectrum disorders and attention deficit hyperactivity disorder in adults	ADHD (N=19) ASD (N=21) TDC (N=21)	Mean age: 28.8-30.8 y	Age: matched Sex: matched IQ: matched ODD/CD: no	Stop signal task Verbal fluency task	Stop signal task-mean reaction time, accuracy rates Verbal fluency task-task performance: No. of correct words generated during the 60s activation period	No significant differences were observed among the ADHD and ASD groups in any of the task-performance indices
Response Inhibition Impairment in High Functioning Autism and Attention Deficit Hyperactivity Disorder: Evidence from Near-Infrared Spectroscopy Data	ADHD (N=16) ASD (N=19) TDC (N=16)	8-14 y	Age: matched Sex: matched IQ: matched ODD/CD: missing	Go/No-go task Stroop task	Go/No-go task-commission errors, reaction time Stroop task-accuracy rates in incongruent blocks, reaction times	In the No-go blocks, there was no significant difference between the ASD and ADHD groups in the number of commission errors. In the Go blocks, there was no significant difference between the two groups in reaction time. In the Stroop task, the two groups did not differ significantly in the accuracy rates or in the reaction times during the incongruent blocks.
Response Inhibition in Adults with Autism Spectrum Disorder Compared to Attention Deficit/Hyperactivity Disorder	ADHD (N=24) ASD (N=24) TDC (N=14)	18-55 y	Age: matched Sex: matched IQ: matched ODD/CD: missing	Stroop test Hayling Sentence Completion test Matching Familiar Figures test	Stroop test- total No. of correct responses, color-word score (total No. of correct responses minus the incorrect responses) Hayling task-reaction time	The ADHD group obtained a significantly lower score than the ASD groups on the Stroop test, reflecting their quicker but less accurate performance. In the Hayling test, the ASD group was significantly slower to complete sentences with connected

					Matching Familiar Figures test- reaction time, No. of errors	words compared to the ADHD group. In the Matching Familiar Figures test, the ADHD group was significantly quicker than the ASD group, but they also made significantly more errors than the ASD group
Note: ADHD= attention-deficit/hyperactivity disorder; ASD= autism spectrum disorder; CD= conduct disorder; IQ= intelligence quotient; ND= no difference; ODD= oppositional defiant disorder; SIG= significant; TDC= typically developing controls						

Table 2. Studies examining the difference in emotional skills between ADHD and ASD

Study	**Participants**	**Age**	**Confounding variables**	**Tasks/ Measures**	**Outcome estimates**	**Results**
An emotion recognition subtyping approach to studying the heterogeneity and comorbidity of autism spectrum Open Access disorders and attention-deficit/ hyperactivity disorder	ADHD (N=111) ASD (N=89) TDC (N=220)	7-18 y	Age: matched on mean chronological age Sex: SIG IQ: SIG ODD/CD: missing	Identification of Facial Emotions task Affective Prosody task from the battery of the Amsterdam Neuropsychological Tasks	Mean reaction time Accuracy rates	ADHD and ASD groups did not differ in their performances in terms of speed-accuracy patterns. Emotion recognition impairments were similarly frequent in ASD as in ADHD, and none of the emotion recognition impairments were particularly linked to ASD or ADHD.
Autistic Traits and Empathy in Children With Attention Deficit Hyperactivity Disorder, Autism Spectrum Disorder and Co-occurring Attention Deficit Hyperactivity Disorder/Autism Spectrum Disorder	ADHD (N=33) ASD (N=77) TDC (N=64)	6-14 y	Age: controlled Sex: ND IQ: analyses were controlled for IQ ODD/CD: missing	The child version of the Empathy Quotient assesses the degree of empathy expressed in real-life situations, experiences, and interests	Questionnaire score	The total score of the ADHD group was significantly higher compared to the ASD group.
Explicit vs. applied theory of mind competence: A comparison of typically developing males, males with ASD, and males with ADHD	ADHD (N=29) ASD (N=67) TDC (N=49)	5-14.08 y	Age: matched Sex: ND IQ: missing ODD/CD: ODD	Theory of Mind Task Battery to assess explicit ToM competence Theory of Mind Inventory to assess applied ToM competence	Composite scores Subscale scores Item scores	In the Theory of Mind Task Battery, the composite score of the ADHD group was significantly higher compared to the ASD group. In the Early Subscale score, no differences between the two groups were found. In the Basic and Advanced Subscales scores, the ASD group significantly underperformed the ADHD group. In the Theory of Mind Inventory, no difference was found between the composite scores of the ASD and the ADHD group. In the Early and Basic Subscales scores, the

						ADHD group significantly outperformed the ASD group. In the Advanced Subscale score, no difference between the two groups was found.
Morphing Task: The Emotion Recognition Process in Children with Attention Deficit Hyperactivity Disorder and Autism Spectrum Disorder	ADHD (N=21) ASD (N=20) TDC(N=21)	7-12 y	Age: missing Sex: missing IQ: missing ODD/CD: no	Emotion recognition morphing Task	Reaction time Error frequency	In the human-face condition, the ADHD group exhibited significantly higher error frequency compared to the ASD group in identifying the emotion of surprise. There were no significant differences between the ADHD and ASD groups in identifying the emotion of disgust. The ADHD group tended to confuse facial expressions of fear with sadness more frequently than the ASD group, while the ASD group more often confused fear with surprise compared to the ADHD group. For the facial expression of surprise, the ASD group responded slower than the ADHD group. In the cartoon-face condition, the ADHD group exhibited significantly higher error frequency compared to the ASD group in identifying the emotion of sadness. Concerning disgust, the ADHD group had a higher percentage of errors relative to the ASD group. In this condition, the ASD group showed overall slower response times compared to the ADHD group.
Neural Correlates of Theory of Mind in Autism Spectrum Disorder, Attention-Deficit/Hyperactivity Disorder, and the Comorbid Condition	ADHD (N=21) ASD (N=19) TDC (N=25)	20-27 y	Age: ND Sex: ND IQ: SIG ODD/CD: missing	Frith-Happé task to assess ToM- Inside the fMRI scan the task was performed fully. Outside the scan, a subset of the tasks' clips was shown to the participants, followed by the question "What do you think is happening during the clip?"	Inside the fMRI scan- accuracy rates Outside the fMRI scan- participants' responses	During the fMRI task, the ADHD group identified goal-directed motions more accurately than the ASD group. During the task outside of the fMRI scanner, No group differences were found in ratings of intention attributions and their appropriateness. The ASD group gave the shortest ToM descriptions, despite receiving more prompts than the ADHD group.
Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD	ADHD (N=111) ASD (N=89) TDC (N=220)	7–18 y	Age: matched on mean age Sex: SIG IQ: SIG ODD/CD: missing	Identification of Facial Emotions task Affective Prosody task from the battery of the Amsterdam	Reaction times Accuracy rates	The ADHD and the ASD groups did not significantly differ in their performances on both tasks, regarding reaction time and accuracy

				Neuropsychological Tasks (ANT)		

Note: ADHD= attention-deficit/hyperactivity disorder; ASD= autism spectrum disorder; CD= conduct disorder; IQ= intelligence quotient; ND= no difference; ODD= oppositional defiant disorder; SIG= significant; TDC= typically developing controls

Table 3. Studies examining the difference in brain structures and functions between ADHD and ASD

Study	Participants	Age	Confounding variables	Tasks/ Measures	Outcome estimates	Results
Association of White Matter Structure With Autism Spectrum Disorder and Attention-Deficit/ Hyperactivity Disorder	ADHD (N=55) ASD (N=69) TDC (N=50)	6-12.9 y	Age: matched Sex: matched IQ: missing ODD/CD: missing	DTI scans	Voxelwise fractional anisotropy Radial diffusivity Mean diffusivity Axial diffusivity (MA)	Lower fractional anisotropy values in the genu, body, and splenium of the corpus callosum among the ASD group compared with the ADHD group. In addition, higher mean diffusivity, radial diffusivity, and axial diffusivity values in the midbody and anterior portions of the corpus callosum among the ASD group compared with the ADHD group
Disorder-Specific Alteration in White Matter Structural Property in Adults With Autism Spectrum Disorder Relative to Adults With ADHD and Adult Controls	ADHD (N=32) ASD (N=23) TDC (N=29)	18-30 y	Age: ND Sex: ND IQ: SIG (analysis was conducted with the exclusion of low IQ) ODD/CD: missing	MRI scans DSI (Diffusion spectrum imaging) scans	Generalized fractional anisotropy values	Lower mean generalized fractional anisotropy values in the right arcuate fasciculus, right cingulum hippocampal part, anterior commissure, and three callosal fibers (VLPFC part, precentral part, superior temporal part) among the ASD group compared with the ADHD group
Disorder-specific gray matter deficits in attention deficit hyperactivity disorder relative to autism spectrum disorder	ADHD (N=44) ASD (N=19) TDC (N=33)	Mean age range: 13.6-14.9 y	Age: ND Sex: ND IQ: SIG ODD/CD: missing	MRI scans	Total gray matter volume Total brain volume White matter volume	The ADHD group had significantly smaller total brain volume and total gray matter volume, and smaller gray matter volume in the left medial frontal region, right posterior cerebellum, and left middle/superior temporal gyrus, compared to the ASD group. No significant group differences in gray matter volumes in the bilateral basal ganglia were observed between the two groups. Also, no significant group differences were observed in white matter volume
Disorder-Specific Predictive Classification of Adolescents with Attention Deficit Hyperactivity Disorder (ADHD) Relative to Autism Using Structural Magnetic Resonance Imaging	ADHD (N=29) ASD (N=19) TDC (N=29)	10-18 y	Age: matched Sex: ND IQ: SIG ODD/CD: no	MRI scans	Gray matter white matter Cerebrospinal fluid volumes Total intracranial volume (sum of gray matter, white matter, and cerebrospinal fluid volumes)	A binary classifier trained to discriminate the ADHD group from the ASD group achieved a balanced accuracy of 85.2%
White matter	ADHD	Mean	Age: matched	DTI scans	Fractional	No significant differences

alterations in autism spectrum disorder and attention-deficit/ hyperactivity disorder in relation to sensory profile	(N=55) ASD (N=105) TDC (N=58)	age between 29.4-31.2 y	Sex: matched IQ: ND ODD/CD: missing		anisotropy Radial diffusivity	in fractional anisotropy values in the corpus callosum among the ASD and ADHD groups. No significant differences in radial diffusivity values in the right posterior part of the corpus callosum among the ASD and the ADHD groups

Note: ADHD= attention-deficit/hyperactivity disorder; ASD= autism spectrum disorder; CD= conduct disorder; IQ= intelligence quotient; ND= no difference; ODD= oppositional defiant disorder; SIG= significant; TDC= typically developing controls

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Discussion

Despite extensive research on ADHD and ASD, there is still a gap in the literature regarding a comprehensive comparison and examination of the similarities and differences between these two disorders. Although the co-occurrence of ADHD and ASD is frequently observed, few investigations have directly compared the two disorders to explore any possible overlap and shared pathophysiology. Therefore, this systematic review aimed to compare ADHD and ASD in the context of three domains: executive functions; emotional skills; and brain structures and functions, to examine the question of whether ADHD and ASD are part of the same spectrum. For this aim, we conducted a systematic review in which we identified 19 relevant articles and reviewed them considering the three aspects above.

First, we examined whether there is a differentiation between ASD-only vs. ADHD-only individuals in terms of executive functions. Executive functions are a set of cognitive processes that regulate and monitor behavior to accomplish goals, encompassing attentional and inhibitory control, working memory, and cognitive flexibility (Diamond, 2013; Craig et al., 2016; Cristofori et al., 2019). While executive function deficits were suggested to play an etiological role in ADHD (Pennington & Ozonoff, 1996; Barkley, 1997; Brown, 2002; T. E. Brown, 2009; Halleland et al., 2012), these deficits were also found in studies comparing ASD to a typically developing control group, particularly in terms of behavioral inhibition and regulation (Ozonoff et al., 1991; Demetriou et al., 2018). Therefore, an open question is whether significant differences in executive functions will be observed when directly comparing the two clinical groups. Our review included eight studies that compared executive functions between ADHD (without ASD) and ASD (without ADHD). Three studies examined response inhibition, from which two did not report group differences (Xiao et al., 2012; Ishii-Takahashi et al., 2014). The third study reported speed-accuracy tradeoff differences between the ADHD and the ASD groups, in which the ADHD group prioritized speed over accuracy, while the ASD group prioritized accuracy over speed (Johnston et al., 2011). Two additional studies examined sustained attention: one study did not report differences between the two groups (Vaidya et al., 2020), while the other found higher intra-subject response variability in the ADHD group relative to the ASD group (Christakou et al., 2013). Two studies examined reward-related behavior, and both of them did not report differences between the two groups (Kohls et al., 2014; Chantiluke et al., 2015). Finally, one study examined working memory and found significantly poorer performance in the ASD group compared to the ADHD group (Wang et al., 2018). In conclusion, the current evidence does not suggest a consistent difference between ADHD-only and ASD-only clinical groups in terms of executive functions. Despite the theoretical claims that executive dysfunction and response inhibition impairments are etiological in the presentation of ADHD, it is clear that these also appear in ASD, at least to a similar extent.

Second, we examined whether ADHD-only and ASD-only individuals differ in emotional skills. We adopt here a broad definition of emotional skills, particularly due to the small number of studies addressing the issue with a direct comparison between the two clinical groups. Specifically, emotional skills can be referred to as the ability to recognize and regulate one's emotions, as well as to recognize those of other people, and are the foundation of self-awareness and interaction with others. ASD is defined by a core of difficulties in perceiving and recognizing emotions, as well as understanding the mental states of others (Ozonoff et al., 1991; Frith, 2001; Tseng et al., 2011). However, individuals with ADHD also exhibited impairments in emotional competencies, such as comprehending and regulating their emotions when compared with a typically developing control group (Cadesky et al., 2000; Miller et al., 2011; Demirci & Erdogan, 2016; Parke et al., 2021). Therefore, it remains unknown whether deficits in emotional skills are more prominent in ASD compared with ADHD. The current review included six studies that explore emotional skills. Three studies examined emotion recognition: two studies of which did not find differences between the two groups (Waddington et al., 2018a; Waddington et al., 2018b); and one that showed mixed findings that were not consistent across all experimental conditions or emotions presented, and thus did not indicate specific differences between the two disorders (Greco et al., 2021). Two further studies examined ToM: one study did not find significant differences between the two groups (Ilzarbe et al., 2020), while the other exhibited several findings indicating better ToM competence among the ADHD group compared to the ASD group (Hutchins et al., 2016). Finally, one study examined empathy and found that the ADHD group exhibited higher levels of empathy compared to the ASD group (Aiello et al., 2021). In conclusion, the literature indicates some preliminary evidence to suggest that ASD is associated with lower empathic skills and ToM abilities compared with ADHD. No significant differences in emotion recognition were found between the two groups. However, overall, there is only a small number of studies directly assessing these skills in ADHD vs. ASD, and the main conclusion is that more research is needed to firmly determine whether these types of deficits are indeed more pronounced in ASD.

Finally, we examined whether there is a distinguishable differentiation concerning brain structures and functions between ADHD-only and ASD-only individuals. studies have indicated that individuals with ADHD and ASD exhibit differences in both brain structure and function compared to typically developing individuals (Krain & Castellanos, 2006; Qiu et al., 2011; Nickl-Jockschat et al., 2012; Rubia et al., 2014; Ecker et al., 2015; Riddle et al., 2017; Bayard et al., 2020). Although there has been research conducted on brain structure and function in both individuals with ADHD and ASD, few studies have directly compared the two groups. Consequently, there are significant gaps in our understanding of the similarities and differences in brain structure and functions between these two disorders. The current review included five studies that explore brain structure and functions. Three studies examined brain connectivity: one study did not find differences between the two groups in fractional anisotropy or radial diffusivity values in the brain (Ohta et al., 2020). However, the other two studies did report that the ASD group had lower fractional anisotropy values, and higher mean diffusivity, radial diffusivity, and axial diffusivity values in several portions of the brain and of the corpus callosum in particular, compared to the ADHD group (Aoki et al., 2017; Chiang et al., 2017). These findings generally indicate less structural organization and integrity of white matter fibers, which suggests weaker connectivity between brain regions among the ASD group. Two studies examined brain structures: One study found that the ADHD group had significantly smaller total brain volume and total gray matter volume, and smaller gray matter volumes in frontal, posterior, and temporal regions of the brain, compared to the ASD group (Lim et al., 2015). The other study did not use a general linear models approach, and instead examined and found that a binary classifier was able to distinguish individuals with ADHD from individuals with ASD with 85.2% accuracy (Lim et al., 2013). In conclusion, the existing literature presents inconsistent findings regarding potential distinctions and similarities in brain structure and functions between ADHD and ASD. While some differences have been observed, such as weaker connectivity between brain regions in ASD and reduced gray and white matter volumes in various brain regions in ADHD, the reported results are not entirely consistent across studies.

To sum up, this review mostly highlights the dire need for systematic studies that will address cognitive and neural differences between ASD-only and ADHD-only individuals. Currently, the literature does not provide a clear answer as to whether ADHD or ASD are uniquely or more strongly associated with specific deficits or neural features. This includes executive dysfunction which is regarded as a core symptom of ADHD, and poorer emotional skills which are considered as core deficits in ASD. While some differences in executive functioning, emotional skills, and brain structure and functions have been observed between the two disorders, these differences are not consistent or significant enough to differentiate the two disorders. Therefore, the evidence suggests that ADHD and ASD may share some commonalities, but more research is needed to determine the extent and nature of these commonalities and whether they reflect a shared underlying pathophysiology.

There are several limitations to this literature review that need to be acknowledged. First, due to the small number of studies that were included in each question, we could not perform an analysis of effect sizes and cannot address publication bias. Second, the necessity to compare ADHD-only and ASD-only populations may have resulted in the confinement of the ASD participants to a specific subgroup within the autism spectrum. In 5 (26%) of the studies included in the current review, it was reported that the ASD group consisted partly or entirely of participants with high-functioning ASD. Moreover, in all the studies examined in the current review, participants had a minimum IQ score of 70. Of these, four studies (21%) comprised participants with a minimum IQ score of 80, and one (5%) included participants with a minimum IQ score of 85. Therefore, we suggest that this circumstance may have led to a predominance of high-functioning ASD participants, as some conceptualizations define high-functioning ASD as individuals with autism who fall within the normal range of intelligence (i.e.,70 or above) (Gillberg, 1998; Hartley & Sikora, 2009), while others describe it as individuals with autism who possess an average or above-average IQ (i.e., 85-115 or above, when 80-90 is considered low average) (Chiang & Lin, 2007; Mayes et al., 2011; Andersen et al., 2013). Consequently, it remains unclear whether these samples represent the ASD population or whether the current findings can be generalized solely to this specific subgroup. Additionally, the review did not account for significant demographic variables such as age and gender. This is particularly important as some studies had a wide age range while others had a narrow range, and some included both sexes while others only included one sex, making it difficult to ascertain the impact of age and sex on the outcomes.

Given the lack of empirical research directly comparing ADHD and ASD, there is a pressing need for future research that adopts a multifaceted approach to investigate these two disorders. By employing diverse methodologies, such as analyzing clinical presentation, neurobiological markers, and therapeutic outcomes, we can attain a more comprehensive understanding of the similarities and differences between these conditions, thereby addressing the current knowledge gaps in this field.

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