**Shared and specific neural correlates in attention-deficit/hyperactivity disorder and autism spectrum disorder: a meta-analysis of 243 task-based functional MRI studies**

Subtitle: Standardized neural activation in ADHD and ASD

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**ABSTRACT**

**Objective:** To investigate shared and specific neural correlates of cognitive functions in attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) by performing a comprehensive meta-analysis and considering a balanced set of neuropsychological tasks across the two disorders.

**Methods**: We searched a broad set of electronic databases up to 4-Dec-2022 for task-based functional magnetic resonance imaging studies investigating differences between ADHD and typically developing controls (TDC) or between ASD and TDC. Spatial coordinates of brain loci differing significantly between cases and controls were extracted. To avoid potential diagnosis-driven selection bias of cognitive tasks, we grouped them according to the Research Domain Criteria framework, and conducted stratified sampling to match cognitive component profiles. We used Activation Likelihood Estimation for the meta-analysis.

**Results:** After screening 20,755 potentially relevant references, we meta-analyzed 243 studies (3084 ADHD (676 females), 2654 ASD (292 females), and 6795 TDC participants (1909 females)). ASD and ADHD showed shared greater-activations in the lingual and rectal gyrus; and shared lower-activations in regions including the middle frontal gyrus, parahippocampal gyrus, and insula. By contrast, we found ASD-specific greater- and lower-activations in regions including left middle temporal gyrus, and middle frontal gyrus, respectively, and ADHD-specific greater- and lower-activations in amygdala and global pallidus, respectively.

**Conclusions**: Although ASD and ADHD showed both shared and disorder-specific standardized neural activations, disorder-specific activations were more prominent than shared ones. Brain functional differences between ADHD and ASD are more likely to reflect diagnosis-related pathophysiology rather than bias from the selection of specific neuropsychological tasks.

**INTRODUCTION**

Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are the two most commonly diagnosed neurodevelopmental disorders. ADHD is characterized by impairing inattention and/or hyperactivity-impulsivity that are inconsistent with developmental levels (1). The core features of ASD are difficulties in social communication alongside restricted interest and repetitive behaviors (RRBs) (1). Although ADHD and ASD diagnostic criteria are eminently different, people with ADHD often present ASD symptoms and vice versa (2, 3). Beside the clinical overlap, ADHD and ASD share genetic underpinning, including rare variants and single nucleotide polymorphisms (4, 5).

To delve into these clinical observations and genetic findings, numerous task-based functional magnetic resonance imaging (tfMRI) studies have sought to identify the neural correlates of ADHD and ASD core symptom dimensions. Reflecting the distinctly different diagnostic criteria, most of the available tfMRI studies selected tasks based on the conceptualization of the pathophysiology of ADHD and ASD (6, 7), respectively. Specifically, tfMRI studies in ADHD have typically used attention and inhibition tasks (8), whereas studies in ASD have frequently relied on emotional face recognition tasks (7). Meta-analytic synthesis of tfMRI studies in ADHD has found atypical activation in the right dorsolateral prefrontal cortex (DLPFC), left putamen, and globus pallidus during attention tasks, with insula and anterior cingulate cortex (ACC) implicated in inhibition (9). In relation to ASD, meta-analytic evidence has found atypical activation in the superior temporal gyrus (STG) and fusiform gyrus (FFG) related to difficulties in social interaction (7, 10-12). RRBs have often been interpreted to reflect deficiencies in cognitive flexibility, which have been associated with the inferior parietal gyrus in tfMRI studies (13). Although these prior analyses provide insights into the neural correlates likely associated with the typical symptoms of each disorder, they are limited by their *a priori* selection of specific tasks for ADHD and ASD, respectively.

In contrast to diagnosis-driven research constrained by diagnostic criteria, the Research Domain Criteria (RDoC) framework organizes mental health research in functional domains, including Cognitive Systems, Positive and Negative Valence Systems, Social Processes, Arousal and Regulatory Systems, and Sensorimotor Systems. In keeping with the RDoC framework, studies have begun to incorporate neuropsychological tasks related to trans-diagnostic symptom domains to determine whether neural correlates are distinct or shared in ADHD and ASD (14, 15). Specifically, attention and reward processing tasks have been administered to individuals with ASD (16, 17), and social tasks have been used to study individuals with ADHD (18, 19). Specific studies have found lower activation in the DLPFC during attention tasks in ASD (20), and atypical processing in the FFG evoked by watching emotional faces in ADHD (21). These results suggest that some of the neural bases of ADHD symptoms among people with ASD are similar to those of people with ADHD and vice versa. However, results from previous tfMRI studies are mixed. Thus, the extent to which brain-behavior relationships (i.e., brain regions underpinning behavioral symptoms and cognition) in ADHD and ASD are shared or differ remains unclear. Gaining insight into this aspect would inform our understanding of the pathophysiology of these two common disorders, with implications for their conceptualization, future diagnostic classifications, and management strategies. Indeed, this would be relevant to the ongoing debate as to whether the current diagnostic categories for neurodevelopmental disorders should be lumped or split (22).

A previous meta-analysis by Lukito et al. addressed the specificity of the neural underpinnings of cognitive control in ADHD and ASD, examining shared and distinct functional abnormalities in individuals with these two conditions (23). They found differences in neural activation during cognitive control tasks between ADHD and ASD. Reduced activation in the ACC and middle frontal gyrus (MFG) was specific to ASD, while greater-than-typical activation in the precuneus and FFG was specific to ASD. By contrast, no atypical activation was specific to ADHD compared with ASD. Although the work by Lukito et al. provided important novel insight by comparing ADHD against ASD, it focused on only one out of six RDoC cognitive domains. There are additional deficits that overlap clinically in other cognitive domains in ADHD and ASD. However, the tfMRI literature on these developmental disorders is strongly biased in the selection of neuropsychological tasks. Hence, based on available evidence synthesis in the field, we cannot validly infer commonalities and differences. Accordingly, a more comprehensive synthesis of the neural profiles of individuals with ASD and ADHD across studies with common tasks in ADHD and ASD would further our understanding of their pathophysiology.

To address this gap, we performed a meta-analysis of tfMRI studies that included either or both individuals with ADHD and those with ASD using datasets which were balanced to include a similar number of studies per domain and task across the two disorders. Given the exploratory nature of the meta-analysis, we did not formulate any a priori hypotheses.

**METHODS**

The study protocol was pre-registered on PROSPERO (CRD42021283877).

**Search**

The search key was a combination of terms for the diagnosis and the terms for the imaging modality. The terms for the diagnosis included either “ADHD” or “autism” and related terms, such as “hyperkinetic” and “Asperger” as well as their wild cards. The terms for the modality included “neuroimaging” and “functional magnetic imaging” but did not specify “task” because this would have missed relevant studies. Specific search terms and syntax are reported in the Supplemental Figure 1. PubMed (MEDLINE), Ovid databases (PsycINFO, EMBASE+EMBASE Classic, Ovid MEDLINE), and Web of Knowledge (Web of Science (Science Citation Index Expanded), Biological Abstracts, BIOSIS, Food Science and Technology Abstracts) were searched without language restriction from inception to 4th December 2022. We also hand-searched references from included studies and reviews to identify any eligible study possibly missed with the electronic search.

**Inclusion and exclusion criteria, screening and data extraction**

Inclusion criteria:

1. Original studies:
2. using tfMRI
3. assessing differences in blood oxygen level dependent (BOLD) signal in ADHD vs. TDC or ASD vs. TDC.
4. recruiting children and/or adults with a categorical diagnosis of ADHD or ASD (and their equivalent constructs), according to the Diagnostic and Statistical Manual of Mental Disorders (DSM, from III to 5) or the International Classification of Diseases (ICD, 10 or previous versions).
5. Studies including individuals of any age and both sexes, recruited from clinical settings or the community, with or without ongoing or previous pharmacological treatment for ADHD or ASD-related problems, were retained.

Exclusion criteria:

1. Studies:
2. comparing only ADHD vs. ASD.
3. recruiting participants whose symptoms partially remitted and no longer fulfilled the diagnostic criteria.
4. assessing only ADHD symptoms, without establishing a categorical diagnosis.
5. recruiting participants with a diagnosis of Minimal Brain Dysfunction (MBD) or with the Deficit in Attention, Motor control, and Perception syndrome (24), as well as studies assessing only ASD symptoms, without a formal diagnosis (e.g., diagnoses based only on the Autism Spectrum Quotient or the Autism Diagnostic Observation Schedule).

In the first stage of screening, two authors (HT and JF) independently screened titles/abstracts for inclusion. A final list was agreed with discrepancies resolved by consensus between the two authors. When consensus was not reached, a third senior author arbitrated (YYA or TI). If any doubt about inclusion existed, the article proceeded to the next stage. The full-text version of the articles passing the first stage screening was assessed for eligibility by two researchers independently. Discrepancies were resolved by consensus between the two authors and, if needed, a third researcher acted as an arbitrator. Two researchers independently extracted demographic, clinical, and neuroimaging data. Where required, we contacted the corresponding author via e-mail to inquire regarding study eligibility or to request additional data needed to include their study in the meta-analysis.

**Labelling of neuropsychological tasks**

Two authors extracted the neuropsychological tasks (HT and FJ). Another author (YYA) assigned the neuropsychological tasks to the corresponding latest version of RDoC Subconstructs (25). Another author confirmed the classification (TI). Each Domain contains corresponding Constructs and Subconstructs, as shown in Table 1. For the meta-analysis, we extracted coordinates of loci in which the BOLD response differed significantly between clinical and control groups.

**Stratified sampling**

Balanced subsampling is a sampling method to create a sub-sample that assures matching in key parameters when the whole sample differs in the distribution of key parameters between groups. We adopted a stratified subsampling method to balance the distribution of neuropsychological tasks between ADHD and ASD. To conduct stratified subsampling, we first focused on the Subconstruct that contained two or more experiments in each of four categories (diagnoses x direction), i.e., ASD-higher-than-TDC, ASD-lower-than-TDC, ADHD-higher-than-TDC, ADHD-lower-than-TDC. Studies satisfying this criterion proceeded to stratified subsampling at the Subconstruct level. Studies that did not proceed to stratified subsampling at the Subconstruct level were aggregated at the Construct level. Constructs with at least two studies in all four categories proceeded to stratified subsampling, while the other Constructs were collapsed to the corresponding Domain. The Domains that did not have at least two studies in all four categories did not proceed to stratified subsampling (Table 2).

**Analysis**

Next we used a random balanced subsampling approach, ensuring that each sample contained an equal number of experiments from each domain. Per disorder (ADHD/ASD) and direction (higher/lower than TDC), we calculated the revised activation likelihood estimation (ALE) for 10,000 of these subsamples to approximate the true underlying effect. The primarily goal of ALE is to identify brain regions in which study results converge, taking into account the spatial uncertainty in each study’s results (26-29). Thus, we excluded studies not reporting significant group differences, as they do contribute to spatial convergence. Results were thresholded using cluster-wise FWE at p<0.05, as per current standard (30). For each dataset, the algorithm outputs a binary brain map indicating voxels for which significant convergence was found. We repeated the subsampling procedures 10,000 times, yielding 10,000 binary convergence maps for each direction and each diagnostic group. We then computed the average of all binary convergence maps per direction and diagnostic group to estimate the voxel-wise proportion of significant convergence over all subsamples. These procedures produced four maps (i.e., two directions for each of the two diagnostic groups), each map yielding the probability of finding significant convergence in a balanced setting (PMap). We then performed conjunction analyses for each direction (i.e., greater- or lower-activations) across the two diagnostic groups. This was done by overlaying the greater-/lower-activation probability maps of each disorder and taking the minimum. In the resulting maps, areas with values over zero were interpreted as being shared across disorders. Studies recruiting both ADHD and ASD were included into both the ADHD and ASD analyses.

**Follow-up analysis**

To get a better understanding of the results of the main 'subsampling ALE', we ran multiple follow-up analyses. In the first analysis we calculated the relative contribution of each RDoC Subconstruct/Construct/Domain towards significant clusters, to assess specificity of construct/domain to cluster relationships. To calculate the relative contribution, we first calculated the proportion of the modeled activation (MA) value per voxel in the significant clusters per experiment per subsample. We then averaged the proportion over all experiments belonging to a certain Domain, which showed the relative contribution of each Domain to each individual voxel of the cluster still on a subsample level. Next, we averaged over subsamples, which showed the contribution on a voxel and Construct/Domain level. Lastly, we took the average over all voxels of the cluster, weighted by the PMap, increasing the impact of frequently activated voxels on the final contribution.

The second analysis we ran was a meta-regression to assess the effect of age on the resulting clusters. This was necessary because we included both developmental as well as adult samples in our literature list. We limited the meta-regression to clusters surviving a 50%-density based thresholding to limit inferences to the most stable results. We then fitted a linear regression model between each experiment's mean age and its total MA contribution to the remaining clusters.

As a third follow-up analysis, we ran meta-analytic connectivity modeling (MACM) and functional decoding on the clusters surviving the 50%-density based thresholding (27, 29-31). MACM is a meta-analytic approach to brain connectivity in which large neuroimaging databases are used to find regions in the brain showing significant convergence with a particular seed-region. In our case, these seed regions are the clusters found in the main analysis, and we used the BrainMap as our database of choice (32, 33). Functional decoding uses the behavioral domain and paradigm class meta-data categories from the BrainMap database to allow for functional characterizations of resulting clusters (34, 35). For this it utilizes both forward and reverse inference. Forward inference assesses the probability of detecting activity in a certain brain region when a specific task or cognitive process is at hand. Conversely, reverse inference unveils the probability of a specific task or cognitive process being present when there is activation in a particular brain region. Together, MACM and functional decoding allow for data-driven conclusions about the clusters resulting from the main 'subsampling ALE'.

**RESULTS**

**Included studies**

As reported in Supplementary Figure 1 (PRISMA 2020 flowchart), the initial search identified 32,069 hits. After deduplication, 20,755 references were screened and 370 studies were deemed potentially eligible for meta-analysis (Supplementary Table 1). From these, 243 (including a total of 3084 participants with ADHD (676 females), 2654 with ASD (292 females), and 6795 TDC (1909 females)) reported data that could be meta-analyzed, including 118 studies recruiting individuals with ADHD, 123 with ASD, and eight recruiting individuals with both ASD and ADHD. Integrated studies used a wide variety of psychological tasks during the scan. For example, among Cognitive Systems tasks, GO/NOGO and n-back tasks were most frequently used. Seven and two ASD studies used these tasks, respectively, while, 10 studies used each of these tasks in ADHD. ASD studies used visual and spatial tasks more frequently, while ADHD studies mainly focused on inhibition tasks. All the studies that recruited both individuals with ASD and those with ADHD had direct comparisons between the two diagnoses. Four studies showed only differences in brain activation between ASD and ADHD, while the other four showed both shared and different brain activations. In general, prior studies showed more differences than shared activations between ASD and ADHD. Although some empirical results were similar to the results of the meta-analysis, such as greater-activation in the MFG and IFG in ASD, most empirical findings were not concordant with the meta-analysis. Details of the included (Sub)Construct/Domain and contrasts are shown in Figure 1 and Supplementary Table 2, respectively. The remaining studies were not included because they did not report peak coordinates of group differences or did not show significant between-group differences.

**Convergence of results across tasks and across ADHD and ASD groups**

Table 2 and Figure 2 display the greater- and lower-activated brain regions that were shared across the ADHD and ASD groups. In comparison to TDC, both ADHD and ASD groups exhibited right-lateralized greater-activations in brain areas including the lingual gyrus (MNI: *x*=2, *y*=-90, *z*=-2, cluster size (*k*) =53) and rectal gyrus (*x*=6, *y*=44, *z*=-26, *k*=51). The lower-activations, however, were localized in the left hemisphere, particularly in the MFG (*x*=-40, *y*=34, *z*=26, *k*=107), and STG (*x*=-54, *y*=-30, *z*=-4, *k*=27) (Figure 2 and Table 2).

**Convergence of results across tasks in ASD-specific and ADHD-specific activations**

Compared to TDC, the ASD group exhibited greater-activations in several cortical regions, including the left MTG (*x*=-46, *y*=-66, *z*=2, *k*=620) and inferior parietal lobule (IPL; *x*=-40, *y*=-52, *z*=42, *k*=591), and subcortically in right hippocampus (*x*=30, *y*=-36, *z*=4, *k*=105), and left putamen (*x*=-26, *y*=-10, *z*=8, *k*=87). In contrast, the ASD group showed lower-activations in cortical regions, such as the left MFG (*x*=-44, *y*=26, *z*=32, *k*=812) and right MTG (*x*=52, *y*=-36, *z*=4, *k*=525), as well as subcortical regions, involving the left amygdala (*x*=-24, *y*=0, *z*=-12, *k*=760), and right hippocampus (*x*=24, *y*=-4, *z*=-20, *k*=148). Figure 3 provides a visual representation of the greater- and lower-activations, and Table 2 contains detailed information (Unthresholded brain activation map is available in Supplementary Figure 2).

In comparison to TDC, the ADHD group demonstrated greater-activations in cortical regions, such as the right insula (*x*=34, *y*=14, *z*=8, *k*=627) and posterior cingulate cortex (PCC; *x*=6, *y*=-50, *z*=10, *k*=203), and subcortical regions, including the right amygdala (*x*=-22, *y*=-2, *z*=-14, *k*=826), and putamen (*x*=20, *y*=2, *z*=2, *k*=406). ADHD-related lower-activations were distributed in cortical regions, such as the right MTG (*x*=60, *y*=-8, *z*=-12, *k*=417) and left IFG (*x*=-46, *y*=15, *z*=0, *k*=318), and subcortical regions, including the right global pallidus (*x*=20, *y*=-8, *z*=-2, *k*=731) and left thalamus (*x*=-8, *y*=-16, *z*=0, *k*=308). Figure 4 illustrates the greater- and lower-activations, and Table 2 provides detailed information (Unthresholded brain activation map is available in Supplementary Figure 3).

**Contribution of RDoC Subconstruct/Construct/Domain to ASD- and ADHD-specific activations**

With regard to ASD, the left MTG (*x*=-46, *y*=-66, *z*=2, *k*=620) and right superior temporal pole (*x*=32, *y*=8, *z*=-28, *k*=111) clusters showing greater activation than TDC were predominantly associated with Social Processes and Attention, respectively (Figure 4, Table 2), while the cluster in the left MFG (*x*=-44, *y*=26, *z*=32, *k*=289) showing lower activation in ASD consisted of a combination of Positive Valence, Social Processes, Cognitive Systems, Visual Perception, and Response Inhibition (Figure 4, Table 2).

With regard to ADHD, the left amygdala cluster (*x*=-22, *y*=-2, *z*=-14, *k*=760) showing greater activation than TDC was predominantly associated with Cognitive Systems, while the cluster in the right MTG (*x*=60, *y*=-8, *z*=-12, *k*=417) showing lower activation in ADHD was predominantly associated with both Visual Perception and Response Inhibition (Figure 4, Table 2).

**Meta-regression**

To examine age-dependent effects, we performed a meta-regression of age. As shown in Supplementary Table 2, no brain regions exhibited a significant association with age (all *P* > 0.06).

**Functional decoding and MACM**

The ASD-related greater activated location in the right IFG (*x*=22, *y*=46, *z*=22) was associated with domains related to the emotional aspect of disgust and cognitive aspect of music (Supplementary Figure S3A). As shown in Supplementary Figure 3B, the corresponding co-activated pattern comprised the ACC, bilateral IFGs and insular cortices. The second ASD-related greater activated location in the ACC (*x*=-2, *y*=36, *z*=24) was associated with domains related to emotion aspects of valence and reward/gain (Supplementary Figure 4A). As shown in Supplementary Figure 4B, the corresponding co-activated pattern contained the bilateral insular cortices, PCC, and thalamus. On the other hand, the ASD-related lower activated location in the ACC (*x*=0, *y*=38, *z*=20) was associated with the emotional aspect of reward/gain (Supplementary Figure 5A). The functional co-activated pattern of this cluster contained the bilateral insular cortices, PCC, thalamus, and nucleus accumbens (Supplementary Figure 5B).

The ADHD-related greater activated location in the left midbrain (*x*=-4, *y*=-34, *z*=-16) was associated with emotional aspects of positive, fear, and reward/gain, cognitive aspects of spatial and reasoning, and perception aspect of gustation (Supplementary Figure 6A). The co-activated pattern of this cluster involved the bilateral insular cortices, ACC, thalamus, right putamen, left globus pallidus, and bilateral cerebellum (Supplementary Figure 6B). The second ADHD-related greater activation location in the left globus pallidus (*x*=-16, *y*=-4, *z*=-5) was associated with the interoceptive aspect of sexuality, emotional aspects of disgust and reward/gain, perception aspect of olfaction, and cognitive aspect of reasoning (Supplementary Figure 7A). The co-activated pattern of this cluster contained the bilateral insular cortices, ACC, thalamus, putamen, and nucleus accumbens (Supplementary Figure 7B). The ADHD-related lower activated location in the left STG (*x*=-58, *y*=-22, *z*=6) was associated with domains related to the perception aspect of audition, cognitive aspects of music, phonology, and speech, and action aspect of speech (Supplementary Figure 8A). The corresponding co-activated pattern of this cluster comprised the bilateral insular cortices, ACC, STGs, thalamus, putamen, and cerebellum (Supplementary Figure 8B).

**DISCUSSION**

In this systematic review and meta-analysis of tfMRI studies aimed at finding shared and distinct neural correlates in ADHD and ASD, we addressed for the first time bias related to diagnosis-driven selection of neuropsychological tasks by using a stratified sampling of psychological tasks. We identified both shared but also disorder-specific convergence of results across tasks and across the two disorders. Overall, disorder-specific abnormalities were more prominent than shared ones. Specifically, we found shared greater-activations in the lingual and rectal gyri and lower-activations in the MFG and STG relative to TDC, regardless of task. By contrast, greater-activations in the MTG and ACC and lower-activation in the MFG and MTG represented convergence of results across tasks specific to ASD, whereas greater-activations in the insula and PCC and lower-activations in the MTG and IFG represented convergence of results across tasks specific to ADHD.

Importantly, our findings are consistent with results of studies using other MRI modalities. For example, abnormalities in the STG, IFG, and MFG have been reported in both ASD and ADHD samples using voxel-based morphometry (31, 32), and resting-state fMRI (33, 34). These consistencies with our results suggest that atypical activation in these brain regions may underlie atypical processing during psychological tasks, rather than being its consequence. However, cross-sectional studies cannot address causality. Future research will need to examine causal relations between atypical morphometry and activation during tasks and during resting state, as well as in relation to symptoms.

Intriguingly, some of the shared abnormalities, e.g. in the STG, have been observed in other mental disorders, such as schizophrenia and bipolar disorder (35-37). Similarly, MRI studies have shown abnormal structure and metabolism in the MFG in schizophrenia and bipolar disorder (38, 39). Prior tfMRI studies showed that the STG and MFG are crucial for attention and social cognition, and for working memory, respectively (40). Given that these cognitive components are nonspecifically impaired across psychiatric disorders, abnormalities in these brain regions may reflect transdiagnostic vulnerability to impaired social functioning, rather than the neural basis of specific symptoms of one diagnosis.

Among disorder-specific activations, ASD groups showed both greater and lower-activations in the ACC. Prior meta-analyses of ASD tfMRI studies repeatedly reported atypical activation in the ACC in social and non-social (41) and reward processing tasks (8). Atypical ACC activation in ASD across neuropsychological tasks is in line with our results, and suggests that the ACC represents a hub in the pathophysiology of ASD. In ADHD, we found greater activation in the insula. Previous meta-analysis of fMRI studies showed that the insula is a site of action of methylphenidate (42), suggesting that the insula is a potential pathophysiological hub in ADHD. In addition, the current meta-analysis showed the largest cluster with lower activation in the globus pallidus. Intriguingly, structural neuroimaging studies with ADHD repeatedly showed abnormal volumes in the globus pallidus (32, 43). These findings suggest that our stratified sampling strategy of neuropsychological tasks may have minimized the effects of tasks and emphasized the brain regions where abnormalities across tasks could be observed.

Our findings of disorder specific abnormalities are at odds with the RDoC framework that posits brain-behavior relationships as largely independent of clinical diagnoses (44). We consider two potential explanations for this unexpected difference. First, although we assigned psychological tasks to RDoC constructs, selection bias factors may have remained. For example, stimuli for ASD typically used voices or eyes, while ADHD studies used letters or colors (45, 46). Although the cues differed, they were assigned to Cognitive Systems as long as the contrast mainly focused on Cognitive Systems. Thus, selection bias was possibly not fully eliminated despite our systematic efforts. Second, individuals with ASD and those with ADHD are often administered different medications, which may produce different secondary symptoms. As we prioritized stratified sampling to minimize task selection bias, we did not exclude studies based on medication use. Differences in those factors might have impacted results. Nevertheless, the available data suggest that what we detected reflects real differences in neural activations between the two diagnoses.

**Limitations**

In addition to possible residual selection bias noted above, we were unable to subdivide the datasets to perform sensitivity analyses, e.g., by separating children and adults or excluding some Domain or Construct. This is because we prioritized stratified sampling, which requires at least two studies in each (Sub)Construct. Moreover, although we extracted the medication status of participants, we could not address effects of concurrent pharmacological treatments, as controlling for medication status would have required access to individual participant data, well beyond the scope of this work. We did not include studies with only a dimensional measurement of symptom severity. Because the aim of the current study was to test the impact of the diagnosis on neural activation, including participants without a categorical diagnosis would have not been consistent with the current research question, and would have increased heterogeneity in clinical presentations. However, reporting only symptom severity would not necessarily mean that participants did not meet a categorical diagnosis. The exclusion of these studies resulted in the reduction of the number of integrated studies. Future quantitative syntheses should include both categorical and dimensional studies, relying on the strengths of both, to overcome heterogeneity and maximize the number of integrated studies. Another exclusionary reason was reporting no-significant differences. Because the primary goal of ALE is to examines spatial convergence rather than effect sizes, studies not reporting significant group differences would not affect this likelihood. In contrast, we meta-analyzed all studies with overlapping participants as long as they adopted different neuropsychological tasks. This decision was based on two reasons. First, it is not possible to completely exclude the possibility of participants overlapping across studies. Second, we assumed that different neuropsychological tasks demand different neural activations. Although studies with known participant overlap indeed showed different neural activation patterns with different tasks, our results may be biased by unknown confounding factors present in participants that appeared more than once in the analysis. Potential unknown confounding factors include unknown genetic vulnerability or environmental factors as well as known confounding factors such as age, sex, and comorbidities. Finally, although we included studies regardless of age, sex, or intelligence, we note that participants of the included studies reflected mainly intellectually high functioning individuals, because performing neuropsychological tasks is more challenging for people with low functioning.

**Conclusions and clinical relevance**

Pooling data from 243 tfMRI studies and using an advanced approach to address task selection bias, we found that individuals with ASD and ADHD shared some brain activation abnormalities, although disorder-specific alterations predominated. Our findings can inform the ongoing clinical debate on whether ADHD and ASD should be merged as “neurodevelopmental conditions” or should be kept as distinct entities. The frequent co-occurrence of ASD and ADHD as well as the shared and specific abnormalities may support the need for more integrated pathways of care. From a clinical and service organization standpoint, considering neurodevelopmental disorders as a more homogeneous construct, rather than separate disorders, may provide more efficient delivery of care. However, our findings should also encourage clinicians to be mindful of their specific cognitive/behavioral features as they may require specific management strategies.

**Author Contributions:**

YYA, SBE, and SC conceptualized and organized the project. HT and JF conducted the initial and full text screening. YYA and TI served as an arbitrator. HT and JF conducted data extraction. JF performed investigation. LF and TI analyzed data. YYA and SC drafted the manuscript. FXC provided a critical review and revised the manuscript. All the authors approved the final version of the manuscript.

**Conflict of Interest:**

None

**Funding/Support:**

This work was partly supported by the Japan Society for the Promotion of Science (21K15719 to YYA). This work was partly supported by the Japan Agency for Medical Research and Development (AMED) under Grant NumberJP18dm0307008.

SBE acknowledges funding by the European Union’s Horizon 2020 Research and Innovation Program (grant agreements 945539 (HBP SGA3) and 826421 (VBC)), the Deutsche Forschungsgemeinschaft (DFG, SFB 1451 & IRTG 2150) and the National Institutes of Health (R01 MH074457).

**Acknowledgment**

We thank Dorothea Floris, Erik de Water, and Hsiang-Yuan Lin for translating articles written in languages other than English. We also thank James R. Booth, John A. Sweeney, Sarah Durston, Eric Feczko, Alexandra Livia Georgescu, Carla A Mazefsky, Ralph-Axel Müller, Ryu-ichiro Hashimoto, Kurt P. Schulz, Benjamin E. Yerys and Eric R. Murphy for providing additional information for analysis. We also thank Yoshiyuki Tachibana and Ryuta Kawashima for their kind guidance.

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**Figure legends**

**Figure. 1. Percentages of experiments in RDoC Domains and Constructs.**

Percentages of experiments are visualized based on the Research Domain Criteria (RdoC) Domains and Constructs in each direction of group comparisons. The upper left doughnut chart shows the percentages of experiments reporting greater-activations in ASD compared with TDC, while the upper right doughnut chart represents those reporting lower-activations in ASD. The bottom left figure represents the percentages of experiments showing greater-activations in ADHD, while the bottom right figure shows those showing lower-activation in ADHD compared with TDC. Additional details are in Table 2 in the Supplement.

**Figure. 2. Shared greater and lower brain activations in ASD and ADHD relative to TDC.**

A. Conjunction analysis of activation likelihood estimation (ALE) meta-analyses with a stratified sampling of psychological tasks identified brain regions showing shared greater activations in ASD and ADHD relative to typically developing controls (TDC).

B. Conjunction analysis of ALE meta-analysis identified brain regions exhibiting shared lower activations in ASD and ADHD relative to TDC. The colors of boundaries represent the corresponding resting-state networks. Additional details are in Table 2.

**Figure. 3. Altered brain activations in the ASD group relative to the TDC group.**A. Activation likelihood estimation (ALE) meta-analysis identified brain regions showing greater activations in the ASD group relative to the typically developing control (TDC) group.
B. ALE meta-analysis identified brain regions showing lower activations in the ASD group relative to the TDC group.
The colors of boundaries represent the corresponding resting-state networks. For the top five largest clusters, the contributions of each RDoC Subconstruct/Construct/Domain were visualized. Additional details are in Table 2.

**Figure. 4. Altered brain activations in the ADHD group relative to the TDC group.**

A. Activation likelihood estimation (ALE) meta-analysis identified brain regions showing greater activations in the ADHD group relative to the typically developing control (TDC) group.

B. ALE meta-analysis identified brain regions showing lower activations in the ADHD group relative to the TDC group.

The colors of boundaries represent the corresponding resting-state networks. For the top five largest clusters, the contributions of each RDoC Subconstruct/Construct/Domain omain were visualized. Additional details are in Table 2.