Title: Mapping common grey matter volume deviation across child and adolescent psychiatric disorders

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Abstract

Childhood and adolescence represent a time notable for the emergence of many psychiatric disorders, where comorbidity and co-occurrence of symptoms are well-documented. However, it remains unclear whether there exists common brain structural disturbance across psychiatric disorders in youth. Here, we conduct a transdiagnostic meta-analysis of 132 structural neuroimaging experiments in youth consisting of multiple psychiatric diagnoses. Compared to healthy peers, youth psychiatric disorders are characterized by reduced grey matter volume (GMV) of amygdala and lateral orbitofrontal cortex and enhanced GMV of ventromedial prefrontal cortex and precuneus. These four regions were then subjected to functional connectivity and decoding analyses based on healthy participant datasets, allowing for a data-driven quantitative inference on psychophysiological functions. These regions and their networks mapped onto systems implicated in negative valence, positive valence, as well as social and cognitive functioning. Together, our findings are consistent with transdiagnostic models of psychopathology, uncovering common structural disturbance across youth psychiatric disorders, potentially reflecting an intermediate transdiagnostic phenotype in association with broad dimensions of youth psychopathology.

Keywords: psychiatric disorders; children and adolescents; grey matter volume; meta-analysis; meta-analytic connectivity modeling (MACM); resting-state functional connectivity (RSFC); functional decoding

1. Introduction

Psychiatric disorders in children and adolescents have become a global public health problem (Costello et al., 2005; Costello et al., 2003; García-Carrión et al., 2019). Psychiatric problems occurring during this period cause irreparable damage in multiple developmental domains including affect, cognition and socialization (Shaw et al., 2010; Tomás et al., 2008). Accordingly, these problems impose great limitations on the chances that individuals can successfully transition to adulthood equipped with optimal physical and mental well-being (Merikangas et al., 2009), resulting in significant suffering for families and society (Kieling et al., 2011; Lawrence et al., 2015). According to a recent meta-analysis (Polanczyk et al., 2015), nearly 15% of children and adolescents worldwide suffer from various manifestations of psychiatric problems. Worse still, adulthood psychiatric disorders often emerge from the vulnerable period of childhood and adolescence (Kessler et al., 2007; Kessler et al., 2005a; Kessler et al., 2005b). Given the prevalence and severity of mental disturbances in this sensitive period, it is crucial to identify potential vulnerability markers and treatment targets.

Childhood and adolescence represent a time of extensive brain development and maturation (Dahl, 2004; Lebel et al., 2008; McAllister and Stein, 2010), during which brain functions and structures are vulnerable to adverse events, such as early-life stress (Carr et al., 2013; Rao et al., 2008). Likewise, the psychopathology of psychiatric disorders among youth is increasingly understood to reflct abnormalities of an immature and vulnerable brain subject to adverse psychosocial, biological and/or environmental factors (Tomás et al., 2008). Furthermore, brain morphological alterations associated with psychopathology are already present before the development of symptoms (Ing et al., 2019; José Javier, 2013; Voets et al., 2008). To better

understand these disturbances in mental health, it is crucial to examine neurobiological patterns associated with psychiatric problems in children and adolescents.

Although most brain imaging studies classify patients into different diagnostic categories based on clinical symptoms (Spitzer et al., 1978), there is a significant overlap of symptoms among multiple clinical diagnoses (Allsopp et al., 2019; Eaton et al., 2015; Kessler et al., 1994; Krueger and Eaton, 2015; Markon, 2010; Nenadic et al., 2015). The lack of clear diagnostic boundaries may be particularly challenging in youth, wherein clinical phenotypes are usually less distinct (Angold et al., 1999). On the basis of disorder persistence, onset, and symptoms, major psychiatric disorders can be clustered into higher-level dimensions (Eaton et al., 2015; Krueger and Eaton, 2015), which are further unified into a general liability factor representing lesser-to-greater severity of psychopathology (known as the p-factor) (Caspi et al., 2014; Caspi and Moffitt, 2018; Lahey et al., 2012; Lahey et al., 2017). Accordingly, a hierarchical model holds that there is an ordered structure of psychopathological symptoms, consisting of four levels: individual symptoms, first-order dimensions (resembling traditional diagnoses), broader second-order factors (e.g., internalizing vs. externalizing) and a general psychopathology factor (i.e., the p-factor) (Lahey et al., 2017; Zald and Lahey, 2017). In light of this framework, widely-used case-control designs in the psychiatric neuroimaging literature reflect the endeavor to map neurobehavioral markers to the first-order dimensions of psychopathology. However, this approach ignores the shared variance among first-level dimensions and thus impedes investigations of transdiagnostic mechanisms of psychopathology that may aid in the development of more efficient screening, diagnostic, and intervention tools.

Indeed, recent evidence suggests that mappings between psychopathology and neurobehavioral systems might be more robust at the higher-order factors rather than at lower first-

order dimensions. For instance, a wide array of psychiatric disorders broadly share a large portion of their common genetic variation (Anttila et al., 2018), suggesting that higher-order factors account for a larger proportion of heritable variance than first-order dimensions (Lahey et al., 2011). Moreover, there are common neural circuit deficits across a variety of psychiatric disorders in adults revealed by neuroimaging meta-analyses of brain structures (Goodkind et al., 2015; Jenkins et al., 2016; Kempton et al., 2011), brain functions during active tasks (McTeague et al., 2017; McTeague et al., 2020; Noordermeer et al., 2016; Sprooten et al., 2017), and resting-state brain functions (Sha et al., 2019). Lastly, recent studies employing a broad dimensional approach have linked alterations of brain function and structure to higher-order psychopathology factors in both youth and adults (Kaczkurkin et al., 2018; Kaczkurkin et al., 2019; Katharina et al., 2018; Neumann et al., 2020; Romer et al., 2018; Shanmugan et al., 2016; Snyder et al., 2017; Weissman et al., 2019). Together, recent theoretical proposals and empirical evidence highlight the importance of identifying neurobiological systems linked to overarching dimensions of psychopathology that cut across diagnoses. A transdiagnostic meta-analysis of brain imaging studies is well-suited to address this issue by synthesizing neural substrates nonspecifically associated with multiple forms of psychopathology.

Here, we examined whether there is a common brain structural disturbance across psychiatric disorders in children and adolescents. The morphometric analysis of brain structure provides a promising opportunity to reveal shared biological mechanisms across psychiatric disorders with the following advantages (Goodkind et al., 2015; Jovicich et al., 2013; Zuo et al., 2019): (i) brain structure is one of the most reliable neuroimaging measures, showing stability over time (Zuo et al., 2019); (ii) voxel-based morphometry (VBM) analysis of brain structure has been widely utilized in the research of child and adolescent psychiatric disorders incorporating standardized

methods and unified contrasts; and (iii) the analysis of whole brain-based data alleviates the need for a priori assumptions regarding which neural circuits are thought to be affected. Therefore, we conducted a transdiagnostic meta-analysis of VBM studies across child and adolescent psychiatric disorders to search for commonalities of structural variation. Moreover, we implemented several complementary analyses based on healthy participant datasets to characterize both functional connectivity and psychological function profiles of regions derived from our meta-analysis.

In particular, we examined both task-based and resting-state functional connectivity of identified brain regions by implementing two well-validated methods: meta-analytic connectivity modeling (MACM, Robinson et al., 2010) and resting-state functional connectivity (RSFC, Biswal et al., 1995). The combinations of these approaches allowed us to uncover a more robust estimation of connectivity profiles across different modalities by revealing consensus connectivity networks (CCN) for regions ensuing from meta-analyses (Chen et al., 2018; Goodkind et al., 2015; Wong et al., 2019; Zhang et al., 2017). These analyses aimed to: (i) characterize the physiological functions of regions derived from meta-analyses following a brain network perspective; and (ii) reveal neural circuits that appear to be particularly vulnerable across psychiatric disorders, due to their connections to brain regions with structural perturbations. That is, the regions of convergent morphological alterations could be considered as nodes in related networks vulnerable to disorder-related structural perturbations. Such a network perspective is particularly relevant to the transdiagnostic approach, since it is likely that higher-order psychopathology factors are mapped to alterations in large-scale networks rather than a small number of regions (Buckholtz and Meyerlindenberg, 2012a; Menon, 2011; van den Heuvel and Sporns, 2019). Accordingly, regions ensuing from meta-analyses and their networks were overlaid to a brain functional network atlas to reveal underlying large-scale network correlates (Chen et al., 2018; Zhang et al., 2017). Lastly,

we examined psychological functions of ensuing brain regions and their networks with functional decoding analyses based on large-scale datasets from the Neurosynth database (Yarkoni et al., 2011). Together, these complementary analytical schemes aimed to provide data-driven quantitative inference on psychophysiological functions of identified regions.

2. Materials and Methods

2.1. Literature search and selection

Systematic and comprehensive searches of the PubMed, ISI Web of Science and Google Scholar databases were performed in September 2018 according to the PRISMA guidelines (Shamseer et al., 2015). The identified studies were further selected, which resulted in the inclusion of 132 experiments (i.e., contrasts) from 87 published VBM articles, consisting of eight types of psychiatric symptom constellations **(Fig. 1)**. More details on the literature search and selection are illustrated in the supplementary methods.

< Insert Fig. 1 here >

2.2. Main Activation Likelihood Estimation (ALE) approach

A coordinate-based meta-analysis of reported structural magnetic resonance imaging (sMRI) studies was conducted, employing the revised ALE algorithm (in-house MATLAB scripts) (Eickhoff et al., 2009). ALE is a modeling technique used for determining the convergence of foci reported from different neuroimaging studies, with published foci in Talairach or MNI space (Turkeltaub et al., 2002). ALE interprets reported foci as spatial probability distributions, whose widths are based on empirical estimates of the spatial uncertainty due to between-subject and between-template variability of the neuroimaging data (Eickhoff et al., 2009). Within each of the

132 experiments used in this analysis, a modulated activation (MA) map, or modelled anatomical map, was created by taking the maximum probability associated with any one focus (always the closest one) for each voxel (Turkeltaub et al., 2012).

The union of the individual MA maps created from the maximum probability associated with the closest focus for each voxel (Turkeltaub et al., 2002) was then calculated to obtain an ALE map across contrasts. This ALE map is assessed against a null distribution of random spatial association between contrasts using a non-linear histogram integration algorithm (Turkeltaub et al., 2012). In addition, the average non-linear contribution of each contrast for each cluster was calculated from the fraction of the ALE values at the cluster with and without the respective contrast (Eickhoff et al., 2016). Based on the calculated contribution, we employed two additional criteria to select significant clusters: (1) the contributions for one cluster should be from at least two contrasts so that the finding would not only be driven by one single contrast; and (2) the average contribution of the most dominant contrasts (MDE) should not exceed 50%, whereas the average contribution of the two most dominant contrasts (2MDEs) should not exceed 80% (Eickhoff et al., 2016). It should be noted that other potential meta-analytic algorithms for brain imaging findings are available, such as Seed-based D Mapping (SDM) (Albajes-Eizagirre et al., 2019; Radua et al., 2012). Previous empirical and simulation studies comparing ALE with SDM have yielded similar results (Albrecht et al., 2019; Samartsidis et al., 2017). While a systematic comparison between different meta-analysis algorithms is beyond the scope of current study, we aimed to follow the best-practice recommendations commonly proposed by developers of different methods (Müller et al., 2018; Radua and Mataix-Cols, 2012).

Applying the ALE algorithm, the reported coordinates of brain structure patterns associated with youth psychiatric disorders converged across contrasts, such that we evaluated two directional

relationships: (1) GMV decreases among patients relative to healthy peers (patients < healthy controls: 96 contrasts, 699 foci, 5338 subjects); and (2) GMV increases among patients relative to healthy peers (patients > healthy controls: 36 contrasts, 232 foci, 1795 subjects). More details of each primary study are illustrated in Supplementary Tables S1-S3.

2.3. LOEO analysis

We implemented a leave-one-experiment-out (LOEO) analysis for each of the two ALE meta-analyses to further ensure that the main meta-analytic results were not driven by the coordinates from a single contrast (see supplementary methods for details). All maps were thresholded using a cluster level family wise error (cFWE) correction ($P < 0.05$) with a cluster formation threshold of $P < 0.001$ using 10,000 permutations for the correction of multiple comparisons.

2.4. Modulation effects

We extracted per-voxel probabilities of aberrant gray matter in the VBM meta-analysis for each of the common regions to investigate moderation of effects by demographic, clinical and imaging-specific factors, including mean age, sex ratio, mean intelligence quotient (IQ), medication status, disorder comorbidity and MRI magnetic field strength (see also Goodkind et al., 2015; Jenkins et al., 2016; Mcteague et al., 2016; McTeague et al., 2017). Nonparametric Kruskal-Wallis *H*, Mann-Whitney *U*, and Spearman's rank correlation tests were utilized as warranted. Moreover, it should be noted that we did not assess modulating effects of some potentially influential factors (e.g., duration of disease) that were not reported in most studies (see also Supplementary Tables S1-S3).

2.5. Functional connectivity analyses

The task-based and resting-state functional connectivities of identified brain regions (i.e., left amygdala, right lOFC, vmPFC and precuneus, see also Results section) were determined with MACM and RSFC. These analyses were based on recent theoretical and empirical evidence indicating that psychological dysfunctions in psychiatric disorders often arise from alterations in large-scale neural networks rather than localized changes in a small number of regions (Buckholtz and Meyerlindenberg, 2012a; Menon, 2011; van den Heuvel and Sporns, 2019). In other words, psychological dysfunction might emerge from functional alterations in brain regions that are anatomically intact but are connected to locations exhibiting structural abnormalities (i.e., remote network effects). For instance, there is evidence showing that structural perturbations result in symptoms through remote functional effects of a distributed network rather than the affected anatomical locations themselves (Corp et al., 2019; Darby et al., 2018; Fox, 2018; Sha et al., 2019). Therefore, functional connectivity analyses could help to uncover neural circuits particularly vulnerable to disorder-related structural perturbations. This network perspective is especially relevant for searching neurobiological markers of broad transdiagnostic dimensions of psychopathology.

On the one hand, task-based functional connectivity was determined with MACM, which delineates patterns of co-activation across thousands of studies using the BrainMap database (http://www.brain map.org/), producing data-driven functional connectivity maps for each aberrant GMV location as a pre-defined region of interest (Langner et al., 2014). On the other hand, resting functional connectivity was examined with whole-brain RSFC analyses, using a publically available connectome database from 192 healthy participants to identify regions functionally connected to each aberrant GMV location at rest (Nooner et al., 2012). The combination of RSFC

and MACM allowed the analysis of convergence (i.e., CCN) between both task-driven and task-independent functional networks related to regions emerging from our ALE structural meta-analysis, which allowed us to evaluate adaptive functionality of these regions with respect to healthy populations (Chen et al., 2018; Goodkind et al., 2015; Wong et al., 2019; Zhang et al., 2017). More details of functional connectivity analyses are provided in supplementary methods.

2.6. Large-scale network analysis

To assess the underlying large-scale network correlates, clusters revealed by meta-analysis, MACM, and RSFC analyses were overlaid onto seven canonical functional cortical networks and a collection of subcortical areas (Choi et al., 2012; Liu et al., 2018; Yeo et al., 2011). Canonical networks include the fronto-parietal network, dorsal attention network, ventral attention network, somatomotor network, visual network, cortical affective network, and default mode network, in addition to a subcortical network (Yeo et al., 2011). The relative distribution was computed by the proportion of activated voxels of a given network versus all activated voxels, while the absolute distribution was calculated by the proportion of activated voxels of a given network versus voxels of that template network (Chen et al., 2018; Zhang et al., 2017).

2.7. Functional decoding

To explore which psychological topics were most relevant to each network of identified brain regions, functional decoding was performed using version 0.6 of the Neurosynth database (Yarkoni et al., 2011). Using all fMRI studies in the database, a data-driven quantitative inference on mental processes associated with the network was performed by training a naïve Bayes classifier. Two sets of studies that activated at least 5% voxels and that did not activate any voxel

of a given cluster were selected respectively as the positive and negative samples of the training set (Vega et al., 2017). The area under the receiver operating characteristic curve was used to measure the performance of the model with a 4-fold cross-validation. This resulted in the conditional probability of psychological topics under each module. Notably, only those topics that survived multiple comparisons using FDR with $P < 0.01$ by implementing a permutation test were reported. Finally, the log odds ratio between the probability of a given topic activating the module and the probability of the topic not activating the module was extracted from the trained naïve Bayes model to generate functional decoding profiles.

3. Results

3.1. Included studies and sample characteristics

Of the 3480 publications initially found in our search, 2785 were excluded after first screening by title and abstract content. After examining the full texts of the remaining 209 publications, 87 published VBM articles contributed to the present meta-analysis (see **Fig. 1** for details on the inclusion procedure). Our final sample included 132 comparisons between child and adolescent psychiatric disorders and healthy controls, representing a total of 3424 patients (aged 6 - 19 years) and 3709 matched healthy individuals (also aged 6 - 19 years). More information about each primary study included in the meta-analysis is included in Tables S1-S3.

3.2.VBM meta-analysis across youth psychiatric disorders

Gray matter decreases: The meta-analysis of VBM studies reporting GMV decreases in patients relative to healthy peers demonstrated consistent maxima in left amygdala and right lateral orbitofrontal cortex (lOFC) **(Fig. 2 & Table 1)**. Fifteen out of 96 contrasts contributed to the cluster

in left amygdala (MDE = 16.22%; 2MDE = 32.23%). Eleven out of 96 contrasts contributed to the cluster in right lOFC (MDE = 17.64%; 2MDE = 34.95%) **(Table S4)**.

Gray matter increases: Examining the contrasts of GMV increases in patients relative to healthy peers demonstrated consistent maxima in left ventromedial prefrontal cortex (vmPFC) and right precuneus **(Fig. 2 & Table 1)**. Five out of 36 contrasts contributed to the cluster in left vmPFC (MDE = 28.09%; 2MDE = 55.47%). Five out of 36 contrasts contributed to the cluster in right precuneus (MDE = 30.68%; 2MDE = 50.77%) **(Table S5)**.

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3.3. LOEO analysis

With respect to the contrasts of GMV decreases in patients compared to healthy peers, consistent maxima in left amygdala and right lOFC were identified **(Fig. S1 & Table S6)**. With respect to the contrasts of GMV increases in patients compared to healthy peers, consistent maxima in left vmPFC and right precuneus were identified (**Fig. S1 & Table S6**). Together, the results of the LOEO approach corroborated the findings of our primary ALE meta-analysis.

3.4. Modulation effects

Per-voxel probabilities of aberrant gray matter in the VBM meta-analysis for each of the identified regions were extracted and examined for effects of demographic, clinical and imaging-specific factors. First, no significant effects of clinical diagnoses were identified (Kruskal-Wallis *H* test: $H < 13.924$; $P > .053$ for all). Next, we considered whether the common gray matter abnormality findings were due to the presence of comorbid diagnosis and medication, and we found that these factors did not account for differences in gray matter aberrant locations (Mann-Whitney *U* test: $U < 1.758$; $P > .079$ for all). Finally, we examined the potential role of

demographic and imaging-specific factors. Gray matter differences were not related to: (i) mean age, IQ and sex ratio using either nonparametric correlations (Spearman *rho* < 0.155; *P* > .133 for all) or Mann-Whitney *U* tests via median-split (*U* < 1.780; *P* > .075 for all); or (ii) MRI magnetic field strength using Mann-Whitney *U* tests (*U* < 1.454; *P* > .146 for all).

3.5.Functional connectivity results

We conducted MACM and RSFC connectivity analyses to further investigate the functional connectivity profiles (i.e., CCN) of left amygdala, right lOFC, right precuneus and left vmPFC **(**see **Fig. 3, Fig. 4, & Tables S7, S8)**. Specifically, the CCN of the left amygdala seed **(**see **Table 2 & Fig. 3A, right panel)** was comprised of the amygdala, hippocampus, parahippocampus, thalamus, putamen, caudate, lateral orbital gyrus, anterior insula, medial frontal gyrus, inferior/middle occipital gyrus, fusiform and precentral gyrus, which were primarily distributed in the subcortical network (relative: 38.26%; absolute: 23.57%) and visual network (relative: 17.51%; absolute: 4.84%) **(Fig. 5A & 5B)**. The CCN of the right lOFC seed **(**see **Table 2 & Fig. 3B, right panel)** were comprised of the lateral orbital gyrus, anterior insula, dorsal anterior cingulate gyrus, superior medial frontal gyrus, fusiform, thalamus, putamen, caudate, hippocampus and amygdala, which were primarily distributed in the fronto-parietal network (relative: 34.57%; absolute: 13.65%), ventral attention network (relative: 19.39%; absolute: 10.96%) and subcortical network (relative: 15.40%; absolute: 12.10%) **(Fig. 5A & 5B)**. The CCN of the right vmPFC seed **(**see **Table 2 & Fig. 4A, right panel)** included the ventral medial frontal gyrus, anterior cingulate gyrus, precuneus, caudate and middle cingulate gyrus, which were primarily distributed in the default mode network (relative: 85.65%; absolute: 6.87%) **(Fig. 5A & 5B)**. The CCN of the right precuneus seed (see **Table 2 & Fig. 4B, right panel**) involved the

precuneus, superior/inferior parietal lobule, inferior temporal gyrus, dorsal anterior cingulate gyrus, middle frontal gyrus and postcentral gyrus, which were primarily distributed in the dorsal attention network (relative: 49.43%; absolute: 9.29%), ventral attention network (relative: 23.34%; absolute: 4.92%) and somatomotor network (relative: 20.07%; absolute: 2.96%) **(Fig. 5A & 5B)**. Separate findings of MACM and RSFC are listed in the supplementary results.

< Insert Fig. 3 & Fig. 4 here >

3.6.Quantitative functional profiling of identified networks

First, the functional decoding analysis revealed that the amygdala-related network was predominantly associated with the psychological functions of face/emotion, emotion, fear, reward, and memory processing. Second, the lOFC-related network was focused on decision-making, conflict, switching, reading, and language processing. Third, the vmPFC-related network was linked to reward, decision-making, awareness, mentalizing, and personality factors. Fourth, the precuneus-related network was associated with attention, action, motor, spatial, and gaze processing. The log odds ratio between the probability of a given topic activating the network and the probability of the topic not activating each network was displayed in a functional decoding profile for each network ($P < 0.01$, FDR corrected) **(Fig. 5C)**.

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4. Discussion

The present meta-analysis aimed to quantitatively delineate the shared neurobiological substrates of child and adolescent psychiatric disorders. We identified a transdiagnostic pattern of gray matter changes across multiple forms of youth psychopathology. Specifically, our results revealed that child and adolescent psychiatric disorders, in comparison to healthy controls, are

characterized by GMV decreases in left amygdala and right lOFC as well as GMV enlargements in left vmPFC and right precuneus. Importantly, our main findings remained robust after validation approaches to eliminate effects solely due to a single experiment. Our findings were also robust to the modulation effects of demographic (e.g., mean age, sex ratio), clinical (e.g., clinical diagnoses, medication state, comorbidity), or imaging-specific (e.g., MRI magnetic field strength) factors. Moreover, large-scale network analyses indicated that these four regions and their functional connectivity profiles are mapped onto multiple brain systems including subcortical, fronto-parietal, attention, and default mode networks, which are linked to adaptive emotional reactivity and regulation, cognitive control, and social functions. Together, our study identified not only the regions of convergent structural perturbations across youth psychiatric disorders but also their derived neural networks and psychological functions from a data-driven approach based on healthy participants. These findings implicate shared neural mechanisms in association with higher-order dimensions of psychopathology cutting across disorder boundaries in youth.

Our findings are consistent with transdiagnostic/dimensional models of psychopathology advocated in recent years (Cuthbert, 2014; Insel et al., 2010; Insel, 2014; Lahey et al., 2017). For instance, the Research Domain Criteria Project (RDoC) asserts that psychiatric disorders may reflect dysfunction in a small number of transdiagnostic functional constructs measured at different levels (e.g., brain-imaging measures) (Insel et al., 2010; Insel and Landis, 2013; Sanislow et al., 2019; Sanislow et al., 2010; Victor et al., 2018). In this regard, brain regions and networks revealed in the current study might correspond to the RDoC dimensional functional constructs of negative/positive valence, cognitive control and social functioning, abnormalities that manifest in disorder-spanning symptoms. Moreover, the current findings are well-aligned with the hierarchical model of psychopathology, such that the shared structural altercations might reflect nonspecific

neural correlates of second-order factors (e.g., externalizing or internalizing) or the general psychopathology factor (Zald and Lahey, 2017). Notably, it is likely that those transdiagnostic functional constructs or higher-order psychopathology factors are embedded in large-scale network disruptions accompanying with structural alterations in key nodes, rather than localized dysfunctions in individual nodes (Buckholtz and Meyerlindenberg, 2012b; Sha et al., 2019; Zald and Lahey, 2017). As discussed below, brain regions and networks revealed in the current study contribute to widespread functional constructs that are related to different dimensions of psychopathology.

Amygdala has been considered as a key node in neural circuits implicated in emotional perception/communication, memory and expression (Blair, 2008; Kirkby et al., 2018; Meffert et al., 2015), which are commonly disrupted across multiple disorders (Ciaramidaro et al., 2018; Eisenberg et al., 2009; Sabharwal et al., 2017) and predictive of treatment outcomes (Gorka et al., 2019). This notion is corroborated by our results indicating a transdiagnostic pattern of GMV loss in the amygdala, which is imbedded in the subcortical limbic system associated with emotional functioning. Similar to our findings of reduced left amygdala volume across disorders in youth, the adult psychopathology literature reveals attenuated amygdala structure across diagnoses, such as anxiety disorders (e.g., Baeken et al., 2010; Blackmon et al., 2011), attention deficit hyperactivity disorder (ADHD) (e.g., Frodl et al., 2010; Nickel et al., 2017), autism spectrum disorder (ASD) (Domes et al., 2013; Kleinhans et al., 2011), and posttraumatic stress disorder (PTSD) (e.g., Ahmed-Leitao et al., 2016; Morey et al., 2012; Paquola et al., 2016). Attenuated amygdala volumes have also been linked to broader transdiagnostic psychopathology dimensions in both youth and adults, including internalizing symptoms (Snyder et al., 2017) and emotional communication deficits (e.g., alexithymia) (Goerlich-Dobre et al., 2015; Ihme et al., 2013; see Xu

et al., 2018 for a meta-analysis). Moreover, anomalous functional connectivity of amygdala with other regions in the subcortical network (e.g., thalamus) is evident in many psychiatric disorders within the context of excessive acquisition and expression of negative emotion (Green et al., 2017; Jalbrzikowski et al., 2019; Yoon et al., 2017). For instance, decreased amygdala connectivity to thalamus in response to threat is associated with anxiety symptoms in a transdiagnostic youth sample (Katharina et al., 2018). Likewise, in both healthy and clinical populations, changes in functional connectivity of amygdala with other subcortical limbic regions (e.g., hippocampus/thalamus) scale with improvement in negative mood following neurofeedback training (Young et al., 2018; Zhu et al., 2019; Zotev et al., 2018). Arguably, structural perturbation of amygdala and related disruptions in the subcortical network are associated with emotion-related symptoms across child and adolescent psychiatric disorders.

lOFC constitutes an important node in a domain-general system engaged by a variety of high-level cognitive control processes ranging from control of attention and memory to response and emotion (Dosenbach et al., 2006; Duncan and John, 2013; Lückmann et al., 2014; Vincent et al., 2008). Accordingly, our findings revealed that lOFC-related neural circuits are mapped to fronto-parietal, ventral attention, and subcortical networks. The fronto-parietal network contributes to task-set maintenance, long-term planning, and response suppression and selection, among other high-order control processes (Cole et al., 2014; Cole et al., 2013; Menon, 2011), whereas the ventral attention network is recruited by the detection of salient stimuli (Corbetta et al., 2008; Kim and Hongkeun, 2014). Other studies have distinguished the functional roles of these networks as initiating/adjusting control or maintaining stable task sets (Dosenbach et al., 2006; Dosenbach et al., 2007). Finally, the connectivity of lOFC with the subcortical network is implicated in successful emotion regulation (Banks et al., 2007; Monk, 2008; Ochsner et al., 2012; Opialla et

al., 2015). In brief, lOFC engages functional connectivity with multiple systems, allowing it to implement cognitive control functions in a domain-general manner. This conjecture is in line with our functional decoding results implicating lOFC in multiple domains.

In accordance with our findings, previous studies have shown transdiagnostic structural and functional abnormalities in lOFC-related networks across a wide range of psychiatric disorders (Carlisi et al., 2017; Patti and Troiani, 2017; Spielberg et al., 2014). For instance, recent transdiagnostic neuroimaging meta-analyses of adult psychopathology have demonstrated shared alterations in the fronto-parietal and ventral attention networks across various disorders (Goodkind et al., 2015; McTeague et al., 2017; Sha et al., 2019). In youth, decreases in lOFC volumes are associated with a general psychopathology factor (Snyder et al., 2017), and cortical thickness of the ventral attention network is reduced in association with second-order fear symptoms (Kaczkurkin et al., 2019). In terms of large-scale network connectivity, different forms of psychopathology share hypoconnectivity between fronto-parietal and default mode networks (Sha et al., 2019), and loss of network separation between these networks scales with a general psychopathology factor in youth (Xia et al., 2018). Moreover, different psychiatric disorders share hypoconnectivity of the ventral attention network with both fronto-parietal and default mode networks, which is, in turn, linked to gray matter reductions in nodes of these networks (Sha et al., 2019). Likewise, changes in functional connectivity of the ventral attention system parallel transdiagnostic improvement in depressive symptoms following cognitive behavioral therapy (Zhen et al., 2018). Lastly, disruptions in structural and functional connectivity of lOFC and a subcortical limbic circuit (e.g., thalamus/caudate) are linked to emotional dysregulation among different psychiatric disorders such as ADHD (Yang et al., 2018), ASD (Turner et al., 2006), and schizophrenia (Hamoda et al., 2019). In summary, it is conceivable that lOFC and related large-

scale networks underlie the functional construct of cognitive control, of which dysfunctions might drive disorder-spanning symptoms.

vmPFC constitutes a hub in the default mode network that is implicated in value-based decision making (Hare et al., 2009), self-referential thinking (D'Argembeau et al., 2005), autobiographical memory (Greicius and Menon, 2004), prospection (Spreng and Grady, 2010), and theory of mind (Matthias et al., 2014; Roy et al., 2012). These adaptive self-related and social cognitive processes represent essential dimensions of mental health (Cotter et al., 2017; Northoff et al., 2006; Zhao et al., 2013), and their disruptions are linked to structural and functional abnormalities in vmPFC as well as the default mode network across psychiatric disorders (Carlisi et al., 2017; Schilbachab et al., 2016; Whitfield-Gabrieli and Ford, 2012). For instance, perturbed structure, activity, and connectivity of the default mode network have been associated with symptom severity (Gong et al., 2017) and the general psychopathology factor in youth (Snyder et al., 2017). Moreover, delayed maturation and dysconnectivity of the default mode network predict general psychopathology scores among both youth and adults (Elliott et al., 2018; Sato et al., 2016). Likewise, development of the default mode network is vulnerable to early-life stress, which constitutes a major risk factor for the development and maintenance of diverse forms of psychopathology (Zeev-Wolf et al., 2019). Lastly, changes in the functional connectivity of the default mode network scale with improvement in depressive symptoms following mindfulness-based cognitive therapy in a transdiagnostic anhedonic sample (Cernasov et al., 2019). Together, the clinical significance of vmPFC and related default mode network has been well established in a myriad of psychiatric conditions (Mohan et al., 2016; Whitfield-Gabrieli and Ford, 2012), and alterations in this system are in line with the transdiagnostic dimensions of psychopathology.

Finally, precuneus and its network are primarily focused within the dorsal attention network contributing to top-down attention orientation to task-relevant features and spatial locations (Cieslik et al., 2010; Corbetta, 2000; Kim and Hongkeun, 2014). These attention processes support cognitive flexibility, enabling us to prioritize the processing of relevant information while suppressing distracters (Lanssens et al., 2020). For instance, deviations from normative maturational trajectories in the dorsal attention network along with other networks predict dysfunction of sustained attention in youth (Kessler et al., 2016). Notably, the dorsal attention network implements executive functions presumably by suppressing the default mode network, demonstrating the anticorrelation between these networks (Owens et al., 2019). Accordingly, reduced functional connectivity between the dorsal attention network and default mode network has been linked to numerous psychiatric disorders, including but not limited to ADHD (Kessler et al., 2014), substance use disorder (Ipser et al., 2018), and major depressive disorder (Yan et al., 2019). Lastly, structural connections of precuneus to multiple regions in the dorsal attention network are altered in association with early-life stress (Teicher et al., 2014). To conclude, alterations in precuneus and the dorsal attention network are associated with attention deficits in many psychiatric disorders.

Several limitations related to the current study should be noted. First, the limited number of experiments on each disorder hindered the examination of diagnosis-specific structural alterations. Relatedly, the current meta-analytic approach did not allow us to distinguish neural correlates associated with the general psychopathology factor from those associated with more specific second-order factors. Both specific and nonspecific neural correlates are important to more comprehensively understand the hierarchical psychopathology structure, which could help to explain both comorbidity and heterogeneity across psychiatric disorders (Zald and Lahey, 2017).

Future studies addressing this issue might map brain imaging measures to different levels of psychopathology simultaneously. Such a hierarchical approach could also help to reveal the complex relationship between multiple functional construct deficits and broad dimensional features of psychopathology, both of which might be mediated by the abnormalities in brain regions and networks ensuing from current study. Second, it remains unclear whether the transdiagnostic morphological alterations represent a proxy for cause or consequence of psychopathology, which awaits to be examined with longitudinal designs. Third, although current findings shed light on large-scale networks plausibly vulnerable to youth psychopathology based on healthy participant datasets, future studies are needed to validate current findings by synthesizing network alterations in youth psychiatric disorders. Lastly, several methodology limitations should also be noted, such that: (i) the ALE meta-analysis provides only measurements of spatial convergence without considering effect sizes; (ii) the number of experiments for each specific disorder diagnosis is not well balanced; and (iii) modulating effects of potentially influential factors such as illness duration and age of illness onset could not be assessed comprehensively as this information was not consistently included across primary studies.

Despite these limitations, the current findings provide novel evidence on shared neural mechanisms across youth psychiatric disorders with respect to common structural perturbations in key nodes of large-scale networks subserving adaptive psychological functioning. These findings provide new insight on early-expressed neurobiological signatures of psychopathology, which could be leveraged for pharmacological and clinical interventions that might be beneficial to broad-spectrum youth psychopathology.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

References

Albajes-Eizagirre, A., Solanes, A., Vieta, E., Radua, J., 2019. Voxel-based meta-analysis via permutation of subject images (PSI): Theory and implementation for SDM. NeuroImage 186, 174-184.

Albrecht, F., Bisenius, S., Neumann, J., Whitwell, J., Schroeter, M.L., 2019. Atrophy in midbrain & cerebral/cerebellar pedunculi is characteristic for progressive supranuclear palsy - A double-validation whole-brain meta-analysis. NeuroImage. Clinical 22, 101722.

Allsopp, K., Read, J., Corcoran, R., Kinderman, P., 2019. Heterogeneity in psychiatric diagnostic classification. Psychiatry research.

Angold, A., Costello, E.J., Erkanli, A., 1999. Comorbidity. The Journal of Child Psychology and Psychiatry and Allied Disciplines 40, 57-87.

Anttila, V., Bulik-Sullivan, B., Finucane, H.K., Walters, R.K., Bras, J., Duncan, L., Escott-Price, V., Falcone, G.J., Gormley, P., Malik, R., 2018. Analysis of shared heritability in common disorders of the brain. Science 360, eaap8757.

Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Phan, K.L., 2007. Amygdala–frontal connectivity during emotion regulation. Social cognitive and affective neuroscience 2, 303-312.

Biswal, B., Zerrin Yetkin, F., Haughton, V.M., Hyde, J.S., 1995. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magnetic resonance in medicine 34, 537-541.

Blair, R.J.R., 2008. The amygdala and ventromedial prefrontal cortex: functional contributions and dysfunction in psychopathy. 363, 2557-2565.

Buckholtz, J.W., Meyerlindenberg, A., 2012a. Psychopathology and the Human Connectome: Toward a Transdiagnostic Model of Risk For Mental Illness. 74, 990-1004.

Buckholtz, J.W., Meyerlindenberg, A., 2012b. Psychopathology and the Human Connectome: Toward a Transdiagnostic Model of Risk For Mental Illness. Neuron 74, 990-1004.

Carlisi, C.O., Norman, L., Murphy, C.M., Christakou, A., Chantiluke, K., Giampietro, V., Simmons, A., Brammer, M., Murphy, D.G., Mataix-Cols, D., Rubia, K., 2017. Comparison of neural substrates of temporal discounting between youth with autism spectrum disorder and with obsessive-compulsive disorder. Psychol Med 47, 2513-2527.

Carr, C.P., Martins, C.M.S., Stingel, A.M., Lemgruber, V.B., Juruena, M.F., 2013. The role of early life stress in adult psychiatric disorders: a systematic review according to childhood trauma subtypes. The Journal of nervous and mental disease 201, 1007-1020.

Caspi, A., Houts, R.M., Belsky, D.W., Goldman-Mellor, S.J., Harrington, H., Israel, S., Meier, M.H., Ramrakha, S., Shalev, I., Poulton, R., 2014. The p factor: one general psychopathology factor in the structure of psychiatric disorders? Clinical Psychological Science 2, 119-137.

Caspi, A., Moffitt, T.E., 2018. All for one and one for all: Mental disorders in one dimension. American Journal of Psychiatry 175, 831-844.

Cernasov, Greene, Kinard, Halverson, Lowery, McLamb, Arnold, 2019. Attenuated Default Mode Network Functional Connectivity is Associated With Improvement in Depressive Symptoms Following Mindfulness-Based Cognitive Therapy in a Transdiagnostic Anhedonic Sample. Biological Psychiatry 85(10), S158-S159.

Chen, T., Benjamin, B., Julia, C., Li, W., Shuqi, Y., B., E.S., Chunliang, F., 2018. A domain-general brain network underlying emotional and cognitive interference processing: evidence from coordinate-based and functional connectivity meta-analyses. Brain Structure & Function.

Choi, E.Y., Yeo, B.T.T., Buckner, R.L., 2012. The organization of the human striatum estimated by intrinsic functional connectivity. Journal of Neurophysiology 108, 2242-2263.

Ciaramidaro, A., Bölte, S., Schlitt, S., Hainz, D., Poustka, F., Weber, B., Freitag, C., Walter, H., 2018. Transdiagnostic deviant facial recognition for implicit negative emotion in autism and schizophrenia. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology

28, 264-275.
Cieslik, E.C., Zilles, K., Kurth, F., Eickhoff, S.B., 2010. Dissociating Bottom-Up and Top-Down Processes in a Manual Stimulus-Response Compatibility Task. Journal of Neurophysiology 104, 1472-1483.
Cole, M.W., Repovš, G., Anticevic, A., 2014. The frontoparietal control system: a central role in mental health. Neuroscientist A Review Journal Bringing Neurobiology Neurology & Psychiatry 20, 652-664.
Cole, M.W., Reynolds, J.R., Power, J.D., Repovs, G., Anticevic, A., Braver, T.S., 2013. Multi-task connectivity reveals flexible hubs for adaptive task control. Nature Neuroscience 16, 1348-1355.
Corbetta, M., 2000. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neuroscience 3.
Corbetta, M., Patel, G., Shulman, G.L., 2008. The Reorienting System of the Human Brain: From Environment to Theory of Mind. Neuron 58, 306-324.
Corp, D.T., Joutsa, J., Darby, R.R., Delnooz, C.C., van de Warrenburg, B.P., Cooke, D., Prudente, C.N., Ren, J., Reich, M.M., Batla, A., 2019. Network localization of cervical dystonia based on causal brain lesions. Brain 142, 1660-1674.
Costello, E.J., Egger, H., Angold, A., 2005. 10-year research update review: the epidemiology of child and adolescent psychiatric disorders: I. Methods and public health burden. Journal of the American Academy of Child & Adolescent Psychiatry 44, 972-986.
Costello, E.J., Mustillo, S., Erkanli, A., Keeler, G., Angold, A., 2003. Prevalence and development of psychiatric disorders in childhood and adolescence. Archives of general psychiatry 60, 837-844.
Cotter, J., Granger, K., Backx, R., Hobbs, M., Barnett, J.H., 2017. Social cognitive dysfunction as a clinical marker: A systematic review of meta-analyses across 30 clinical conditions. Neuroscience & Biobehavioral Reviews 84.
Cuthbert, B.N., 2014. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. World Psychiatry 13, 28-35.
D'Argembeau, F, C., Linden, 2005. Self-referential reflective activity and its relationship with rest: a PET study. Neuroimage 25, 616-624.
Dahl, R.E., 2004. Adolescent brain development: a period of vulnerabilities and opportunities. Keynote address. Annals of the New York Academy of Sciences 1021, 1-22.
Darby, R.R., Horn, A., Cushman, F., Fox, M.D., 2018. Lesion network localization of criminal behavior. 115, 601-606.
Dosenbach, N.U., Visscher, K.M., Palmer, E.D., Miezin, F.M., Petersen, S.E., 2006. A core system for the implementation of task sets. Neuron 50, 799-812.
Dosenbach, N.U.F., Fair, D.A., Miezin, F.M., Cohen, A.L., Wenger, K.K., Dosenbach, R.A.T., Fox, M.D., Snyder, A.Z., Vincent, J.L., Raichle, M.E., 2007. Distinct brain networks for adaptive and stable task control in humans. 104, 11073-11078.
Duncan, John, 2013. The Structure of Cognition: Attentional Episodes in Mind and Brain. Neuron 80, 35-50.
Eaton, N.R., Rodriguez-Seijas, C., Carragher, N., Krueger, R.F., 2015. Transdiagnostic factors of psychopathology and substance use disorders: a review. Social psychiatry and psychiatric epidemiology 50, 171-182.
Eickhoff, S.B., Laird, A.R., Grefkes, C., Wang, L.E., Zilles, K., Fox, P.T., 2009. Coordinate-based activation likelihood estimation meta-analysis of neuroimaging data: A random-effects approach based on empirical estimates of spatial uncertainty. Human Brain Mapping 30, 2907-2926.
Eickhoff, S.B., Nichols, T.E., Laird, A.R., Hoffstaedter, F., Amunts, K., Fox, P.T., Bzdok, D., Eickhoff, C.R., 2016. Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation. Neuroimage 137, 70-85.
Eisenberg, N., Spinrad, T.L., Eggum, N.D., 2009. Emotion-Related Self-Regulation and Its Relation to Children's Maladjustment. Annual Review of Clinical Psychology 6, 495.

Elliott, M.L., Romer, A., Knodt, A.R., Hariri, A.R., 2018. A Connectome Wide Functional Signature of Transdiagnostic Risk for Mental Illness. Biological Psychiatry, S0006322318314161.
Fox, M.D., 2018. Mapping symptoms to brain networks with the human connectome. New England Journal of Medicine 379, 2237-2245.
García-Carrión, R., Villarejo-Carballido, B., Villardón-Gallego, L., 2019. Children and Adolescents Mental Health: A Systematic Review of Interaction-Based Interventions in Schools and Communities. Frontiers in psychology 10.
Goerlich-Dobre, Lamm, C., Pripfl, J., Habel, U., Votinov, M., 2015. The left amygdala: A shared substrate of alexithymia and empathy. Neuroimage 122, S1053811915007235.
Gong, Q., Hu, X., Pettersson-Yeo, W., Xu, X., Lui, S., Crossley, N., Wu, M., Zhu, H., Mechelli, A., 2017. Network-level dysconnectivity in drug-naïve first-episode psychosis: dissociating transdiagnostic and diagnosis-specific alterations. Neuropsychopharmacology 42, 933-940.
Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., Ortega, B.N., Zaiko, Y.V., Roach, E.L., Korgaonkar, M.S., 2015. Identification of a common neurobiological substrate for mental illness. JAMA psychiatry 72, 305-315.
Gorka, S.M., Young, C.B., Klumpp, H., Kennedy, A.E., Francis, J., Ajilore, O., Langenecker, S.A., Shankman, S.A., Craske, M.G., Stein, M.B., Phan, K.L., 2019. Emotion-based brain mechanisms and predictors for SSRI and CBT treatment of anxiety and depression: a randomized trial. Neuropsychopharmacology 44, 1639-1648.
Green, S.A., Hernandez, L., Bookheimer, S.Y., Dapretto, M., 2017. Reduced modulation of thalamocortical connectivity during exposure to sensory stimuli in ASD. Autism research : official journal of the International Society for Autism Research 10, 801-809.
Greicius, M.D., Menon, V., 2004. Default-Mode Activity during a Passive Sensory Task: Uncoupled from Deactivation but Impacting Activation. Journal of Cognitive Neuroscience 16, 1484-1492.
Hamoda, H.M., Makhlouf, A.T., Fitzsimmons, J., Rathi, Y., Makris, N., Mesholam-Gately, R.I., Wojcik, J.D., Goldstein, J., McCarley, R.W., Seidman, L.J., Kubicki, M., Shenton, M.E., 2019. Abnormalities in thalamo-cortical connections in patients with first-episode schizophrenia: a two-tensor tractography study. Brain Imaging Behav 13, 472-481.
Hare, T.A., Camerer, C.F., Rangel, A., 2009. Self-Control in Decision-Making Involves Modulation of the vmPFC Valuation System. Science 324, 646-648.
Ihme, K., Dannlowski, U., Lichev, V., Stuhrmann, A., Grotegerd, D., Rosenberg, N., Kugel, H., Heindel, W., Arolt, V., Kersting, A., 2013. Alexithymia is related to differences in gray matter volume: A voxel-based morphometry study. Brain Research 1491, 60-67.
Ing, A., Sämann, P.G., Chu, C., Tay, N., Biondo, F., Robert, G., Jia, T., Wolfers, T., Desrivières, S., Banaschewski, T., 2019. Identification of neurobehavioural symptom groups based on shared brain mechanisms. Nature Human Behaviour, 1-13.
Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D.S., Quinn, K., Sanislow, C., Wang, P., 2010. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am Psychiatric Assoc.
Insel, T., Landis, S.C., 2013. Twenty-Five Years of Progress: The View from NIMH and NINDS. Neuron 80, 561-567.
Insel, T.R., 2014. The NIMH research domain criteria (RDoC) project: precision medicine for psychiatry. American Journal of Psychiatry 171, 395-397.
Ipser, J.C., Uhlmann, A., Taylor, P., Harvey, B.H., Wilson, D., Stein, D.J., 2018. Distinct intrinsic functional brain network abnormalities in methamphetamine-dependent patients with and without a history of psychosis. Addict Biol 23, 347-358.
Jalbrzikowski, M., Murty, V.P., Tervo-Clemmens, B., Foran, W., Luna, B., 2019. Age-Associated Deviations of Amygdala Functional Connectivity in Youths With Psychosis Spectrum Disorders: Relevance to Psychotic

Symptoms. American Journal of Psychiatry.
Jenkins, L.M., Barba, A., Campbell, M., Lamar, M., Shankman, S.A., Leow, A.D., Ajilore, O., Langenecker, S.A., 2016. Shared white matter alterations across emotional disorders: A voxel-based meta-analysis of fractional anisotropy. NeuroImage: Clinical 12, 1022-1034.
José Javier, M.H., 2013. Brain structural and functional changes in adolescents with psychiatric disorders. International Journal of Adolescent Medicine & Health 25, 245-256.
Jovicich, J., Marizzoni, M., Sala-Llonch, R., Bosch, B., Bartrés-Faz, D., Arnold, J., Benninghoff, J., Wiltfang, J., Roccatagliata, L., Nobili, F., 2013. Brain morphometry reproducibility in multi-center 3 T MRI studies: a comparison of cross-sectional and longitudinal segmentations. Neuroimage 83, 472-484.
Kaczkurkin, A.N., Moore, T.M., Calkins, M.E., Ciric, R., Detre, J.A., Elliott, M.A., Foa, E.B., Garcia de la Garza, A., Roalf, D.R., Rosen, A., 2018. Common and dissociable regional cerebral blood flow differences associate with dimensions of psychopathology across categorical diagnoses. Molecular Psychiatry.
Kaczkurkin, A.N., Park, S.S., Sotiras, A., Moore, T.M., Calkins, M.E., Cieslak, M., Rosen, A.F.G., Ciric, R., Xia, C.H., Cui, Z., Sharma, A., Wolf, D.H., Ruparel, K., Pine, D.S., Shinohara, R.T., Roalf, D.R., Gur, R.C., Davatzikos, C., Gur, R.E., Satterthwaite, T.D., 2019. Evidence for Dissociable Linkage of Dimensions of Psychopathology to Brain Structure in Youths. Am J Psychiatry 176, 1000-1009.
Katharina, Kircanski, Lauren, White, Wan-Ling, Tseng, Jillian, Lee, Wiggins, 2018. A Latent Variable Approach to Differentiating Neural Mechanisms of Irritability and Anxiety in Youth.
Kempton, M.J., Salvador, Z., Munafò, M.R., Geddes, J.R., Simmons, A., Frangou, S., Williams, S.C., 2011. Structural neuroimaging studies in major depressive disorder: meta-analysis and comparison with bipolar disorder. Archives of general psychiatry 68, 675-690.
Kessler, D., Angstadt, M., Sripada, C., 2016. Growth Charting of Brain Connectivity Networks and the Identification of Attention Impairment in Youth. JAMA Psychiatry 73, 481-489.
Kessler, D., Angstadt, M., Welsh, R.C., Sripada, C., 2014. Modality-spanning deficits in attention-deficit/hyperactivity disorder in functional networks, gray matter, and white matter. The Journal of neuroscience : the official journal of the Society for Neuroscience 34, 16555-16566.
Kessler, R.C., Amminger, G.P., Aguilar-Gaxiola, S., Alonso, J., Lee, S., Ustün, T.B., 2007. Age of onset of mental disorders: a review of recent literature. Curr Opin Psychiatry 20, 359-364.
Kessler, R.C., Berglund, P., Demler, O., Jin, R., Merikangas, K.R., Walters, E.E., 2005a. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. JAMA Psychiatry 62, 593-602.
Kessler, R.C., Chiu, W.T., Demler, O., Walters, E.E., 2005b. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Archives of general psychiatry 62, 617-627.
Kessler, R.C., McGonagle, K.A., Zhao, S., Nelson, C.B., Hughes, M., Eshleman, S., Wittchen, H.-U., Kendler, K.S., 1994. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Archives of general psychiatry 51, 8-19.
Kieling, C., Baker-Henningham, H., Belfer, M., Conti, G., Ertem, I., Omigbodun, O., Rohde, L.A., Srinath, S., Ulkuer, N., Rahman, A., 2011. Child and adolescent mental health worldwide: evidence for action. Lancet 378, 1515-1525.
Kim, Hongkeun, 2014. Involvement of the dorsal and ventral attention networks in oddball stimulus processing: A meta-analysis. Human Brain Mapping 35, 2265-2284.
Kirkby, L.A., Luongo, F.J., Lee, M.B., Nahum, M., Van Vleet, T.M., Rao, V.R., Dawes, H.E., Chang, E.F., Sohal, V.S., 2018. An Amygdala-Hippocampus Subnetwork that Encodes Variation in Human Mood. Cell.
Krueger, R.F., Eaton, N.R., 2015. Transdiagnostic factors of mental disorders. World Psychiatry 14, 27-29.
Lückmann, H.C., Jacobs, H.I.L., Sack, A.T., 2014. The Cross-functional Role of Frontoparietal Regions in Cognition–Internal Attention as the Overarching Mechanism. Progress in Neurobiology 116.
Lahey, B.B., Applegate, B., Hakes, J.K., Zald, D.H., Hariri, A.R., Rathouz, P.J., 2012. Is there a general factor

699 of prevalent psychopathology during adulthood? Journal of abnormal psychology 121, 971-977.
700 Lahey, B.B., Krueger, R.F., Rathouz, P.J., Waldman, I.D., Zald, D.H., 2017. A hierarchical causal taxonomy of
701 psychopathology across the life span. Psychological bulletin 143, 142-186.
702 Lahey, B.B., Van Hulle, C.A., Singh, A.L., Waldman, I.D., Rathouz, P.J., 2011. Higher-Order Genetic and
703 Environmental Structure of Prevalent Forms of Child and Adolescent Psychopathology. Archives of General
704 Psychiatry 68, 181.
705 Langner, R., Rottschy, C., Laird, A.R., Fox, P.T., Eickhoff, S.B., 2014. Meta-analytic connectivity modeling
706 revisited: Controlling for activation base rates. Neuroimage 99, 559-570.
707 Lanssens, A., Pizzamiglio, G., Mantini, D., Gillebert, C.R., 2020. Role of the dorsal attention network in
708 distracter suppression based on features. Cognitive neuroscience 11, 37-46.
709 Lawrence, D., Johnson, S., Hafekost, J., Boterhoven de Haan, K., Sawyer, M., Ainley, J., Zubrick, S.R., 2015.
710 The mental health of children and adolescents: Report on the second Australian child and adolescent
711 survey of mental health and wellbeing.
712 Lebel, C., Walker, L., Leemans, A., Phillips, L., Beaulieu, C., 2008. Microstructural maturation of the human
713 brain from childhood to adulthood. Neuroimage 40, 1044-1055.
714 Liu, J., Liao, X., Xia, M., He, Y., 2018. Chronnectome fingerprinting: Identifying individuals and predicting
715 higher cognitive functions using dynamic brain connectivity patterns. Hum Brain Mapp 39, 902-915.
716 Müller, V.I., Cieslik, E.C., Laird, A.R., Fox, P.T., Radua, J., Mataix-Cols, D., Tench, C.R., Yarkoni, T., Nichols, T.E.,
717 Turkeltaub, P.E., 2018. Ten simple rules for neuroimaging meta-analysis. Neuroscience & Biobehavioral
718 Reviews 84, 151-161.
719 Markon, K., 2010. Modeling psychopathology structure: A symptom-level analysis of Axis I and II disorders.
720 Psychological medicine 40, 273-288.
721 Matthias, Schurz, Joaquim, Radua, Markus, Aichhorn, Fabio, Richlan, Josef, Perner, 2014. Fractionating
722 theory of mind: A meta-analysis of functional brain imaging studies.
723 McAllister, T.W., Stein, M.B., 2010. Effects of psychological and biomechanical trauma on brain and
724 behavior. Annals of the New York Academy of Sciences 1208, 46.
725 Mcteague, L.M., Goodkind, M.S., Etkin, A., 2016. Transdiagnostic impairment of cognitive control in mental
726 illness. Journal of Psychiatric Research 83, 37-46.
727 McTeague, L.M., Huemer, J., Carreon, D.M., Jiang, Y., Eickhoff, S.B., Etkin, A., 2017. Identification of
728 common neural circuit disruptions in cognitive control across psychiatric disorders. American Journal of
729 Psychiatry 174, 676-685.
730 McTeague, L.M., Rosenberg, B.M., Lopez, J.W., Carreon, D.M., Huemer, J., Jiang, Y., Chick, C.F., Eickhoff, S.B.,
731 Etkin, A., 2020. Identification of Common Neural Circuit Disruptions in Emotional Processing Across
732 Psychiatric Disorders. American Journal of Psychiatry, appi. ajp. 2019.18111271.
733 Meffert, H., Brislin, S.J., White, S.F., Blair, J.R., 2015. Prediction errors to emotional expressions: the roles
734 of the amygdala in social referencing. Soc Cogn Affect Neurosci 10, 537-544.
735 Menon, V., 2011. Large-scale brain networks and psychopathology: a unifying triple network model. Trends
736 in Cognitive Sciences 15, 483-506.
737 Merikangas, K.R., Nakamura, E.F., Kessler, R.C., 2009. Epidemiology of mental disorders in children and
738 adolescents. Dialogues in clinical neuroscience 11, 7.
739 Mohan, A., Roberto, A.J., Lorenzo, A., Jones, K., Lapidus, K.A.B., 2016. The Significance of the Default Mode
740 Network (DMN) in Neurological and Neuropsychiatric Disorders: A Review. Yale Journal of Biology &
741 Medicine 89, 49-57.
742 Monk, C.S., 2008. The development of emotion-related neural circuitry in health and psychopathology.
743 Development and psychopathology 20, 1231-1250.
744 Nenadic, I., Maitra, R., Langbein, K., Dietzek, M., Lorenz, C., Smesny, S., Reichenbach, J.R., Sauer, H., Gaser,
745 C., 2015. Brain structure in schizophrenia vs. psychotic bipolar I disorder: a VBM study. Schizophrenia
746 research 165, 212-219.

Neumann, A., Muetzel, R.L., Lahey, B.B., Bakermans-Kranenburg, M.J., van, I.M.H., Jaddoe, V.W., Hillegers, M.H.J., White, T., Tiemeier, H., 2020. White Matter Microstructure and the General Psychopathology Factor in Children. J Am Acad Child Adolesc Psychiatry.

Nooner, K.B., Colcombe, S.J., Tobe, R.H., Mennes, M., Benedict, M.M., Moreno, A.L., Panek, L.J., Brown, S., Zavitz, S.T., Li, Q., 2012. The NKI-Rockland Sample: A Model for Accelerating the Pace of Discovery Science in Psychiatry. Frontiers in Neuroscience 6, 152.

Noordermeer, S.D., Luman, M., Oosterlaan, J., 2016. A systematic review and meta-analysis of neuroimaging in oppositional defiant disorder (ODD) and conduct disorder (CD) taking attention-deficit hyperactivity disorder (ADHD) into account. Neuropsychology review 26, 44-72.

Northoff, G., Heinzel, A., Greck, M.d., Bermpohl, F., Dobrowolny, H., Panksepp, J., 2006. Self-referential processing in our brain—A meta-analysis of imaging studies on the self. 31, 440-457.

Ochsner, K.N., Silvers, J.A., Buhle, J.T., 2012. Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. Annals of the New York Academy of Sciences 1251, E1.

Opialla, S., Lutz, J., Scherpiet, S., Hittmeyer, A., Jäncke, L., Rufer, M., Grosse Holtforth, M., Herwig, U., Brühl, A.B., 2015. Neural circuits of emotion regulation: a comparison of mindfulness-based and cognitive reappraisal strategies. European archives of psychiatry and clinical neuroscience 265, 45-55.

Owens, Yuan, Hahn, Albaugh, Allgaier, Chaarani, Garavan, 2019. Confirmatory Investigation of Psychiatric and Neuropsychological Correlates of Default Mode Network and Dorsal Attention Network Autocorrelation.

Patti, M.A., Troiani, V., 2017. Orbitofrontal sulcogyral morphology is a transdiagnostic indicator of brain dysfunction. Neuroimage Clinical 17, 910.

Polanczyk, G.V., Salum, G.A., Sugaya, L.S., Arthur, C., Rohde, L.A., 2015. Annual Research Review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. Journal of Child Psychology & Psychiatry 56, 345–365.

Radua, J., Mataix-Cols, D., 2012. Meta-analytic methods for neuroimaging data explained. Biology of Mood & Anxiety Disorders 2, 6.

Radua, J., Mataix-Cols, D., Phillips, M.L., El-Hage, W., Kronhaus, D.M., Cardoner, N., Surguladze, S., 2012. A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. European Psychiatry 27.

Rao, U., Hammen, C., Ortiz, L.R., Chen, L.-A., Poland, R.E., 2008. Effects of early and recent adverse experiences on adrenal response to psychosocial stress in depressed adolescents. Biological psychiatry 64, 521-526.

Robinson, J.L., Laird, A.R., Glahn, D.C., Lovallo, W.R., Fox, P.T., 2010. Metaanalytic connectivity modeling: delineating the functional connectivity of the human amygdala. Human brain mapping 31, 173-184.

Romer, A.L., Knodt, A.R., Houts, R., Brigidi, B.D., Moffitt, T.E., Caspi, A., Hariri, A.R., 2018. Structural alterations within cerebellar circuitry are associated with general liability for common mental disorders. Molecular Psychiatry.

Roy, M., Shohamy, D., Wager, T.D., 2012. Ventromedial prefrontal-subcortical systems and the generation of affective meaning. 16, 0-156.

Sabharwal, A., Kotov, R., Szekely, A., Leung, H.C., Barch, D.M., Mohanty, A., 2017. Neural markers of emotional face perception across psychotic disorders and general population. Journal of abnormal psychology 126, 663-678.

Samartsidis, P., Montagna, S., Johnson, T.D., Nichols, T.E., 2017. The Coordinate-Based Meta-Analysis of Neuroimaging Data. Statistical Science 32, 580-599.

Sanislow, C.A., Ferrante, M., Pacheco, J., Rudorfer, M.V., Morris, S.E., 2019. Advancing translational research using nimh research domain criteria and computational methods. Neuron 101, 779-782.

Sanislow, C.A., Pine, D.S., Quinn, K.J., Kozak, M.J., Garvey, M.A., Heinssen, R.K., Wang, P.S.-E., Cuthbert,

B.N., 2010. Developing constructs for psychopathology research: research domain criteria. Journal of abnormal psychology 119, 631.
Sato, J.R., Salum, G.A., Gadelha, A., Crossley, N., Vieira, G., Manfro, G.G., Zugman, A., Picon, F.A., Pan, P.M., Hoexter, M.Q., Anés, M., Moura, L.M., Del'Aquilla, M.A.G., Amaro, E., Jr., McGuire, P., Lacerda, A.L.T., Rohde, L.A., Miguel, E.C., Jackowski, A.P., Bressan, R.A., 2016. Default mode network maturation and psychopathology in children and adolescents. Journal of child psychology and psychiatry, and allied disciplines 57, 55-64.
Schilbachab, Hoffstaedtercd, Müllercd, 2016. Transdiagnostic commonalities and differences in resting state functional connectivity of the default mode network in schizophrenia and major depression. Neuroimage Clinical 10, 326-335.
Sha, Z., Wager, T.D., Mechelli, A., He, Y., 2019. Common dysfunction of large-scale neurocognitive networks across psychiatric disorders. Biological psychiatry 85, 379-388.
Shamseer, L., Moher, D., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L.A., 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 349, g7647-g7647.
Shanmugan, S., Wolf, D.H., Calkins, M.E., Moore, T.M., Ruparel, K., Hopson, R.D., Vandekar, S.N., Roalf, D.R., Elliott, M.A., Jackson, C., 2016. Common and Dissociable Mechanisms of Executive System Dysfunction Across Psychiatric Disorders in Youth. American Journal of Psychiatry, appi.ajp.2015.2011.
Shaw, P., Gogtay, N., Rapoport, J., 2010. Childhood psychiatric disorders as anomalies in neurodevelopmental trajectories. Human brain mapping 31, 917-925.
Snyder, H.R., Hankin, B.L., Sandman, C.A., Head, K., Davis, E.P., 2017. Distinct Patterns of Reduced Prefrontal and Limbic Gray Matter Volume in Childhood General and Internalizing Psychopathology. Clinical Psychological Science A Journal of the Association for Psychological Science 5.
Spielberg, J.M., Miller, G.A., Warren, S.L., Sutton, B.P., Banich, M., Heller, W., 2014. Transdiagnostic dimensions of anxiety and depression moderate motivation-related brain networks during goal maintenance. Depression and anxiety 31, 805-813.
Spitzer, R.L., Endicott, J., Robins, E., 1978. Research diagnostic criteria: rationale and reliability. Archives of general psychiatry 35, 773-782.
Spreng, R.N., Grady, C.L., 2010. Patterns of Brain Activity Supporting Autobiographical Memory, Prospection, and Theory of Mind, and Their Relationship to the Default Mode Network. 22, 1112-1123.
Sprooten, E., Rasgon, A., Goodman, M., Carlin, A., Leibu, E., Lee, W.H., Frangou, S., 2017. Addressing reverse inference in psychiatric neuroimaging: Meta-analyses of task-related brain activation in common mental disorders. Human brain mapping 38, 1846-1864.
Teicher, M.H., Anderson, C.M., Ohashi, K., Polcari, A., 2014. Childhood Maltreatment: Altered Network Centrality of Cingulate, Precuneus, Temporal Pole and Insula. Biological Psychiatry 76, 297-305.
Tomás, P., Matcheri, K., Giedd, J.N., 2008. Why do many psychiatric disorders emerge during adolescence? Nature Reviews Neuroscience 9, 947-957.
Turkeltaub, P.E., Eden, G.F., Jones, K.M., Thomas, 2002. Meta-Analysis of the Functional Neuroanatomy of Single-Word Reading: Method and Validation. Neuroimage 16, 765-780.
Turkeltaub, P.E., Eickhoff, Laird, A.R., Fox, M., Fox, P., 2012. Minimizing Within-Experiment and Within-Group Effects in Activation Likelihood Estimation Meta-Analyses. Human Brain Mapping 33, 1-13.
Turner, K.C., Frost, L., Linsenbardt, D., McIlroy, J.R., Müller, R.-A., 2006. Atypically diffuse functional connectivity between caudate nuclei and cerebral cortex in autism. 2, 34.
van den Heuvel, M., Sporns, O., 2019. A cross-disorder connectome landscape of brain dysconnectivity. Nature reviews. Neuroscience.
Vega, A.D.L., Yarkoni, T., Wager, T.D., Banich, M.T., Vega, A.D.L., Yarkoni, T., Wager, T.D., Banich, M.T., Vega, A.D.L., Yarkoni, T., 2017. Large-scale Meta-analysis Suggests Low Regional Modularity in Lateral Frontal

842 Cortex. Cerebral Cortex, 1-15.
843 Victor, T.A., Khalsa, S.S., Simmons, W.K., Feinstein, J.S., Savitz, J., Aupperle, R.L., Yeh, H.W., Bodurka, J.,
844 Paulus, M.P., 2018. Tulsa 1000: a naturalistic study protocol for multilevel assessment and outcome
845 prediction in a large psychiatric sample. Bmj Open 8, e016620.
846 Vincent, J.L., Kahn, I., Snyder, A.Z., Raichle, M.E., Buckner, R.L., 2008. Evidence for a Frontoparietal Control
847 System Revealed by Intrinsic Functional Connectivity. Journal of Neurophysiology 100, 3328-3342.
848 Voets, N.L., Hough, M.G., Douaud, G., Matthews, P.M., James, A., Winmill, L., Webster, P., Smith, S., 2008.
849 Evidence for abnormalities of cortical development in adolescent-onset schizophrenia. Neuroimage 43,
850 665-675.
851 Weissman, D.G., Jenness, J.L., Colich, N.L., Miller, A.B., Sambrook, K.A., Sheridan, M.A., McLaughlin, K.A.,
852 2019. Altered Neural Processing of Threat-Related Information in Children and Adolescents Exposed to
853 Violence: A Transdiagnostic Mechanism Contributing to the Emergence of Psychopathology. J Am Acad
854 Child Adolesc Psychiatry.
855 Whitfield-Gabrieli, S., Ford, J.M., 2012. Default mode network activity and connectivity in psychopathology.
856 Annual review of clinical psychology 8, 49-76.
857 Wong, T.Y., Sid, A., Wensing, T., Eickhoff, S.B., Habel, U., Gur, R.C., Nickl-Jockschat, T., 2019. Neural networks
858 of aggression: ALE meta-analyses on trait and elicited aggression. Brain Structure and Function 224, 133-
859 148.
860 Xia, C.H., Zongming, M., Rastko, C., Shi, G., F., B.R., N., K.A., E., C.M., A., C.P., Angel, G.d.l.G., N., V.S., 2018.
861 Linked dimensions of psychopathology and connectivity in functional brain networks. Nature
862 Communications 9, 3003-.
863 Xu, Pengfei, Opmeer, Esther, M., van, Tol, Marie-Jose, Goerlich, Katharina, 2018. Structure of the
864 alexithymic brain: A parametric coordinate-based meta analysis.
865 Yan, C.G., Chen, X., Li, L., Castellanos, F.X., Bai, T.J., Bo, Q.J., Cao, J., Chen, G.M., Chen, N.X., Chen, W., Cheng,
866 C., Cheng, Y.Q., Cui, X.L., Duan, J., Fang, Y.R., Gong, Q.Y., Guo, W.B., Hou, Z.H., Hu, L., Kuang, L., Li, F., Li,
867 K.M., Li, T., Liu, Y.S., Liu, Z.N., Long, Y.C., Luo, Q.H., Meng, H.Q., Peng, D.H., Qiu, H.T., Qiu, J., Shen, Y.D., Shi,
868 Y.S., Wang, C.Y., Wang, F., Wang, K., Wang, L., Wang, X., Wang, Y., Wu, X.P., Wu, X.R., Xie, C.M., Xie, G.R.,
869 Xie, H.Y., Xie, P., Xu, X.F., Yang, H., Yang, J., Yao, J.S., Yao, S.Q., Yin, Y.Y., Yuan, Y.G., Zhang, A.X., Zhang, H.,
870 Zhang, K.R., Zhang, L., Zhang, Z.J., Zhou, R.B., Zhou, Y.T., Zhu, J.J., Zou, C.J., Si, T.M., Zuo, X.N., Zhao, J.P.,
871 Zang, Y.F., 2019. Reduced default mode network functional connectivity in patients with recurrent major
872 depressive disorder. Proc Natl Acad Sci U S A 116, 9078-9083.
873 Yang, Z., Li, H., Tu, W., Wang, S., Ren, Y., Yi, Y., Wu, T., Jiang, K., Shen, H., Wu, J., Dong, X., 2018. Altered
874 patterns of resting-state functional connectivity between the caudate and other brain regions in
875 medication-naïve children with attention deficit hyperactivity disorder. Clinical imaging 47, 47-51.
876 Yarkoni, T., Poldrack, R.A., Nichols, T.E., Van Essen, D.C., Wager, T.D., 2011. Large-scale automated synthesis
877 of human functional neuroimaging data. Nature methods 8, 665.
878 Yeo, T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W.,
879 Zöllei, L., Polimeni, J.R., 2011. The organization of the human cerebral cortex estimated by intrinsic
880 functional connectivity. Journal of neurophysiology 106, 1125-1165.
881 Yoon, S., Kim, J.E., Hwang, J., Kang, I., Jeon, S., Im, J.J., Kim, B.R., Lee, S., Kim, G.H., Rhim, H., Lim, S.M.,
882 Lyoo, I.K., 2017. Recovery from Posttraumatic Stress Requires Dynamic and Sequential Shifts in Amygdalar
883 Connectivities. Neuropsychopharmacology 42, 454-461.
884 Young, K.D., Siegle, G.J., Misaki, M., Zotev, V., Phillips, R., Drevets, W.C., Bodurka, J., 2018. Altered task-
885 based and resting-state amygdala functional connectivity following real-time fMRI amygdala
886 neurofeedback training in major depressive disorder. Neuroimage Clinical 17, 691-703.
887 Zald, D.H., Lahey, B.B., 2017. Implications of the Hierarchical Structure of Psychopathology for Psychiatric
888 Neuroimaging. Biol Psychiatry Cogn Neurosci Neuroimaging, S2451902217300332.
889 Zeev-Wolf, M., Levy, J., Goldstein, A., Zagoory-Sharon, O., Feldman, R., 2019. Chronic Early Stress Impairs

Default Mode Network Connectivity in Preadolescents and their Mothers. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging.
Zhang, R., Geng, X., Lee, T.M.C., 2017. Large-scale functional neural network correlates of response inhibition: an fMRI meta-analysis. Brain Structure & Function.
Zhao, W., Luo, L., Li, Q., Kendrick, K.M., 2013. What Can Psychiatric Disorders Tell Us about Neural Processing of the Self? Frontiers in Human Neuroscience 7, 485.
Zhen, Y., Shi, G., Nicolas, H., 2018. Network changes associated with transdiagnostic depressive symptom improvement following cognitive behavioral therapy in MDD and PTSD.
Zhu, Y., Gao, H., Tong, L., Li, Z., Wang, L., Zhang, C., Yang, Q., Yan, B., 2019. Emotion Regulation of Hippocampus Using Real-Time fMRI Neurofeedback in Healthy Human. Front Hum Neurosci 13, 242.
Zotev, V., Phillips, R., Misaki, M., Wong, C.K., Bodurka, J., 2018. Real-time fMRI neurofeedback training of the amygdala activity with simultaneous EEG in veterans with combat-related PTSD. Neuroimage Clinical 19, 106-121.
Zuo, X.-N., Xu, T., Milham, M.P., 2019. Harnessing reliability for neuroscience research. Nature human behaviour 3, 768-771.

Figure Legends

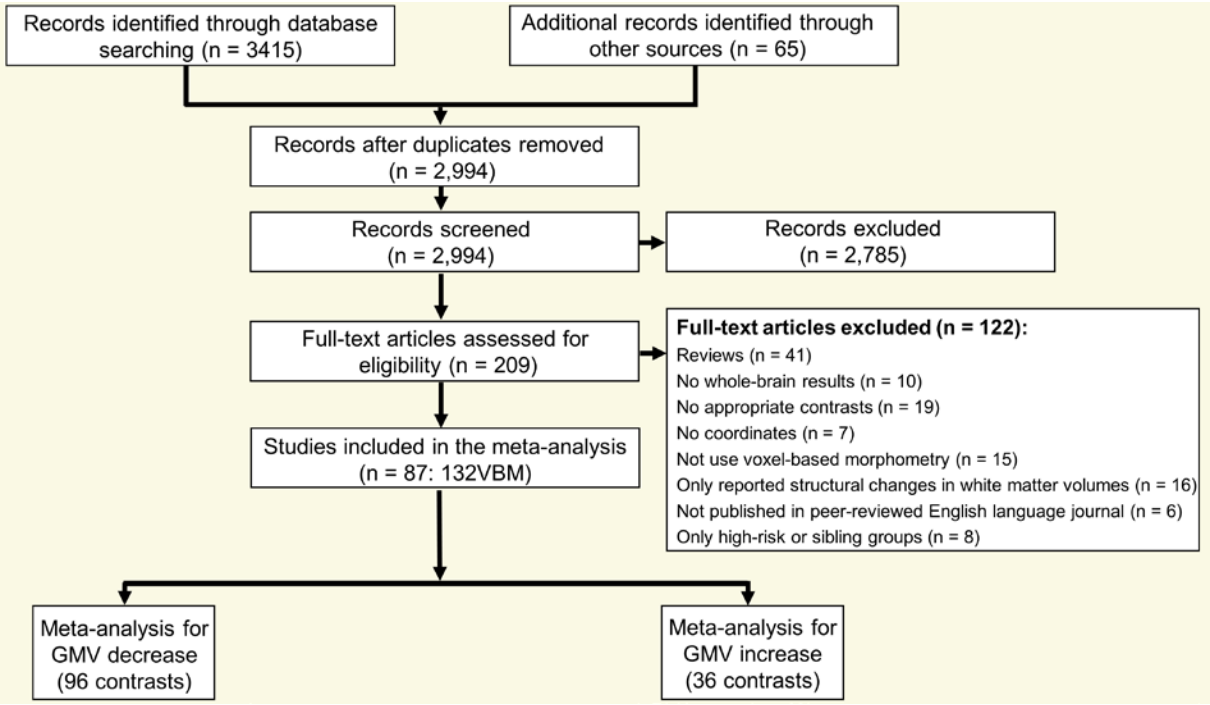
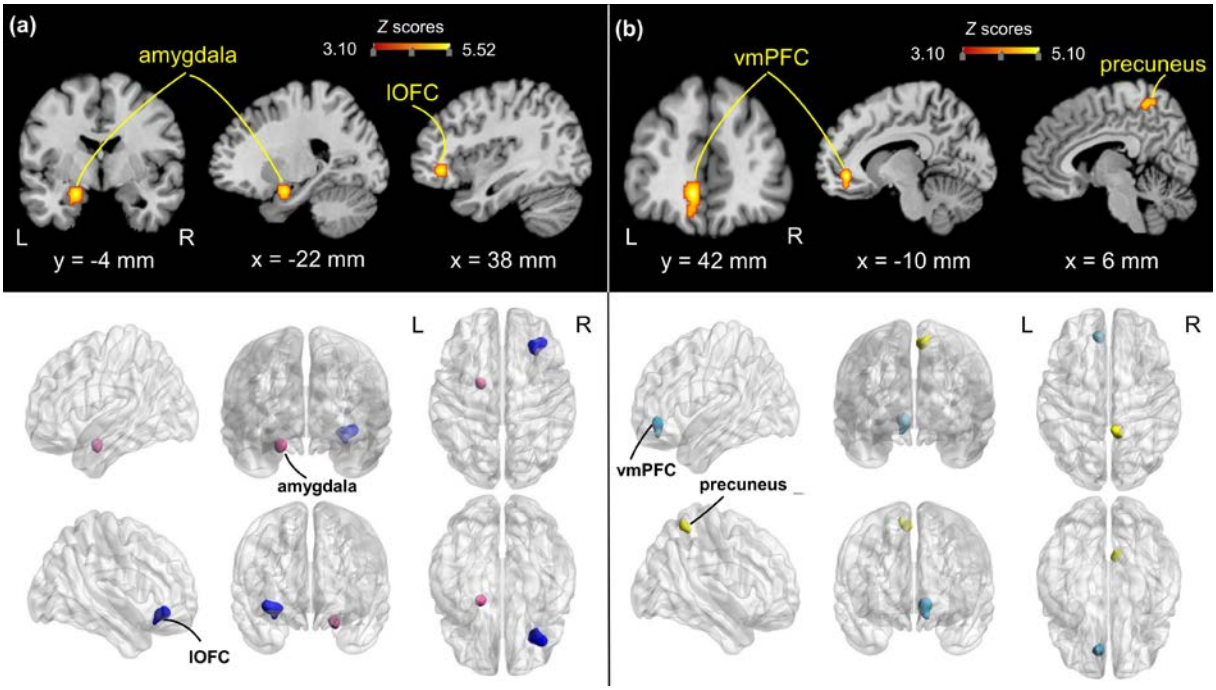


Figure 1. Flow chart of the study selection process for the meta-analysis. GMV, gray matter volume; VBM, voxel-based morphometry.



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911 **Figure 2. Significant clusters from the meta-analysis of patients versus healthy controls contrast for**
912 **GMV differences in sMRI studies. (a) GMV decrease: patients < controls; (b) GMV increase: patients**
913 **> controls (cluster-level family-wise error correction (*P* < 0.05) with a cluster-forming threshold of *P***
914 **< 0.001 using 10,000 permutations).** L, left; R, right; vmPFC, ventromedial prefrontal cortex; lOFC, lateral
915 orbital frontal cortex.

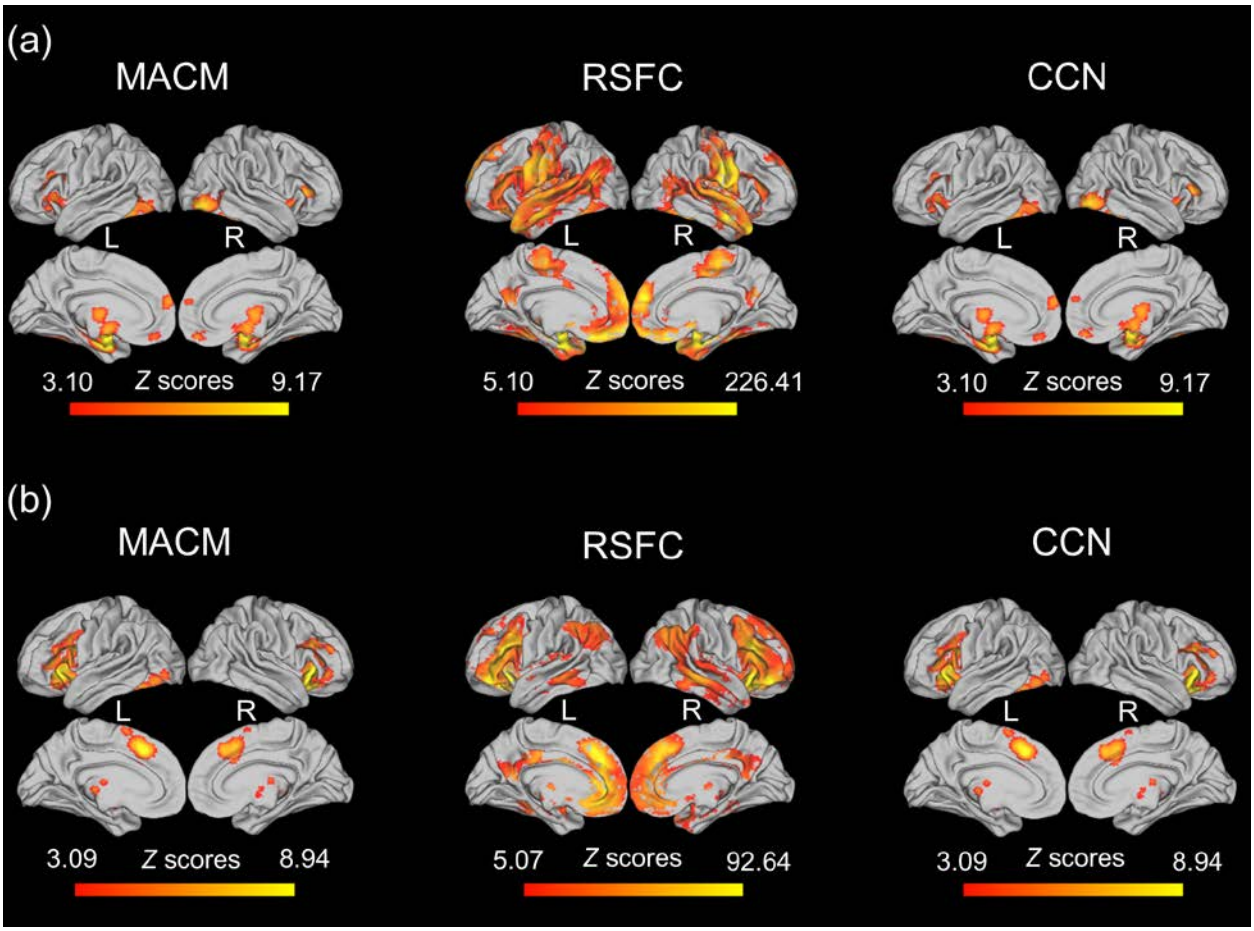


Figure 3. Results for the task-based connectivity analysis (MACM) and task-free connectivity analysis (RSFC) for the regions of GMV decreases in patients versus controls. (a) left panel: MACM results for amygdala; middle panel: RSFC results for amygdala; right panel: MACM and RSFC results for amygdala. (b) left panel: MACM results for lOFC; middle panel: RSFC results for lOFC; right panel: MACM and RSFC results for lOFC (voxel-wise *P* (FWE) < 0.05). L, left; R, right; lOFC, lateral orbital frontal cortex; vmPFC, ventromedial prefrontal cortex. CCN, consensus connectivity networks.

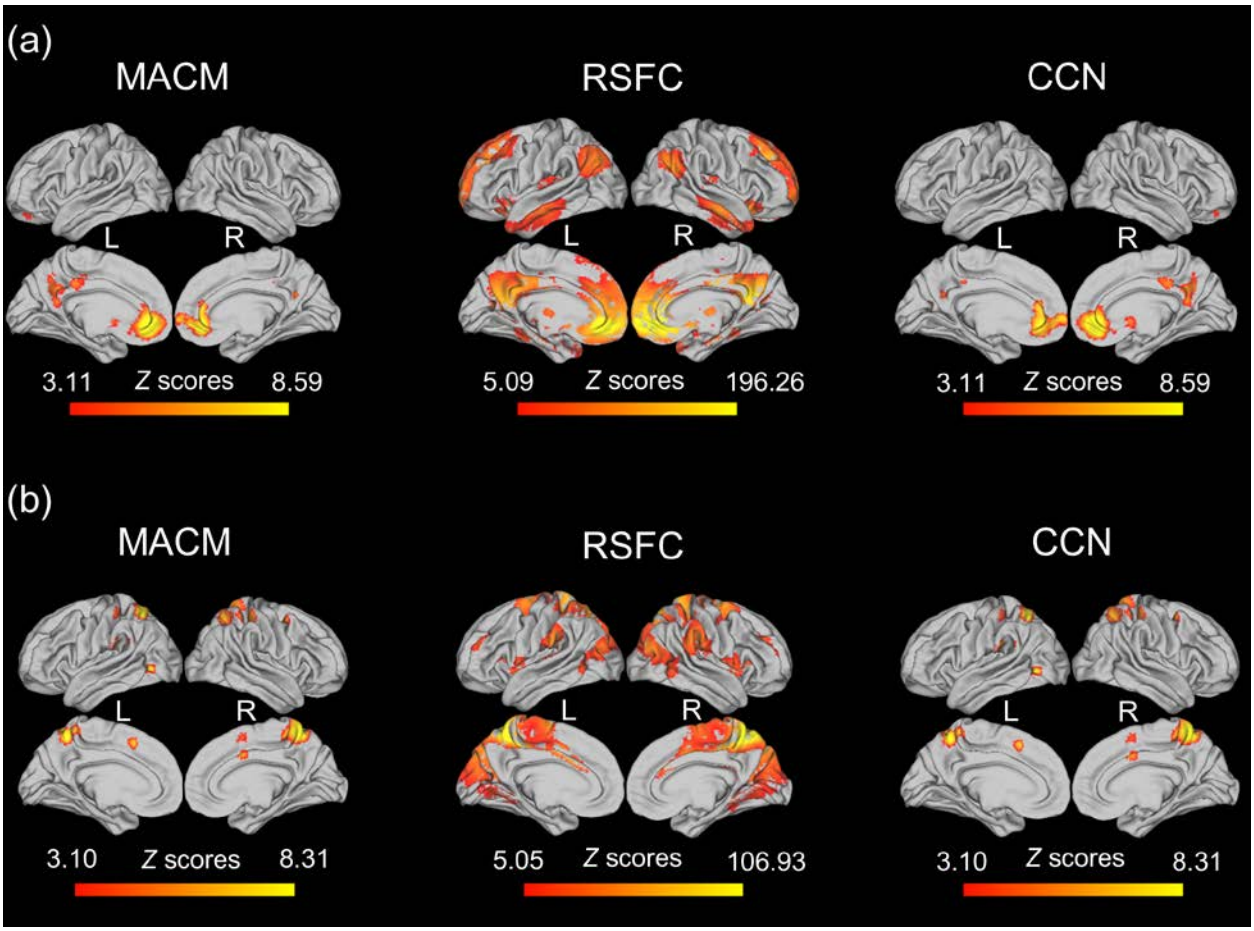
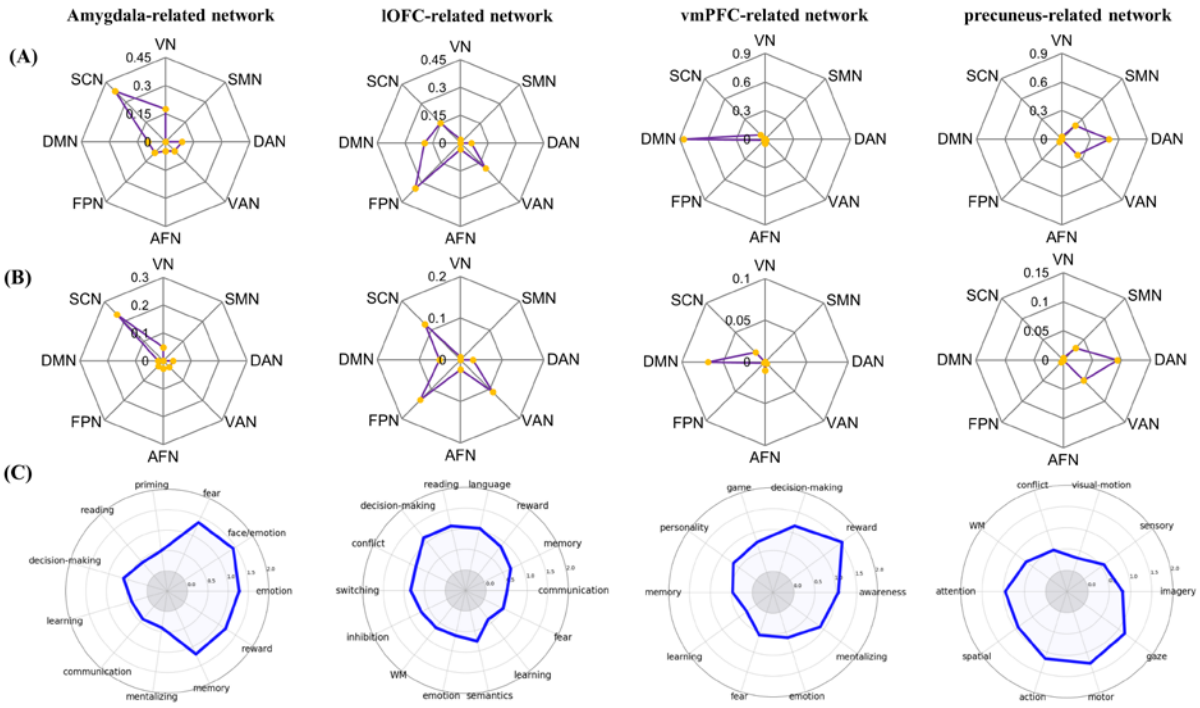


Figure 4. Results for the task-based connectivity analysis (MACM) and task-free connectivity analysis (RSFC) for the regions of GMV increases in patients versus controls. (a) left panel: MACM results for vmPFC; middle panel: RSFC results for vmPFC; right panel: MACM and RSFC results for vmPFC. (b) left panel: MACM results for precuneus; middle panel: RSFC results for precuneus; right panel: MACM and RSFC results for precuneus (voxel-wise *P* (FWE) < 0.05). L, left; R, right; vmPFC, ventromedial prefrontal cortex. CCN, consensus connectivity networks.



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931 **Figure 5. Network distribution of significant clusters and functional decoding for the common**
932 **clusters for the amygdala-related network, lOFC-related network, vmPFC-related network and**
933 **precuneus-related network. a Relative network distribution of clusters from primary meta-analyses.**
934 **b Absolute network distribution of clusters from primary meta-analyses. c. Functional decoding for**
935 **contributing networks.** lOFC, lateral orbital frontal cortex; vmPFC, ventromedial prefrontal cortex; VN,
936 visual network; SMN, somatomotor network; DAN, dorsal attention network; VAN, ventral attention network;
937 CAN, cortical affective network; FPN, fronto-parietal network; DMN, default mode network; SCN, subcortical
938 regions.

Table 1. Significant clusters from the meta-analysis of patients versus healthy controls contrast for GMV differences in sMRI studies (GMV decrease and increase)

Laterality	Cluster no.	Brain Regions	BA	MNI Coordinates (mm)			peak Z score	Cluster Size (mm^3)
				x	y	z		
Group differences (GMV decrease)								
L	1	Amygdala	-	-20	-2	-20	5.52	1016
R	2	lateral orbital frontal cortex	47	38	36	-8	5.36	1752
Group differences (GMV increase)								
L	1	ventromedial prefrontal cortex	10	-10	42	-6	5.10	848
R	2	Precuneus	7/5	6	-46	58	4.24	968

P(FWE) < 0.05 at the cluster level with a cluster-forming threshold of P < 0.001 using 10,000 permutations.

942 **Table 2. MACM and RSFC results for amygdala, lOFC, vmPFC, and precuneus.**

Laterality	Cluster no.	Brain Regions	BA	MNI Coordinates (mm)			Peak intensity	Cluster Size (mm^3)
				x	y	z		
Amygdala								
L/R	1	amygdala/hippocampus/ /parahippocampal/thalamus/ putamen/caudate/uncus	-	-22	-4	-18	9.17	41408
R	2	fusiform	37	42	-50	-20	6.51	1944
L	3	fusiform	37	-42	-48	-20	5.54	5232
R	4	medial frontal gyrus	11	0	46	-16	4.86	1176
R	5	inferior occipital gyrus/middle occipital gyrus	19	44	-78	-8	7.12	6080
L	6	lateral orbitofrontal cortex/anterior insula	13/47	-34	26	-2	5.62	3592
L	7	inferior frontal gyrus	47	-50	24	-6	5.98	1512
R	8	inferior frontal gyrus	46	54	32	6	5.60	1712
L	9	medial frontal gyrus	10	-4	60	18	5.20	1416
L	10	precentral gyrus	9	-48	6	32	4.66	1632
lOFC								
L	1	lateral orbitofrontal cortex/anterior insula	9/47	-32	28	-6	8.35	31280
R	2	lateral orbitofrontal cortex/anterior insula	11/47	32	28	-8	8.94	21968
L	3	inferior temporal gyrus	19/37	-44	-72	-10	4.82	2184
R	4	thalamus/putamen/caudate	-	12	-14	2	6.17	7552

		hippocampus						
L/R	5	dorsal anterior cingulate cortex/superior medial frontal gyrus	8/32	-4	24	42	8.31	10712
vmPFC								
L/R	1	ventromedial prefrontal cortex/anterior cingulate cortex	10/24	10	42	-8	8.59	16472
R	2	caudate	-	8	6	-4	5.18	1808
R	3	precuneus	7/31	6	-52	32	4.92	3064
R	4	middle cingulate cortex	31	8	-24	42	4.39	976
Precuneus								
L/R	1	precuneus/superior parietal lobule/inferior parietal lobule	5/7	8	-50	60	8.31	17096
L	2	inferior parietal lobule	40	-58	-32	26	4.98	1160
R	3	dorsal anterior cingulate cortex	6/32	6	8	38	5.16	2584
L	4	inferior occipital gyrus	37	-44	-68	-2	5.17	800
R	5	postcentral gyrus	40	34	-48	58	5.40	2496
R	6	middle frontal gyrus	6	40	2	54	4.31	808
L	7	postcentral gyrus	3	-42	-32	56	5.08	1104

943

Supplementary Information

Supplementary Methods

Literature search and selection

The keywords for the search used the combination of three categories of relevant terms as follows: (1) sample category: “teenager” OR “adolescent” OR “adolescence” OR “juvenile” OR “teen” OR “youth” OR “young” OR “youngster” OR “child” OR “children” OR “pediatric”; (2) imaging modalities: “VBM” OR “voxel-based morphometry” OR “sMRI” OR “anatomical magnetic resonance images” OR “structural imaging”; and (3) disorder diagnosis: “schizophrenia” OR “schizophreniform” OR “psychopathy” OR “psychopathic” OR “psychopath” OR “mentally disordered” OR “PCL-R” OR “attention deficit hyperactivity disorder” OR “ADHD” OR “conduct disorder” OR “conduct problems” OR “disruptive behavior disorders” OR “oppositional defiant disorder” OR “intermittent explosive disorder” OR “callous unemotional” OR “disruptive behavior” OR “defiant behavior” OR “externalizing” OR “intermittent explosive” OR “affective disorders” OR “bipolar disorder” OR “unipolar disorders” OR “mania” OR “manic disorder” OR “dissociative disorder” OR “dysthymia” OR “major depressive disorder” OR “MDD” OR “depression” OR “obsessive compulsive disorder” and “OCD” OR “generalized anxiety disorder” OR “GAD” OR “mood and anxiety disorders” OR “anxiety disorder” OR “panic disorder” OR “agoraphobia” OR “phobia” OR “autism spectrum disorders” OR “ASD” OR “Asperger” OR “Asperger syndrome” OR “post-traumatic stress disorder” OR “stress disorder” OR “PTSD” OR “post-traumatic stress” OR “eating disorders” OR “anorexia nervosa” OR “eating disorders” OR “bulimia nervosa” OR “binge and heavy drinking” OR “overweight” OR “obesity” OR “cannabis” OR “marijuana” OR “marihuana” OR “THC” OR “tetrahydrocannabinol” OR “delta-9-

967 tetrahydrocannabinol" OR "cigarette-smoking" OR "nicotine" OR "alcohol misuse" OR "alcohol
968 abuse" OR "alcohol addiction" OR "heavy drinking" OR "binge drinking" OR "alcohol
969 dependence" OR "substance abuse" OR "substance use disorder" OR "SUD" OR "internet gaming
970 disorder" OR "internet addiction" OR "IGD". In addition, we explored several other sources,
971 including (1) the BrainMap database (http://brainmap.org); (2) the reference lists of selected article,
972 relevant reviews or meta-analyses (Goodkind et al., 2015; Hu et al., 2017; Liu et al., 2017; Merz
973 et al., 2018; Nenadic et al., 2015; Rogers and Brito, 2016; Seitz et al., 2016); and (3) direct searches
974 on the names of frequently occurring authors.

975 The obtained studies were assessed for inclusion according to the following criteria (see also
976 Goodkind et al., 2015; McTeague et al., 2017; Sha et al., 2019): First, each article reported results
977 from an empirical study published in a peer-reviewed English language journal. Second, each
978 study referred to at least one psychiatric versus control group comparison on structural brain
979 imaging data. The psychiatric disorder group was defined as a group of children and adolescents
980 with a formal clinical diagnosis aged 6-19, whereas the control group was defined as a sample of
981 healthy peers. The age range was based on the Convention on the Rights of the Child and World
982 Health Organization (WHO) regarding the age classification of children and adolescents (Unicef,
983 1989; WHO, 2017), as well as inclusion criteria employed in previous meta-analyses including
984 children and adolescents (Gebel et al., 2018; Ikeda et al., 2018; Seo and Sa, 2010). Finally, the
985 current meta-analysis focused on studies that employed structural magnetic resonance imaging
986 (sMRI), and reported whole brain GMV alterations (rather than region of interest [ROI] analyses)
987 in a standardized stereotaxic space (Talairach or Montreal Neurological Institute, MNI). Note that
988 for the papers reporting Talairach coordinates, a conversion to MNI coordinates was employed
989 using the icbm2tal algorithm (Lancaster et al., 2010) implemented in the GingerALE software

(version 2.3.6, http://www.brainmap.org/). Subsequently, several additional steps were employed to further refine the option of the reported results, such that results were excluded if (i) the age of participants in any groups was not within the range of 6 - 19 years; (ii) the psychiatric group included high-risk relatives of psychiatric disorder or undiagnosed individuals with psychotic characteristics; or (iii) participants in psychiatric group were a history of neurological diseases i.e. epilepsy, brain tumor, brain lesion or meningitis. Moreover, when group comparison differences were reported at both the baseline and follow-up phases, the results at follow-up were excluded; if group comparison differences were reported using different parameters (e.g., with versus without head motion correction), secondary results were excluded (see also Sha et al., 2019). Filtering search results according to these inclusion/exclusion criteria yielded a total of 132 studies (i.e., contrasts) from 87 published VBM articles **(**see **Table S1-S3** for details information with regard to each study**)**, consisting of eight types of psychiatric symptom constellations: (1) attention deficit hyperactivity disorder (29 contrasts); (2) anxiety disorders, including obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder (22 contrasts); (3) mood disorders, including major depressive disorder and bipolar disorder (10 contrasts); (4) behavior disorders, including conduct disorder, disruptive behavior disorders, and oppositional behavior disorder (17 contrasts); (5) autism spectrum disorders (29 contrasts); (6) eating disorders (8 contrasts); (7) substance use disorders, including alcohol use disorder, fetal alcohol spectrum disorder, cocaine-exposed youth, and toluene abusers (7 contrasts); and (8) psychosis, including first-episode psychosis and schizophrenia (10 contrasts).

Validation analysis

On each fold, one contrast was excluded and the ALE meta-analysis was conducted on the remaining N-1 contrasts. Afterwards, we conducted a conjunction analysis on the ALE results of > 80% folds to identify the brain regions that were robustly engaged. As such, the identified brain regions were present in > 80% folds of the LOEO analysis (Feng et al., 2018; Feng et al., 2015). These analyses were employed to validate our main ALE meta-analysis findings. All maps were thresholded using a cluster level family wise error (cFWE) correction ($P < 0.05$) with a cluster formation threshold of $P < 0.001$ using 10,000 permutations for correcting multiple comparisons (Eklund et al., 2016; Woo et al., 2014). This analysis was employed to validate our main ALE meta-analysis findings.

Functional connectivity analyses: MACM analyses

Based on ALE meta-analysis results, the functional coactivation of each GMV region differing between patients and controls (left amygdala, right lOFC, right precuneus and left vmPFC) was determined by MACM analyses using the BrainMap Database (Laird et al., 2009). MACM analyses focus on co-activation likelihood with respect to regions of interest, that is, a high co-activation likelihood across experiments implies a high co-activation likelihood within a given subset or domain, and thus uncovers network relationships with a high degree of generality at task state (Toro et al., 2008). Specifically, the BrainMap database (http://www.brain map.org/) was used, which at the time of assessment contained coordinates of reported activation foci and associated meta-data of more than 8400 neuroimaging experiments. For our analysis, for the left amygdala, 250 contrasts and 2806 foci from 3979 participants were identified; for the right lOFC, 200 contrasts and 2708 foci from 3118 participants were identified; for the left vmPFC, 89

contrasts and 931 foci from 1316 participants were identified; and for the right precuneus, 46 contrasts and 637 foci from 679 participants were identified. First, whole-brain peak coordinates of all those studies from BrainMap were downloaded if the study reported at least one focus of activation within each ROI. Next, coordinates were analyzed using the ALE algorithm (as described above) to detect areas of convergence of coactivation with each seed. Finally, the ALE maps were FWE corrected at the cluster level ($P < 0.05$) with a cluster forming threshold of $P < 0.001$ and converted into Z scores for display.

Functional connectivity analyses: RSFC analyses

To complement task-based connectivity derived from MACM analyses, whole-brain RSFC of the brain regions identified from ALE meta-analysis as ROIs was assessed. Specifically, resting-state fMRI images of 192 healthy volunteers were obtained from the Enhanced Nathan Kline Institute-Rockland Sample (http://fcon_1000.projects.nitrc.org/indi/enhanced/) (Nooner et al., 2012). The enhanced NKI-RS is a community-ascertained, lifespan sample in which age, ethnicity, and socioeconomic status are representative of the general population (Horn and Blankenburg, 2016). The enhanced NKI-RS dataset has been widely used in previous studies including those conducting meta-analysis (Krall et al., 2015; Wong et al., 2019).

Preprocessing for resting-state functional connectivity. RSFC analysis was conducted between all identified regions. Resting-state fMRI images of 192 healthy adults (65% female, 20-75 years old, mean [± SD] age = 46.4 ± 16.7 years, no current psychiatric or neurologic diagnosis) were obtained from the Enhanced Nathan Kline Institute – Rockland Sample (Nooner et al., 2012). The local ethics committee of the Heinrich-Heine University in Düsseldorf approved re-analysis

of the data. During resting-state imaging acquisition, subjects were instructed to look at a fixation cross, not thinking about anything and not falling asleep. Images were acquired on a Siemens TimTrio 3T scanner using BOLD contrast and gradient-echo EPI pulse sequence with the following parameters: TR, 1.4 s; TE, 30 ms; flip angle, 6; voxel size, 2.0 mm × 2.0 mm × 2.0 mm; slice number, 64 slices. Physiological and movement artifacts were removed from the RS data using FIX (FMRIB's ICA-based Xnoiseifier, version 1.061 as implemented in FSL 5.0.9; Griffanti et al., 2014; Salimikhorshidi et al., 2014), which decomposed the data into independent components (ICs) and identified noise components using a large number of distinct spatial and temporal features via pattern classification. Unique variance related to the identified artefactual ICs was then regressed from the data together with 24 movement parameters (including derivatives and second-order effects as previously described and evaluated) (Satterthwaite et al., 2013). Data were further preprocessed using SPM8 (Wellcome Trust Centre for Neuroimaging, London) and in-house Matlab scripts. The first four scans were excluded prior to further analyses, and the remaining EPI images were corrected for head movement using a two-pass (alignment to the initial volume followed by an alignment to the mean after the first pass) affine registration. The mean EPI image for each subject was then spatially normalized to the ICBM-152 reference space using the "unified segmentation" approach (Ashburner and Friston, 2005). The resulting deformation was applied to the individual EPI volumes, which were subsequently smoothed with a 5-mm FWHM Gaussian kernel to improve the signal-to-noise ratio and to compensate for residual anatomic variations.

Seed-based analysis. Implementing a seed-based analysis, the functional connectivity (bivariate correction) between the average BOLD signals from given seed regions (left amygdala, right lOFC, right precuneus and left vmPFC) and all other voxels in the brain was computed. The

voxel-wise correlation coefficients were then transformed into Fisher' s Z scores and tested for consistency across subjects by a second-level analysis of variance (ANOVA, including appropriate nonsphericity correlation). Results were FWE-corrected at a threshold of $P < 0.05$ (corresponding to $T = 4.92$) at the voxel-level.

Functional decoding

The database consists of 11,406 fMRI studies and over 410,000 activity peaks that cover all-sided published neuroimaging literature. The observations for each study contains the peak activities for all contrasts reported in the study's table and the frequency of all words in the article abstract. Notably, a set of psychological 60 topics were used (Vega et al., 2017), which was derived by the latent Dirichlet allocation topic modeling to remedy the redundancy and potential ambiguity in word terms (Blei et al., 2003).

Supplementary Results

MACM and RSFC results

For left amygdala, MACM analyses revealed functional connectivity with amygdala extending to hippocampus, parahippocampal, thalamus, putamen, caudate, and lOFC/anterior insula, medial frontal gyrus, inferior occipital gyrus/middle occipital gyrus, fusiform and precentral gyrus **(Table S7 & Fig. 3A, left panel)**. For right lOFC, MACM analyses revealed functional connectivity patterns with lOFC/anterior insula, dorsal anterior cingulate cortex/superior medial frontal gyrus, fusiform and thalamus extending to putamen, caudate,

hippocampus **(Table S7 & Fig. 3B, left panel)**. For left vmPFC, MACM analyses revealed functional connectivity patterns with vmPFC/anterior cingulate cortex, precuneus, caudate and middle cingulate cortex **(Table S7 & Fig. 4A, left panel)**. And for right precuneus, they revealed functional connectivity patterns with precuneus/superior parietal lobule/inferior parietal lobule, inferior temporal gyrus, dorsal anterior cingulate cortex, middle frontal gyrus and postcentral gyrus **(Table S7 & Fig. 4B, left panel)**.

RSFC analyses revealed that task-free functional connectivity patterns were, on the whole, consistent with MACM analyses. In particular, left amygdala was significantly connected with regions including amygdala extending to hippocampus, parahippocampal, thalamus, putamen, angular, caudate, and hypothalamus, dorsal anterior cingulate cortex, brainstem and cerebellum **(Table S8 & Fig. 3A, middle panel)**, whereas right lOFC was significantly connected with lOFC extending to anterior insula, anterior cingulate cortex, middle temporal gyrus, superior temporal gyrus, angular, thalamus, amygdala, and inferior temporal gyrus, inferior occipital gyrus, hypothalamus, fusiform, precentral gyrus and cerebellum **(Table S8 & Fig. 3B, middle panel)**. Left vmPFC was significantly connected with vmPFC extending to inferior frontal gyrus, middle temporal gyrus, superior temporal gyrus, posterior cingulate, precuneus, and supplementary motor area, superior parietal gyrus/angular gyrus and cerebellum **(Table S8 & Fig. 4A, middle panel)**, and right precuneus was significantly connected with precuneus extending to inferior parietal lobule, superior parietal lobule, middle temporal gyrus, posterior cingulate, and superior temporal gyrus, inferior temporal gyrus, inferior parietal gyrus/superior temporal gyrus, brainstem, lentiform nucleus, caudate, parahippocampal gyrus, thalamus, fusiform and cerebellum **(Table S8 & Fig. 4B, middle panel)**.

Supplementary Figures

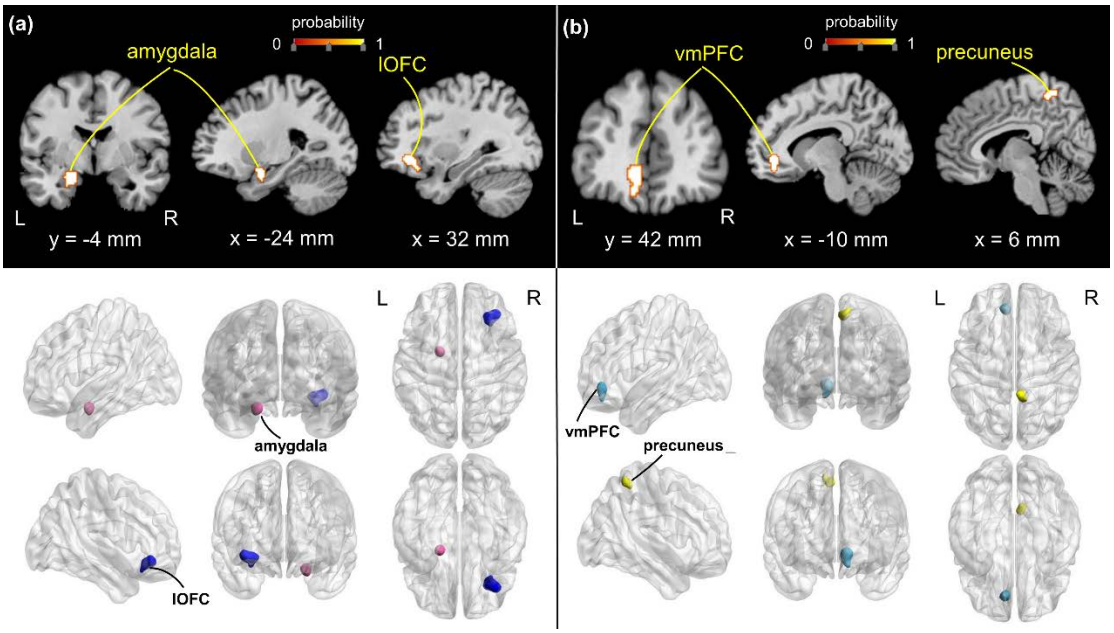

Figure S1. Significant clusters identified in >80% folds of the leave-one-experiment-out analysis of patients versus healthy controls contrast for GMV differences in sMRI studies. (a) GMV decrease: patients < controls; (b) GMV increase: patients > controls. L, left; R, right; vmPFC, ventromedial prefrontal cortex; lOFC, lateral orbital frontal cortex.

1128 **Table S1. Summary of studies included for the meta-analyses.**

Study	Subject sample	N	Contrast	No. of foci
patients < HC				
Brieber et al. (2004)	ADHD/HC	30	HC > ADHD	9
Bonath et al. (2018)	ADHD/HC	36	HC > ADHD	12
Lim et al. (2013)	ADHD/HC	58	HC > ADHD	6
Vilgis et al. (2016)	ADHD/HC	79	HC > ADHD	14
Carmona et al. (2005)	ADHD/HC	50	HC > ADHD	17
Yang et al. (2008)	ADHD/HC	114	HC > ADHD	6
Kobel et al. (2010)	ADHD/HC	26	HC > ADHD	1
Sasayama et al. (2010)	ADHD/HC	35	HC > ADHD	6
Sasayama et al. (2010)	ADHD/HC	25	HC > ADHD	14
Overmeyer et al. (2001)	ADHD/HC	34	HC > ADHD	9
Villemonteix et al. (2015)	ADHD/HC	29	HC > ADHD	1
Jagger-Rickels et al. (2018)	ADHD/HC	73	HC > ADHD	15
Jagger-Rickels et al. (2018)	ADHD/RD/HC	106	HC > disorder group (ADHD/RD)	19
Jagger-Rickels et al. (2018)	ADHD/HC	48	HC > ADHD	5
Iannaccone et al. (2015)	ADHD/HC	36	HC > ADHD	3

Kappel et al. (2014)	ADHD/HC	24	HC > ADHD	3
Li et al. (2015)	ADHD/HC	60	HC > ADHD	2
Mcalonan et al. (2007)	ADHD/HC	59	HC > ADHD	8
Wang et al. (2007)	ADHD/HC	24	HC > ADHD	4
Almeida Montes et al. (2011)	ADHD/HC	23	HC > ADHD	1
Almeida Montes et al. (2011)	ADHD/HC	18	HC > ADHD	1
Stevens et al. (2012)	ADHD/HC	48	HC > ADHD	1
Cheng et al. (2011)	ASD/HC	50	HC > ASD	11
Cheng et al. (2011)	ASD/HC	38	HC > ASD	13
Hower Kwon et al. (2004)	ASD/HC	24	HC > ASD	3
Hower Kwon et al. (2004)	ASD/HC	33	HC > ASD	1
Brieber et al. (2004)	ASD/HC	30	HC > ASD	6
Kaufmann et al. (2013)	ASD/HC	20	HC > ASD	1
Ni et al. (2018)	ASD/HC	142	HC > ASD	6
Ni et al. (2018)	ASD/HC	114	HC > ASD	6
Salmond et al. (2005)	ASD/HC	32	HC > ASD	2
Mcalonan et al. (2005)	ASD/HC	34	HC > ASD	13

McAlonan et al. (2008)	ASD/HC	72	HC > ASD	8
McAlonan et al. (2008)	ASD/HC	71	HC > ASD	4
McAlonan et al. (2008)	ASD/HC	88	HC > ASD	9
Boddaert et al. (2004)	ASD/HC	33	HC > ASD	4
Foster et al. (2015)	ASD/HC	84	HC > ASD	5
Ke et al. (2008)	ASD/HC	32	HC > ASD	1
D'Mello et al. (2015)	ASD/HC	70	HC > ASD	3
D'Mello et al. (2016)	ASD with early language delay/HC	48	HC > ASD	2
D'Mello et al. (2016)	ASD without early language delay/HC	57	HC > ASD	1
Janssen et al. (2008)	BD/HC	71	HC > BD	1
Castro-Fornieles et al. (2018)	BD/HC	85	HC > BD	3
Gao et al. (2013)	BD/HC	36	HC > BD	1
Adleman et al. (2012)	BD/SMD/HC	201	HC > BD and SMD	3
Dickstein et al. (2005)	BD/HC	40	HC > BD	3
Gold et al. (2016)	BD/HC	73	HC > BD	4
Singh et al. (2012)	BD/HC	50	HC > BD	1
Sterzer et al. (2007)	CD/HC	24	HC > CD	3

Sebastian et al. (2016)	CD/HC	89	HC > CD	34
Sebastian et al. (2016)	CD and high levels of CU traits/HC	58	HC > CD	37
Sebastian et al. (2016)	CD and low levels of CU traits/HC	60	HC > CD	9
Fahim et al. (2011)	DBD/HC	47	HC > DBD	8
Fahim et al. (2012)	ODD/HC	38	HC > ODD	1
Huebner et al. (2008)	CD/HC	46	HC > CD	3
Dalwani et al. (2011)	SUD and CD/HC	44	HC > SUD and CD	4
Stevens et al. (2012)	CD/HC	48	HC > CD	31
Olvera et al. (2014)	CD/HC	48	HC > CD	8
Zhang et al. (2018)	CD/HC	120	HC > CD	3
Dalwani et al. (2015)	SUD and CD/HC	43	HC > SUD and CD	9
Castro-Fornieles et al. (2008)	AN/HC	21	HC > AN	3
Bomba et al. (2015)	AN/HC	19	HC > AN	5
Fujisawa et al. (2015)	AN/HC	34	HC > AN	2
Gaudio et al. (2011)	AN without haloperidol treatment/HC	22	HC > AN	3
Gaudio et al. (2011)	AN with haloperidol treatment/HC	26	HC > AN	10
Monzon et al. (2017)	AN/HC	20	HC > AN	25

Mainz et al. (2012)	AN/HC	38	HC > AN	19
Dahlberg et al. (2015)	ED/HC	43	HC > ED	1
Mueller et al. (2013)	ANX/HC	102	HC > ANX	4
Strawn et al. (2015)	GAD/HC	65	HC > GAD	3
Strawn et al. (2013)	ANX/HC	43	HC > ANX	2
Michael et al. (2005)	ANX/HC	51	HC > ANX	2
Michael et al. (2005)	ANX/HC	39	HC > ANX	1
Hagan et al. (2015)	MDD/HC	145	HC > MDD	1
Carmona et al. (2009)	OCD/HC	36	HC > OCD	36
Gilbert et al. (2009)	OCD/HC	20	HC > OCD	3
Chen et al. (2013)	OCD/HC	20	HC > OCD	46
Luisa Lázaro et al. (2009)	OCD/HC	30	HC > OCD	2
Szeszko et al. (2008)	OCD/HC	63	HC > OCD	3
Janssen et al. (2008)	psychosis/HC	76	HC > psychosis	3
Pagsberg et al. (2007)	psychosis/HC	53	HC > psychosis	1
Ahmed et al. (2012)	PTSD/HC	53	HC > PTSD	3
Keding et al. (2015)	PTSD/HC	54	HC > PTSD	5

Soh et al. (2015)	FASD/HC	48	HC > FASD	18
Rando et al. (2013)	cocaine exposed/HC	63	HC > cocaine exposed	3
Aydin et al. (2009)	toluene abusers/HC	35	HC > toluene abusers	12
Brooks et al. (2014)	AUD/HC	116	HC > AUD	2
Dalvie et al. (2017)	AUD/HC	116	HC > AUD	3
Dalvie et al. (2014)	AUD/HC	116	HC > AUD	1
Janssen et al. (2008)	SCZ/HC	76	HC > SCZ	2
Castro-Fornieles et al. (2018)	SCZ/HC	104	HC > SCZ	5
Yoshihara et al. (2008)	SCZ/HC	36	HC > SCZ	1
Douaud et al. (2007)	SCZ/HC	50	HC > SCZ	23
Voets et al. (2008)	SCZ/HC	50	HC > SCZ	20
Zhang et al. (2017)	SCZ/HC	52	HC > SCZ	3
Zhang et al. (2015)	SCZ/HC	67	HC > SCZ	1
patients > HC				
Brieber et al. (2004)	ADHD/HC	30	ADHD > HC	6
Villemonteix et al. (2015)	ADHD/HC	31	ADHD > HC	1
Kaya et al. (2018)	ADHD/HC	37	ADHD > HC	10

Iannaccone et al. (2015)	ADHD/HC	36	ADHD > HC	2
Kappel et al. (2014)	ADHD/HC	24	ADHD > HC	5
Wang et al. (2007)	ADHD/HC	24	ADHD > HC	2
Stevens et al. (2012)	ADHD/HC	48	ADHD > HC	4
Cheng et al. (2011)	ASD/HC	50	ASD > HC	24
Cheng et al. (2011)	ASD/HC	38	ASD > HC	18
Brieber et al. (2004)	ASD/HC	30	ASD > HC	2
Kaufmann et al. (2013)	ASD/HC	20	ASD > HC	2
Ni et al. (2018)	ASD with dysregulation/HC	114	ASD > HC	3
Salmond et al. (2005)	ASD/HC	32	ASD > HC	16
Lin et al. (2017)	ASD/HC	86	ASD > HC	1
Foster et al. (2015)	ASD/HC	84	ASD > HC	42
Ke et al. (2008)	ASD/HC	32	ASD > HC	6
D'Mello et al. (2015)	ASD/HC	70	ASD > HC	3
De Brito et al. (2009)	CD/HC	48	CD > HC	33
Fahim et al. (2012)	ODD/HC	38	ODD > HC	1
Huebner et al. (2008)	CD/HC	46	CD > HC	1

Dalwani et al. (2011)	SUD and CD/HC	44	SUD and CD > HC	1
Zhang et al. (2018)	CD/HC	120	CD > HC	5
Mueller et al. (2013)	GAD/HC	102	GAD > HC	4
Strawn et al. (2015)	AXN/HC	65	AXN > HC	1
Strawn et al. (2013)	AXN /HC	43	AXN > HC	2
Liao et al. (2013)	GAD/HC	51	GAD > HC	1
Wehry et al. (2015)	MDD/HC	55	MDD > HC	4
Wehry et al. (2015)	MDD/HC	53	MDD > HC	2
Gilbert et al. (2009)	OCD/HC	20	OCD > HC	2
Szeszko et al. (2008)	OCD/HC	63	OCD > HC	10
Britton et al. (2010)	OCD/HC	35	OCD > HC	4
Huyser et al. (2013)	OCD/HC	58	OCD > HC	3
Zarei et al. (2011)	OCD/HC	52	OCD > HC	3
Carrion et al. (2009)	PTSD/HC	48	PTSD > HC	3
Soh et al. (2015)	FASD/HC	48	FASD > HC	1
Cullen et al. (2013)	antecedents of SCZ/HC	40	antecedents of SCZ > HC	4

Abbreviation: HC = healthy controls. ADHD = attention deficit hyperactivity disorder. ASD = autism spectrum disorder. ANX = anxiety disorder. GAD = generalized anxiety disorder. AN= anorexia nervosa. AUD = alcohol use disorder. BD = bipolar disorder. CD = conduct disorder. DBD = disruptive behavior

disorders. ED = eating disorders. FASD = fetal alcohol spectrum disorder. MDD = major depressive disorder. OCD = obsessive compulsive disorder. ODD = oppositional defiant disorder. PTSD = posttraumatic stress disorder. SCZ = schizophrenia. SUD = substance use disorder. CU = callous unemotional. RD = reading disability. SMD = Severe Mood Dysregulation.

Table S2. Detailed demographic characteristics of studies included in the meta-analysis.

Study	Patient M/F	HCs M/F	Patient age mean (SD)	HCs age mean (SD)	Patient GMV (SD)	HCs GMV (SD)	Patient IQ (SD)	HCs IQ (SD)
patients < HC								
Brieber et al. (2004)	15/0	15/0	13.13(1.4)	13.3(1.8)	NA	NA	104.1(15.8)	107.7(12.7)
Bonath et al. (2018)	18/0	18/0	13.6(1.7)	14.1(1.3)	784 (49.6)	804 (49.5)	106.8(11.6)	108.1(12.9)
Lim et al. (2013)	29/0	29/0	13.8(1.84)	14.4(2.48)	749 (59.9)	790 (53.5)	97.2 (6.91)	109 (10.4)
Vilgis et al. (2016)	48/0	31/0	12.58(2.21)	12.75(1.96)	NA	NA	above 70	above 70
Carmona et al. (2005)	21/4	21/4	10.82(3)	11.18(3.21)	744.39 (50.44)	784.55 (45.15)	above 80	above 80
Yang et al. (2008)	35/22	34/23	11.1(NA)	11.7(NA)	M:745.19(46.29); F:673.50(48.81)	M:763.39(51.48); F:708.35(65.32)	97.9 (NA)	102.5

Kobel et al. (2010)	14/0	12/0	10.43(1.34)	10.92(1.62)	NA	NA	NA	NA
Sasayama et al. (2010)	13/5	12/5	ADHD along: 8.9(2.4); ADHD comorbid with CD/ODD: 11.9(3.4)	10(2.4)	NA	NA	ADHD along: 90.9(10.7); ADHD comorbid with CD/ODD: 89.2(13.9)	NA
Sasayama et al. (2010)	6/2	12/5	8.9(2.4)	10(2.4)	NA	NA	90.9(10.7)	NA
Overmeyer et al. (2001)	15/3	15/1	10.4(1.7)	10.3(2.2)	873.9 (122.5)	870.5 (109.1)	99.0 (14.9)	NA
Villemonteix et al. (2015)	0/15	0/14	10.2(1.2)	9.7(1.2)	NA	NA	103.8(12.1)	112.7(9.5)
Jagger-Rickels et al. (2018)	18/23	18/14	9.61(1.39)	9.66(1.38)	NA	NA	above 79	above 79
Jagger-Rickels et al. (2018)	34/40	18/14	ADHD:9.61(1.39); RD:9.24(1.35); ADHD comorbid with RD:9.13(1.54)	9.66(1.38)	NA	NA	above 79	above 79

Jagger-Rickels et al. (2018)	10/6	18/14	9.13(1.54)	9.66(1.38)	NA	NA	above 79	above 79
Iannaccone et al. (2015)	11/7	9/9	14.5(1.52)	14.82(1.24)	NA	NA	114.45(10.32)	108.46(17.75)
Kappel et al. (2014)	10/4	8/2	9.8(1.3)	11(1.3)	NA	NA	104.6(15.5)	111.9(16.2)
Li et al. (2015)	30/0	30/0	10.37(1.9)	10.37(1.6)	NA	NA	107.1(14.4)	121.7(14.0)
Mcalonan et al. (2007)	28/0	31/0	9.9(2)	9.6(1.8)	NA	NA	109.9 (21.3)	116.5 (17.3)
Wang et al. (2007)	12/0	12/0	13.4(0.9)	13.5(0.4)	NA	NA	114(13)	103(18)
Almeida Montes et al. (2011)	0/11	0/12	7.18(1.4)	7.83(1.46)	NA	NA	105.18 (13.85)	109.66 (11.34)
Almeida Montes et al. (2011)	0/8	0/10	14.87(1.12)	14.9(1.19)	NA	NA	104 (7.95)	105 (9.95)
Stevens et al. (2012)	19/5	16/8	15.7(1.55)	16(1.47)	NA	NA	98.3(15.04)	97.4(7.94)

Cheng et al. (2011)	25/0	25/0	13.7(2.5)	13.5(2.1)	NA	NA	101.6(18.9)	109.0(9.5)
Cheng et al. (2011)	13/0	25/0	NA	13.5(2.1)	NA	NA	NA	109.0(9.5)
Hower Kwon et al. (2004)	11/0	13/0	13.6(2.4)	13.6(3.1)	NA	NA	NA	NA
Hower Kwon et al. (2004)	20/0	13/0	HFA: 14(3.3); ASD: 13.6(2.4)	13.6(3.1)	NA	NA	NA	NA
Brieber et al. (2004)	15/0	15/0	14.2(1.9)	13.3(1.8)	NA	NA	106.8(21.4)	107.7(12.7)
Kaufmann et al. (2013)	8/2	8/2	14.7(5)	13.8(5.3)	NA	NA	102.3(15.9)	109.5(6.4)
Ni et al. (2018)	81/0	61/0	ASD + with dysregulation: 13(2); ASD - with dysregulation: 12(2.2)	12.4(2.4)	ASD + with dysregulation: 810.8(59.9); ASD - with dysregulation: 800.4(62.5)	798.9(53.8)	ASD + with dysregulation:108.3(15.1); ASD - with dysregulation:105.6(12.0)	112.0(10.9)

Ni et al. (2018)	53/0	61/0	13(2)	12.4(2.4)	810.8(59.9)	798.9(53.8)	108.3(15.1)	112.0(10.9)
Salmond et al. (2005)	13/1	6/12	12.9(0.7)	12.6(0.7)	NA	NA	102(4)	104(2)
Mcalonan et al. (2005)	16/1	16/1	12(1.8)	11(1.2)	594.1(31.5)	626.2(29.1)	101(10.0)	114(14.1)
McAlonan et al. (2008)	14/3	47/8	NA	NA	NA	NA	117.4(18.4)	117.1(18.1)
McAlonan et al. (2008)	13/3	47/8	NA	NA	NA	NA	109.1(16.9)	117.1(18.1)
McAlonan et al. (2008)	27/6	47/8	NA	NA	NA	NA	113.2(17.9)	117.1(18.1)
Boddaert et al. (2004)	16/5	7/5	9.3(2.2)	10.8(2.7)	NA	NA	41.9(21.3), assessed with WISC-R and Brunet-Lezine developmental test	NA
Foster et al. (2015)	38/0	46/0	12.4(2.9)	12.6(3)	NA	NA	102.5(17)	113.1(12)
Ke et al. (2008)	14/3	12/3	8.88(1.96)	9.73(1.67)	NA	NA	108.76(19.07)	109.80(19.22)

D'Mello et al. (2015)	30/5	21/14	10.4(1.6)	10.4(1.5)	NA	NA	above 79	above 79
D'Mello et al. (2016)	13/0	21/14	10.23(1.23)	10.36(1.52)	NA	NA	above 80	above 80
D'Mello et al. (2016)	18/4	21/14	11.01(1.6)	10.36(1.52)	NA	NA	above 80	above 80
Janssen et al. (2008)	13/7	35/16	16.5(1)	15.4(1.6)	NA	NA	76 (21), estimated by the cubes and vocabulary tests	102 (15)
Castro-Fornieles et al. (2018)	9/6	48/22	16.5(0.7)	15.3(1.5)	740.9 (59.1)	762.4(64.4)	77.9 (20.6)	105.8 (16.1)
Gao et al. (2013)	6/12	6/12	15.1(1.81)	14.1(1.61)	NA	NA	98.5 (13.5)	105(7.72)
Adleman et al. (2012)	83/50	36/32	BD:14.2(2.6); SMD:12.7(2.4)	13.9(2.3)	NA	NA	BD:110(15); SMD:107(14)	111(14)
Dickstein et al. (2005)	13/7	13/7	13.4(2.5)	13.3(2.3)	NA	NA	109(13.6)	114(13.3)
Gold et al. (2016)	14/6	24/29	14.6(2.3)	13.8(2.5)	746.4(70.0)	752.7(76.8)	107.3(9.0)	109.9(10.5)

Singh et al. (2012)	13/13	10/14	15.7(1.6)	14.9(1.4)	NA	NA	106(9.2)	112(11.0)
Sterzer et al. (2007)	12/0	12/0	12.75(0.49)	12.5(0.45)	NA	NA	100.6(3.7)	107.2(3.0)
Sebastian et al. (2016)	60/0	29/0	CD-H-CU:14.35(1.64); CD-L-CU:14.16(1.58)	13.6(1.53)	NA	NA	CD-H-CU:97.97 (13.84); CD-L-CU:104.07 (11.53)	105.21(11.94)
Sebastian et al. (2016)	29/0	29/0	14.35(1.64)	13.6(1.53)	NA	NA	97.97 (13.84)	105.21(11.94)
Sebastian et al. (2016)	31/0	29/0	14.16(1.58)	13.6(1.53)	NA	NA	104.07 (11.53)	105.21(11.94)
Fahim et al. (2011)	10/12	13/12	8.39(0.1)	8.36(0.07)	NA	NA	13.00(4.85), assessed by WPPSI-R Block design; 20.28(7.07),assessed by Vocabulary score	14.68(4.50); 20.66 (5.95)
Fahim et al. (2008)	8/10	10/10	8.39(0.1)	8.36(0.07)	870(79)	849(71)	22.00(3.77), assessed by WPPSI-R Block design; 14.00(4.00), assessed by Vocabulary score	23.23(5.18); 15.00 (6.00)
Huebner et al. (2008)	23/0	23/0	14.5(1.6)	14.2(1)	768(50)	816(57)	96.7(9.6)	98.9(6.1)

Dalwani et al. (2011)	25/0	19/0	16.64(0.23)	16.59(0.37)	NA	NA	98.08(1.68)	105.21(2.08)
Stevens et al. (2012)	16/8	16/8	16(1.29)	16(1.47)	NA	NA	91.3(13.18)	97.4(7.94)
Olvera et al. (2014)	16/8	16/8	15.83(1.05)	15.3(1.14)	NA	NA	91.90 (15.45)	98.55 (10.74)
Zhang et al. (2018)	60/0	60/0	15.3(1)	15.5(0.7)	NA	NA	97.0(12.3)	105.4(8.8)
Dalwani et al. (2015)	0/22	0/21	16.09(0.2)	16.67(0.25)	NA	NA	94.26(2.23)	103.95(2.26)
Castro-Fornieles et al. (2009)	1/11	1/8	14.5(1.5)	14.6(3.2)	NA	NA	NA	NA
Bomba et al. (2015)	0/11	0/8	13.63(2.77)	13.25(2.43)	NA	NA	no mental retardation	no mental retardation
Fujisawa et al. (2015)	0/20	0/14	14.15(1.814)	14.93(1.592)	686.08(66.202)	762.11(35.020)	96.10(12.60)	100.07(6.855)
Gaudio et al. (2011)	0/6	0/16	15.7(1.5)	15.1(1.5)	NA	NA	NA	NA

Gaudio et al. (2011)	0/10	0/16	14.9(1.7)	15.1(1.5)	NA	NA	NA	NA
Monzon et al. (2017)	0/10	0/10	16.1(0.33)	17.25 (0.33)	NA	NA	NA	NA
Mainz et al. (2012)	0/19	0/19	15.7(1.5)	15.6(1.9)	605(89)	738(99)	108.8(8.5)	106.8(15.7)
Dahlberg et al. (2015)	0/15	0/28	15(1.36)	14.3(1.09)	696(55.32)	720(78.52)	NA	NA
Mueller et al. (2013)	17/22	35/28	Met:11.3(2.6); Val:13.7(2.5)	Met:13.5(3.1); Val:13.9(2.5)	NA	NA	Met:109.1(12.6); Val:110.4(11.63)	Met:116.0(10.3); Val:113.3(14.8)
Strawn et al. (2015)	10/28	12/15	14.4(3)	14.8(3.9)	NA	NA	above 70	above 70
Strawn et al. (2013)	7/8	11/17	13(2)	13(2)	NA	NA	105(9)	108(11)
Michael et al. (2005)	8/9	16/18	12.9(2.3)	12.4(2.2)	NA	NA	112(12)	113(12)
Michael et al. (2005)	NA	16/18	NA	12.4(2.2)	NA	NA	above 70	above 70

Hagan et al. (2015)	28/81	11/25	15.56(1.27)	15.65(1.45)	NA	NA	96.59(11.45)	100.94(10.93)
Carmona et al. (2007)	13/5	13/5	12.86(2.76)	13.03(3.04)	NA	NA	above 80	above 80
Gilbert et al. (2009)	6/4	6/4	13.26(2.46)	12.97(2.68)	NA	NA	no mental retardation	no mental retardation
Chen et al. (2013)	4/4	6/6	11.7(2.7)	11.8(2.2)	672.2(40.9)	739.8(63.3)	94.8(9.8)	108.6(6.0)
Luisa Lázaro et al. (2009)	8/7	8/7	13.7(2.5)	14.3(2.5)	NA	NA	NA	NA
Szeszko et al. (2008)	14/23	9/17	13(2.7)	13(2.6)	NA	NA	no mental retardation	no mental retardation
Janssen et al. (2008)	19/6	35/16	15.5(1.8)	15.4(1.6)	NA	NA	83(18)	102 (15)
Pagsberg et al. (2007)	11/13	11/18	15.7(NA)	16(NA)	826(82)	848(75)	89(NA)	112(NA)
Ahmed et al. (2012)	11/10	15/17	16.17(1.68)	14.49(2.23)	NA	NA	NA	NA

Keding et al. (2015)	9/18	14/13	14.2(2.7)	13.6(3)	NA	NA	102.2(12.2)	108.8(12.9)
Soh et al. (2015)	13/16	11/8	Alert-treated FASD group:9.46(NA);delayed-treatment control FASD group:9.88(NA)	10.05(NA)	NA	NA	Alert-treated FASD group:84.46(NA);delayed-treatment control FASD group:93.81(NA)	112.42(NA)
Rando et al. (2013)	23/19	14/7	M:15(1.13); F:14.37(0.68)	M:14.64(0.63); F:14.43(0.54)	NA	NA	above 80	above 80
Aydin et al. (2009)	15/0	20/0	15.53(1.3)	15.6(1.09)	NA	NA	63.06(15.97), assessed by WISC-III	100.40(4.00)
Brooks et al. (2014)	25/33	25/33	14.9(0.8)	14.7(0.8)	754(81)	779(82)	no mental retardation	no mental retardation
Dalvie et al. (2017)	25/33	25/33	14.98(NA)	14.77(NA)	NA	NA	no mental retardation	no mental retardation
Dalvie et al. (2014)	25/33	25/33	14.98(NA)	14.77(NA)	NA	NA	no mental retardation	no mental retardation
Janssen et al. (2008)	19/6	35/16	15.4(1.8)	15.4(1.6)	NA	NA	80(20)	102 (15)
Castro-Fornieles et al. (2018)	24/10	48/22	15.2(1.7)	15.3(1.5)	762.2(72.9)	762.4(64.4)	83.1 (16.1)	105.8 (16.1)

Yoshihara et al. (2008)	9/9	9/9	15.8(1.3)	15.8(1.8)	621.3(29.5)	657.2(60.4)	72.8(15.3)	97.3(11.8)
Douaud et al. (2007)	18/7	17/8	M:16.5(1.3); F:15.9(1.5)	M:16.2(1.37); F:15.6(1.3)	NA	NA	87(14)	108(15)
Voets et al. (2008)	18/7	17/8	16.25(1.4)	16(1.5)	NA	NA	87(14)	108(15)
Zhang et al. (2017)	13/13	13/13	16.87(1.05)	16.81(0.75)	NA	NA	above 70	above 70
Zhang et al. (2015)	17/20	17/13	15.5(1.8)	15.3(1.6)	NA	NA	above 70	above 70
patients > HC								
Brieber et al. (2004)	15/0	15/0	13.3(1.4)	13.3(1.8)	NA	NA	104.1(15.8)	107.7(12.7)
Villemonteix et al. (2015)	18/0	13/0	10.4(1.6)	9.9(1.2)	NA	NA	107.4(9.3)	109.1(10.9)
Kaya et al. (2018)	14/5	12/6	10.32(1.95)	10.17(2.04)	NA	NA	113.53(20.76)	119.67(15.32)

Iannaccone et al. (2015)	11/7	9/9	14.5(1.52)	14.82(1.24)	NA	NA	114.45(10.32)	108.46(17.75)
Kappel et al. (2014)	10/4	8/2	9.8(1.3)	11(1.3)	NA	NA	104.6(15.5)	111.9(16.2)
Wang et al. (2007)	12/0	12/0	13.4(0.9)	13.5(0.4)	NA	NA	114(13)	103(18)
Stevens et al. (2012)	19/5	16/8	15.7(1.55)	16(1.47)	NA	NA	98.3(15.04)	97.4(7.94)
Cheng et al. (2011)	25/0	25/0	13.7(2.5)	13.5(2.1)	NA	NA	101.6(18.9)	109.0(9.5)
Cheng et al. (2011)	13/0	25/0	NA	13.5(2.1)	NA	NA	NA	109.0(9.5)
Brieber et al. (2004)	15/0	15/0	14.2(1.9)	13.3(1.8)	NA	NA	106.8(21.4)	107.7(12.7)
Kaufmann et al. (2013)	8/2	8/2	14.7(5)	13.8(5.3)	NA	NA	102.3(15.9)	109.5(6.4)
Ni et al. (2018)	53/0	61/0	13(2)	12.4(2.4)	810.8(59.9)	798.9(53.8)	108.3(15.1)	112.0(10.9)

Salmond et al. (2005)	13/1	6/12	12.9(0.7)	12.6(0.7)	NA	NA	102(4)	104(2)
Lin et al. (2017)	38/0	48/0	13.2(2.6)	12.8(2.7)	807.376(59.851)	800.435(47.520)	103.6(18.8)	112.7(12.0)
Foster et al. (2015)	18/0	46/0	12.4(2.9)	12.6(3)	NA	NA	102.5(17)	113.1(12)
Ke et al. (2008)	14/3	12/3	8.88(1.96)	9.73(1.67)	NA	NA	108.76(19.07)	109.80(19.22)
D'Mello et al. (2015)	30/5	21/14	10.4(1.6)	10.4(1.5)	NA	NA	above 79	above 79
De Brito et al. (2009)	23/0	25/0	11.7(NA)	11.5(NA)	NA	NA	95.4(10.59)	106.9(10.59)
Fahim et al. (2008)	8/10	10/10	8.39(0.1)	8.36(0.07)	870(79)	849(71)	22.00(3.77), assessed by WPPSI-R Block design; 14.00 (4.00), assessed by Vocabulary score	23.23(5.18); 15.00 (6.00)
Huebner et al. (2008)	23/0	23/0	14.5(1.6)	14.2(1)	768(50)	816(57)	96.7(9.6)	98.9(6.1)
Dalwani et al. (2011)	25/0	19/0	16.64(0.23)	16.59(0.37)	NA	NA	98.08(1.68)	105.21(2.08)

Zhang et al. (2018)	60/0	60/0	15.3(1)	15.5(0.7)	NA	NA	97.0(12.3)	105.4(8.8)
Mueller et al. (2013)	17/22	35/28	Met:11.3(2.6); Val:13.7(2.5)	Met:13.5(3.1); Val:13.9(2.5)	NA	NA	Met:109.1(12.6); Val:110.4(11.63)	Met:116.0(10.3); Val:113.3(14.8)
Strawn et al. (2015)	10/28	12/15	14.4(3)	14.8(3.9)	NA	NA	above 70	above 70
Strawn et al. (2013)	7/8	11/17	13(2)	13(2)	NA	NA	105(9)	108(11)
Liao et al. (2013)	13/13	12/13	GAD + childhood maltreatment:17(0.2); GAD-childhood maltreatmen:16.67(0.22)	HC + childhood Maltreatment：16.58(0.22); HC - childhood maltreatment: 16.85(0.21)	NA	NA	no mental retardation	no mental retardation
Wehry et al. (2015)	3/11	14/27	14(3)	13(2)	NA	NA	above 70	above 70
Wehry et al. (2015)	3/9	14/27	14(4)	13(2)	NA	NA	above 70	above 70

Gilbert et al. (2009)	6/4	6/4	13.26(2.46)	12.97(2.68)	NA	NA	no mental retardation	no mental retardation
Szeszko et al. (2008)	14/23	9/17	13(2.7)	13(2.6)	NA	NA	no mental retardation	no mental retardation
Britton et al. (2010)	9/6	13/7	13.5(2.4)	13.6(2.4)	NA	NA	NA	NA
Huyser et al. (2013)	11/18	11/18	13.78(2.58)	13.6(2.73)	NA	NA	9.4(3.0), assessed by WPPSI-R Block design; 10.9(2.4), assessed by Vocabulary score	11.3(2.6); 12.0(1.4)
Zarei et al. (2011)	14/12	14/12	16.6(1.5)	16.5(1.4)	910.027(52.578)	877.379 (41.505)	109.4(12.5)	110.8(10.3)
Carrion et al. (2009)	14/10	14/10	11(2.24)	11(2.73)	NA	NA	no mental retardation	no mental retardation
Soh et al. (2015)	13/16	11/8	Alert-treated FASD group:9.46(NA);delayed-treatment control FASD group:9.88(NA)	10.05(NA)	NA	NA	Alert-treated FASD group:84.46(NA);delayed-treatment control FASD group:93.81(NA)	112.42(NA)
Cullen et al. (2013)	14/6	9/11	11.1(1)	11.3(0.8)	NA	NA	107(13)	113(10)

Abbreviation : M: male. F: female. HC = healthy controls. GMV = grey matter volume. ADHD = attention deficit hyperactivity disorder. CD = conduct disorder. ODD = oppositional defiant disorder. ASD = autism spectrum disorder. HFA = High functioning autism. BD = bipolar disorder. SMD = Severe Mood Dysregulation. CD-H-CU = conduct disorder and high levels of callous unemotiona traits. CD-L-CU = conduct disorder and low levels of callous unemotiona traits. FASD = fetal alcohol spectrum disorder. GAD = generalized anxiety disorder. RD = reading disability. Met = Met allele carriers. Val = Val/Val homozygotes. IQ = intelligence quotient. WISC = Wechsler intelligence scale for children. WPPSI = Wechsler Preschool and Primary Scale of Intelligence. NA = not available.

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Table S3. Detailed clinical and imaging-specific characteristics of studies included in the meta-analysis.

Study	Duration of diseases	Age at onset	medication status	comorbidity	diagnostic criteria	MRI magnetic field strength
patients < HC						
Brieber et al. (2004)	NA	NA	10 patients were currently on psychostimulants	comorbid ANX, enuresis, or ODD	DSM-IV and ICD-10	1.5 T
Bonath et al. (2018)	NA	NA	14 patients had medication history with intake of methylphenidate	comorbid combined type, inattentive, or ODD	DSM-IV	3 T
Lim et al. (2013)	NA	NA	6 patients received regular methylphenidate medication	non-comorbid	DSM-IV	3 T
Vilgis et al. (2016)	NA	NA	36 patients were non-medicated	comorbid ANX, Persistent Depressive, ODD, or CD	DSM-IV	3 T
Carmona et al. (2005)	NA	NA	medication	comorbid Anxiety, Depression, Simple phobia, Tics, Obsessions, Nightmares, or Insomnia	DSM-IV-TR	1.5 T

Yang et al. (2008)	NA	NA	49 patients received methylphenidate	comorbid chronic motor tic disorder, ANX, learning disorders	DSM-IV	1.5 T
Kobel et al. (2010)	NA	NA	medication	comorbid ODD, CD, or GAD	DSM-IV	3 T
Sasayama et al. (2010)	NA	NA	NA	comorbid ODD, or CD	DSM-IV-TR	1.5 T
Sasayama et al. (2010)	NA	NA	NA	non-comorbid	DSM-IV-TR	1.5 T
Overmeyer et al. (2001)	NA	NA	18 patients received methylphenidate;1 patient desipramine;1 patient d-amphetamine	non-comorbid	DSM-IV	1.5 T
Villemonteix et al. (2015)	NA	NA	medication-free	non-comorbid	DSM-IV-R	3 T
Jagger-Rickels et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV	1.5 T
Jagger-Rickels et al. (2018)	NA	NA	NA	comorbid ADHD, or RD	DSM-IV	1.5 T
Jagger-Rickels et al. (2018)	NA	NA	NA	comorbid RD	DSM-IV	1.5 T

Iannaccone et al. (2015)	NA	NA	13 patients received Methylphenidate medication	comorbid Affective disorder, Adjustment disorder, ANX/phobias, Dyscalculia, or CD	DSM-IV-TR and ICD-10	3 T
Kappel et al. (2014)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T
Li et al. (2015)	NA	NA	medication-free	comorbid ODD	DSM-IV	3 T
Mcalonan et al. (2007)	NA	NA	medication	comorbid anxiety, ODD, CD, Hyperactive subtype, Inattentive subtype, or Combined subtype	DSM-IV	1.5 T
Wang et al. (2007)	NA	NA	NA	non-comorbid	DSM-IV	3 T
Almeida Montes et al. (2011)	NA	NA	medication-free	non-comorbid	DSM-IV-TR	1 T
Almeida Montes et al. (2011)	NA	NA	medication-free	non-comorbid	DSM-IV-TR	1 T
Stevens et al. (2012)	NA	NA	NA	comorbid CD	DSM-IV	3 T
Cheng et al. (2011)	NA	NA	medication-free	comorbid Asperger’s syndrome and pervasive developmental disorders	DSM-IV	1.5 T

Cheng et al. (2011)	NA	NA	medication-free	comorbid Asperger's syndrome and pervasive developmental disorders	DSM-IV	1.5 T
Hower Kwon et al. (2004)	NA	NA	NA	non-comorbid	DSM-IV	3 T
Hower Kwon et al. (2004)	NA	NA	NA	non-comorbid	DSM-IV	3 T
Brieber et al. (2004)	NA	NA	2 patients were taking atypical neuroleptic	comorbid ANX, enuresis, or ODD	DSM-IV and ICD-10	1.5 T
Kaufmann et al. (2013)	NA	NA	NA	non-comorbid	DSM-IV-TR	1.5 T
Ni et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV and ICD-10	3 T
Ni et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV and ICD-10	3 T
Salmond et al. (2005)	NA	NA	medication-free	non-comorbid	ASAS	1.5 T
Mcalonan et al. (2005)	NA	NA	medication-free	non-comorbid	ICD-10	1.5 T

McAlonan et al. (2008)	NA	NA	medication-free	comorbid Asperger's syndrome or had a history of delayed language acquisition	DSM-IV	1.5 T
McAlonan et al. (2008)	NA	NA	medication-free	had a history of delayed language acquisition	DSM-IV	1.5 T
McAlonan et al. (2008)	NA	NA	medication-free	had a history of delayed language acquisition	DSM-IV	1.5 T
Boddaert et al. (2004)	NA	NA	medication-free for at least a month before MRI	comorbid mental retardation	DSM-IV	1.5 T
Foster et al. (2015)	NA	NA	NA	non-comorbid	ADOS and ADOS-2	3 T
Ke et al. (2008)	NA	NA	NA	non-comorbid	DSM-IV	1.5 T
D'Mello et al. (2015)	NA	NA	NA	non-comorbid	DSM-IV	3 T
D'Mello et al. (2016)	NA	NA	NA	had a history of delayed language acquisition	DSM-IV	3 T
D'Mello et al. (2016)	NA	NA	NA	non-comorbid	DSM-IV	3 T

Janssen et al. (2008)	16.2 (0.9)	10.0 (10.4)	medication	non-comorbid	DSM-IV	1.5 T
Castro-Fornieles et al. (2018)	NA	NA	medication	non-comorbid	K-SADS-PL, PANSS, PAS	1.5 T
Gao et al. (2013)	13.8 (1.69)	15.6 (13.0)	2 patients were non-medicated	diagnosed with comorbidity	DSM-IV	3 T
Adleman et al. (2012)	before age 12	at least 12 months	medication-free	comorbid illnesses	DSM-IV	1.5 T
Dickstein et al. (2005)	10.1(3.2)	NA	1 patient were non-medicated	comorbid ADHD, Anxiety, or Psychosis	DSM-IV	1.5 T
Gold et al. (2016)	before age 10	NA	medication	comorbid Anxiety, GAD, Social phobia, Panic disorder, ADHD, ODD, CD, MDD, pervasive developmental disorder, separation ANX, Eliminating Disorders or Tic/Tourette disorders	DSM-V	3 T
Singh et al. (2012)	NA	NA	medication	non-comorbid	DSM-IV-TR	3 T
Sterzer et al. (2007)	before age 10	NA	NA	comorbid ADHD	DSM-IV and ICD-10	1.5 T

Sebastian et al. (2016)	NA	NA	medication-free	non-comorbid	CASI-CD	1.5 T
Sebastian et al. (2016)	NA	NA	medication-free	non-comorbid	CASI-CD	1.5 T
Sebastian et al. (2016)	NA	NA	medication-free	non-comorbid	CASI-CD	1.5 T
Fahim et al. (2011)	NA	NA	medication-free	comorbid CD, or ODD	DSM-V	1.5 T
Fahim et al. (2008)	NA	NA	medication-free	non-comorbid	DSM-V	1.5 T
Huebner et al. (2008)	NA	NA	medication-free	comorbid ADHD	DSM-IV	1.5 T
Dalwani et al. (2011)	NA	NA	2 patients were medicated	non-comorbid	DSM-IV	3 T
Stevens et al. (2012)	NA	NA	NA	non-comorbid	DSM-IV	3 T
Olvera et al. (2014)	10	NA	medication	comorbid BD, CD, ODD, PTSD, MDD, or ADHD	DSM-IV	3 T

Zhang et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV-TR	3 T
Dalwani et al. (2015)	NA	NA	medication	comorbid SUD and CD	DSM-IV	3 T
Castro-Fornieles et al. (2009)	8.3(3.1)	NA	NA	non-comorbid	DSM-IV-TR	1.5 T
Bomba et al. (2015)	NA	14.45(10.92)	medication-free	non-comorbid	DSM-IV	1.5 T
Fujisawa et al. (2015)	12.60(1.818)	23.55(17.022)	medication-free	non-comorbid	DSM-IV	3 T
Gaudio et al. (2011)	15.3(1.6)	4.3(2.7)	medication-free	non-comorbid	DSM-IV-TR	1.5 T
Gaudio et al. (2011)	14.4(1.8)	5.8(3.5)	medication	non-comorbid	DSM-IV-TR	1.5 T
Monzon et al. (2017)	NA	NA	NA	non-comorbid	DSM-V	3 T
Mainz et al. (2012)	NA	NA	3 patients were medicated	comorbid OCD, or MDD	DSM-IV	3 T

Dahlberg et al. (2015)	NA	8.67(5.43)	medication-free	comorbid illnesses	DSM-IV	3 T
Mueller et al. (2013)	NA	NA	medication-free	comorbid GAD, Social Phobia, Specific phobia, Separation ANX, depression, ODD, ADHD, Ticdisorder, Enuresis	K-SADS-PL	3 T
Strawn et al. (2015)	NA	NA	medication-free	non-comorbid	K-SADS-PL	3 T
Strawn et al. (2013)	NA	NA	medication-free	non-comorbid	K-SADS-PL	4 T
Michael et al. (2005)	NA	NA	7 patients were medicated	comorbid MDD	DSM-IV	3 T
Michael et al. (2005)	NA	NA	7 patients were medicated	non-comorbid	DSM-IV	3 T
Hagan et al. (2015)	NA	NA	medication-free	comorbid ANX	DSM-IV	3 T
Carmona et al. (2007)	NA	NA	medication	comorbid tic disorder but did not meet criteria for Tourette's disorder	DSM-IV-TR	1.5 T
Gilbert et al. (2009)	NA	NA	NA	comorbid illnesses	DSM-IV	1.5 T

Chen et al. (2013)	NA	8(3.4)	medication-free	non-comorbid	DSM-IV	3 T
Luisa Lázaro et al. (2009)	NA	NA	medication	non-comorbid	DSM-IV	1.5 T
Szeszko et al. (2008)	NA	NA	medication	comorbid ANX, ODD, ADHD without hyperactivity, ADHD with hyperactivity, or trichotillomania	DSM-IV	1.5 T
Janssen et al. (2008)	15.0 (2.1)	12.0 (10.4)	medication	non-comorbid	DSM-IV	1.5 T
Pagsberg et al. (2007)	13.6(2.84)	NA	medication	non-comorbid	ICD-10	1.5 T
Ahmed et al. (2012)	NA	NA	medication-free	comorbid MDD, Separation ANX, ADHD	DSM-IV-TR	1.5 T
Keding et al. (2015)	NA	46 (36)	9 patients were medicated	comorbid psychiatric illness, or depressive disorders	DSM-IV	3 T
Soh et al. (2015)	NA	NA	medication	comorbid ADHD	ascertained through the Motherisk Clinic at the Hospital for Sick Children	1.5 T
Rando et al. (2013)	NA	NA	medication-free	non-comorbid	self-reports on the Youth Risk Behavior Survey and	3 T

					urine toxicology results from laboratory-analyzed samples	
Aydin et al. (2009)	12.76(1.83)	31.86(18.74)	medication-free	non-comorbid	abused toluene-containing solvents by inhalation for a period of at least 6 months	1.5 T
Brooks et al. (2014)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T
Dalvie et al. (2017)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T
Dalvie et al. (2014)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T
Janssen et al. (2008)	15.0 (9.3)	8.3 (12.1)	medication	non-comorbid	DSM-IV	1.5 T
Castro-Fornieles et al. (2018)	NA	NA	medication	diagnosed with schizoaffective disorder, or SCZ	K-SADS-PL, PANSS, PAS	1.5 T
Yoshihara et al. (2008)	under 16 years	1.2(0.9)	1 patient were non-medicated	non-comorbid	DSM-IV	1.5 T
Douaud et al. (2007)	14.9(1.6)	1.4(0.7)	medication	3 patients and 1 control fulfilled criteria for mild learning disability	DSM-IV	1.5 T

Voets et al. (2008)	15(1.5)	1.4(0.7)	medication	non-comorbid	DSM-IV	1.5 T
Zhang et al. (2017)	16.51(1.01)	3.61(3.50)	medication-free, no more than 3 days of antipsychotic treatment before clinical assessment and MRI scan	non-comorbid	DSM-IV	3 T
Zhang et al. (2015)	NA	16.0(14.4)	medication-free	non-comorbid	DSM-IV-TR	3 T
patients > HC						
Brieber et al. (2004)	NA	NA	10 patients were currently on psychostimulants	comorbid ANX, enuresis, or ODD	DSM-IV and ICD-10	1.5 T
Villemonteix et al. (2015)	NA	NA	medication-free	non-comorbid	DSM-IV-R	3 T
Kaya et al. (2018)	NA	NA	medication-free	had a negative history of neurological and psychiatric disease	DSM-IV	1.5 T
Iannaccone et al. (2015)	NA	NA	13 patients received Methylphenidate medication	comorbid affective disorder, adjustment disorder, ANX/phobias, dyscalculia, or CD	DSM-IV-TR and ICD-10	3 T
Kappel et al. (2014)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T

Wang et al. (2007)	NA	NA	NA	non-comorbid	DSM-IV	3 T
Stevens et al. (2012)	NA	NA	NA	comorbid CD	DSM-IV	3 T
Cheng et al. (2011)	NA	NA	medication-free	comorbid Asperger's syndrome and pervasive developmental disorders	DSM-IV	1.5 T
Cheng et al. (2011)	NA	NA	medication-free	comorbid Asperger's syndrome and pervasive developmental disorders	DSM-IV	1.5 T
Brieber et al. (2004)	NA	NA	2 patients were taking atypical neuroleptic	comorbid ANX, enuresis, or ODD	DSM-IV and ICD-10	1.5 T
Kaufmann et al. (2013)	NA	NA	NA	non-comorbid	DSM-IV-TR	1.5 T
Ni et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV and ICD-10	3 T
Salmond et al. (2005)	NA	NA	medication-free	non-comorbid	ASAS	1.5 T
Lin et al. (2017)	NA	NA	medication-free	non-comorbid	DSM-IV-TR	3 T

Foster et al. (2015)	NA	NA	NA	non-comorbid	ADOS and ADOS-2	3 T
Ke et al. (2008)	NA	NA	NA	non-comorbid	DSM-IV	1.5 T
D'Mello et al. (2015)	NA	NA	NA	non-comorbid	DSM-IV	3 T
De Brito et al. (2009)	NA	NA	NA	non-comorbid	SDQ and APSD	3 T
Fahim et al. (2008)	NA	NA	medication-free	non-comorbid	DSM-V	1.5 T
Huebner et al. (2008)	NA	NA	medication-free	comorbid ADHD	DSM-IV	1.5 T
Dalwani et al. (2011)	NA	NA	2 patients were medicated	non-comorbid	DSM-IV	1.5 T
Zhang et al. (2018)	NA	NA	NA	non-comorbid	DSM-IV-TR	3 T
Mueller et al. (2013)	NA	NA	medication-free	comorbid GAD, social Phobia, specific phobia, separation ANX, depression, ODD, ADHD, Ticdisorder, Enuresis	K-SADS-PL	3 T

Strawn et al. (2015)	NA	NA	medication-free	non-comorbid	K-SADS-PL	3 T
Strawn et al. (2013)	NA	NA	medication-free	non-comorbid	K-SADS-PL	4 T
Liao et al. (2013)	NA	NA	medication-free	non-comorbid	DSM-IV	3 T
Wehry et al. (2015)	NA	NA	NA	non-comorbid	DSM-IV	4 T
Wehry et al. (2015)	NA	NA	NA	comorbid anxiety	DSM-IV	4 T
Gilbert et al. (2009)	NA	NA	NA	comorbid illnesses	DSM-IV	1.5 T
Szeszko et al. (2008)	NA	NA	medication	comorbid ANX, ODD, ADHD without hyperactivity, ADHD with hyperactivity, or trichotillomania	DSM-IV	1.5 T
Britton et al. (2010)	NA	4.1(2.0)	medication	comorbid illness	DSM-IV	3 T
Huyser et al. (2013)	12.17(3.0)	2.6(2.3)	medication-free	non-comorbid	CY-BOCS	3 T

Zarei et al. (2011)	11.2(2.8)	5.3(3.4)	16 patients were medicated	non-comorbid	CY-BOCS	1.5 T
Carrion et al. (2009)	NA	NA	NA	comorbid depression, social phobia, ADHD, separation ANX, GAD, or simple phobia	DSM-IV	1.5 T
Soh et al. (2015)	NA	NA	medication	comorbid ADHD	ascertained through the Motherisk Clinic at the Hospital for Sick Children	1.5 T
Cullen et al. (2013)	NA	NA	medication-free	comorbid speech and motor delays/abnormalities, emotional symptoms, peer relationship problems, CD, and hyperactivity inattention, or multiple "certainly true' PLEs	psychotic-like experience questionnaire	3 T

Abbreviation : HC = healthy controls. ADHD = attention deficit hyperactivity disorder. GAD = generalized anxiety disorder. ANX = anxiety disorder. BD = bipolar disorder. CD = conduct disorder. MDD = major depressive disorder. ODD = oppositional defiant disorder. PTSD = posttraumatic stress disorder. SUD = substance use disorder. OCD = obsessive compulsive disorder. SCZ = schizophrenia. RD = reading disability. DSM = The Diagnosticand Statistical Manual of Mental Disorders. ICD = International Classification of Diseases. ADOS = Autism Diagnostic Observation Schedule. K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Age Children – Present and Lifetime Version. PANSS = Positive and Negative Syndrome Scale. PAS = Premorbid Adjustment Scale. ASAS = Australian Scale for Asperger's Syndrome. CASI-CD = Child and Adolescent Symptom Inventory Conduct Disorder subscale. SDQ = Strengths and Difficulties Questionnaire. APSD = Antisocial Process Screening Device. CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale. NA = not available.

Table S4. Average contribution of each experimental contrast for significant clusters identified for the meta-analysis comparing GMV decreases in patients versus healthy controls across sMRI studies.

Cluster No.	Study	N	Contrast	Average contribution (%)
amygdala [-20 -4 -20]	Brieber et al. (2004)	30	HC > ADHD	7.55
	Sasayama et al. (2010)	35	HC > ADHD	2.02
	Sasayama et al. (2010)	25	HC > ADHD	8.03
	Brieber et al. (2004)	30	HC > ASD	0.69
	Gao et al. (2013)	36	HC > BD	2.01
	Dickstein et al. (2005)	20	HC > BD	1.38
	Sterzer et al. (2007)	24	HC > CD	8.36
	Huebner et al. (2008)	46	HC > CD	13.29
	Stevens et al. (2012)	48	HC > CD	16.22
	Monzon et al. (2017)	20	HC > AN	7.31
	Michael et al. (2005)	51	HC > GAD	13.88
	Michael et al. (2005)	39	HC > GAD	16.01
	Chen et al. (2013)	20	HC > OCD	0.22
	Rando et al. (2013)	63	HC > cocaine-exposed	2.73
	Bonath et al. (2013)	36	HC > ADHD	0.26
lateral orbital frontal cortex [32 32 -10]	Carmona et al. (2005)	50	HC > ADHD	11.01
	Cheng et al. (2011)	50	HC > ASD	10.8
	Cheng et al. (2011)	38	HC > ASD	9.58
	Sebastian et al. (2015)	89	HC > CD	17.64

Sebastian et al. (2015)	58	HC > CD with high CU trait	17.31
Sebastian et al. (2015)	60	HC > CD with low CU trait	8.44
Sterzer et al. (2007)	48	HC > CD	7.26
Monzon et al. (2017)	20	HC > AN	5.52
Chen et al. (2013)	20	HC > OCD	5.66
Castro-Fornieles et al. (2018)	104	HC > SCZ	3.57
Fahim et al. (2011)	47	HC > DBD	3.06

Abbreviation: HC = healthy controls. ADHD = attention deficit hyperactivity disorder. ASD = autism spectrum disorder. AN= anorexia nervosa. BD = bipolar disorder. CD = conduct disorder. DBD = disruptive behavior disorders. GAD = generalized ANX. OCD = obsessive compulsive disorder. SCZ = schizophrenia. CU = callous unemotional.

Table S5. Average contribution of each experimental contrast for significant clusters identified for the meta-analysis comparing GMV increases in patients versus healthy controls across sMRI studies.

Cluster No.	Study	N	Contrast	Average contribution (%)
ventromedial prefrontal cortex [-10 42 -8]	Kappel et al. (2014)	24	ADHD > HC	27.14
	Cheng et al. (2011)	50	ASD > HC	28.09
	Cheng et al. (2011)	38	ASD > HC	27.38
	Szeszko et al. (2008)	63	OCD > HC	1.17
	Britton et al. (2010)	35	OCD > HC	16.22
precuneus [8 -48 60]	Cheng et al. (2011)	50	ASD > HC	19.41
	Cheng et al. (2011)	38	ASD > HC	30.68
	Strawn et al. (2013)	43	GAD > HC	20.09
	Wehry et al. (2015)	53	MDD > HC	14.43
	Szeszko et al. (2008)	63	OCD > HC	15.29

Abbreviation: HC = healthy controls. ADHD = attention deficit hyperactivity disorder. ASD = autism spectrum disorder. GAD = generalized ANX. OCD = obsessive compulsive disorder. MDD = major depressive disorder.

Table S6. Significant clusters identified in > 80% folds of the leave-one-experiment-out analysis of patients versus healthy controls contrast for GMV differences in sMRI studies (GMV decreases and increases)

Laterality	Cluster no.	Brain Regions	BA	MNI Coordinates (mm)			Probability	Cluster Size (mm^3)
				x	y	z		
Group differences (GMV reduction)								
L	1	amygdala	-	-24	-4	-28	1	1016
R	2	lateral orbital frontal cortex	47	32	24	-20	1	1752
Group differences (GMV increase)								
L	1	ventromedial prefrontal cortex	10	-14	40	-20	1	848
R	2	precuneus	7/5	8	-46	54	1	968

P(FWE) < 0.05 at the cluster level with a cluster-forming threshold of P < 0.001 using 10,000 permutations.

Table S7. MACM results for amygdala, lOFC, vmPFC, and precuneus.

Laterality	Cluster no.	Brain Regions	BA	MNI Coordinates (mm)			Peak intensity	Cluster Size (mm^3)
				x	y	z		
Amygdala								
L/R	1	amygdala/hippocampus /parahippocampal/ thalamus/putamen/ caudate/uncus	-	-22	-4	-18	9.17	41408
R	2	fusiform	37	42	-50	-20	6.52	1944
L	3	fusiform	37	-42	-48	-20	5.54	5232
L/R	4	medial frontal gyrus	11	0	46	-16	4.86	1176
R	5	inferior occipital gyrus/middle occipital gyrus	19/37	44	-78	-8	7.12	6080
L	6	lateral orbitofrontal cortex/anterior insula	13/47	-34	26	-2	5.64	3592
L	7	inferior frontal gyrus	47	-50	24	-6	5.98	1512
R	8	inferior frontal gyrus	46	54	32	6	5.60	1712
L	9	medial frontal gyrus	10	-4	60	18	5.20	1416
L	10	precentral gyrus	9	-48	6	32	4.66	1632
lOFC								
L/R	1	lateral orbitofrontal cortex/anterior insula	13/47	-32	28	-6	8.35	31280
L/R	2	lateral orbitofrontal cortex/anterior insula	13/47	32	28	-8	8.94	21968
L	3	fusiform	37	-44	-72	-10	4.82	2184
R	4	thalamus	-	12	-14	2	6.17	7552

L/R	5	dorsal anterior cingulate cortex/superior medial frontal gyrus	8/32	-4	24	42	8.31	10712
vmPFC								
L/R	1	ventromedial prefrontal cortex/anterior cingulate cortex	10/32	-10	42	-8	8.59	16472
L	2	caudate	-	-8	6	-4	5.18	1808
L	3	precuneus	7/31	-6	-52	32	4.92	3064
L	4	middle cingulate cortex	31	-8	-24	42	4.39	976
precuneus								
L/R	1	precuneus/superior parietal lobule/inferior parietal lobule	5/7	8	-50	60	8.31	17096
L	2	inferior temporal gyrus	37	-44	-68	-2	5.17	800
L	3	inferior parietal lobule	40	-58	-32	26	4.98	1160
R	4	dorsal anterior cingulate cortex	6/32	6	8	38	5.17	2584
R	5	inferior parietal lobule	40	34	-38	58	5.41	2496
R	6	middle frontal gyrus	6	40	2	54	4.31	808
L	7	postcentral gyrus	3	-42	-30	56	5.08	1104

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Table S8. RSFC results for amygdala, lOFC, vmPFC, and precuneus.

Laterality	Cluster no.	Brain Regions	BA	MNI Coordinates (mm)			Peak intensity	Cluster Size (mm^3)
				x	y	z		
Amygdala								
L/R	1	amygdala/hippocampus/parahippocampal/thalamus/putamen/angular/caudate/extra-nuclear/insula/anterior cingulate cortex	-	-24	-4	-22	226.41	496512
L/R	2	cerebellum	-	-6	-52	-44	14.32	9872
L	3	cerebellum	-	-22	-56	-48	6.66	280
L	4	cerebellum	-	-22	-80	-40	7.31	344
L	5	brainstem	-	-8	-24	-42	7.58	592
L	6	cerebellum	-	-20	-90	-38	6.77	96
R	7	brainstem	-	14	-22	-36	5.87	96
L	8	brainstem	-	-14	-24	-22	6.49	64
L	9	hypothalamus	-	-2	4	-20	16.15	104
L	10	dorsal anterior cingulate cortex	32	-10	18	32	5.85	64

lOFC								
L/R	1	lateral orbitofrontal cortex/medial frontal gyrus/anterior cingulate cortex/insula/middle temporal gyrus/superior temporal gyrus/inferior parietal lobule/angular/thalamus/amygdala	10/ 40	30	30	-12	92.64	444248
L/R	2	cerebellum	-	2	-52	-38	18.26	10816
L/R	3	cerebellum	-	-34	-72	-46	19	15760
L	4	cerebellum	-	36	-70	-40	10.84	3864
L	5	superior temporal gyrus	38	-34	12	-38	6.43	208
L	6	fusiform	36	-26	-6	-40	5.66	48
R	7	fusiform	28	26	-8	-36	5.91	88
R	8	fusiform	20	38	-14	-32	8.44	200
L	9	inferior temporal gyrus	20	-48	-8	-34	5.99	104
L	10	middle temporal gyrus	21	-48	8	-34	5.97	88
R	11	cerebellum	-	2	-48	-22	5.68	40
-	12	hypothalamus	-	0	4	-20	7.95	40
L	13	inferior occipital gyrus	18	-22	-102	-10	6.8	112
R	14	inferior occipital gyrus	18	28	-100	-6	8.95	392

L	15	middle temporal gyrus	22	-48	-44	4	7.3	136
L	16	middle temporal gyrus	22	-62	-60	14	6.89	112
R	17	precentral gyrus	6	54	4	14	6.38	208
vmPFC								
L/R	1	ventromedial prefrontal cortex/inferior frontal gyrus/middle temporal gyrus/superior temporal gyrus/posterior cingulate/precuneus	10/ 21	-6	42	-8	195.26	344392
L/R	2	cerebellum	-	8	-50	-46	28.77	11704
L/R	3	cerebellum	-	48	-56	-46	30.53	10776
L	4	cerebellum	-	-48	-60	-44	21.68	6824
R	5	cerebellum	-	24	-40	-32	7.82	176
L	6	cerebellum	-	-8	-46	-28	6.22	56
R	7	cerebellum	-	0	-44	-16	5.62	40
L	8	cerebellum	-	-2	-54	-12	5.75	48
R	9	angular gyrus/superior temporal gyrus/inferior parietal lobule	39/ 40	54	-68	34	31.83	14872
L	10	superior parietal gyrus/middle temporal gyrus/inferior parietal lobule	39/ 40	-44	-78	36	36.21	19608

L	11	supplementary motor area	6	-6	-24	58	5.72	88
R	12	supplementary motor area	6	6	-24	60	7.41	168
precuneus								
L/R	1	precuneus/inferior parietal lobule/superior parietal lobule/middle temporal gyrus/posterior cingulate	6/7	6	-50	58	106.93	358952
R	2	brainstem	-	2	-42	-50	6.5675	72
R	3	superior temporal gyrus	38	26	8	-48	10.8	752
R	4	brainstem	-	10	-22	-42	7.76	120
L	5	brainstem	-	-4	-38	-38	5.9	152
R	6	inferior temporal gyrus	20	34	0	-42	5.98	64
R	7	fusiform	36	32	-18	-32	9.7	200
L	8	inferior parietal gyrus/superior temporal gyrus	13/ 40	-66	-30	22	30.52	33320
R	9	cerebellum	-	0	-72	-24	8.86	376
L	10	parahippocampal gyrus	-	-32	-28	-28	7.86	64
L	11	fusiform	36	-46	-42	-24	12.49	712
R	12	inferior frontal gyrus	47	18	10	-22	16.33	392

L	13	inferior frontal gyrus	47	-16	8	-20	7.18	48
L	14	cerebellum	-	-12	-94	-20	7.15	56
L	15	fusiform	18	-38	-82	-20	7.73	160
R	16	superior frontal gyrus	11	24	66	-12	14.81	328
L	17	cerebellum	-	-6	-92	-18	9.42	152
L	18	lentiform nucleus	-	-16	-4	-6	12.21	1328
R	19	thalamus	-	18	-22	14	10.25	2144
R	20	lentiform nucleus	-	18	-4	-6	10.77	704
R	21	caudate	-	8	24	0	11.27	168
R	22	middle frontal gyrus/superior frontal gyrus	9/10	34	46	28	27.98	9376
L	23	middle frontal gyrus/superior frontal gyrus	9/10	-36	50	28	24.23	6360

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Supplementary Reference

Ashburner, J., Friston, K.J., 2005. Unified segmentation. Neuroimage 26, 839-851.

Blei, D.M., Ng, A.Y., Jordan, M.I., 2003. Latent dirichlet allocation. Journal of machine Learning research 3, 993-1022.

Eklund, A., Nichols, T.E., Knutsson, H., 2016. Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. Proc Natl Acad Sci U S A 113, 7900-7905.

Feng, C., Becker, B., Huang, W., Wu, X., Eickhoff, S.B., Chen, T., 2018. Neural substrates of the emotion-word and emotional counting Stroop tasks in healthy and clinical populations: A meta-analysis of functional brain imaging studies. Neuroimage 173, 258-274.

Feng, C., Luo, Y.-J., Krueger, F., 2015. Neural Signatures of Fairness-Related Normative Decision Making in the Ultimatum Game: A Coordinate-Based Meta-Analysis. Human Brain Mapping 36, 591-602.

Gebel, A., Lesinski, M., Behm, D.G., Granacher, U., 2018. Effects and dose–response relationship of balance training on balance performance in youth: a systematic review and meta-analysis. Sports Medicine 48, 2067-2089.

Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., Ortega, B.N., Zaiko, Y.V., Roach, E.L., Korgaonkar, M.S., 2015. Identification of a common neurobiological substrate for mental illness. JAMA psychiatry 72, 305-315.

Griffanti, L., Salimi-Khorshidi, G., Beckmann, C.F., Auerbach, E.J., Douaud, G., Sexton, C.E., Zsoldos, E., Ebmeier, K.P., Filippini, N., Mackay, C.E., 2014. ICA-based artefact removal and accelerated fMRI acquisition for improved resting state network imaging. Neuroimage 95, 232-247.

Horn, A., Blankenburg, F., 2016. Toward a standardized structural–functional group connectome in MNI space. Neuroimage 124, 310.

Hu, X., Du, M., Chen, L., Li, L., Zhou, M., Zhang, L., Liu, Q., Lu, L., Mreedha, K., Huang, X., 2017. Meta-analytic investigations of common and distinct grey matter alterations in youths and adults with obsessive-compulsive disorder. Neuroscience & Biobehavioral Reviews 78, S0149763415302797.

Ikeda, E., Stewart, T., Garrett, N., Egli, V., Mandic, S., Hosking, J., Witten, K., Hawley, G., Tautolo, E.S., Rodda, J., 2018. Built environment associates of active school travel in New Zealand children and youth: A systematic meta-analysis using individual participant data. Journal of Transport & Health 9, 117-131.

Krall, S.C., Rottschy, C., Oberwelland, E., Bzdok, D., Fox, P.T., Eickhoff, S.B., Fink, G.R., Konrad, K., 2015. The role of the right temporoparietal junction in attention and social interaction as revealed by ALE meta-analysis. Brain Structure & Function 220, 587-604.

Laird, A.R., Eickhoff, S.B., Kurth, F., Fox, P.M., Uecker, A.M., Turner, J.A., Robinson, J.L., Lancaster, J.L., Fox, P.T., 2009. ALE Meta-Analysis Workflows Via the Brainmap Database: Progress Towards A Probabilistic Functional Brain Atlas. Frontiers in Neuroinformatics 3, 23.

Lancaster, J., Tordesillas-Gutierrez, D., M, Salinas, F., Evans, A., Zilles, K., Mazziotta, J., Fox, P., 2010. Bias between MNI and Talairach coordinates analyzed using the ICBM-152 brain template. Human Brain Mapping 28, 1194-1205.

Liu, J., Yao, L., Zhang, W., Xiao, Y., Liu, L., Gao, X., Shah, C., Li, S., Tao, B., Gong, Q., 2017. Gray matter abnormalities in pediatric autism spectrum disorder: a meta-analysis with signed differential mapping. Eur Child Adolesc Psychiatry 26, 933-945.

McTeague, L.M., Huemer, J., Carreon, D.M., Jiang, Y., Eickhoff, S.B., Etkin, A., 2017. Identification of common neural circuit disruptions in cognitive control across psychiatric disorders. American Journal of Psychiatry 174, 676-685.

Merz, E.C., He, X., Noble, K.G., 2018. Anxiety, depression, impulsivity, and brain structure in children and adolescents. Neuroimage Clinical 20, 243-251.

Nenadic, I., Maitra, R., Langbein, K., Dietzek, M., Lorenz, C., Smesny, S., Reichenbach, J.R., Sauer, H., Gaser, C., 2015. Brain structure in schizophrenia vs. psychotic bipolar I disorder: a VBM study. Schizophrenia research 165, 212-219.

Nooner, K.B., Colcombe, S.J., Tobe, R.H., Mennes, M., Benedict, M.M., Moreno, A.L., Panek, L.J., Brown, S., Zavitz, S.T., Li, Q., 2012. The NKI-Rockland Sample: A Model for Accelerating the Pace of Discovery Science in Psychiatry. Frontiers in Neuroscience 6, 152.

Rogers, J.C., Brito, S.A.D., 2016. Cortical and Subcortical Gray Matter Volume in YouthsWith Conduct

Problems: A Meta-analysis. Jama Psychiatry 73, 64-72.
Salimikhorshidi, G., Douaud, G., Beckmann, C.F., Glasser, M.F., Griffanti, L., Smith, S.M., 2014. Automatic denoising of functional MRI data: combining independent component analysis and hierarchical fusion of classifiers. Neuroimage 90, 449-468.
Satterthwaite, T.D., Elliott, M.A., Gerraty, R.T., Ruparel, K., Loughead, J., Calkins, M.E., Eickhoff, S.B., Hakonarson, H., Gur, R.C., Gur, R.E., 2013. An improved framework for confound regression and filtering for control of motion artifact in the preprocessing of resting-state functional connectivity data. Neuroimage 64, 240-256.
Seitz, J., Herpertz-Dahlmann, B., Konrad, K., 2016. Brain morphological changes in adolescent and adult patients with anorexia nervosa. Journal of Neural Transmission 123, 1-11.
Seo, D.-C., Sa, J., 2010. A meta-analysis of obesity interventions among US minority children. Journal of Adolescent Health 46, 309-323.
Sha, Z., Wager, T.D., Mechelli, A., He, Y., 2019. Common dysfunction of large-scale neurocognitive networks across psychiatric disorders. Biological psychiatry 85, 379-388.
Toro, R., Fox, P.T., Paus, T., 2008. Functional coactivation map of the human brain. Cerebral cortex 18, 2553-2559.
Unicef, 1989. Convention on the Rights of the Child.
Vega, A.D.L., Yarkoni, T., Wager, T.D., Banich, M.T., Vega, A.D.L., Yarkoni, T., Wager, T.D., Banich, M.T., Vega, A.D.L., Yarkoni, T., 2017. Large-scale Meta-analysis Suggests Low Regional Modularity in Lateral Frontal Cortex. Cerebral Cortex, 1-15.
WHO, 2017. Global accelerated action for the health of adolescents (AA-HA!): guidance to support country implementation.
Wong, T.Y., Sid, A., Wensing, T., Eickhoff, S.B., Habel, U., Gur, R.C., Nickl-Jockschat, T., 2019. Neural networks of aggression: ALE meta-analyses on trait and elicited aggression. Brain Structure and Function.
Woo, C.W., Krishnan, A., Wager, T.D., 2014. Cluster-extent based thresholding in fMRI analyses: Pitfalls and recommendations. Neuroimage 91, 412-419.