Common and Distinct Neural Patterns of Attention-Deficit/Hyperactivity Disorder and Borderline Personality Disorder: A Multimodal Functional and Structural Meta-analysis

Nanfang Pan, Song Wang, Kun Qin, Lei Li, Ying Chen, Xun Zhang, Han Lai, Xueling Suo, Yajing Long, Yifan Yu, Shiyu Ji, Joaquim Radua, John A. Sweeney, and Qiyong Gong

ABSTRACT

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) and borderline personality disorder (BPD) have partially overlapping symptom profiles and are highly comorbid in adults. However, whether the behavioral similarities correspond to shared neurobiological substrates is not known.

METHODS: An overlapping meta-analysis of 58 ADHD and 66 BPD whole-brain articles incorporating observations from 3401 adult patients and 3238 healthy participants was performed by seed-based d mapping. Brain maps were subjected to meta-analytic connectivity modeling and data-driven functional decoding analyses to identify associated neural circuit alterations and relations to behavioral dimensions.

RESULTS: Both groups exhibited hypoactivated abnormalities in the left inferior parietal lobule, and altered clusters of the bilateral superior temporal gyrus were disjunctive in ADHD and BPD. No overlapping structural abnormalities were found. Multimodal alterations of ADHD were located in the right putamen and of BPD in the left orbitofrontal cortex.

CONCLUSIONS: The transdiagnostic neural bases of ADHD and BPD in temporoparietal circuitry may underlie overlapping problems of behavioral control, while disorder-specific substrates in frontostriatal circuitry may account for their distinguishing features in motor and emotion domains, respectively.

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Attention-deficit/hyperactivity disorder (ADHD), manifested in clinical features of inattention, hyperactivity, and impulsivity (1), is a common neurodevelopmental disorder persisting into adulthood and impacting 2.5% of adults worldwide (2,3). Borderline personality disorder (BPD) is also characterized by behavioral impulsivity and affective dysregulation that contributes to interpersonal instability and severe stigma (4), with a prevalence of 1.3% in the general population (5). ADHD and BPD frequently co-occur within the adult clinical population and in relatives owing to shared familial and heritable risk factors (6,7). Approximately 38% of BPD cases have comorbid ADHD (8), and the lifetime comorbidity of BPD is 33% among ADHD patients (9). Individuals diagnosed with childhood ADHD are at increased risk for BPD in adulthood (7), and the presence of BPD in individuals with ADHD may lead to unfavorable treatment outcome (10).

Overlapping clinical characteristics of ADHD and BPD consist of impulsive behaviors and emotional instability (11,12). Behavioral disinhibition has been recognized as a shared functional impairment in ADHD and BPD, in which impulsivity is a prominent psychopathological dimension characterized by premature and ill-considered actions in both conditions (8,13). Accordingly, anomalies of prefrontal-striatal activity reflected the neuropathological mechanism of impulsivity domain in ADHD (14,15), and disturbances in prefrontal-parietal circuitry might be responsible for response disinhibition when considering BPD samples (16). The other core area of symptomatic overlap is emotional instability—hasty and inflated alterations in affective states (17), centering on dysfunctional frontoparieto-limbic systems (18,19). Though sharing these similarities, individuals with BPD tend to have trouble controlling emotions related to their inner experience (20), while the affective and motoric hyperreactivity of ADHD patients is often a response to external events (21,22).

A neuroimaging meta-analysis of ADHD has suggested that volumetric reduction of the orbitofrontal and temporal cortices and blunted activation of inferior frontal gyrus (IFG), temporal, and striatal substrates have relevance to impairments in executive functions in adulthood (23,24). In BPD, gray matter reduction and hyperactivation of the amygdala contributed to disturbed emotion processing as a hallmark of BPD (25), coupled with brain abnormalities in the orbitofrontal, dorsal prefrontal, and striatal regions linked to behavioral disinhibition (13,26). Thus, ADHD and BPD may have shared neural substrates apart from those behavioral similarities, indicating a transdiagnostic phenotype following a common
psychopathological pathway (7,27). Individuals with common neural markers may confer high risks for the comorbid condition, and additional attention is warranted to achieve a more effective treatment response in clinical management (11,28).

Identifying their disjunctive neural mechanisms may potentially facilitate differential diagnosis. Regarding insufficient studies investigating their comorbidities and making comparisons directly (8,29,30), a systematic understanding of the conjunctive and disjunctive neural alterations with these disorders remains to be established. Overlapping and comparative meta-analytic approaches offer a promising approach for addressing this issue.

Herein, we performed a multimodal meta-analysis of functional and structural neuroimaging studies to map the common and disorder-specific brain abnormalities in adults with ADHD and BPD (25,31,32). Obtained neural markers were then subjected to meta-analytic connectivity modeling (MACM) and data-driven functional decoding analyses to identify the associated neural circuit alterations and their relation to behavioral dimensions (33,34).

METHODS AND MATERIALS

Literature Selection and Database Construction

Prior to obtaining any dataset, we preregistered our meta-analytic plan on the Open Science Framework (registration doi: 10.17605/OSF.IO/KFZQN). We performed a comprehensive literature search in PubMed, Web of Science, and Embase for whole-brain functional magnetic resonance imaging (fMRI) or voxel-based morphometry (VBM) studies based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria before March 2, 2021 (35). Studies were included in the meta-analysis if they compared adult patients with ADHD or BPD (ages 18–65 years) with healthy individuals on blood oxygen level–dependent signals or gray matter volume (GMV) (details of the search and article eligibility criteria in the Supplemental Methods).

A total of 124 whole-brain articles were included in the current meta-analysis (ADHD-fMRI, 45 articles [proportion of cognitive/emotion experiments = 31/16]; BPD-fMRI, 52 articles [proportion of cognitive/emotion experiments = 19/33]; ADHD-VBM, 14 articles; BPD-VBM, 14 articles; one article reported parallel anatomic and functional findings and three articles enrolling duplicated samples were excluded in further analysis). These articles incorporated eligible observations from 3401 adult patients (ADHD, 1816; BPD, 1585) and 3238 healthy participants (procedures of literature search and included articles in Figure 1 and Table S1). All included studies were evaluated for quality and limitation to infer the importance of these findings with a 12-point Imaging Methodology Quality Assessment Checklist (36) (for details, see the Supplemental Methods).

We extracted peak coordinates for brain functional or structural abnormalities and corresponding t values from those articles. Then, we coded each study with sample size, mean age, and sex ratio, as well as for parameters of scanner (i.e.,

Figure 1. Flowcharts of the literature search and selection criteria for articles on attention-deficit/hyperactivity disorder (ADHD) and borderline personality disorder (BPD) in the meta-analysis. Panel (A) shows the literature search for articles on fMRI, and panel (B) for article on the VBM method. DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; ROI, region of interest; rs-fMRI, resting-state functional magnetic resonance imaging; SBM, surface-based morphometry; VBM, voxel-based morphometry.
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tesla and slice thickness), statistical approach (i.e., kernel smoothing and multiple corrections), and reported clusters. For patient groups, the proportion receiving psychiatric medication and comorbid conditions were recorded. The task and corresponding Research Domain Criteria construct and domain were labeled for included fMRI studies (detailed database construction in the Supplemental Methods and Table S2) (37).

We conducted separate disorder- and modality-specific analyses to obtain conjunctive and comparative findings (38,45). A comparative coordinate-based meta-analytic approach could identify both common and distinct patterns of two disorders, and it has the potential to inform the emergence of diagnostic biomarkers for comorbid conditions (31,46). To avoid the likelihood that the false positive rate is higher than a preferred degree in the worst-case scenario, the SDM adjusts the raw union of probabilities to the desired threshold (45). To threshold the statistical maps of neural abnormalities of ADHD and BPD, we applied the familywise error rate correction with threshold-free cluster enhancement statistics at \( p < .05 \) and cluster size >10 voxels to control for multiple comparisons and obtain robust findings (detailed introduction of SDM-PSI and procedures of overlapping analysis in the Supplemental Methods) (32).

Meta-analytic Connectivity Modeling

Meta-analytic coactivation analysis examines regions that typically are active in prior imaging research with those found to be abnormal in a clinical or psychophysiological study (47,48), allowing for a practical interpretation of the interaction across the whole brain and adding complementary information to task-related and resting-state functional connectivity studies (33,49,50). We delineated the coactivated neural circuits of identified peaks by extracting the peak coordinates and integrated findings of articles that reported activation in the seed regions to yield a convergent coactivation brain map in the Neurosynth package (http://www.neurosynth.org) (51). A 5-mm sphere was created for peaks of the identified clusters to search the candidate coactivated brain regions with the false discovery rate correction \( (p < .01) \) to reduce the false positive connectomes (33). To characterize neural coactivation at the large-scale network level, we overlaid the coactivation patterns into the default mode network (DMN), central executive network (CEN), dorsal attention network, ventral attention network (VAN), somatomotor network, visual network, and cortical affective network (52,53) and calculated the similarity of coactivation patterns to these networks (introduction of Neurosynth and details of MACM and related analysis in the Supplemental Methods) (33).

Functional Decoding

Functional decoding analysis allows for a data-driven understanding to bridge the gap between psychophysiological functioning and MRI-derived brain alterations (54,55). We used Neurosynth to decode the pooled neural anomalies, as it currently contains a large-scale neuroimaging database and encodes articles with interactive psychological terms (54). The Pearson correlation coefficients of psychological terms were calculated between the term-based activation maps and our modeled brain maps (54), and we recorded the terms with the top 10 highest correlation coefficients (55). Furthermore, we gathered the correlation coefficients of five behavioral domains (i.e., action, cognition, emotion, interoception, and perception) derived from a paradigm taxonomy and presented with their relative proportions (56,57) to determine the most prominent behavioral domain related to suprathreshold brain regions (details of functional decoding and behavioral domains in the Supplemental Methods and Table S3).

Ancillary Analyses

We conducted separate disorder- and modality-specific analyses to supplement with overlapping analysis. Meta-regression analysis was employed to examine the potential role of demographic factors and medication status at the whole-brain level (23). Following the main meta-analyses, we extracted the Hedges’ \( g \) imputations for peak coordinates of clusters and performed Spearman’s correlation, Mann-Whitney \( U \), and Kruskal-Wallis \( H \) tests to explore the modulatory effects of confounding variables (57). For fMRI studies, we calculated the contribution of included experiments attributed to each Research Domain Criteria domain for identified clusters based on Hedges’ \( g \) imputations. Additionally, we conducted cognition and emotion subgroup analyses to investigate specific brain functional profiles. Publication bias and between-study heterogeneity were assessed via funnel plots, Egger’s test, and \( I^2 \) statistics (details of ancillary analyses in the Supplemental Methods) (44).

RESULTS

Sample Characteristics

Among 122 eligible studies in the meta-analysis, no statistical difference between patient groups was noted in the sample...
size-weighted t tests in age (fMRI: $t_{df} = 0.510, p = .611$; VBM: $t_{df} = 0.052, p = .969$), but BPD studies consisted of a larger proportion of females than ADHD studies in both modalities (fMRI: $t_{df} = 11.027, p < .001$; VBM: $t_{df} = 5.621, p < .001$). The proportion of medicated patients did not differ by diagnosis ($\chi^2_{df} = 0.020, p = .889$) (Table 1).

### Overlapping Analysis Across Disorders

The overlapping analysis indicated that functional abnormalities of the left inferior parietal lobule (IPL) were conjunctive in ADHD and BPD cases (peak coordinates: $-40, -50, 52; Z = 4.454; k = 23$; shared hypoactivation pattern), and those of the left anterior superior temporal gyrus (STG)/temporal pole (peak coordinates: $-48, -2, -14; Z = 3.688; k = 82$) and right posterior STG (peak coordinates: $52, -38, 18; Z = 4.255; k = 44$) (Table 2 and Figure 2) were disjunctive (reduced response in ADHD but hyperactivation in BPD). The meta-analytic connectivity of the left IPL mainly overlaid on the CEN (% relative distribution [%RD]: 12.13%), the left STG on the DMN (%RD: 15.49%), and the right STG on the VAN (%RD: 10.60%) (Figure 2 ; Table S5). The convergent findings of the left IPL and right STG were predominantly correlated with the action domain (% correlation coefficient: 47.33% and 27.61%, respectively), while the left STG/temporal pole was linked to the cognition domain (% correlation coefficient: 39.82%) (Figure 2; Table S6). No conjunctive or disjunctive brain structural abnormalities were found between ADHD and BPD, though both structural patterns involved a part of the left orbitofrontal cortex (OFC) that had different specific anatomic locations (Table 3).

### Overlapping Analysis Across Modalities

In ADHD, multimodal conjunction analysis revealed that the cluster in the right putamen (peak coordinates: $30, 10, 4; Z = 4.585; k = 145$) exhibited both blunted functional activation and decreased GMV in contrast with control subjects, while those of the left OFC/anterior cingulate cortex (ACC) converged in multimodality in individuals with BPD (peak coordinates: $-4, 34, -10; Z = 4.044; k = 56$) (Table 2 and Figure 3). When overlaying the findings of MACM analysis, the coactivation pattern of the right putamen was largely located in the VAN and that of the left OFC in the DMN (%RD: 11.79% and 23.15%, respectively) (Figure 3; Table S5). The multimodal abnormality of ADHD was predominantly associated with the action domain, while that of BPD was associated with the perception domain (% correlation coefficient: 48.75% and 36.53%, respectively) (Figure 3; Table S6). No disjunctive findings in multimodality were found in either ADHD or BPD.

### Ancillary Analyses

Separate analyses of ADHD cases alone compared with healthy individuals demonstrated hypoactivation in regions including the bilateral IFG/insula/STG, bilateral IPL, left supplementary motor area, right cerebellum, and left OFC and GMV reduction in the right putamen, left OFC, and right supramarginal gyrus (SMG). Patients with BPD exhibited hyperactivation in the bilateral STG, right precuneus, left supramarginal gyrus, and right parahippocampal gyrus/amygdala; reduced activation in left superior parietal lobule/IPL and ventral ACC; and GMV reduction in the left OFC and left middle occipital gyrus relative to control subjects (Table 3). Coactivation patterns in MACM analysis are shown in Table S5 and Figure S1, as anomalies of ADHD mainly coactivated with the CEN, while those of BPD linked with the VAN. Functional decoding analysis revealed that most of the identified clusters of ADHD were primarily associated with the action domain.
while those of BPD were diverse (Table S6 and Figure S2). The top 10 psychophysical terms correlated with those brain abnormalities to infer its main functioning are shown in Table S7, as the left IPL of overlapping analysis predominately correlated with “retention” and “execution,” the left STG correlated with “music” and “speak,” the right STG correlated with “pain” and “listening,” and the right putamen, from distinct multimodal analysis, correlated with “sensation” and “motor” and left OFC with “decision” and “value.”

Meta-regression analysis revealed that sex modulated the neuropathological processing in the right putamen in ADHD and that in the left cerebellum and right ACC in BPD. Additionally, the medication status modulated structural alterations of the right putamen, SMG, and left OFC in ADHD, but no significant clusters were identified in the fMRI modality. In BPD, medication status was associated with structural patterns in the right insula and functional patterns in the left amygdala (details and findings of age in Table S8). The modulatory effects of medication status on brain structural patterns of ADHD and BPD overlapped in the right putamen/insula. Among confounding variables of interests, sex and age played critical roles in identified clusters (20 out of 25 clusters and 7 out of 25 clusters, respectively) (Table S9). The Research Domain Criteria domain of cognitive systems was prevalent in functional profiles of ADHD (all contributions >38%) and in that of negative valence systems in profiles of BPD (all contributions >38%), and the differences of contributions did not reach statistical significance within disorders for any clusters (Table S10). In subgroup analysis for fMRI studies, ADHD samples exhibited hypoactivations in the right cerebellum, bilateral insula, left supplementary motor area, left superior frontal gyrus, right IPL, and right striatum relative to healthy control subjects in the cognition category, while BPD cases showed functional abnormalities in the right parahippocampal gyrus, right STG, right inferior temporal gyrus, and left ACC in the emotion category (Table S11). Interstudy heterogeneity was not significant among all identified clusters according to $I^2$ statistics (all $I^2 < 10\%$) (details and publication bias results in Table S12).

**DISCUSSION**

The current multimodal meta-analysis provides a comprehensive delineation of the similarities and differences in the neural bases of ADHD and BPD in adulthood underlying their shared and distinct clinical features. Following up on overlapping functional patterns centered on the left IPL and bilateral STG, the identified clusters coactivated with the CEN, DMN, and VAN in the large-scale MACM analysis and data-driven functional decoding indicated that these patterns mainly corresponded to the action and cognition domains. Structural abnormalities of both disorders emerged in the left...
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Multimodal Neural Patterns Underlying ADHD and BPD

Table 3. Disorder-Specific Brain Abnormalities of ADHD and BPD

<table>
<thead>
<tr>
<th>Contrast/Brain Region</th>
<th>BA</th>
<th>MNI Coordinates (x, y, z)</th>
<th>Z</th>
<th>p Value</th>
<th>Cluster Size</th>
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<tbody>
<tr>
<td>ADHD vs. HC in fMRI</td>
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<tr>
<td>HC &gt; ADHD</td>
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<tr>
<td>L inferior frontal gyrus/insula/superior temporal gyrus</td>
<td>47/48</td>
<td>-52, 12, 10</td>
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<td>.001</td>
<td>3626</td>
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<td>R inferior frontal gyrus/insula/superior temporal gyrus</td>
<td>38/47/48</td>
<td>32, 18, -2</td>
<td>6.178</td>
<td>.001</td>
<td>2165</td>
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<td>R inferior parietal lobule</td>
<td>39/40</td>
<td>44, -58, 50</td>
<td>5.628</td>
<td>.002</td>
<td>654</td>
</tr>
<tr>
<td>L supplementary motor area</td>
<td>6</td>
<td>-2, 4, 58</td>
<td>5.382</td>
<td>.001</td>
<td>632</td>
</tr>
<tr>
<td>R cerebellum</td>
<td>37</td>
<td>36, -50, -38</td>
<td>4.541</td>
<td>.002</td>
<td>380</td>
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<tr>
<td>L orbitofrontal cortex</td>
<td>10</td>
<td>-38, 58, -2</td>
<td>4.373</td>
<td>.018</td>
<td>80</td>
</tr>
<tr>
<td>L inferior parietal lobule</td>
<td>40</td>
<td>-40, -48, 48</td>
<td>5.110</td>
<td>.012</td>
<td>52</td>
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<tr>
<td>BPD vs. HC in fMRI</td>
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<td>BPD &gt; HC</td>
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<tr>
<td>R superior temporal gyrus</td>
<td>22/24</td>
<td>58, -30, 18</td>
<td>5.475</td>
<td>.001</td>
<td>1386</td>
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<td>L superior/middle temporal gyrus/temporal pole</td>
<td>20/21/38</td>
<td>-46, -22</td>
<td>5.927</td>
<td>.001</td>
<td>1297</td>
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<tr>
<td>R parahippocampal gyrus/amygdala</td>
<td>28/34/36</td>
<td>28, -4, -28</td>
<td>6.293</td>
<td>.001</td>
<td>590</td>
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<tr>
<td>R precuneus</td>
<td>23</td>
<td>16, -68, 26</td>
<td>5.886</td>
<td>.001</td>
<td>164</td>
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<tr>
<td>L superior frontal gyrus</td>
<td>10</td>
<td>-8, 58, 12</td>
<td>5.039</td>
<td>.018</td>
<td>65</td>
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<tr>
<td>HC &gt; BPD</td>
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<tr>
<td>L superior/inferior parietal lobule</td>
<td>7/40</td>
<td>-26, -54, 58</td>
<td>5.469</td>
<td>.001</td>
<td>350</td>
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<tr>
<td>L ventral anterior cingulate cortex</td>
<td>11/25</td>
<td>-6, 32, -6</td>
<td>4.937</td>
<td>.009</td>
<td>160</td>
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<tr>
<td>Cerebellum</td>
<td>-</td>
<td>2, -60, -38</td>
<td>4.592</td>
<td>.042</td>
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<td>ADHD vs. HC in sMRI</td>
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<td>HC &gt; ADHD</td>
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<tr>
<td>R putamen</td>
<td>48</td>
<td>28, 4, 8</td>
<td>5.722</td>
<td>.001</td>
<td>420</td>
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<td>L orbitofrontal cortex</td>
<td>11</td>
<td>0, 46, -26</td>
<td>5.060</td>
<td>.027</td>
<td>57</td>
</tr>
<tr>
<td>R supramarginal gyrus</td>
<td>40</td>
<td>62, -44, 34</td>
<td>4.329</td>
<td>.045</td>
<td>22</td>
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<tr>
<td>BPD vs. HC in sMRI</td>
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<tr>
<td>BPD &gt; HC</td>
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<tr>
<td>L orbitofrontal cortex</td>
<td>11</td>
<td>-6, 40, -14</td>
<td>5.134</td>
<td>.002</td>
<td>540</td>
</tr>
<tr>
<td>L middle occipital gyrus</td>
<td>17/18</td>
<td>-20, -98, 4</td>
<td>5.118</td>
<td>.007</td>
<td>190</td>
</tr>
</tbody>
</table>

Suprathreshold clusters were identified at FWE rate correction with $p_{FWE} < .05$ and cluster size >10 voxels. Breakdown clusters are shown in Table S4.

ADHD, attention-deficit/hyperactivity disorder; BA, Brodmann area; BPD, borderline personality disorder; fMRI, functional magnetic resonance imaging; FWE, familywise error; HC, healthy control; L, left; MNI, Montreal Neurological Institute; R, right; sMRI, structural magnetic resonance imaging.

OFC, yet without shared profiles. The multimodal meta-analysis demonstrated that converging brain functional and structural alterations were located in the right putamen in ADHD and in the left OFC in BPD, with linkage to the VAN and DMN and predominant involvement of the action and perception domains, respectively. These findings shed light on the similarities and divergences of brain alterations associated with ADHD and BPD in multimodal dimensions, which may facilitate mechanistic understanding of the two disorders, provide potential information about the basis for their shared behavioral features, and in the longer term, potentially facilitate differential diagnosis and provide interventional targets for treatment discovery programs.

Common Neural Abnormalities in ADHD and BPD

The overlapping functional abnormality in the left IPL may be responsible for the psychopathological model of the comorbid condition of ADHD and BPD in clinical settings. The prior model was constructed based on the view that behavioral disinhibition derived from alterations in the frontostriatal circuitry and attention deficits were triggered by those in frontoparietal systems (58). However, considering symptomatic overlaps of ADHD and BPD, we rephrased the model given that the reduced activation of the left IPL is linked with deficits in attention (59), which serve as the bases of disinhibitory control and impulsivity in healthy populations, individuals with ADHD, and individuals with BPD (15,25,60,61). As a key node in the CEN (62), the IPL serves as a multidimensional integrator binding cognitive and affective information processing (63,64). Abnormalities of the IPL may indicate the executive network disruption in the neuropathological processing underlying cognitive control and decision making (65). Findings of the left IPL in a transdiagnostic approach may contribute to problems of reduced attentional control and behavioral disinhibition that are associated with both ADHD and BPD (2,15,66).

The overlapping but disjunctive functional patterns in the bilateral STG have relevance to the cognition and action domains, and their coactivated brain regions are largely instantiated in VAN and DMN. A hypoactivated STG/temporal pole in adults with ADHD impinged on cognition as a result of dysfunctional temporal processing (24), and a hyperresponsive
bilateral STG has been linked to impaired cognitive processing (25,67). Specifically, regions of the STG engage in action observation that contributes to regulating motor actions and impulsivity (68–70), and the STG has connections with limbic systems underlying the integration of emotion processing (71). As above, although functional abnormalities of ADHD and BPD overlapped in the STG and were anchored to the cognition and action realms, the inverse activation direction suggests diverse psychopathological mechanisms in the two disorders (72,73). Clarifying the differential behavioral effects of these two patterns of abnormality may represent a promising direction for future studies (74).

Both ADHD and BPD cases exhibited a GMV decrease in the medial OFC that coactivated with the DMN, yielding different locations (the gyrus rectus and part of the ACC, respectively) and functional decoding (interoception and emotion domains). One role of the OFC is to flexibly adjust adaptive behaviors through reward processing to optimize goal-directed action (75,76). For correlated psychophysical terms in Neurosynth, the OFC cluster of ADHD was mainly associated with “craving” and that of BPD with “value” and “decision.” Thus, while the OFC is impacted in both disorders, somewhat different regions are involved with potential differences in behavioral aspect (1,29). The lack of converging structural alterations seems in conflict with the common phenomenon that ADHD co-occurs with BPD (8), regarding the fact that neuroimaging researchers selectively and exclusively enroll ADHD and BPD cases to emphasize case-control differences at the expense of the representativeness (23).

**Distinct Multimodal Abnormalities in ADHD Versus BPD**

The divergent brain functional and structural alterations of ADHD and BPD were located in the right putamen and left OFC/ACC, respectively. The connectivity between the OFC and striatum accounts for reinforcement learning and behavioral flexibility (15,77). Notably, high trait impulsivity, as a transdiagnostic symptom shared by ADHD and BPD, has been associated with decreased functional activation and integrity of myelination in circuitry including the medial OFC/ACC and striatum (78,79). In the MACM analysis, the coactivated spatial pattern of the right putamen for ADHD cases is closely aligned with the VAN, which partially explains their maladaptive cognitive and emotional processing of external stimuli and dysfunctions of inhibitory control in ADHD (65). The coactivated network of the left OFC for BPD individuals was most similar to DMN, which may account for the associated loss of dynamic control for attention reorienting between internal and external events (80). Functional decoding indicated that the cluster of the putamen was anchored on the action domain.
and the OFC on the perception domain. Striatal alterations in individuals with ADHD may contribute to their dysfunction in the bottom-up processing of behavioral control regarding its role in the action realm (31,81), while the abnormal OFC pattern in individuals with BPD underlies their processing emotional events, alexithymia, and integrating emotional experience with adaptive action planning—potentially contributing to their increased risk for impulsive self-injury (82,83). Notably, our disjunctive findings should be interpreted with caution regarding the possibility that differences in task paradigms restricted us from a comprehensive understanding toward neural substrates of ADHD and BPD, and regarding the possibility that those distinct abnormalities would be identified in both disorders as more unbiased evidence emerged.

Disorder-Specific Abnormalities in ADHD and BPD

In functional alteration patterns, individuals with ADHD showed hypoactivation in the bilateral IFG/insula/STG. Psychological functions of the IFG have been generally recognized as a brake on affective processing and behavioral actions (84,85), which is of clinical relevance for the dysfunction of inhibition and executive control in ADHD (86). Among individuals with ADHD and comorbid BPD, microstructural abnormalities of IFG co-occurring with limbic alterations were linked to dysfunctional emotion regulation and other behavioral features (50). In BPD cases, abnormalities were found in the left superior frontal gyrus, superior parietal lobule, and right parahippocampal gyrus/amygdala. Psychological functions of frontal components correspond to top-down cognitive control and emotion regulation, of parietal ones to behavioral integration and social mentalizing, and of limbic substrates to salience detection and emotion processing (15,20). These regions together comprise a fronto-parieto-limbic circuitry that accounts for emotion regulation (19). In addition, patterns of GMV reduction were also found in brain regions of the right putamen and SMG in ADHD and the left middle occipital gyrus in BPD. Given the predominant linkage with the action domain, the SMG contributes to action reprogramming for rapid adaptation to external alterations and to maintaining the memory flow of serial orders (87,88). Apart from relating to visuospatial functioning, the middle occipital gyrus processes the category-selective attention via facial recognition (89). Notably, large-scale mega-analyses revealed that reduced volume of subcortical regions was not found in adults, but rather was found only in children with ADHD compared with typically developing control subjects, suggesting a neuro-pathological model of altered subcortical trajectories (90,91).

Potential Role of Medication Status

The meta-regression analysis revealed that modulated brain structural alterations of ADHD and BPD overlapped in the right putamen/insula pertaining to current medication treatment. The putamen is a potential therapeutic target for ADHD given its role in behavioral inhibition and control (92), and psychotropic treatment was linked to neural responses in the insula in individuals with BPD (93). While individual relation of imaging to particular medications is not possible for a meta-analysis such as ours, these findings highlight the potential value of studying how treatments typically provided to patients with ADHD and patients with BPD may modulate these particular brain regions to reduce behavioral disturbances.

Limitations

First, our findings may not generalize to pediatric or geriatric populations. Because pediatric BPD is not well studied compared with pediatric ADHD, only articles recruiting adult participants were included in the meta-analysis. Second, the representativeness of our transdiagnostic findings might be weakened due to study issues such as differences in sex ratios or differences in the use of emotional and cognitive fMRI task paradigms between the two disorders of interest. Differences in sex ratios of included samples result from different susceptibility of sex populations in community samples (4,94), and various predominant clinical manifestations contribute to biased research interest and differences in task paradigms (6). Adding sex to covariates in the meta-analysis may reconcile the concern, but further studies accounting for the general clinical presentation of those disorders might be of great interest. Finally, data to permit direct association of brain alterations and behavior at the individual level were not available, so we used data-driven approaches to provide suggestive behavioral linkages with our regional brain findings.

Conclusions

The current meta-analysis, to our knowledge, is the first to investigate the multimodal transdiagnostic neural patterns of ADHD and BPD, and it includes data-driven functional decoding and meta-analytic connectivity approaches. Our study depicts a comprehensive presentation of common and distinct neural bases of ADHD and BPD, which indicates shared abnormal patterns in the temporoparietal profile and distinct patterns in frontostriatal circuitry. These findings provide novel transdiagnostic information regarding two psychiatric conditions that share clinical features of behavioral disinhibition and affective reactivity (6). Understanding of the distinct disrupted neurocircuits with each disorder could help establish better pathophysiological models and facilitate differential diagnosis. Further, the transdiagnostic and disorder-specific neural bases of illness have the potential to serve as therapeutic targets in the development of novel treatments for ADHD and BPD, and to better understand mechanisms for their high comorbidity rates and overlapping symptom profiles (92,93), which is one of the goals of psychoradiology (95–98).

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Multimodal Neural Patterns Underlying ADHD and BPD

ARTICLE INFORMATION
From the Huashan MR Research Center (NP, SW, KQ, LL, YC, XZ, HL, XS, YL, YY, SJ), JAS, QG, Department of Radiology, West China Hospital of Sichuan University; Functional and Molecular Imaging Key Laboratory of Sichuan Province (NP, SW, KQ, LL, YC, XZ, HL, XS, YL, YY, SJ), West China Hospital of Sichuan University; and Research Unit of Psychoradiology (NP, SW, KQ, LL, YC, XZ, HL, XS, YL, YY, SJ), Chinese Academy of Medical Sciences, Chengdu; and Department of Radiology (QG), West China Xiamen Hospital of Sichuan University, Xiamen, China; Imaging of Mood- and Anxiety-Related Disorders Group (JR), Institut d’Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain; Department of Psychiatry Studies (JR), Institute of Psychiatry, Psychology, and Neuroscience, King’s College London, London, United Kingdom; and the Department of Psychiatry (JAS), University of Cincinnati, Cincinnati, Ohio.

NP and SW contributed equally to this work as joint first authors.
Address correspondence to Qiyong Gong, M.D., Ph.D., at qiyonggong@hmrc.org.cn, or Song Wang, Ph.D., at wangs_psych@163.com.

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