Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria

Braz J Psychiatry. 2026;48:e20254350
doi:10.47626/1516-4446-2025-4350
Brazilian Psychiatric Association

CC BY

ORIGINAL ARTICLE

Brain functional connectivity and inhibitory control in Tourette syndrome with and without comorbid attention-deficit/hyperactivity disorder

Wenyan **Zhang**,[1,2*] Xianbin **Wang**,[1,2*] Zhongyi **Liu**,[1,2] Anyi **Zhang**,[1,2] Hongna **Li**,[1,2] Qing **Zhao**,[1,2] Zhongliang **Jiang**,[1,2] Jirui **Wang**,[1,2] Kai **Yang**,[1,2] Weiwei **Men**,[3,4] Xu **Hong**,[5] Tianyuan **Lei**,[1,2] Yonghua **Cui**[1,2]

[1]*Department of Psychiatry, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China.* [2]*Laboratory for Clinical Medicine, Capital Medical University, Beijing, China.* [3]*Center for MRI Research, Academy for Advanced Interdisciplinary Studies, Peking University, Beijing, China.* [4]*Beijing City Key Laboratory for Medical Physics and Engineering, Institute of Heavy Ion Physics, School of Physics, Peking University, Beijing, China.* [5]*Cloud Services Innovation Laboratory, Institute of Intelligent Science and Technology, China Electronics Technology Group Corporation, Beijing, China.* * *These authors contributed equally to this work.*

Objective: Tourette syndrome is often comorbid with attention-deficit/hyperactivity disorder and is associated with inhibitory control deficits. However, the differences in whole-brain functional connectivity between Tourette syndrome with and without ADHD and their neural basis for inhibitory control remain unclear. This study examines functional connectivity differences between these groups and their association with inhibitory control.
Methods: We recruited 52 children with Tourette syndrome (30 with Tourette syndrome only and 22 with Tourette syndrome + attention-deficit/hyperactivity disorder) from Beijing Children's Hospital. Resting-state functional magnetic resonance imaging was used to construct individual functional connectivity networks, and inhibitory control was assessed using the Go/No-Go task. Group differences in whole-brain functional connectivity were analyzed using the network-based statistic approach, which identifies connected subnetworks showing significant differences between groups while controlling for multiple comparisons. Multivariate linear regression models were used to examine associations between functional connectivity and inhibitory control, adjusting for comorbid attention-deficit/hyperactivity disorder.
Results: Compared to the Tourette syndrome only group, the Tourette syndrome + attention-deficit/hyperactivity disorder group showed decreased functional connectivity involving the default mode, somatomotor, and limbic networks. In both groups, inhibitory control was positively correlated with functional connectivity, predominantly involving the default mode, frontoparietal, somatomotor, and attention networks. The groups did not differ significantly in functional connectivity related to inhibitory control.
Conclusions: Although differences in functional connectivity were observed between the Tourette syndrome and Tourette syndrome + attention-deficit/hyperactivity disorder groups, both had similar functional connectivity associated with inhibitory control. These findings highlight the neural impact of attention-deficit/hyperactivity disorder in Tourette syndrome and provide insights for future clinical interventions.

Keywords: Tourette syndrome; attention-deficit/hyperactivity disorder; inhibitory control; functional connectivity

Introduction

Tourette syndrome (TS) is a common neurodevelopmental disorder that emerges in childhood, characterized by involuntary motor and vocal tics.[1,2] The lifetime prevalence of any psychiatric comorbidity in individuals with TS is approximately 86%,[3] with attention-deficit/hyperactivity disorder (ADHD) being the most frequent, affecting 60-80% of these individuals.[4] There is a close clinical relationship between TS and ADHD, with evidence of symptom-level interactions between the two conditions.[5] Extensive clinical research has shown that individuals with comorbid ADHD experience significantly greater quality of life impairment that those with TS alone.[6-9]

Correspondence: Yonghua Cui, National Center for Children's Health, Capital Medical University, Beijing Children's Hospital, 56 Nanlishi Road, Beijing, 100101, China.
E-mail: cuiyonghua@bch.com.cn
Submitted May 28 2025, accepted Sep 04 2025.

How to cite this article: Zhang W, Wang X, Liu Z, Zhang A, Li H, Zhao Q, et al. Brain functional connectivity and inhibitory control in Tourette syndrome with and without comorbid attention-deficit/hyperactivity disorder. Braz J Psychiatry. 2025;47:e20254350. Epub 2025 Oct 5. http://doi.org/10.47626/1516-4446-2025-4350

However, the neural mechanisms underlying this increased impairment remain unclear.

Recent advancements in non-invasive functional magnetic resonance imaging (fMRI) have provided valuable tools for investigating the abnormal neural mechanisms underlying TS. Resting-state fMRI measures brain activity without external tasks or stimuli, revealing intrinsic networks based on synchronized spontaneous activity.[10,11] Resting-state brain activity has been shown to reflect task-induced activity patterns.[12-14] Numerous studies have identified widespread functional abnormalities in TS patients across multiple brain regions, particularly within the cortico-striato-thalamo-cortical circuit.[15-18] Research on the functional connectivity (FC) of the brain in individuals with TS comorbid with ADHD remains scarce, with only a few studies addressing FC in this comorbid population. The available studies indicate no significant differences in resting-state FC between TS only and TS + ADHD groups.[19,20] However, task-based fMRI studies using the stop-signal task have found that TS + ADHD children exhibit stronger activation in the right inferior frontal gyrus, left insula, and middle and temporal gyri, particularly during failed inhibition.[21] Moreover, considering the brain's compensatory and coordinated nature, the functional brain networks in TS + ADHD patients should not be viewed as a simple additive effect of the dysfunctions seen in each disorder individually.[22] Instead, the interaction between these two conditions may lead to network reorganization, resulting in more complex FC patterns.[23] Therefore, a detailed comparison of the neural mechanisms underlying TS only and TS + ADHD is crucial for uncovering the underlying neurobiological processes.

Inhibitory control refers to an individual's ability to suppress inappropriate behaviors due to immediate impulses.[24] Individuals with TS typically have impaired inhibitory control, which is considered a key factor in poor regulation of tics.[22] Meta-analytic findings indicate that TS patients generally have mild to moderate deficits in inhibitory control, and this impairment is significantly exacerbated when comorbid with ADHD.[25] However, the neural mechanisms underlying these inhibitory control deficits remain unclear.

Early studies have shown that both TS and ADHD involve dysfunction in the basal ganglia-thalamocortical pathways.[26] However, when the two conditions co-occur, brain function may reorganize, leading to distinct neural mechanisms of inhibitory control compared to TS alone.[23] This interaction may result in more complex brain network changes, engaging different regions. As a result, treatments like deep brain stimulation[27] or repetitive transcranial magnetic stimulation[28,29] may require different targets in patients with comorbid TS and ADHD. Conventional targets used for TS alone may be less effective in the comorbid group. Therefore, investigating the FC differences between TS only and TS + ADHD groups is essential for both clinical treatment and scientific understanding.

To address the above issues, our study explored FC patterns associated with comorbid TS and ADHD. Specifically, we: 1) compared the differences in FC between the TS only group and the TS with ADHD group; and 2) investigated the distributional differences in FC related to inhibitory control between these two groups.

Methods

Participants and clinical information

We recruited 60 patients with TS between March 2023 and September 2024 from Beijing Children's Hospital, Capital Medical University. The inclusion criteria were: 1) a diagnosis of TS according to DSM-5 criteria; 2) age between 6 and 18 years; 3) assessment of psychiatric comorbidities by an experienced child psychiatrist (YC) during clinical interviews based on DSM-5 criteria (those with any psychiatric comorbidities other than ADHD, e.g., autism spectrum disorder, schizophrenia, intellectual disability, obsessive-compulsive disorder, mood disorders, or anxiety disorders were excluded based on these evaluations); 4) no severe physical illnesses; 5) age-appropriate cognitive function (i.e., capable of completing neuropsychological tests); 6) no substance abuse or dependence; and 7) no contraindications to MRI. After data preprocessing, the study included 52 children diagnosed with TS (30 with TS only, 22 with TS + ADHD).

Clinical assessments

All participants completed a Go/No-Go task to measure inhibitory control.[30,31] The Go/No-Go task produced several performance metrics, including correct response time, commission error rate, overall error rate, and omission error rate. Among these, we selected the inverse efficiency score as it provides a stable and comprehensive measure of inhibitory control.[32] The inverse efficiency score was calculated using the following formula:

$$IES = \frac{Mean\ Correct\ Response\ Time}{1 - Commision\ Error\ Rate}$$

Magnetic resonance imaging acquisition

The imaging acquisition protocol included structural MRI and resting-state fMRI sessions, performed on a 3.0-T SIEMENS Prisma scanner with 32-channel head coil (Prisma, Siemens, Germany). The participants were instructed to open their eyes, avoid head movements, remain alert, and refrain from thinking about anything specific during the resting-state fMRI data acquisition. FMRI data were collected using a multiband-accelerated echo-planar imaging sequence to ensure full brain coverage (repetition time = 800 ms, echo time = 30 ms, flip angle = 60°, field of view = 216 × 216 mm^2, 60 slices, 2.4-mm slice thickness, acceleration factor = 6; the total time for this session is 8 min). Additionally, a high-resolution T1-MPRAGE structural image was acquired for coregistration purposes (repetition time =

2,300 ms; echo time = 3.12 ms; flip angle = 7°; field of view = 205 × 205 mm^2, 0.8-mm slice thickness).

Functional magnetic resonance imaging data preprocessing

To ensure data quality and prepare the fMRI data for subsequent analyses, several preprocessing steps were performed using the Data Processing & Analysis for Brain Imaging[33] toolbox. First, the initial 10 time points of each fMRI dataset were discarded to allow for signal stabilization. Next, slice timing correction was applied to compensate for differences in acquisition times across slices within each volume. This was followed by motion correction, where all volumes were realigned to the first volume. The realigned fMRI volumes were then coregistered with the corresponding T1-weighted structural images and normalized to the standard Montreal Neurological Institute space using a unified segmentation algorithm. To enhance the signal-to-noise ratio and account for individual differences in brain anatomy, Gaussian spatial smoothing with a full-width at half-maximum of four mm was applied. Further preprocessing steps included linear detrending to eliminate low-frequency drifts, nuisance signal regression, and temporal filtering with a band-pass filter of 0.01-0.1 Hz to isolate low-frequency fluctuations associated with intrinsic brain activity. Nuisance covariates include Friston's 24 head motion parameters, signals from white matter, cerebrospinal fluid, and whole brain, as well as volumes with excessive motion (framewise displacement > 0.5 mm).[34-36]

In summary, a total of 60 TS patients consented to participate in the study. Three participants did not complete the MRI scan, and five were excluded due to excessive head motion or anatomical abnormalities. To ensure data quality, head motion thresholds were set at < 3 mm of translation and < 3° of rotation. Only participants with a mean framewise displacement < 0.5 mm were retained for analysis, and volumes exceeding this threshold were further censored during nuisance regression to reduce the potential impact of transient motion artifacts.

Construction of functional connectivity networks

After preprocessing, the fMRI data underwent further analysis to extract average time series from regions of interest and estimate FC patterns for each participant. The fMRI data were parcellated into 200 cortical regions using the Schaefer atlas[37] and into 32 subcortical regions based on a separate parcellation scheme proposed by Tian et al.[38] Subsequently, the mean time series were extracted from 232 regions of interest, and pairwise connectivity was computed using Pearson correlation coefficients. Negative values in the correlation matrices were set to zero, as they are generally considered to lack meaningful interpretation in functional brain networks.[39] Subsequently, network sparsity thresholding was applied using a fixed threshold of 0.15, yielding networks that emphasize robust and biologically meaningful connections. The resulting values were then transformed using Fisher's r-to-z transformation, yielding a 232 × 232 connectivity matrix for each participant.

To further summarize the findings, the 200 cortical regions were classified into seven canonical functional networks as defined by Yeo et al.[40]: the visual, somatomotor, dorsal attention, ventral attention, default mode, frontoparietal, and limbic networks.

Statistical methods

Demographic statistics

Continuous variables are reported as means and SD, while categorical variables are presented as counts and percentages of the total. Independent samples *t*-tests or chi-square tests were used to compare demographic and clinical characteristics between the study groups.

Analysis of functional connectivity in brain networks

We employed the network-based statistic (NBS) approach to examine functional brain connectivity networks, using the NBS toolbox MATLAB.[41] This method controls for multiple comparisons and applies permutation testing to assess the significance of connected node subsets.[42] By comparing the size of observed network components to those generated through permutations, NBS determines the statistical significance of the connections, making it well-suited for complex data with small groups.[43] This method controls the family-wise error rate at the cluster level with $p < 0.05$. In our analysis, we selected a threshold *t*-value of 3.5 to compute significantly different connections and reduce false positive results due to random fluctuations.

We conducted three experiments using NBS. First, we applied NBS to analyze the differences in functional brain connectivity networks between the TS only group and the TS + ADHD group. In this model, we controlled for age, sex, and mean framewise displacement (contrast and design matrix: Supplementary Table S1). Second, we tested whether the neural correlates of inhibitory control differed between the TS only and TS + ADHD groups. The models included sex, age, and mean framewise displacement as covariates and incorporated the group × inhibitory control interaction term as a key variable of interest (contrast and design matrix: Supplementary Table S2). Finally, for models that were not significant (indicating no significant difference in the relationship between inhibitory control and FC), we further assessed models without interaction terms (two groups were merged into one group; contrast and design matrix: Supplementary Table S3). Multivariate linear regression models were used to evaluate the relationship between inhibitory control and FC within the NBS framework. The results of the FC analyses were visualized in three-dimensional graphical representations using the BrainNet Viewer toolbox.[44]

Ethics statement

Written consent was obtained from the participants' parents or guardians, and verbal assent was provided

by the participants. The study was approved by the Ethics Committee of Beijing Children's Hospital, Capital Medical University.

Results

Participant characteristics

The demographic and clinical characteristics of the 30 children with TS only and the 22 children with TS + ADHD included in the final analysis are presented in Table 1. Of these, 17 (32.7%) were not taking any medication, while 35 (67.3%) were receiving pharmacological treatment. Specifically, five participants (9.6%) were taking tiapride, 20 (38.5%) were taking aripiprazole, one (1.9%) was taking clonidine, and nine (17.3%) were taking traditional Chinese medicine. No participants were taking psychostimulant medications.

Comparison of network-level functional connectivity between Tourette syndrome only and Tourette syndrome + attention-deficit/hyperactivity disorder groups

The TS + ADHD group had significantly weaker FC than the TS only group within a subnetwork comprising 40 nodes and 47 connections ($p < 0.001$) (Figure 1A). These altered connections predominantly involved the somatomotor, default mode, limbic, and subcortical networks, which together accounted for nearly 90% of the observed differences (Figures 1B and C). The affected network was characterized by long-range within-hemisphere connections between the somatomotor cortex and regions of the limbic system, default network, and prefrontal cortex; interhemispheric connections linking the somatomotor cortex, limbic areas, and contralateral default network regions; and long-range cortico-subcortical connections involving the amygdala and caudate nucleus. These findings indicate disrupted inter-network communication and impaired brain-wide integration rather than isolated within-network dysfunction. The most prominent node-level alterations were located in the right somatomotor cortex, left temporal lobe, left prefrontal cortex, and right parietal lobe. The coordinates of these specific nodes are listed in Supplementary Table S4.

Correlations between functional connectivity and inhibitory control in pure Tourette syndrome and Tourette syndrome + attention-deficit/hyperactivity disorder groups

For inhibition control, we found that comorbidity with ADHD had no significant interaction with FC or inhibition control scores ($p > 0.05$). As shown in Figure 2A, the slopes of the linear fit for FC values in the networks significantly correlated with inhibition control scores and did not differ significantly between TS with and without comorbid ADHD.

Moreover, post-hoc NBS analysis without interaction terms identified a subnetwork in which FC was significantly positively correlated with inhibition control scores ($p = 0.014$). This subnetwork consisted of 54 nodes and 57 edges. The subnetwork predominantly involved the default networks (24.6%), followed by the frontoparietal (15%), somatomotor (14%), and ventral attention (14%) networks, together accounting for approximately 70% of the functional connections associated with inhibitory control scores (Figure 2B). Specifically, this subnetwork was characterized by long-distance front-to-back connectivity between the prefrontal and occipital lobes, as well as long-range connections across the cortex (such as the frontal and temporal lobes) and subcortical regions (basal ganglia, including the nucleus accumbens and putamen) (Figure 2C). The nodes with the greatest number of significant edges included the left lateral prefrontal cortex, the dorsal prefrontal cortex, the medial prefrontal cortex, the right frontal operculum/insula, the right posterior regions, and the left parietal cortex (Figure 2C). The coordinates of the specific nodes are provided in Supplementary Table S5.

Discussion

This study explored FC differences between TS only and TS + ADHD children, as well as the distributional differences in abnormal connectivity related to inhibitory control between the two groups. Overall, compared to the TS only group, the TS + ADHD group had weaker FC, particularly between the somatomotor, default, limbic, and subcortical networks (including basal ganglia regions). However, brain connectivity patterns related to inhibitory

Table 1 Demographic and clinical characteristics

Variable	Pure TS (n=30)	TS + ADHD (n=22)	Group test statistic	p-value
Age (years)	11.30 (1.80)	11.40 (2.10)	t = -0.11	0.91
Sex (male), n (%)	22 (73.3)	18 (81.8)	χ^2 = 0.02	0.90
Inhibitory control score				
Correct response time	395.70 (77.40)	403.20 (47.10)	t = -0.40	0.69
Commission error rate	11.10 (3.80)	11.80 (2.80)	t = -0.70	0.70
Overall error rate	19.30 (7.20)	20.10 (5.70)	t = -0.39	0.49
Omission error rate	8.20 (6.40)	8.10 (6.50)	t = 0.06	0.95
Mean FD	0.18 (0.07)	0.20 (0.09)	t = -0.93	0.36

Data presented as mean (SD), unless otherwise specified.
ADHD = attention-deficit/hyperactivity disorder; FD = framewise displacement; TS = Tourette syndrome.

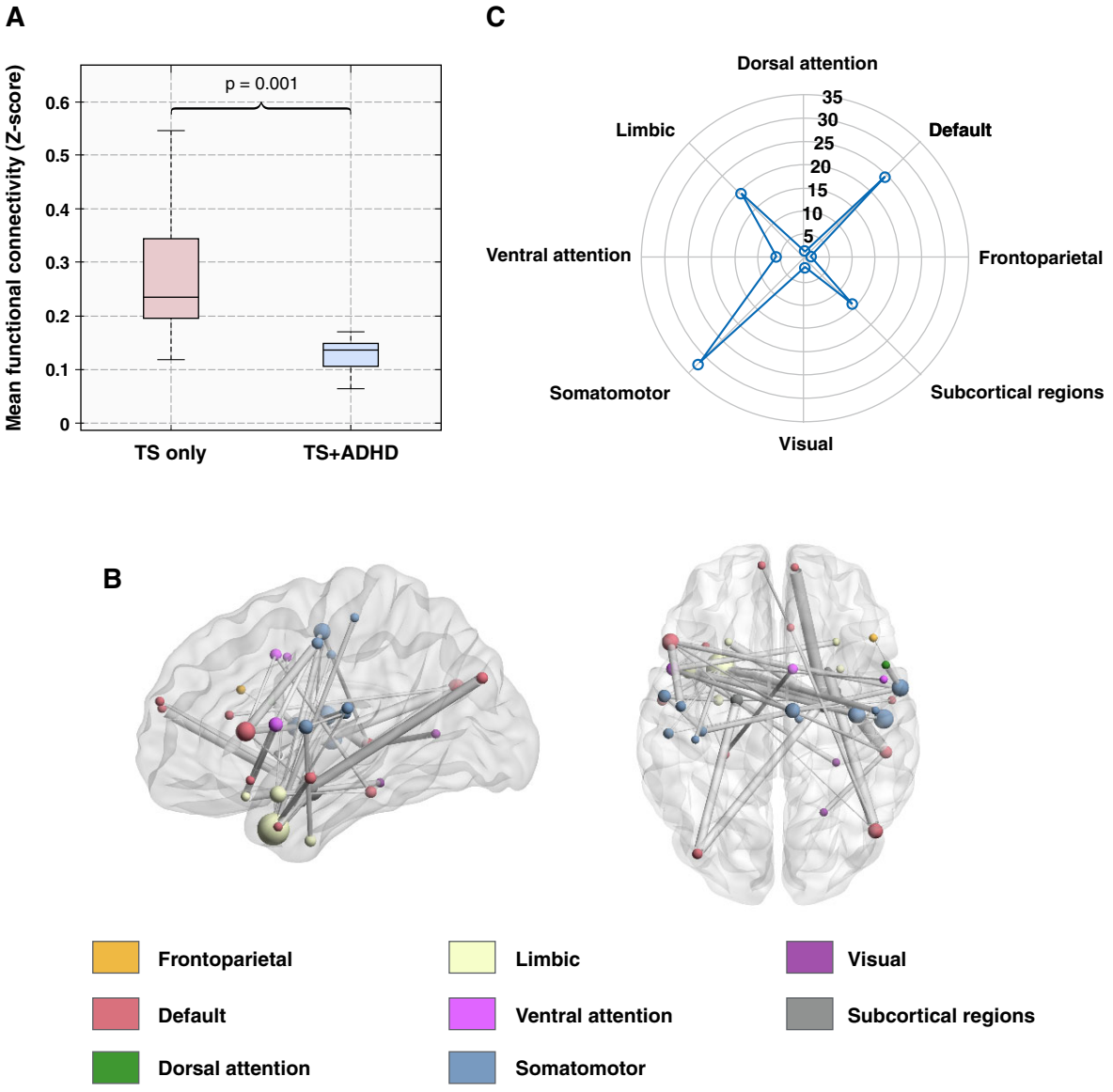


Figure 1 Differences in network-level functional connectivity between pure Tourette syndrome (TS) and TS + attention-deficit/hyperactivity disorder (ADHD) groups. A) Mean functional connectivity differences in significant edges between the TS only and TS + ADHD groups. B) Functional connectivity differences between the TS only and TS + ADHD groups. Functional connectivity was significantly weaker in the TS + ADHD group than the TS only group. Node refers to the number of significant edges connected to that node, while edge refers to the *t*-value of each edge from the statistical analysis. C) Proportion of each functional network involved in the significant edges.

control were similar between the groups, primarily involving the default network, followed by the frontoparietal, somatomotor, and ventral attention networks.

Our findings of reduced FC involving the default mode, somatomotor, and limbic networks in children with TS and comorbid ADHD are consistent with large-scale mega-analyses reporting altered default mode network interactions in ADHD.[45-47] Specifically, these studies highlight disrupted inter-network integration, particularly involving the default mode networks and attention-related networks, as a potential neurobiological signature of attentional dysregulation. While our sample focused on TS-related comorbidity and showed decreased connectivity, large-scale ADHD samples have reported both hypo- and hyperconnectivity, suggesting that connectivity alterations may vary by comorbidity profile, developmental stage, or symptom expression.

We found more pronounced alterations in the limbic and subcortical networks, particularly in the basal ganglia, in the TS + ADHD group, which aligns with the known pathophysiological overlap between the two disorders.[26,48] The basal ganglia, including regions such as the nucleus accumbens and putamen, play a central role in motor control, reward processing, and cognitive functions.[49] Their involvement in both TS and ADHD suggests shared mechanisms within these networks,

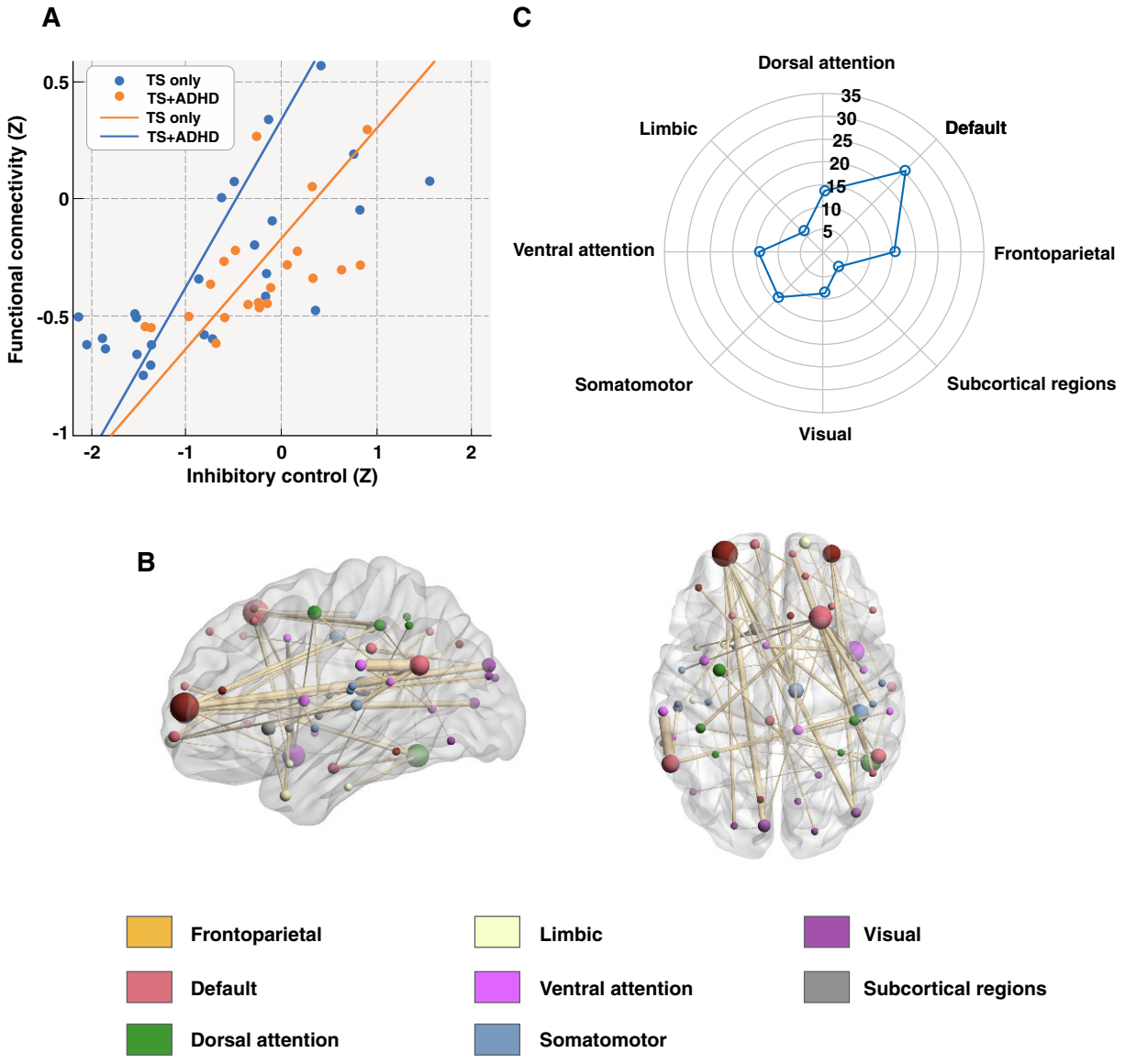


Figure 2 Correlation of functional connectivity with inhibitory control in the Tourette syndrome (TS) only and TS + attention-deficit/hyperactivity disorder (ADHD) groups. A) Linear regression curves of functional connectivity and inhibition control scores for the TS only group and the TS + ADHD group. B) Functional connectivity was significantly correlated with inhibition control. Node refers to the number of significant edges connected to that node, while edge refers to the *t*-value of each edge from the statistical analysis. C) Proportion of each functional network involved in the significant edges related to inhibitory control.

potentially underlying both tic-related symptoms and deficits in attentional regulation.[26,50,51] However, our results contrast with earlier studies that reported no significant FC differences between TS only and TS + ADHD groups.[20] This discrepancy may be due to methodological variations, such as sample size, data preprocessing strategies, or the specific FC measures employed. Furthermore, it is essential to consider the interactive nature of these two disorders. As we hypothesized, the co-occurrence of ADHD in TS may lead to network reorganization, resulting in more complex connectivity patterns than those observed in TS only. This potential reorganization may explain why our TS + ADHD group had altered connectivity in regions traditionally associated with both motor control and cognitive functions, reflecting the intricate interplay between motor and cognitive circuits in ADHD comorbidity.

We also found that the neural deficit patterns in inhibitory control were similar between the TS only and TS + ADHD groups. This suggests that the neural mechanisms underlying inhibitory control in TS patients are fixed, regardless of comorbid ADHD. Specifically, FC deficits primarily occurred in the default networks, followed by the frontoparietal, somatomotor, and ventral attention networks. However, despite FC abnormalities in both TS groups, there were no significant differences in the clinical manifestation of inhibitory control between the TS + ADHD group and the TS only group. This suggests

that comorbid ADHD does not exacerbate inhibitory control deficits. These findings support the hypothesis of ''compensatory activity,'' whereby the brain may reallocate neural resources typically used for task-directed inhibitory control to manage symptomatic behaviors, such as inattention and hyperactivity.[52] As a result, this compensatory neural activity may obscure deficits in inhibitory control, preventing them from manifesting as more pronounced symptoms. Although research on whole-brain resting-state networks related to inhibitory control is limited, a few task-based studies suggest that the prefrontal cortex, particularly in regions involved in the default, frontoparietal, and ventral attention networks, serves as the source of inhibitory control. Abnormal activation in these regions may lead to excessive excitation in motor areas (involved in somatomotor) and subcortical regions, compensating for inhibitory control deficits.[53]

Despite providing valuable insights into the neural mechanisms of inhibitory control, clinical symptoms, and whole-brain FC in the TS only and TS + ADHD groups, several limitations should be acknowledged. First, FC was assessed using resting-state fMRI. Although this method is effective for characterizing intrinsic brain networks, it does not capture task-evoked neural dynamics. Future studies incorporating task-based fMRI could provide a more comprehensive understanding of the functional mechanisms underlying inhibitory control and tic-related symptoms. Second, the study focused exclusively on a pediatric population, without examining potential age-related differences in TS + ADHD comorbidity. Longitudinal studies or research involving adult populations are needed to investigate developmental trajectories and age-specific neural mechanisms. Third, only a single behavioral index of inhibitory control was used. Future research should adopt a multidimensional assessment approach to more comprehensively elucidate the neural correlates of inhibitory control in TS. Fourth, the relatively modest sample size may limit the generalizability and reproducibility of our findings. While the observed effects reached statistical significance, recent large-scale studies (e.g., Marek et al.[54]) have highlighted that findings from smaller neuroimaging samples may be less stable and could overestimate effect sizes. As such, our results should be interpreted with appropriate caution and further validated in future studies with larger, independent cohorts. Fifth, we chose to use the Schaefer atlas because its functionally-defined parcellation enhances functional homogeneity within each parcel, thereby providing a more accurate representation of regional brain activity.[54] Since using a single atlas may introduce some bias, in future work we plan to employ multiple atlases to obtain a more comprehensive and complementary perspective. Sixth, although the participants were not taking central stimulants or other medications with a major impact on brain function, some patients were taking medications to treat tic symptoms, which could have affected brain function. In future studies, medication use should be strictly controlled. Finally, while resting-state fMRI offers a broad overview of functional brain organization, it may not fully capture the complexity of neural regulation. Integrating multimodal neuroimaging techniques, such as structural MRI, diffusion tensor imaging, or electroencephalography, could provide a more complete picture of the relationship between brain structure and function. Additionally, including a healthy control group in future research will help distinguish clinical populations from typically developing individuals.

FC differences were observed between the TS only and TS + ADHD groups. However, both groups showed similar connectivity patterns associated with inhibitory control, suggesting that comorbid ADHD may not substantially alter the FC basis of inhibitory control in TS. These findings contribute to a better understanding of the neurobiological correlates of TS and its comorbidity with ADHD, and can inform future research aimed at developing clinical applications and intervention strategies.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (grant 82171538), the Natural Science Foundation of Beijing Municipality (grant 7244339), the Beijing High-level Public Health Technology Talent Construction Project (no. 2022-2-007), and the Joint Basic-Clinical Laboratory of Pediatric Epilepsy and Cognitive Developmental (3-1-013-03).

The authors would like to thank the participants for completing the study.

Disclosure

The authors report no conflicts of interest.

Data availability statement

The data used during the current study are available from the corresponding author on reasonable request.

Author contributions

WZ: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing.
XW: Conceptualization, Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing.
ZL: Conceptualization, Supervision, Writing – original draft, Writing – review & editing.
AZ: Conceptualization, Data curation, Writing – original draft.
HL: Conceptualization, Data curation, Writing – original draft.
QZ: Writing – original draft, Writing – review & editing.
ZJ: Conceptualization, Data curation, Writing – original draft.
JW: Conceptualization, Data curation, Writing – review & editing.
KY: Conceptualization, Data curation, Writing – review & editing.
WM: Data curation, Methodology, Software.
XH: Data curation, Software.

TL: Conceptualization, Data curation, Writing – original draft, Writing – review & editing.
YC: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing.
All authors have read and approved of the final version to be published.

Handling Editor: Natan Gosmann

References

1 Robertson MM, Eapen V, Singer HS, Martino D, Scharf JM, Paschou P, et al. Gilles de la Tourette syndrome. Nat Rev Dis Primers. 2017;3:16097.
2 Gu Y, Li Y, Cui Y. Correlation between premonitory urges and tic symptoms in a Chinese population with tic disorders. Pediatr Investig. 2020;4:86-90.
3 Brandt V, Essing J, Jakubovski E, Müller-Vahl K. Premonitory urge and tic severity, comorbidities, and quality of life in chronic tic disorders. Mov Disord Clin Pract. 2023;10:922-32.
4 El Malhany N, Gulisano M, Rizzo R, Curatolo P. Tourette syndrome and comorbid ADHD: causes and consequences. Eur J Pediatr. 2015;174:279-88.
5 Zhang W, Jiang Z, Zhang A, Yu L, Wang X, Hong X, et al. Network analysis of Tourette syndrome and attention-deficit/hyperactivity disorder symptoms in children and adolescents. Child Adolesc Psychiatry Ment Health. 2024;18:118.
6 Eddy CM, Cavanna AE, Gulisano M, Agodi A, Barchitta M, Calì P, et al. Clinical correlates of quality of life in Tourette syndrome. Mov Disord. 2011;26:735-8.
7 Conte G, Costanza C, Novelli M, Scarselli V, Arigliani E, Valente F, et al. Comorbidities and disease duration in Tourette syndrome: impact on cognition and quality of life of children. Children (Basel). 2024;11:226.
8 Hu SJ, Li Y, Yang QH, Yang K, Jun JH, Cui YH, et al. Family functioning mediation in tic severity and quality of life for children with Tourette syndrome. World J Psychiatry. 2024;14:1641-51.
9 Li X, Guo Y, Wei S, Chen J, Wu Y. Research progress on the influence of opioids on fetal neurodevelopment during pregnancy. Life Res. 2020;3:68-77.
10 Van Dijk KR, Hedden T, Venkataraman A, Evans KC, Lazar SW, Buckner RL. Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization. J Neurophysiol. 2010;103:297-321.
11 Raimondo L, Oliveira IAF, Heij J, Priovoulos N, Kundu P, Leoni RF, et al. Advances in resting state fMRI acquisitions for functional connectomics. Neuroimage. 2021;243:118503.
12 Smith SM, Fox PT, Miller KL, Glahn DC, Fox PM, Mackay CE, et al. Correspondence of the brain's functional architecture during activation and rest. Proc Natl Acad Sci U S A. 2009;106:13040-5.
13 Wu J, Srinivasan R, Kaur A, Cramer SC. Resting-state cortical connectivity predicts motor skill acquisition. Neuroimage. 2014;91:84-90.
14 Boly M, Balteau E, Schnakers C, Degueldre C, Moonen G, Luxen A, et al. Baseline brain activity fluctuations predict somatosensory perception in humans. Proc Natl Acad Sci U S A. 2007;104:12187-92.
15 Jeppesen SS, Debes NM, Simonsen HJ, Rostrup E, Larsson HB, Skov L. Study of medication-free children with Tourette syndrome do not show imaging abnormalities. Mov Disord. 2014;29:1212-6.
16 Maiquez BM, Sigurdsson HP, Dyke K, Clarke E, McGrath P, Pasche M, et al. Entraining movement-related brain oscillations to suppress tics in Tourette syndrome. Curr Biol. 2020;30:2334-42.e3.
17 Branca C, Bortolato M. The role of neuroactive steroids in tic disorders. Neurosci Biobehav Rev. 2024;160:105637.
18 Wang X, Zhang W, Men W, Hong X, Cui Y, Lei T. Functional connectivity of the precuneus and posterior cingulate cortex moderates the relationship between tic symptoms and premonitory urge in Tourette syndrome. Eur Child Adolesc Psychiatry. 2025.
19 Openneer TJC, Marsman JC, van der Meer D, Forde NJ, Akkermans SEA, Naaijen J, et al. A graph theory study of resting-state functional connectivity in children with Tourette syndrome. Cortex. 2020;126:63-72.
20 Jurgiel J, Miyakoshi M, Dillon A, Piacentini J, Loo SK. Additive and interactive effects of attention-deficit/hyperactivity disorder and tic disorder on brain connectivity. Biol Psychiatry Cogn Neurosci Neuroimaging. 2023;8:1094-102.
21 Openneer TJC, van der Meer D, Marsman JC, Forde NJ, Akkermans SEA, Naaijen J, et al. Impaired response inhibition during a stop-signal task in children with Tourette syndrome is related to ADHD symptoms: a functional magnetic resonance imaging study. World J Biol Psychiatry. 2021;22:350-61.
22 Jackson GM, Draper A, Dyke K, Pépés SE, Jackson SR. Inhibition, disinhibition, and the control of action in Tourette syndrome. Trends Cogn Sci. 2015;19:655-65.
23 Spronk M, Keane BP, Ito T, Kulkarni K, Ji JL, Anticevic A, et al. A whole-brain and cross-diagnostic perspective on functional brain network dysfunction. Cereb Cortex. 2021;31:547-61.
24 Nigg JT. On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. Psychol Bull. 2000;126:220-46.
25 Morand-Beaulieu S, Grot S, Lavoie J, Leclerc JB, Luck D, Lavoie ME. The puzzling question of inhibitory control in Tourette syndrome: A meta-analysis. Neurosci Biobehav Rev. 2017;80:240-62.
26 Sheppard DM, Bradshaw JL, Purcell R, Pantelis C. Tourette's and comorbid syndromes: obsessive compulsive and attention deficit hyperactivity disorder. A common etiology? Clin Psychol Rev. 1999;19:531-52.
27 Martinez-Ramirez D, Jimenez-Shahed J, Leckman JF, Porta M, Servello D, Meng FG, et al. Efficacy and safety of deep brain stimulation in Tourette syndrome: the international Tourette syndrome deep brain stimulation public database and registry. JAMA Neurol. 2018;75:353-9.
28 Hsu CW, Wang LJ, Lin PY. Efficacy of repetitive transcranial magnetic stimulation for Tourette syndrome: A systematic review and meta-analysis. Brain Stimul. 2018;11:1110-8.
29 Ju P, Zhao D, Ma L, Chen J. Biomarker development perspective: Exploring comorbid chronic pain in depression through deep transcranial magnetic stimulation. Journal of Translational Internal Medicine. 2024;12:123-8.
30 Van Royen A, Van Malderen E, Desmet M, Goossens L, Verbeken S, Kemps E. Go or no-go? An assessment of inhibitory control training using the GO/NO-GO task in adolescents. Appetite. 2022;179:106303.
31 Van der Bij J, den Kelder RO, Montagne B, Hagenaars MA. Inhibitory control in trauma-exposed youth: a systematic review. Neurosci Biobehav Rev. 2020;118:451-62.
32 Liesefeld HR, Janczyk M. Combining speed and accuracy to control for speed-accuracy trade-offs(?) Behavior Research Methods. 2019;51:40-60.
33 Yan CG, Wang XD, Zuo XN, Zang YF. DPABI: Data Processing & Analysis for (Resting-State) Brain Imaging. Neuroinformatics. 2016;14:339-51.
34 Chong S, Wang S, Gao T, Yuan K, Han Y, Shi L, et al. Glymphatic function decline as a mediator of core memory-related brain structures atrophy in aging. Journal of Translational Internal Medicine. 2025;13:65-77.
35 Ghaderi S, Mohammadi S. Utility of ultra-high-field magnetic resonance imaging in the detection and management of brain metastases. Med Adv. 2024;2:199-201.
36 Wu Q, Niu Y, Chen D, Lin H, Tan M, Hu Y, et al. Optical coherence tomography angiography features of retinal artery occlusion before and after intra-arterial thrombolysis. Med Adv. 2023;1:115-22.
37 Schaefer A, Kong R, Gordon EM, Laumann TO, Zuo XN, Holmes AJ, et al. Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. Cereb Cortex. 2018;28:3095-114.
38 Tian Y, Margulies DS, Breakspear M, Zalesky A. Topographic organization of the human subcortex unveiled with functional connectivity gradients. Nature Neurosci. 2020;23:1421-32.
39 Murphy K, Fox MD. Towards a consensus regarding global signal regression for resting state functional connectivity MRI. Neuroimage. 2017;154:169-73.
40 Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011;106:1125-65.

41 Zalesky A, Fornito A, Bullmore ET. Network-based statistic: identifying differences in brain networks. Neuroimage. 2010;53:1197-207.
42 Serin E, Zalesky A, Matory A, Walter H, Kruschwitz JD. NBS-Predict: a prediction-based extension of the network-based statistic. Neuroimage. 2021;244:118625.
43 Normand F, Gajwani M, Côté DC, Allard A. NBS-SNI, an extension of the network-based statistic: abnormal functional connections between important structural actors. Netw Neurosci. 2024;8:44-80.
44 Xia M, Wang J, He Y. BrainNet Viewer: a network visualization tool for human brain connectomics. PLoS One. 2013;8:e68910.
45 Norman LJ, Sudre G, Bouyssi-Kobar M, Jiao M, Gligorovic S, Jean J, et al. Cross-sectional mega-analysis of resting-state alterations associated with autism and attention-deficit/hyperactivity disorder in children and adolescents. Nat Mental Health. 2025;3:709-23.
46 Norman LJ, Sudre G, Price J, Shaw P. Subcortico-cortical dysconnectivity in ADHD: a voxel-wise mega-analysis across multiple cohorts. Am J Psychiatry. 2024;181:553-62.
47 Norman LJ, Sudre G, Price J, Shastri GG, Shaw P. Evidence from "big data" for the default-mode hypothesis of ADHD: a mega-analysis of multiple large samples. Neuropsychopharmacology. 2023;48:281-9.
48 Riva D, Taddei M, Bulgheroni S. The neuropsychology of basal ganglia. Eur J Paediatr Neurol. 2018;22:321-6.
49 Graybiel AM. Habits, rituals, and the evaluative brain. Annu Rev Neurosci. 2008;31:359-87.
50 Worbe Y, Malherbe C, Hartmann A, Pélégrini-Issac M, Messé A, Vidailhet M, et al. Functional immaturity of cortico-basal ganglia networks in Gilles de la Tourette syndrome. Brain. 2012;135:1937-46.
51 Senín-Calderón C, Scurtu MC, Ceballos-Munuera C, Perona-Garcelán S, Rodríguez-Testal JF. Cognitive vulnerability to depression or overestimation of premenstrual dysphoric symptoms? Behav Psychol. 2023;31:479-500.
52 Chevrier A, Schachar RJ. BOLD differences normally attributed to inhibitory control predict symptoms, not task-directed inhibitory control in ADHD. J Neurodev Disord. 2020;12:8.
53 Jung J, Jackson SR, Parkinson A, Jackson GM. Cognitive control over motor output in Tourette syndrome. Neurosci Biobehav Rev. 2013;37:1016-25.
54 Chen X, Liao X, Dai Z, Lin Q, Wang Z, Li K, et al. Topological analyses of functional connectomics: A crucial role of global signal removal, brain parcellation, and null models. Hum Brain Mapp. 2018;39:4545-64.