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Clinical symptoms and functional impairment in attention deficit hyperactivity disorder (ADHD) co-morbid tic disorder (TD) patients: a cluster-based investigation

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Abstract

Background Attention deficit hyperactivity disorder (ADHD) and tic disorder (TD) are two common neurodevelopmental disorders that frequently occur in childhood, and these two disorders often coexist. Cluster analysis provides a novel perspective on the heterogeneity of these commonly observed clinical disorders.

Methods We recruited patients with comorbid ADHD and TD from Beijing Children's Hospital between May 2022 and August 2023, collecting data on their symptoms and functional impairments. The number of clusters was determined using the elbow method, and K-means clustering was conducted. Fisher discriminant analysis and silhouette score were used for validation. Additionally, we assessed premonitory urge, strengths, and difficulties among groups. We also collected samples with ADHD alone and performed cluster analyses.

Results The number of clusters for the ADHD comorbid TD sample was determined to be two by the elbow method. The results of the cluster analysis showed that the ADHD comorbid TD sample could be divided into the severe TD group and the severe ADHD group. The severe TD group exhibits more pronounced tic symptoms, yet their age, ADHD symptoms, and functional impairment are all significantly lower than those of the severe ADHD group. Compared to samples with ADHD alone, the distribution of age and functional impairment among individuals does not change with the addition of TD symptoms, maintaining a parallel relationship with the severity of ADHD symptoms.

Conclusion Patients with co-occurring ADHD and TD can be classified into two clusters based on age, symptoms, and functional impairment. In clinical interventions for these patients, while ADHD may require more attention, it is also crucial to identify the core symptoms of the patients. The heterogeneity in clinical symptom presentations highlights the need for individualized treatment approaches.

Keywords Attention deficit hyperactivity disorder, Tic disorder, Cluster, Symptom, Functional impairment

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in childhood, characterized by inattention and hyperactivity/impulsivity, which significantly affect quality of life and functioning [1]. In addition to the core symptoms of inattention and hyperactivity/impulsivity, individuals with ADHD often exhibit a range of associated issues, including conduct and behavioral problems, learning difficulties, and emotional symptoms [2]. Among these, anxiety and depression are the most prevalent emotional comorbidities associated with ADHD [3]. Individuals with ADHD are three times more likely to develop an anxiety disorder compared to those without ADHD [4]. Furthermore, they often demonstrate poorer social skills and experience more learning difficulties [5, 6]. Emotional symptoms frequently co-occur with ADHD and can influence other comorbid conditions; for instance, symptoms such as anxiety and anger can trigger or exacerbate behavioral problems, while depression is often accompanied by various somatic symptoms [7]. Approximately 50% or 20% of individuals with ADHD also have oppositional defiant disorder (ODD) or conduct disorder (CD) [8], which can manifest as strained peer relationships and challenges in adapting to social situations, further worsening functional impairments. Learning difficulties are commonly reported in individuals with ADHD, with estimates indicating that 15% to 50% experience reading difficulties [9] and 5% to 30% face challenges in mathematics [10]. Additionally, these individuals tend to have higher dropout rates and lower attendance rates [11], which has a significant impact on overall functioning.

Tic disorders (TD), like ADHD, are neurodevelopmental disorders characterized by sudden, rapid, repetitive, and uncontrollable vocal and/or motor tics [12]. Individuals with TD often have comorbidities, such as behavioral problems [13, 14], emotional problems [15], premonitory urges (PUs) [16], and ADHD [12]. TD patients may experience emotional problems, mainly due to a sense of shame associated with the condition and its impact on their academic and social lives [17]. Emotional and behavioral problems are often closely related, and some TD patients may experience sudden outbursts of anger [18], which can lead to inappropriate behavior. Research has shown a significantly higher likelihood of violent behavior among young individuals with TD compared to control groups [19]. This highlights the frequent occurrence of emotional and behavioral problems in TD patients.

ADHD is a common psychiatric comorbidity in individuals with TD and has a noticeable impact on them [12]. It has been reported that approximately half of children with TD also have ADHD [20], and about 20% of ADHD patients have TD [21]. When TD coexists with ADHD, the series of behavioral problems, including aggressive behavior, are mainly driven by ADHD [22], and the severity of ADHD is the most prominent factor predicting the impact on the patient's quality of life [23]. Some studies have mentioned a certain overlap in the etiology between ADHD and TD [13], indicating a clear connection and interaction between the two disorders. This highlights the importance of investigating the order of interventions for individuals with comorbidities in clinical interventions. Additionally, a recent study has found that a set of risk genes have a similar effect size in males with Tourette syndrome (TS) and ADHD, which may be one of the reasons why TS and ADHD commonly occur in males.

Although significant progress has been made in the etiological research of ADHD and TD, psychiatric disorders are still considered diseases with unclear etiopathology. It is widely accepted that these disorders result from the combined influence of multiple factors on individuals [24]. Furthermore, due to factors such as sample size, selection of assessment criteria, reproducibility of study findings, and the lack of standardized or unified procedures, etiological research on ADHD and TD is still ongoing, and no universally accepted conclusions have been reached that can be widely generalized [25]. However, the symptom overlap exhibited by individuals with ADHD and TD (e.g., both can lead to emotional or behavioral problems) and the severe functional impairments they experience are well established. This makes it feasible for our study to identify patient subgroups by focusing on individual symptoms and functional impairments. Through the clustering of symptoms and patient subgroups, we aim to identify distinct disease outcome characteristics among the different subgroups, which may then inform tailored interventions to promote better outcomes for individuals.

The research domain criteria (RDoC) is one of the current research hotspots, providing a new approach and classification for addressing the heterogeneity observed in clinical diseases and drawing attention to the exploration of disease subgroups [26]. Cluster analysis is a quantitative statistical tool for identifying disease subtypes, which does not require prior labeling and can directly identify subgroups based on data-driven approaches [27]. Cluster analysis ranks data based on the degree of similarity between data and identifies subgroups with greater commonalities, facilitating a deeper understanding of unique feature combinations within the sample [28]. When applied to patients with ADHD comorbid with TD, cluster analysis can uncover subgroups with shared characteristics and distinct differences beyond diagnostic criteria. This not only enhances our understanding of

subgroup features within ADHD comorbid TD patients but also enables comparisons between subgroups, providing theoretical guidance for clinical interventions. Zhang et al. divided ADHD patients into four groups based on the characteristics of psychopathology and neuropsychology and found different patterns of disease features or impairments among the groups. Through intergroup comparisons, they identified specific executive functions as key intervention targets for ADHD [29]. Additionally, many other studies using different clustering variables have identified differences in various characteristics of ADHD patients, such as cognitive control abilities, reaction time, and these subgroups often cluster into three or four categories [30, 31]. However, previous clustering studies on ADHD and TD have mostly focused on individual disorders, with very few studies on clustering and research specific to the ADHD co-morbid TD.

This study employed clustering analysis on patients with comorbid ADHD and TD. The clustering was based on age, the common symptoms/issues, and functional impairments discussed earlier in relation to ADHD and TD. The aim of this study is to explore the heterogeneity within samples of ADHD comorbid with TD through cluster analysis and to discuss whether functional impairments are associated with specific disorders or symptoms, providing a theoretical reference for clinical interventions. Additionally, while existing studies primarily focus on separate disorders, this study serves as a supplementary exploration of cluster analysis in ADHD comorbid with TD samples.

Methods

Participants

All participants in this study were children and adolescents who sought medical attention at Beijing Children's Hospital from May 2022 to August 2023. Inclusion criteria: (1) met the DSM-5 diagnostic criteria for ADHD and TD and were diagnosed with ADHD and TD after evaluation by a clinician at or above the attending physician level; (2) aged between 5 and 17 years; (3) newly diagnosed with ADHD and TD, with no prior medication use; (4) patients and their guardians provided informed consent and signed a written informed consent form. Exclusion criteria: (1) presence of other psychiatric disorders or intellectual disabilities; (2) significant physical illnesses that could potentially affect the study results. Ultimately, a total of 2,019 participants with comorbid ADHD and TD (sample 1) were included in this study. All physicians involved in the diagnostic process underwent consistency training on diagnostic criteria before the start of this study to ensure uniformity of diagnostic standards and accuracy of diagnoses.

Additionally, we collected a sample of individuals with ADHD alone (sample 2). Inclusion criteria for this sample included meeting the diagnostic criteria for ADHD according to DSM-5 and being newly diagnosed with ADHD. The remaining inclusion and exclusion criteria were consistent with those for the sample with comorbid ADHD and TD. Ultimately, we collected data from 5,519 individuals with ADHD alone. Due to space limitations, the analysis results for this sample are included in the supplementary material.

This study has been approved by the Ethics Committee of Beijing Children's Hospital, China.

Measures-comorbid ADHD and TD sample

Conners Parent Symptom Questionnaire (PSQ): The PSQ [32] is a parent-rated questionnaire used to collect data on participants' ADHD symptoms. It consists of 48 items that can be grouped into 6 dimensions: character problems, psychosomatic problems, anxiety problems, hyperactivity/impulsiveness, learning problems, and hyperactivity index. Higher scores in each dimension indicate more severe problems in that area. The hyperactivity index dimension assesses the severity of ADHD symptoms and overlaps with the other five dimensions in scoring items, so it was not included in the subsequent clustering analysis. The Chinese version of the PSQ has a Cronbach's alpha of 0.92 [33].

The Yale Global Tic Severity Scale (YGTSS): The YGTSS is a clinician-rated tool used to assess the frequency, intensity, complexity, and other characteristics of vocal and motor tics in individuals with tic disorder. The maximum score for tic severity is 50 (25 for vocal tics and 25 for motor tics), with higher scores indicating more severe tics. In this study, motor tics, vocal tics, and total tic scores were utilized as variables for cluster analysis. The scale has demonstrated good reliability in previous measurements within Chinese samples, with a Cronbach's alpha of 0.91 [34].

Weiss Functional Impairment Rating Scales (WFIRS): The WFIRS is a parent-rated questionnaire used to assess functional impairments in patients. It comprises 50 items that evaluate functional impairments across six dimensions: family, social activities, school, self-management, life skills, and adventure activities. Higher scores indicate more severe functional impairments within each dimension. The WFIRS has demonstrated good reliability and validity [35]. In this study, the Cronbach's alpha for the two samples was 0.94 and 0.92, respectively.

Premonitory Urge for Tics Scale (PUTS): The PUTS is used to assess the premonitory urges in individuals with tic disorder. This self-report questionnaire consists of 9 items, each rated on a four-point scale. The scores are summed to obtain a total score, with higher scores

indicating a greater level of premonitory urges. The scale has demonstrated good reliability and validity [36]. Our team has also validated its measurement properties in a previous study involving Chinese samples [34]. In the present study, the Cronbach's alpha for sample 2 was 0.78.

Strengths and Difficulties Questionnaire (SDQ): The SDQ (parent form) [37] was utilized to investigate the difficulties and social support experienced by patients. The SDQ consists of 25 items and can be divided into 5 dimensions (hyperactivity, peer, emotional, conduct, and prosocial) or 2 dimensions (difficulties and social support). Higher scores in the prosocial dimension indicate a higher level of patient engagement in social activities. In this study, the analysis of clustering results was conducted using the difficulties and social support dimensions. The questionnaire has demonstrated good reliability and validity [37]. The Cronbach's alpha for the two samples in this study were 0.74 and 0.71, respectively.

For YGTSS, assessment is conducted by two mental health professionals. They underwent standardized training prior to the assessment to ensure consistency in evaluations. The intraclass correlation coefficient (ICC) calculation yielded a value greater than 0.75, indicating good reliability [38]. The PSQ, WFIRS, and SDQ assessments are completed by the participants' fathers or mothers, while the PUTS assessment is conducted independently by the participants. If there are any questions regarding the items, the two aforementioned mental health professionals provide clarification without influencing the selection results.

Measures-sample with ADHD alone

The ADHD sample was assessed using the PSQ and the WFIRS. As both the PSQ and WFIRS have been previously described, their details will not be reiterated here.

Procedure and analysis

First, before data analysis, the data from both samples were standardized using z-score transformation [39]. These standardized data were then utilized for all subsequent analyses. Collinearity checks were performed on the independent variables of both samples, revealing that the variance inflation factor (VIF) for all variables was below 3, indicating no collinearity among the independent variables. Thus, subsequent analyses could be conducted.

Second, K-means clustering analyses were performed separately on each sample using age, symptom dimensions (5 dimensions of PSQ and 3 dimensions of YGTSS for sample 1; 5 dimensions of PSQ for sample 2), and functional impairment as categorical variables. K-means clustering is a widely used method in cluster analysis [40]. As an unsupervised machine learning technique, it identifies homogeneous subgroups within unlabeled data based on input features, minimizing within-cluster variation to achieve data classification [41]. Prior to clustering, we used the elbow method [42] to determine the optimal number of clusters for both samples, which was found to be 2 (Figure S1 and Figure S2). The elbow method calculates the sum of squared errors (SSE) within different clusters, identifying the optimal number of clusters as the point where the decrease in SSE begins to slow [43]. Between-group comparisons were then conducted. Sample 1 achieved convergence after 11 iterations, while sample 2 achieved convergence after 19 iterations.

We also performed Fisher discriminant analysis [29] on the clustering results and calculated the silhouette score [44] as well as the SDQ and PUTS scores for each cluster to validate the effectiveness of our clustering from both statistical and clinical perspectives. Fisher discriminant analysis reduces the dimensionality of data by maximizing inter-class differences and minimizing intra-class differences. In addition to providing classification results, it can also calculate the proportion of samples classified identically to their original labels [45]. The silhouette score measures the similarity of a data point to its own cluster compared to other clusters, ultimately providing an index for assessing cluster compactness and separation. A higher silhouette score indicates better clustering performance for the corresponding number of clusters [46]. In this study, the optimal number of clusters determined by the silhouette score was consistent with that determined using the elbow method.

Between-group comparisons were conducted using chi-square tests and t-tests. The specific process is illustrated in Fig. 1.

The elbow method was implemented using R version 4.2.2. Clustering and data analysis were conducted using SPSS 26.0 and R version 4.2.2, while graphs were generated with GraphPad Prism 9.

Results

General information

Sample 1 (patients comorbid ADHD and TD) included a total of 2,019 participants, while sample 2 (patients with ADHD only) comprised 5,519 participants. In sample 1, 82.4% ($n=1,664$) were male and 17.6% ($n=355$) were female, with an average age (*SD*) of 8.71 (2.07) years. In sample 2, 75.9% ($n=4,191$) were male and 29.1% ($n=1,328$) were female, with an average age (*SD*) of 8.95 (2.42) years.

Clustering results

Sample 1 comprised 2,019 cases, and after clustering, the sample sizes for the two clusters were 1,140 and 879,

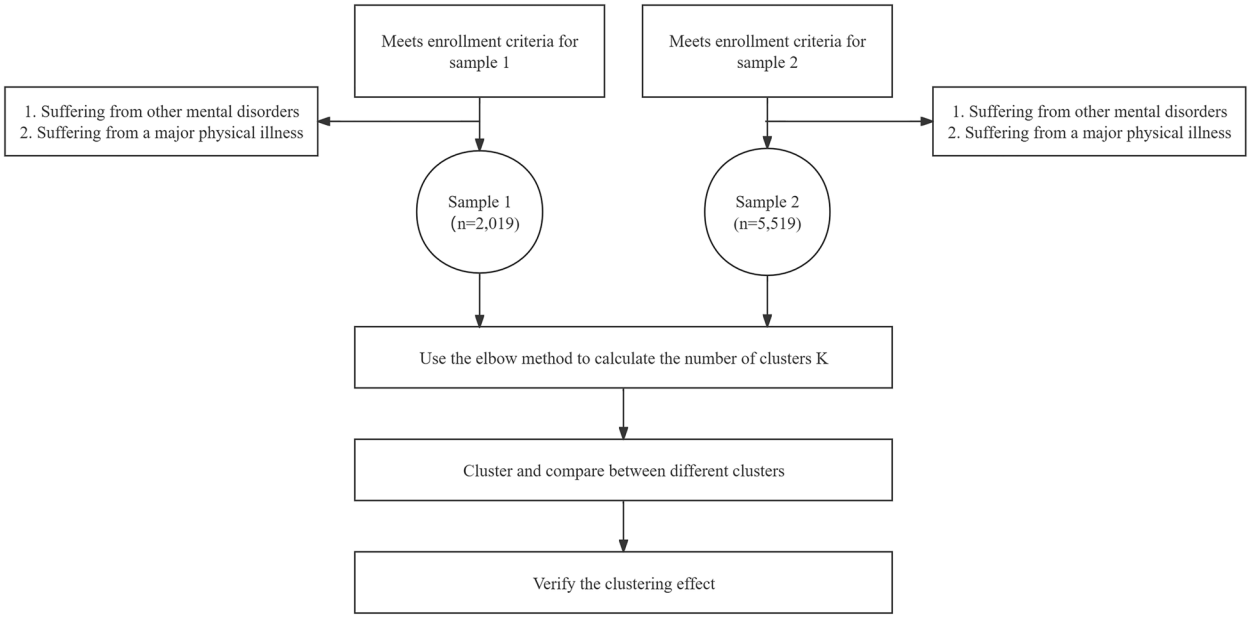

Fig. 1 Process of the research. Note: sample 1 represents ADHD co-morbid TD samples, sample 2 represents ADHD alone samples. In Sample 1, the clustering variables were age, symptoms (PSQ, YGTSS), and functional impairment (WFIRS); in Sample 2, the clustering variables were age, symptoms (PSQ), and functional impairment (WFIRS). In "Verify the clustering effect," both Sample 1 and Sample 2 underwent Fisher discriminant analysis. Additionally, Sample 1 included the calculation of silhouette score and a comparison of SDQ and PUTS differences between clusters

respectively. Sample 2 included 5,519 cases, the sample sizes after clustering were 2,317 and 3,202, respectively. Using Fisher discriminant analysis, the classification accuracy of sample 1 and sample 2 was 95.3% and 95.7% (Table S1 and Table S2), indicating a good level of classification. In sample 1, the z-scores for age, symptoms, and functional impairment of the two clusters can be seen in Fig. 2. Based on age, symptoms, and functional impairment, the clusters can be categorized as follows: severe TD group (cluster 1) and severe ADHD group (cluster 2). The severe TD group had the most severe TD symptoms, and the severe ADHD group exhibited the most severe ADHD symptoms and the highest level of functional impairment. In addition, the age of the severe ADHD group was significantly higher than that of the severe TD group. In sample 2, the clusters were categorized as follows: severe impairment group (cluster 1) and mild impairment group (cluster 2). The cluster with higher age and more symptoms also showed more functional impairment (Figure S3).

Demographic information between groups

In sample 1, the average age (*SD*) for the two clusters was 8.44 years (1.935) and 9.07 years (2.182), respectively, and in sample 2 was 9.33 years (2.473) and 8.67 years (2.345). Regarding gender distribution, in sample 1, cluster 1 includes 916 males and 224 females, while cluster 2 comprises 748 males and 131 females. Chi-square testing revealed a significant difference in gender distribution between these groups ($\chi^2 = 7.714$, $p = 0.005$). In sample 2, cluster 1 includes 1,761 males and 556 females, and cluster 2 has 2,430 males and 772 females. Chi-square testing indicated no significant difference in gender distribution between these groups ($\chi^2 = 0.009$, $p = 0.923$).

Comparison of symptoms and functional impairment between groups

In sample 1, we found that the severe TD group (cluster 1) had the highest scores for TD symptoms but had low scores for ADHD symptoms. On the other hand, the severe ADHD group (cluster 2) had the highest scores for ADHD symptoms and functional impairment but low scores for TD symptoms. The differences between the clusters were statistically significant (Table 1).

We also calculated the symptom and functional impairment scores for the two groups in sample 2 and conducted intergroup comparisons. The symptom and functional impairment scores showed a stepwise distribution, with cluster 1 (severe impairment group) having higher scores and age than cluster 2 (mild impairment group, Table S3).

Validation of clustering results

We calculated the silhouette scores for the number of clusters ranging from 1 to 10 in sample 1 and found that the highest silhouette score occurs when the number of

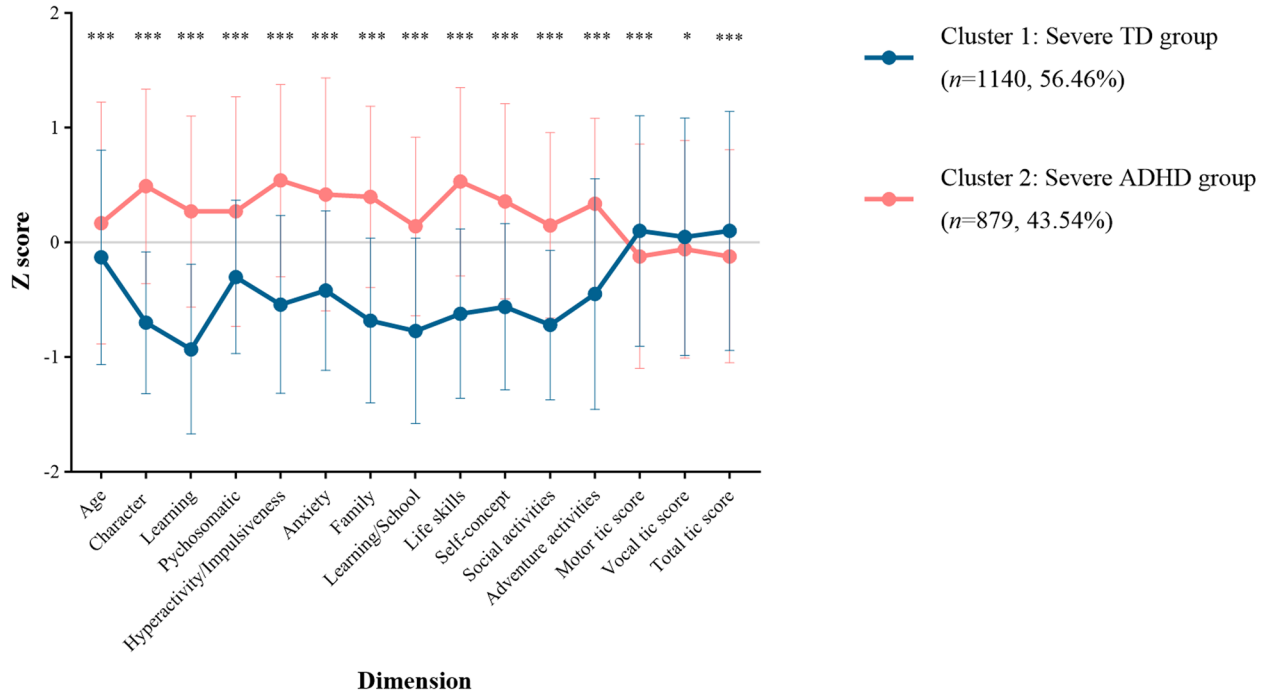

Fig. 2 Z Scores for age, symptoms and functional impairment in ADHD co-morbid TD sample. Note: The horizontal axis represents all dimensions of the clustering variables, while the vertical axis represents the Z-scores of each variable. The asterisks on each dimension represent the results of the comparison of the differences between the two groups, *** represents $p < 0.001$, ** represents $0.001 \leq p < 0.01$, and * represents $0.01 \leq p < 0.05$

Table 1 Comparison of symptoms and functional impairment in two clusters of ADHD co-morbid TD sample

Item	Dimension	Cluster 1: Severe TD group $n = 1,140$		Cluster 2: Severe ADHD group $n = 879$		*t*	*p*	*Cohen'd*
		Mean	*SD*	*Mean*	*SD*			
Age	/	-0.13	0.935	**0.17**	1.054	-6.79	**< 0.001**	-0.31
Conners Z score	Character	-0.70	0.618	**0.49**	0.848	-34.87	**< 0.001**	-1.63
	Learning	-0.93	0.740	**0.27**	0.833	-33.56	**< 0.001**	-1.53
	Pychosomatic	-0.30	0.667	**0.27**	1.002	-14.60	**< 0.001**	-0.69
	Hyperactivity/Impulsiveness	-0.54	0.774	**0.54**	0.840	-29.85	**< 0.001**	-1.34
	Anxiety	-0.42	0.694	**0.42**	1.014	-21.12	**< 0.001**	-0.99
WFRIS Z score	Family	-0.68	0.718	**0.40**	0.790	-31.68	**< 0.001**	-1.44
	Learning/ School	-0.77	0.808	**0.14**	0.779	-25.34	**< 0.001**	-1.14
	Life skills	-0.62	0.738	**0.53**	0.821	-32.64	**< 0.001**	-1.49
	Self-concept	-0.56	0.724	**0.36**	0.851	-25.79	**< 0.001**	-1.18
	Social activities	-0.72	0.652	**0.15**	0.807	-26.12	**< 0.001**	-1.20
	Adventure activities	-0.45	1.005	**0.34**	0.740	-20.48	**< 0.001**	-0.88
YGTSS Z score	Motor tic score	**0.10**	1.006	-0.12	0.979	4.90	**< 0.001**	0.22
	Vocal tic score	**0.05**	1.036	-0.06	0.949	2.54	**0.011**	0.11
	Total tic score	**0.10**	1.043	-0.12	0.928	4.98	**< 0.001**	0.22

The table shows the Z-scores for each variable for the two clusters in sample 1, as well as the results of the between-group comparisons. In two clusters, larger mean values (with significant differences) and significant p-values are highlighted in bold

clusters is 2 (Figure S4). In addition, we also compared the scores of the PUTS and SDQ in sample 1. We found no significant differences among the two groups in terms of PUTS. In the analysis of the two dimensions of SDQ, the severe ADHD group had higher scores on the difficulty dimension than the severe TD group and lower scores on the social support dimension than the severe TD group (Table 2), which is consistent with our clustering results showing the same trend.

Discussion

Compared with previous studies, this research focuses on age and outcomes resulting from the disorder (symptoms and functional impairment), adding to the clustering study findings on patients with ADHD comorbid with TD. This study identified clusters within the patients with comorbid ADHD and TD (sample 1) based on their age, symptoms, and functional impairment. It also compared the age, symptoms, and functional impairment of each cluster. Additionally, we compared the PUs and SDQ scores among the clusters in sample 1. The cluster analysis divided the sample into two subgroups: the severe TD group (cluster 1) and the severe ADHD group (cluster 2).

We found that in sample 1, although the severe TD group exhibited greater severity in vocal tics, motor tics, and overall tic levels, the functional impairment of the severe TD group was less pronounced than that of the severe ADHD group. This finding aligns with previous research on electroencephalography (EEG) in ADHD and TD patients, which suggests that when ADHD and TD coexist, ADHD is the primary factor contributing to individual functional impairment [47]. Many other studies investigating the comorbidity of ADHD and TD have also found that patients with comorbid ADHD and TD experience greater cognitive deficits compared to those with isolated TD [48]. This situation may be attributed to the slower information processing speed observed in ADHD patients, which is indicative of poorer behavioral functioning [49, 50] and leads to more peer-related issues [51].

We also found that the severe ADHD group was older than the severe TD group, which may be related to the greater functional impairment observed in this group. Previous studies have indicated that ADHD symptoms in older children are more likely to be overlooked [52]; for instance, parents might think, "My child is just inattentive or mischievous, not ill." In contrast, TD symptoms may be recognized by parents earlier, as they may wonder, "Why is my child making strange movements or expressions?" Additionally, as individuals age, their social roles and identities become more complex, leading to a more diverse impact of ADHD on functioning [53]. This multifaceted impact may lead to greater functional impairments, as highlighted in previous studies. With increasing age, issues such as disruptive behavior, poor social skills, and learning difficulties may progressively emerge [54]. This also supports our findings, indicating that compared to the severe TD group, the severe ADHD group not only has older patients but also exhibits more severe functional impairments. Age may exacerbate the impact of ADHD on individual functioning, which is a valuable discovery. At the same time, it is important to note that, given the minimal differences in TD symptoms and the driving effects of ADHD symptoms and age, the effect size of TD symptoms in the cluster analysis may be limited. This finding aligns with our earlier observations that ADHD serves as the primary driver of functional impairments in ADHD comorbid TD samples. However, this hypothesis requires further validation in future studies, such as using samples with greater variability in TD symptoms.

Compared to sample 2, the inclusion of TD symptoms did not significantly affect the clustering results, and the degree of functional impairment remained consistent with the severity of ADHD symptoms. However, some studies have suggested that the presence of TD symptoms in ADHD patients may have a minimal impact on individual functioning, whereas the emergence of ADHD symptoms in TD patients can severely affect functioning and potentially lead to more psychopathological issues

Table 2 Comparison of PUTS and SDQ scores among the two groups in the ADHD co-morbid TD sample

Item	Dimension	Cluster 1: Severe TD group *n* = 1,140		Cluster 2: Severe ADHD group *n* = 879		*t*	*p*	*Cohen's d*
		Mean	*SD*	*Mean*	*SD*			
PUTS Z score	/	0.01	1.014	-0.01	0.983	0.353	0.724	0.02
SDQ Z score	Difficulty	-0.49	0.807	**0.44**	0.936	-23.59	**< 0.001**	-1.08
	Social support	**0.21**	0.935	-0.17	0.947	9.055	**< 0.001**	0.41

The table shows the Z-scores of PUTS and SDQ for the two clusters in sample 1, as well as the results of the between-group comparisons. In two clusters, larger mean values (with significant differences) and significant p-values are highlighted in bold

[55–57]. Combining these findings, we believe that when intervening with patients who have both ADHD and TD, assessing the core symptoms should be a primary focus, as the expression of these symptoms may vary significantly among these patients. Based on our findings, we suggest prioritizing interventions targeting ADHD symptoms in patients with ADHD comorbid with TD when ADHD symptoms are prominent. Patients with comorbid ADHD and TD often experience significant functional impairments. Therefore, we recommend a multimodal intervention approach that includes pharmacological treatment, psychotherapy, behavioral therapy, and family support [58]. It is worth noting that some studies have reported a transient increase in tics with the use of central stimulants, making atomoxetine a potentially viable option. Atomoxetine may improve ADHD symptoms and, in turn, positively influence TD symptoms [59]. When TD symptoms are more prominent or are perceived by patients as their primary concern, we recommend addressing TD symptoms while concurrently treating ADHD symptoms to achieve better overall functional outcomes. In such cases, CBT (cognitive-behavioral therapy) may be a feasible choice, as its efficacy in treating TD is less influenced by the presence of ADHD symptoms [60]. It is important to emphasize that while our findings provide theoretical support for clinical interventions, the progression of mental disorders may sometimes deviate from theoretical expectations. Therefore, clinicians should adhere to a key principle of psychiatric treatment: individualized treatment.

In patients with comorbid ADHD and TD (sample 1), there was no significant difference in PUs among the two groups, which was within our expectations. Although some studies suggest that PUs often precede tics, PUs may be distinct symptoms from tics, and existing meta-analytic results show a low correlation between PUs and tic severity [61]. We also found that the severe ADHD group exhibited more difficulties and lower social support, which further validates the effectiveness of our clustering, as this group demonstrated greater functional impairment.

Our study utilized a clustering approach based on symptoms and functional impairment, providing new subgroups for two distinct samples. Additionally, we considered the co-occurrence of ADHD and TD within the sample analyses, providing a theoretical basis for clinical diagnostic prioritization and serving as a strong complement to previous research. However, our study still has certain limitations. Firstly, our study data are entirely derived from parent-completed questionnaires, which inevitably introduces recall bias, potentially affecting the survey results. Subjectivity is also a factor that can affect the accuracy of report results. Parents may provide different perspectives on various questions or symptoms based on their personal judgment. Additionally, parents can only observe their child's behavior at home, so reports on behavior in school or social settings may be inaccurate. Parent–child relationships, personal values, and other factors may also influence the accuracy of the parent's report. Secondly, this study is a cross-sectional study, which limits our ability to determine causal relationships and dynamic changes between variables. In cluster analysis, the dynamic changes of variables can help us observe the trend of each clustering variable, thereby allowing for a more accurate assessment of the differences between subgroups and the effects of variables. Additionally, cross-sectional surveys may suffer from selection bias related to the chosen time point, as the selected time or period may not fully represent the entire population. Thirdly, this study included only symptoms and individual functional impairments as disease characteristics for clustering, which may limit the comprehensiveness of the clustering results. Fourthly, in our sample, the number of males exceeds that of females. This imbalance in the sample may potentially influence the clustering results, thereby affecting the interpretation of the findings. Fifthly, because the hyperactivity index items in the PSQ overlap with those of other dimensions, this dimension was excluded from the clustering analysis. This presents a limitation in our study: the assessment of ADHD symptoms was not comprehensive, potentially overlooking certain inattention symptoms. To address this issue, future research should employ more detailed assessment tools for ADHD, such as the SNAP-IV (Swanson, Nolan, and Pelham Rating Scale-IV), to better elucidate the role of ADHD in comorbid samples. Moreover, balancing the sex ratio and conducting longitudinal studies can help us validate the dynamic changes between variables, as well as better identify changes between clustering subgroups and clarify the effects of variables in subgroup differences. In longitudinal design, it is important to consider the disease progression and the difficulty and benefits of information collection, with designs for both short-term and long-term time points, such as collecting data at 1 month, 3 months, 6 months, and 1 year after the onset of the disease. Finally, incorporating more objective characteristics of ADHD and TD, such as EEG, fMRI results, and hematological markers, should be incorporated to overcome the limitations associated with relying solely on scale-based evaluations and enhance the clustering analysis, yielding more comprehensive subgrouping results.

Conclusion

Patients with co-occurring ADHD and TD can be classified into two clusters based on age, symptoms, and functional impairment. In clinical interventions for these patients, while ADHD may require more attention, it is also crucial to identify the core symptoms of the patients. The heterogeneity in clinical symptom presentations highlights the need for individualized treatment approaches.

Supplementary Information

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Supplementary Materia 1.

Supplementary Material 2.

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Authors' contributions
Zhongliang Jiang was responsible for data collection, data analysis, data interpretation, conceptualisation, visualisation, writing—original draft and writing—editing. Hui Xu, Anyi Zhang, Liping Yu, Xianbin Wang, Wenyan Zhang was responsible for conceptualisation, validation and writing—review. Yonghua Cui and Ying Li was responsible for project administration, supervision, validation, writing—review&editing.

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Data availability
Due to confidentiality agreements with the participants, we are unable to publicly disclose the data. In case of special circumstances, please contact the corresponding author to request access to the data.

Declarations

Ethics approval and consent to participate
This study has been approved by the Ethics Committee of Beijing Children's Hospital, China. All respondents and their guardians agreed to participate in this study and signed written consent.

Consent for publication
All authors have seen the manuscript and approved its submission to *BMC Psychiatry*.

Competing interests
The authors declare no competing interests.

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