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Subtypes of tic disorders in children and adolescents: based on clinical characteristics

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Abstract

Background Tic disorder (TD) is a diverse neurodevelopmental disorder with various symptoms and comorbidities. Traditional classifications based on age onset and duration fail to adequately characterize the full clinical features of TD. This study aims to redefine TD subtypes by a comprehensive analysis of clinical features and comorbidities.

Methods We assessed 139 children and adolescents aged 6–18 years using 14 scales covering 43 dimensions. The k-means clustering algorithm was used to identify distinct TD subtypes. Differences between these subtypes were analyzed using *t*-tests and network analysis, with high expected influence (EI) metric representing key symptoms within each subtype.

Results We identified two distinct subtypes of TD, with 21.6% of participants classified as subtype1 and 78.4% as subtype2. Subtype1 exhibited more severe symptoms across TD, obsessive-compulsive spectrum disorders, and attention deficit hyperactivity disorder assessments compared to subtype2, with significant differences observed in 81.4% of the scale features. Network analysis revealed differences in core symptoms between the two subtypes; subtype1 primarily involved hyperactivity and vital activities, whereas subtype2 primarily involved attention deficit, hyperactivity and conduct. Furthermore, comparisons with DSM-5 classifications revealed distinct patterns, indicating the novel nature of the identified subtypes.

Conclusion Our study identified two novel TD subtypes, highlighting its heterogeneity. Subtype 1 had more severe attention deficits and impulsivity, requiring comprehensive treatment, while subtype 2 had milder symptoms, focusing on support and monitoring. These findings provide insights into TD classification and may help refine treatment strategies. However, the cross-sectional design limits causal interpretations, and reliance on parent-reported data may introduce bias.

Keywords Tic disorder, Subtype classification, Clinical characteristics, Cluster analysis

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Introduction

Tic disorders (TD) are characterized by sudden, rapid, repetitive, and non-rhythmic movements or vocalizations [1]. TD typically manifests during childhood and is one of the most common movement disorders among children [1, 2]. According to our national survey on childhood psychiatric disorders, TD are reported to have a prevalence of 2.5% in China, and the incidence of TD has been gradually increasing [3]. The most common comorbidities associated with TD are attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). TD is a heterogeneous syndrome encompassing a variety of symptom patterns, course trajectories, and treatment responses, possibly arising from distinct biological imbalances or disturbances [1, 4–6]. Comprehensive characterization and identification of TD's clinical subtypes are crucial for enhancing our understanding of patient-specific etiological mechanisms, thus facilitating the development of biologically informed, patient-specific diagnoses and treatments.

Currently, the most widely recognized classification of TD remains the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), which categorizes three primary types based on age of onset and duration: Tourette syndrome (TS), chronic TD, and transient TD [7]. The main differences among these classifications hinge on the presence of concurrent motor and vocal tics and whether the duration of TD exceeds one year. There is continuity among these types; transient TD may evolve into chronic TD, which in turn can progress to TS. Additionally, the clinical manifestations and diagnostic criteria of the International Classification of Diseases, 11th Revision [8] and the Chinese Classification of Mental Disorders, Third Edition [9], align closely with those of the DSM-5.

However, growing evidence suggests that the DSM-5 classification system has limitations [10]. One fundamental issue is its reliance on symptom-based descriptions rather than underlying pathophysiological mechanisms, which may not adequately capture the heterogeneity of TD [11]. Furthermore, the current classification does not account for the impact of comorbidities, which play a significant role in disease presentation, prognosis, and treatment response [12]. Recent studies have explored alternative classification approaches, such as data-driven subtyping using machine learning or cluster analysis, which may offer a more nuanced understanding of TD heterogeneity [1, 4]. Given these considerations, there is a need to move beyond traditional classification systems to develop more refined and clinically meaningful subtypes.

Despite significant progress in the research on diagnosis and treatment of TD, considerable challenges remain, particularly due to the complexity of comorbid conditions. TD in most children is often accompanied by other psychiatric symptoms, including ADHD, OCD, autism spectrum disorder (ASD), depression, anxiety, sleep disorders, migraines, and self-harming behaviors [2, 13, 14]. Among children with TD, 86% had one or more neurodevelopmental or mental health comorbidities, while 58% had two or more comorbidities [15]. ADHD, characterized by inattention, hyperactivity, and impulsivity that impair functioning or development, has an average prevalence of 50–60% in individuals with TS, predominantly affecting men [16]. OCD, a neurotic disorder characterized by the presence of obsessive and/or compulsive behaviors, is also very common in people with TS, with a lifetime incidence of 50.0% [17]. Therefore, it is essential to consider the comorbid symptoms when subtyping TD.

Many recent studies have applied data-driven approaches based on biological, neuroimaging, and other multidimension data to investigate the heterogeneity of neurodevelopmental disorders, such as ADHD, OCD, and ASD [18–20]. The data-driven approach can address the heterogeneity of TD patients by using computational methods to identify patterns from initial data or observations and applying heuristic rules to find and establish relationships among internal features, thereby uncovering various theorems or laws [21]. Previous studies have used data-driven approaches to classify TS into two to five distinct subtypes [22–24]. However, these classifications exhibit considerable variability in the number and characteristics of identified subtypes, indicating a lack of consensus on meaningful classification criteria. Moreover, most of these studies focus solely on TS, excluding chronic and transient TD, which limits their applicability to the broader spectrum of tic disorders. These gaps highlight the need for a more comprehensive and standardized classification framework that encompasses the full heterogeneity of TD [1]. Refining TD subtypes has important clinical implications, as it allows for a more individualized approach to diagnosis and treatment. Additionally, identifying core symptoms within specific subtypes could inform targeted therapeutic strategies, such as behavioral interventions or pharmacological treatments that address key underlying mechanisms. A more precise subtyping framework may also improve prognosis prediction, enabling earlier and more effective intervention strategies [4, 25].

To address these issues, our study employed a machine learning algorithm integrating multiple dimensional scales related to TD, ADHD, and OCD, alongside network analysis to identify core symptoms that may play pivotal roles in the onset or persistence of each subtype [26, 27]. We assessed 139 children and adolescents, aged 6–18 years, using 14 scales covering 43 dimensions. We focus on three main areas: (i) using cluster analysis algorithm to classify TD based on their clinical characteristics and common comorbidities such as ADHD and OCD;

(ii) describing similarities and differences in the newly defined TD subtypes, including clinical symptoms and treatment patterns; and (iii) comparing traditional TD classification based on DSM-5 with the new subtypes. Our findings contribute to a deeper understanding of the clinical heterogeneity of tic disorders and offer a pathway to define disease subtypes based on clinical features. This provides a meaningful reference for future studies aiming to integrate multidimensional data, including genomics and neuroimaging, to further refine classification systems [4].

Methods

Participants

This study was conducted from May 2022 to June 2023 at psychiatric outpatient department at Beijing Children's Hospital, Capital Medical University included 139 children diagnosed with TD. A total of 4,306 children completed assessments related to TD, of which 297 completed assessments related to OCD, and 2417 completed assessments related to ADHD. Among those who completed all three assessments, 154 children were identified. Inclusion criteria were as follows: (1) according to the DSM-5 diagnostic criteria, the clinical diagnosis of TD in this study was determined during outpatient visits by two board-certified child psychiatrists with attending physician or higher qualifications, based on clinical symptoms, supplemented by dimensional scale assessments; (2) age between 6 and 18 years; (3) a clinical diagnosis of TD without comorbid psychiatric disorders other than OCD and ADHD; (4) absence of epilepsy or other neurological disorders; and (5) exclusion of questionnaires with duplicate entries, random responses, or missing data (i.e., those with identical answers throughout or incomplete responses). The final sample size was determined to be 139 cases, of all 82.0% were male ($n = 114$), 18.0% were female ($n = 25$), with an average age of 10.13 years (standard deviation, SD = 2.18). All children underwent TD, OCD, and ADHD-related interviews conducted simultaneously by psychiatrists and outpatient patients. Informed consent was obtained from patients and their parents. The study was approved and conducted by the Medical Ethics Committee of Beijing Children's Hospital (No. IEC-C-006-A04-V.07.).

Measures

We collected basic characteristics of the patients, including demographic information, medical history, comorbidities, and clinical information on existing mental disorders, through the Children's Mental Health Intelligent Digital System. In addition to general information, the following measures were implemented. Tic disorder-related characteristics were assessed using the Yale Global Tic Severity Scale (YGTSS), Parent Tic Questionnaire (PTQ), Premonitory Urge for Tics Scale (PUTS), Motor Obsessive-compulsive and Vocal Evaluation Scale (MOVES), and Gilles de la Tourette Syndrome Quality of Life Scale (GTS-QOL). Obsessive-compulsive disorder-related characteristics were assessed using the Sensory Phenomena Assessment Scale (SPAS), Children Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), and Obsessive-Compulsive Inventory-Revised (OCI-R). ADHD-related characteristics were assessed using the Conners' Comprehensive Behavior Rating Scales Parent Questionnaire (CBRS), Strengths and Difficulties Questionnaire (SDQ), Child ADHD Rating Scale (C-ADHD-RS), Werry-Weiss-Peters Activity Rating Scale (WWPARS), Swanson Nolan and Pelham-IV-26 Rating Scales (SNAP-IV-26), and Weiss Functional Impairment Scale Parent Form (WFIRS-P). All the scale evaluators were child psychiatrists or psychological technicians who had received scale evaluation training. The assessment process followed strict protocols, which included the use of standardized instructions and ensuring that all assessments were conducted in a uniform testing environment. To ensure consistency, 15% of assessments were video-recorded for supervisor review (Yonghua Cui), with discrepancies resolved through consensus meetings. This approach was implemented to minimize potential bias and variability in the data collection process. The details of each scale are as follows:

Tic disorder symptoms measures

The Gilles de La tourette Syndrome–Quality of life scale (GTS-QOL) GTS-QOL [28] is divided into 4 parts, with a total of 27 questions, the average score of statistical factors ranges from 0 to 4 points. These 4 parts are mental and psychological activities of daily life, strong ideas and behaviors, and cognitive functions. Each question had five different options, representing different levels of severity, and the subjects chose different levels of severity based on how they had felt over the previous four weeks [28]. The reliability and validity of Chinese children and adolescents' samples of GTS-QOL have been completed by our team [29], all internal consistency reliability estimates (Cronbach's alpha) of English, Italian, French, Japanese and other versions exceeded 0.7 [30–33]. The Cronbach's alpha coefficient of GTS-QOL obtained from this sample size was 0.92.

Parent tic questionnaire (PTQ) PTQ [34] is a parent-rated tic severity scale with 54 questions used to assess the frequency and intensity of individual tics in children, including a total score of motor tics, vocal tics, and total score. Motor tic scores range from 0 to 112, vocal tic scores range from 0 to 104 and total scores range from 0 to 216. PTQ demonstrated good internal consistency ($\alpha = 0.80$ to 0.86)

[35]. The Cronbach's alpha coefficient of PTQ obtained from this sample size was 0.88.

Premonitory urge for tics scale (PUTS) PUTS [36] comprises 9 questions, each rated on a 4-point scale: not at all, a little, somewhat, and very much. The total score reflects the presence and frequency of premonitory urges before tics and potential relief experienced after tics. Scores range from 9 (lowest) to 36 (highest), with 12.5–24.5 indicating moderate premonitory urges, 25-30.5 indicating high intensity possibly associated with significant impairment, and 31 or above indicating extremely high intensity possibly with severe (physical or intellectual) deficits [19, 31]. Cronbach's alpha of PUTS in Chinese exceeded 0.7 [37]. The Cronbach's alpha coefficient of PUTS for this sample size is 0.77.

Movement, Obsessive-compulsive and vocal evaluation scale (MOVES) MOVES [38, 39] focuses on children's self-evaluation of tic symptoms, with scores influenced by age. It particularly emphasizes obsessive-compulsive symptoms associated with tic symptoms. Scores range from 0 (no symptoms) to over 40 (severe symptoms) with 20 questions. It has good internal consistency, Cronbach's alpha ranging from 0.62 and 0.89 [40]. The Cronbach's alpha coefficient for MOVES performed by this sample size is 0.88.

The yale global tic severity scale (YGTSS) The YGTSS [41] is designed to assess the total severity of tic symptoms through a series of dimensions, such as number, frequency, intensity, complexity, and interference with 16 questions. Clinical experience with multiple tics is required for use of the YGTSS. According to total score, the severities of tic symptoms are divided into three grades: mild (< 25 points), moderate (25–50 points), severe (> 50 points). The Cronbach's alpha of YGTSS ranges from 0.58 to 0.90 [42]. The Cronbach's alpha coefficient of YGTSS obtained from this sample size was 0.81.

Obsessive-compulsive disorder symptoms measures

Sensory phenomenon assessment scale (SPAS) SPAS [43] is an observer-rated scale, professionals assess patients based on their performance over the past week with 5 questions. The scale consists of two parts: a symptom list of common sensory symptoms and a severity assessment covering dimensions such as quantity, frequency, tension, conversion degree, and functional impairment. Scores range from 0 to 25, with different ranges indicating no symptoms, mild, moderate, and severe levels of sensory symptoms. The Cronbach's α coefficients for SPAS is 0.84 [43]. The Cronbach's alpha coefficient of SPAS obtained from this sample size was 0.83.

Children Yale-Brown Obsessive-Compulsive scale (CY-BOCS) CY-BOCS [44] evaluate the severity of obsessive thoughts and compulsive behaviors over the past week. This scale assigns scores from 0 to 4 for each of the 10 items, yielding a total CY-BOCS severity score. Scores below 6 indicate no obsessive thoughts and behaviors, while scores above 25 indicate severe symptoms. CY-BOCS showed Cronbach's alpha values of 0.81 [45]. The Cronbach's alpha coefficient of CY-BOCS obtained from this sample size was 0.91.

The obsessive-compulsive inventory-revised (OCI-R) OCI-R [46] comprises 18 items in six subscales, it assesses the associated distress of each item in the past month on a 5-point Likert scale from 'not at all' (0) to 'extremely' (4). The total score ranges from 0 to 72 and the subscale scores from 0 to 12. It takes about 5 min to complete. 0–10 points: obsessive-compulsive symptoms were not obvious; 10–20 points: suspected obsessive symptoms; 20–30 points: mild to moderate level of obsessive symptoms; 30–40 points: moderate to severe obsessive-compulsive symptoms; > 40 points: extremely severe obsessive-compulsive symptoms. The OCI-R showed excellent internal consistency (Cronbach's alpha = 0.92) [47]. The Cronbach's alpha coefficient of OCI-R obtained from this sample size was 0.90.

Attention deficit hyperactivity disorder symptoms measures

Conners' comprehensive behavior rating scales parent questionnaire (CBRS) CBRS is a symptom questionnaire completed by parents [48]. It consists of 48 items covering behavior problems, learning problems, psychosomatic problems, impulsivity-hyperactivity, anxiety, and a hyperactivity index. The answers are rated based on a four-point Likert scale ranging from 0 (never) to 3 (almost always). The psychometric properties of the revised scale appear adequate as demonstrated by good internal reliability coefficients [49]. The Cronbach's alpha coefficient of CBRS obtained from this sample size was 0.95.

Strengths and difficulties questionnaire (SDQ) Comprising five subscales, this questionnaire [50] assesses emotional symptoms, conduct problems, hyperactivity-inattention, peer relationship problems, and prosocial behavior. Scores indicate the severity of difficulties and strengths. SDQ has total 25 items, all items are rated on a three-point scale (0 = not true, 1 = somewhat true and 2 = certainly true). The SDQ exhibited strong internal consistency (overall Cronbach's alpha coefficient was 0.81 [51]. The Cronbach's alpha coefficient of SDQ obtained from this sample size was 0.74.

Child ADHD rating scale (C-ADHD-RS) The Children's ADHD Behavior Scale is a norm for Chinese children formulated by Shanghai ADHD Cooperative Group. It consists of 14 questions and is scored from 0 to 3, with a total of 42 points [52]. More than 10 points indicates that children may have ADHD behavior abnormalities. The screen tone scale is completed by parents and reflects the severity of the child's behavioral symptoms of ADHD. According to our own data verification, the scale has a high internal consistency, Cronbach's alpha coefficient is 0.91.

Werry-weiss-peters activity rating scale (WWPARS) WWPARS is a parent scale used to assess a child's activity level and is used to clinically assess the symptoms of ADHD in children [53]. With 22 items assessing a child's activity level during various activities, parents score on a scale from 0 to 2, with higher scores indicating higher activity levels. WWPARS has good internal consistency, Cronbach's alpha is 0.75 [54]. The Cronbach's alpha coefficient of WWPARS obtained from this sample size was 0.90.

Chinese version of swanson nolan and pelham, version IV scale, parent form (SNAP-IV) Comprising 26 items, SNAP-IV [55] assesses three dimensions: inattention, hyperactivity-impulsivity, and oppositional defiant symptoms, each item is rated on a four-point rating scale (0 = 'not at all', 2 = 'just a little', 3 = 'quite a bit', and 4 = 'very much'). Scores represent the degree of symptoms. The scale has good internal consistency, Cronbach's alpha ranges 0.88 to 0.90 [56]. The Cronbach's alpha coefficient of SNAP-IV-26 obtained from this sample size is 0.95.

Weiss functional impairment scale parent form (WFIRS-P) WFIRS-P [57] is specifically designed to assess ADHD-specific social functioning, this scale comprises 50 items rated by parents across six domains: family, learning/school, life skills, self-concept, social activities, and risky activities. The items of the WFIRS-P are scored on a four-point Likert-type rating scale: 0 (never or not at all), 1 (sometimes or somewhat), 2 (often or much) or 3 (very often or very much). Cronbach's alpha coefficient exceeded 0.7 for all domains [58]. The Cronbach's alpha coefficient of WFIRS-P obtained from this sample size is 0.92.

K-means clustering algorithm

We employed the k-means clustering method to classify clinical scales associated with TD, OCD, and ADHD symptoms. K-means clustering was selected in this study due to its simplicity, efficiency, interpretability, and widespread application in psychiatric research for subgroup identification [59–61]. Prior to clustering, we performed min-max normalization to standardize the total scores and sub-dimensions ($n = 43$) across various scales. Simultaneously, we chose between 2 and 10 clusters, employing the squared Euclidean distance measurement, and selecting the highest silhouette coefficient to determine the optimal clustering results. The squared Euclidean distance was used as the primary distance metric, as it as it aligns with the objective function of the K-means algorithm and facilitates stable clustering performance. To ensure the robustness of our clustering results, we further conducted sensitivity analyses by comparing the performance of alternative distance metrics, including cosine and cityblock distances, against the squared Euclidean distance [62]. The silhouette coefficient was adopted as an internal evaluation index to assess the validity of the clustering solutions, as it simultaneously reflects the compactness within clusters and the separation between clusters, providing a reliable and interpretable assessment of the clustering structure [63, 64]. Because results can vary with the initial selection of points, we repeated the k-means algorithm 100 times to mitigate bias from the random initial selection of cluster centroids and select the most stable results to ensure that the identified clusters are robust and repeatable over multiple runs (see Figure S1) [65].

Network analysis

Network analysis of psychopathology allows for detailed analyses of symptom interactions, providing an effective method to explore the clinical patterns between TS and comorbid symptoms [66, 67]. To further explore the differences in clinical profiles between TD subtypes, we constructed a network of clinical features for each subtype. In the network model, each symptom is represented as a node (the dimensions in which there are significant differences between subtypes), while the association between two symptoms, measured by Spearman's correlation coefficient because of the scores on each dimension of the scale are not normally distributed, is represented as an edge. The expected influence (EI) metric was employed to quantify the importance of each node in the network, calculated as the sum of the edge weights for each node [68, 69]. Nodes with higher EI values are considered more important and have a central position in the network [70].

Clinical treatment patterns

To investigate whether the new subtypes exhibited different treatment patterns, we used the average number of follow-up visits as a representative metric of treatment patterns for the new subtypes and conducted t-tests to assess the differences between the new subtypes according to the sample size of the last two subtypes.

Table 1 Demographic and clinical characteristics of children patients with TD

Characteristics	Total sample (*N* = 139)	Subtype 1 (*N* = 30)	Subtype2 (*N* = 109)
N (%)			
Gender			
Male	114 (82.01)	26 (86.67)	88 (80.73)
Female	25 (17.99)	4 (13.33)	21 (10.27)
DSM-5 subtype			
TS	59 (42.44)	14 (46.67)	45 (41.28)
CTD	40 (28.78)	9 (30.00)	31 (28.44)
TTD	40 (28.78)	7 (23.33)	33 (30.28)
Mean (SD)			
Age	10.13 (2.18)	10.57 (2.12)	10.00 (2.19)
Follow-up visits	1.32 (1.58)	0.83 (0.95)	1.46 (1.70)

Abbreviations: TS: Tourette syndrome; CTD: Chronic tic disorder; TTD: Transient tic disorder; SD, Standard deviation

Statistical analysis

Descriptive analysis was used to characterize the demographic features of the sample. Independent-samples t-tests were performed to compare the differences in clinical characteristics and the number of follow-up visits between the two newly identified TD subtypes. To control for the risk of type I errors due to multiple comparisons, the false discovery rate (FDR) correction was applied to adjust p-values, with a significance threshold set at $p < 0.05$ [71]. All statistical analyses were performed using SPSS version 26.0 and MATLAB R2023a (Windows version). Sample and effect size calculations were conducted using Python 3.9 and G*Power software (version 3.1) (See supplementary materials for specific calculations). Data visualization was performed using GraphPad Prism version 9.

Result

Demographic information

Among the 139 participants, 82.0% were male ($n = 114$), 18.0% were female ($n = 25$), with an average age of 10.13 years (SD = 2.18). Diagnoses included 28.1% with simple TD, 38.1% with TD comorbid with ADHD, and 33.8% with TD comorbid with other psychiatric disorders. We classified TD according to DSM-5 into Tourette syndrome (TS), Chronic tic disorder (CTD), and Transient tic disorder (TTD), the total sample of our study comprises 59 (42.44%) TS, 40 (28.78%) CTD, and 40 (28.78%) TTD (see Table 1).

Clustering analysis

Using the k-means algorithm and the silhouette coefficient, we determined that a 2-cluster solution was optimal for patients with TD. Subtype1 comprises 30 individuals (21.6%), while subtype2 comprises 109 individuals (78.4%). The scales and dimensionality scores of the two new subtypes are detailed in Table (2). Subtype1

Table 2 Scale and dimension scores of two new subtypes of tic disorder

Characteristics	Total sample (*N* = 139)	Subtype 1 (*N* = 30)	Subtype2 (*N* = 109)
YGTSS motor	12.03 (4.73)	12.70 (5.18)	11.84 (4.61)
YGTSS vocal	6.54 (5.28)	7.27 (5.19)	6.34 (5.31)
YGTSS impairment	2.81 (5.52)	4.33 (5.68)	2.39 (5.53)
YGTSS	21.37 (10.36)	24.30 (10.63)	20.57 (10.18)
PTQ	32.01 (22.24)	42.73 (26.85)	29.06 (19.95)
PUTS	15.65(4.16)	17.03 (4.25)	15.28 (4.08)
MOVES-OCD	0.56 (0.50)	1.01 (0.60)	0.43 (0.39)
MOVES-tics	0.84 (0.55)	1.19 (0.49)	0.75 (0.52)
MOVES-relevant	0.40 (0.51)	0.78 (0.68)	0.30 (0.39)
MOVES	12.81 (9.15)	20.70 (10.13)	10.63 (7.57)
GTS-QOL-physical	0.54 (0.66)	1.15 (0.86)	0.37 (0.46)
GTS-QOL-OCD	0.45 (0.56)	0.78 (0.78)	0.36 (0.45)
GTS-QOL-psychological	0.84 (0.79)	1.60 (0.97)	0.61 (0.59)
GTS-QOL-cognitive	0.98 (0.82)	1.99 (0.93)	0.71 (0.51)
GTS-QOL-satisfaction	77.84 (21.89)	66.67 (25.91)	80.92 (19.70)
SPAS	5.78 (5.13)	8.10 (5.22)	5.15 (4.94)
CY-BOCS-thoughts	2.10 (3.45)	2.93 (4.57)	1.87 (3.06)
CY-BOCS-behavior	3.16 (4.06)	3.90 (4.71)	2.95 (3.86)
CY-BOCS	5.26 (6.66)	6.83 (8.41)	4.83 (6.07)
OCI-R	10.19 (10.05)	19.83 (12.61)	7.53 (7.31)
CBRS-conduct	0.89 (0.53)	1.58 (0.41)	0.70 (0.38)
CBRS-study	1.29 (0.73)	2.23 (0.57)	1.03 (0.52)
CBRS-psychosoma	0.33 (0.36)	0.60 (0.46)	0.26 (0.29)
CBRS-HI	1.28 (0.68)	2.12 (0.47)	1.04 (0.53)
CBRS-anxiety	0.70 (0.52)	1.08 (0.68)	0.59 (0.40)
CBRS-index	1.10 (0.58)	1.92 (0.35)	0.87 (0.40)
SDQ-emotion	3.06 (2.13)	4.53 (2.10)	2.66 (1.97)
SDQ-conduct	2.50 (1.22)	3.47 (1.39)	2.24 (1.04)
SDQ-hyperactivity	4.75 (1.49)	5.40 (1.35)	4.57 (1.49)
SDQ-association	4.24 (1.39)	4.43 (1.50)	4.19 (1.36)
SDQ-social	6.41 (2.00)	5.70 (2.16)	6.61 (1.91)
C-ADHD-RS	12.33 (8.26)	23.13 (9.00)	9.36 (4.92)
WWPARS	14.20 (9.11)	21.53 (9.45)	12.18 (7.94)
SNAP-IV-26-AD	1.30 (0.75)	2.18 (0.64)	1.06 (0.59)
SNAP-IV-26-index	0.64 (0.58)	1.39 (0.67)	0.43 (0.33)
SNAP-IV-26-OD	0.91 (0.65)	1.76 (0.57)	0.68 (0.44)
SNAP-IV-26	0.95 (0.58)	1.78 (0.50)	0.72 (0.34)
WFIRS-P-family	0.52 (0.50)	1.06 (0.62)	0.37 (0.35)
WFIRS-P-study	0.34 (0.40)	0.78 (0.46)	0.21 (0.28)
WFIRS-P-life skill	0.82 (0.43)	1.21 (0.49)	0.71 (0.35)
WFIRS-P-self management	0.63 (0.65)	1.18 (0.80)	0.48 (0.52)
WFIRS-P-social	0.55 (0.44)	0.98 (0.51)	0.43 (0.33)
WFIRS-P-activity	0.19 (0.18)	0.38 (0.21)	0.14 (0.12)

Abbreviations: YGTSS, Yale Global Tic Severity Scale; PTQ, Parent Tic Questionnaire; PUTS, Premonitory Urge for Tics Scale; MOVES, Motor Obsessive-compulsive and Vocal Evaluation Scale; GTS-QOL, Gilles de la Tourette Syndrome Quality of Life Scale; SPAS, Sensory Phenomena Assessment Scale; CY-BOCS, Children Yale-Brown Obsessive-Compulsive Scale; OCI-R, Obsessive-Compulsive Inventory-Revised; CBRS, Conners' Comprehensive Behavior Rating Scales Parent Questionnaire; HI, hyperactive impulsive; SDQ, Strengths and Difficulties Questionnaire; C-ADHD-RS, Child ADHD Rating Scale; WWPARS, Werry-Weiss-Peters Activity Rating Scale; SNAP-IV-26, Swanson Nolan and Pelham-IV-26 Rating Scales; AD, Attention deficit; OD, Oppositional defiance; WFIRS-P, Weiss Functional Impairment Scale Parent Form

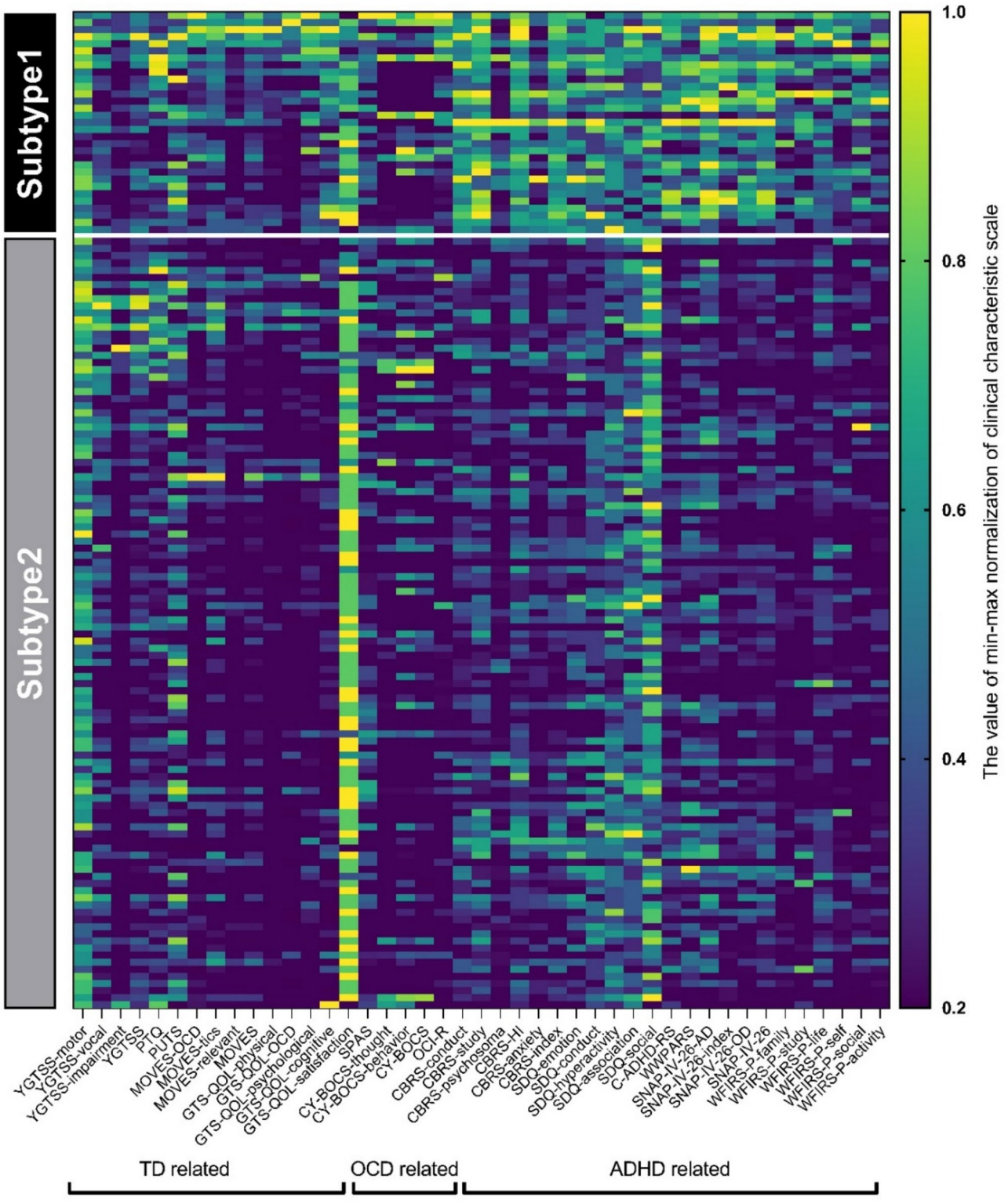

Fig. 1 (See legend on next page.)

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Fig. 1 Heatmap of TD related characteristics scale in 2-cluster solution. The heatmap consisted of 43 dimensions of clinical features of all participants, and the data were standardized and divided into 30 subtype1 and 109 subtype2 subjects according to k-means clustering analysis. **Abbreviation**: YGTSS, Yale Global Tic Severity Scale; PTQ, Parent Tic Questionnaire; PUTS, Premonitory Urge for Tics Scale; MOVES, Motor Obsessive-compulsive and Vocal Evaluation Scale; OCD, obsessive-compulsive disorder; GTS-QOL, Gilles de la Tourette Syndrome Quality of Life Scale; SPAS, Sensory Phenomena Assessment Scale; CY-BOCS, Children Yale-Brown Obsessive-Compulsive Scale; OCI-R, Obsessive-Compulsive Inventory-Revised; CBRS, Conners' Comprehensive Behavior Rating Scales Parent Questionnaire; HI, hyperactive impulsive; SDQ, Strengths and Difficulties Questionnaire; C-ADHD-RS, Child ADHD Rating Scale; WWPARS, Werry-Weiss-Peters Activity Rating Scale; SNAP-IV-26, Swanson Nolan and Pelham-IV-26 Rating Scales; AD, Attention deficit; OD, Oppositional defiance; WFIRS-P, Weiss Functional Impairment Scale Parent Form

exhibited higher overall scores on various features compared to subtype2, indicating more severe manifestations in assessments for TD, OCD, and ADHD (Fig. 1). To assess the robustness of our clustering results, we further evaluated two additional distance metrics—cosine and cityblock—in addition to the default Euclidean distance. Across all comparisons, the two-cluster solution consistently demonstrated the most appropriate clustering structure for the TD sample.

Differences in clinical features between subtypes

We found that 81.4% ($n = 35$) of scale features showed significant differences (after FDR corrected $p < 0.05$). In the C-ADHD-RS, OCI-R, and WWPARS scale total scores, all dimensions of CBRS, the cognitive, physical, and psychological dimensions of GTS-QOL, the tics and OCD dimensions and total scores of the MOVES scale, the emotion and conduct dimensions of the SDQ scale, all dimensions and total scores of SNAP-IV-26, and all dimensions of WFIRS-P, there were significant differences between the subtypes of the two TD ($p < 0.001$). For the total score of the SPAS, PTQ, and PUTS scales, the relevant dimension of MOVES, the social and hyperactivity dimension of SDQ, and the satisfaction dimension of GTS-QOL, the subtypes of the two TD were significantly different ($p < 0.05$). However, in all dimensions of YGTSS and CY-BOCS and the association dimension of SDQ, there was no significant difference between the subtypes of the two TD ($p > 0.05$) (Fig. 2).

Network analysis

The psychopathology network for the two new subtypes is shown in Fig. 3. Subtype1 has more negative correlation than subtype2, and the overall correlation is lower (Fig. 3A). The expected influence (EI) metric represents the core symptoms in both subtypes. We find the top five characteristics of EI in subtype1, which are the hyperactivity index and impulsive hyperactivity dimension of CBRS, the life skills and risk-taking activity dimension of WFIRS-P and the total score of SNAP-IV-26 (Fig. 3B). The top five characteristics of EI in subtype2 are the attention deficit dimension and total score of SNAP-IV-26, the hyperactivity index and conduct dimension of CBRS, and the total score of C-ADHD-RS (Fig. 3B).

Comparison with DSM-5 clinical classification

To compare our newly identified subtypes with traditional clinical classifications, we calculated the proportions of the traditional subtypes within the two new subtypes. Subtype1 comprises 45 (41.28%) TS, 31 (28.44%) CTD, and 33 (30.28%) TTD, whereas subtype2 comprises 14 (46.67%) TS, 9 (30.00%) CTD, and 7 (23.33%) TTD. The Chi-square test revealed no significant differences in the proportions between the two subtypes ($p = 0.78$) (Fig. 4).

Differences in clinical treatment patterns between subtypes

To investigate whether the new subtypes exhibited different treatment patterns, we utilized the average number of follow-up visits as a representative metric of treatment patterns. Subtype1 had an average follow-up frequency of 0.83 (SD = 0.95), while subtype2 had an average of 1.46 (SD = 1.70). We observed a significant statistical difference in clinical treatment patterns between the two groups ($p = 0.01$) (Fig. 5).

Discussion

This study employs a data-driven approach based on extensive clinical features to identify two new subtypes of tic disorder (TD) that differ significantly from traditional classifications in the DSM-5. This finding suggests that traditional classification methods may not fully reflect the heterogeneity of clinical presentations in patients with TD. These new subtypes reveal the internal heterogeneity of TD and could guide personalized treatment and prognosis.

We compared the two new TD subtypes with the traditional DSM-5 classification and found that each individual new subtype included three traditional categories: provisional tic disorder, chronic tic disorder, and Tourette syndrome (TS). This suggests that the data-driven subtypes do not correspond one-to-one with existing diagnostic categories. Instead, both subtypes span several traditional diagnoses, suggesting that our classification captures underlying clinical or neurobiological dimensions that go beyond the DSM-5 framework. It does not imply that a new subtype corresponds to one or two traditional types. Importantly, this new classification is not intended to replace the DSM-5 system but to provide a complementary perspective that may enhance clinical

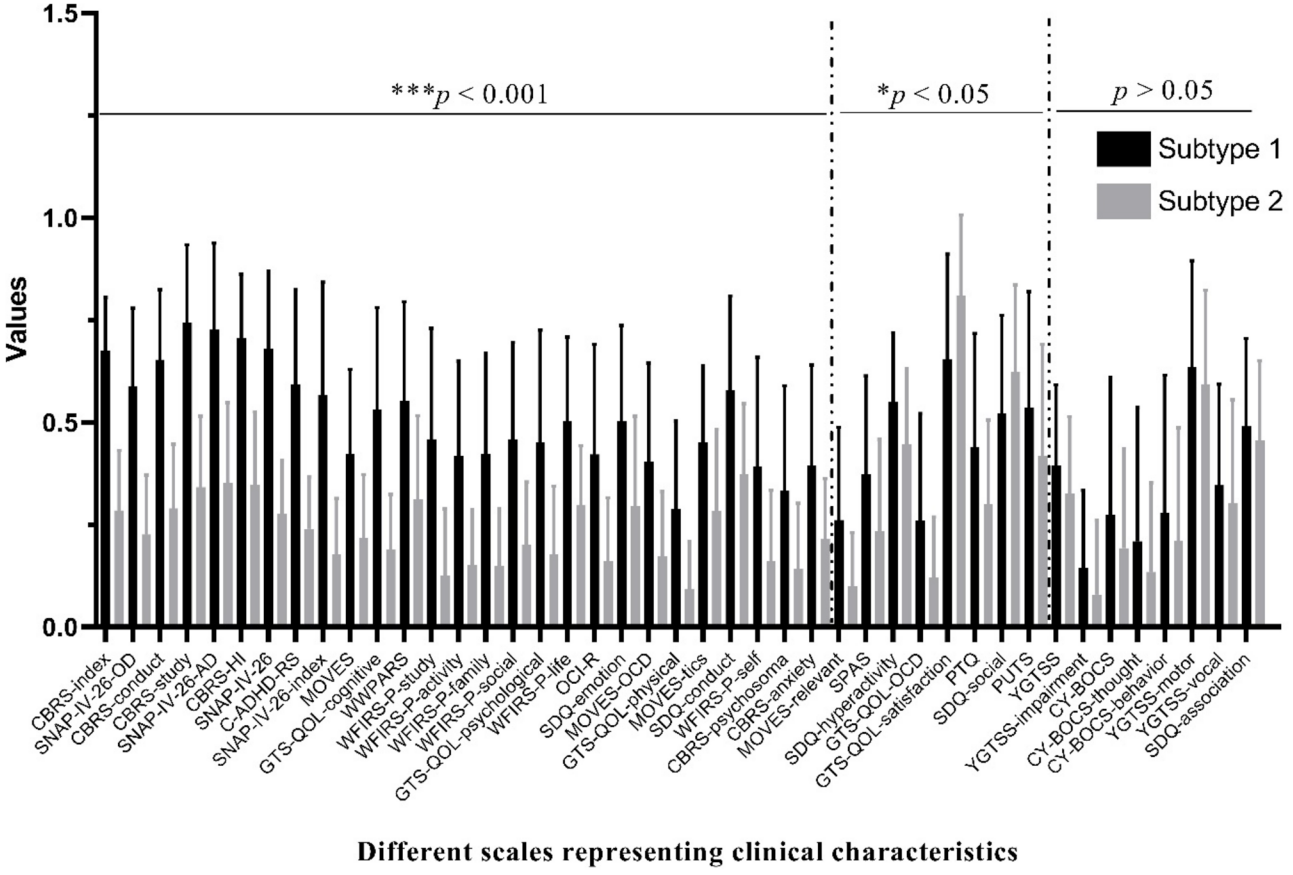

Fig. 2 The scale differences between the two subtypes. Values represent the mean and standard deviation of scores in each dimension. Order the *p*-values after FDR correction from smallest to largest, from left to right. Note: * and *** represent the corrected *p* value < 0.05 and < 0.001 of subtype1 and 2 feature values of each dimension's difference. **Abbreviation**: CBRS, Conners' Comprehensive Behavior Rating Scales Parent Questionnaire; SNAP-IV-26, Swanson Nolan and Pelham-IV-26 Rating Scales; AD, Attention deficit; OD, Oppositional defiance; HI, hyperactive impulsive; C-ADHD-RS, Child ADHD Rating Scale; MOVES, Motor Obsessive-compulsive and Vocal Evaluation Scale; GTS-QOL, Gilles de la Tourette Syndrome Quality of Life Scale; WWPARS, Werry-Weiss-Peters Activity Rating Scale; WFIRS-P, Weiss Functional Impairment Scale Parent Form; OCI-R, Obsessive-Compulsive Inventory-Revised; SDQ, Strengths and Difficulties Questionnaire; OCD, obsessive-compulsive disorder; SPAS, Sensory Phenomena Assessment Scale; PTQ, Parent Tic Questionnaire; PUTS, Premonitory Urge for Tics Scale; YGTSS, Yale Global Tic Severity Scale; CY-BOCS, Children Yale-Brown Obsessive-Compulsive Scale

assessment and guide more personalized intervention strategies.

Subtype 1 has higher overall scores in features than subtype 2, suggesting that subtype 1 has more severe symptoms than subtype 2 on the TD, OCD and ADHD scales. Specifically, subtype 2 scored higher on satisfaction evaluation of GTS-QOL and prosocial behavior of SDQ, but subtype 1 scored higher on the rest. According to the results of this study, subtype 1 may represent more severe TD, whereas subtype 2 may represent milder TD. The differences in severity between the two subtypes identified are partially consistent with previous research on the heterogeneity of tic disorders [1, 4–6, 11]. However, our findings go further by revealing unique patterns in our current sample - one subtype shows a particularly high levels of impulsivity and hyperactivity, whereas the other shows more pronounced deficits in attention and less severe tic symptoms overall. These distinct profiles suggest that our data may not only confirm the variability found in previous work, but also indicate the influence of different underlying pathophysiological mechanisms [72, 73].

Significant differences were found in over 80% of the clinical features in the TD, ADHD, and OCD scales used in this study. No significant differences were found between the subtypes in terms of YGTSS and CY-BOCS scores. This may suggest that the subtypes identified in this study reflect broader psychosocial and functional dimensions beyond the mere severity of tics or comorbid OCD symptoms. These differences in core symptom distributions provide clinicians with a data-driven basis for distinguishing TD subtypes and suggest that treatment strategies may need to be tailored accordingly.

Previous studies have typically focused solely on categorizing TS without considering the other two subtypes of TD. Using a variety of methods, including hierarchical

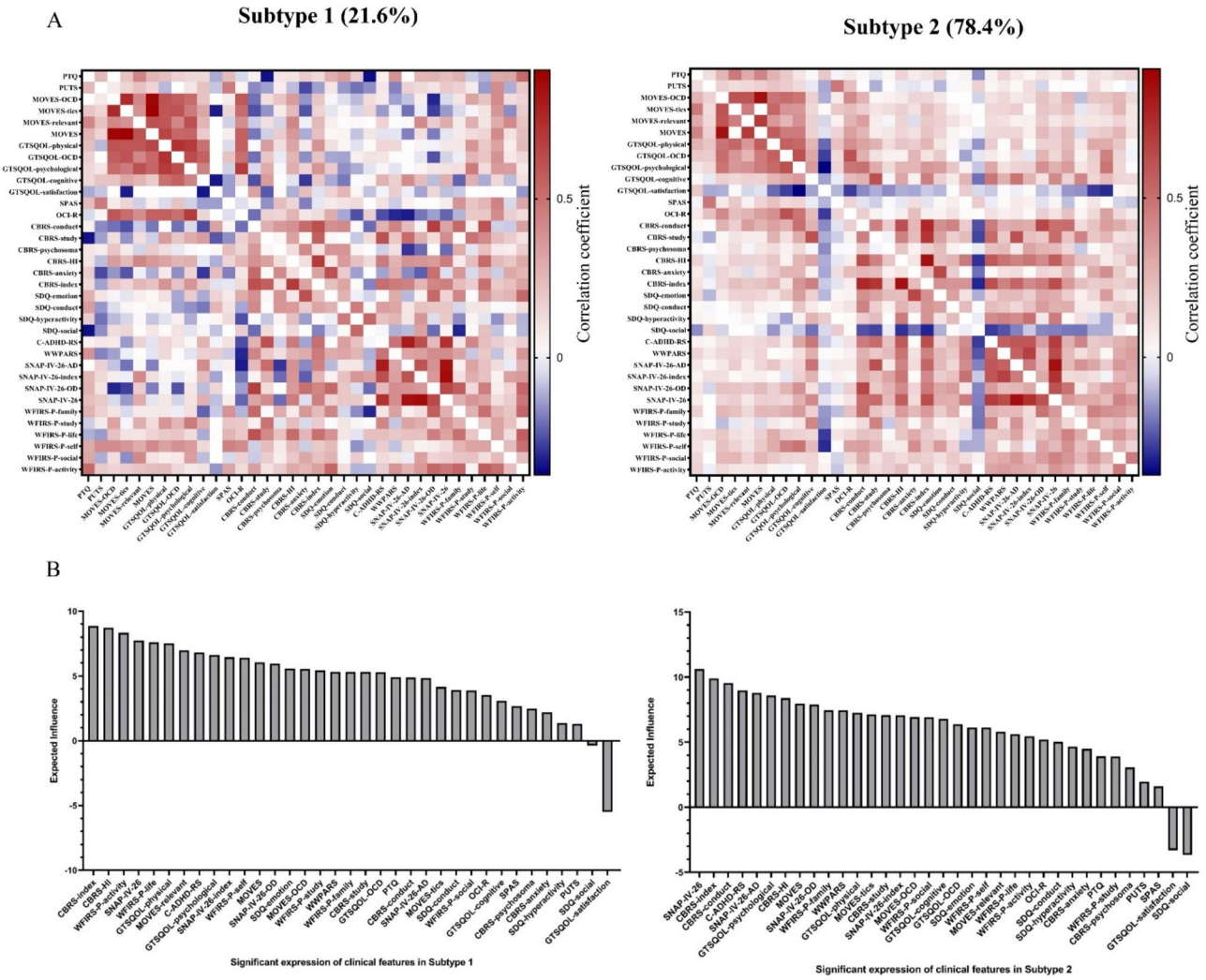

Fig. 3 Network analysis of two new subtypes. **(A)** Constructing a network of clinical features for each subtype (FDR corrected $p < 0.05$). **(B)** Expected Influence. EI values for 35 dimensions, ranking from largest to smallest. **Abbreviation**: PTQ, Parent Tic Questionnaire; PUTS, Premonitory Urge for Tics Scale; MOVES, Motor Obsessive-compulsive and Vocal Evaluation Scale; OCD, obsessive-compulsive disorder; GTS-QOL, Gilles de la Tourette Syndrome Quality of Life Scale; SPAS, Sensory Phenomena Assessment Scale; OCI-R, Obsessive-Compulsive Inventory-Revised; CBRS, Conners' Comprehensive Behavior Rating Scales Parent Questionnaire; HI, hyperactive impulsive; SDQ, Strengths and Difficulties Questionnaire; C-ADHD-RS, Child ADHD Rating Scale; WWPARS, Werry-Weiss-Peters Activity Rating Scale; SNAP-IV-26, Swanson Nolan and Pelham-IV-26 Rating Scales; AD, Attention deficit; OD, Oppositional defiance; WFIRS-P, Weiss Functional Impairment Scale Parent Form

clustering and principal component factor analysis, these studies have revealed multiple facets of these disorders beyond traditional diagnostic criteria. For example, one study examined tic symptoms in 85 TS patients and identified four significant factors: aggressive phenomena, motor and phonic tic symptoms, compulsive phenomena, and tapping [23]. Another study focused on TS patients and found three distinct factors: complex motor tics, attention deficit/hyperactivity symptoms with aggressive behaviors, and complex vocal tics [24]. Another study focused on the phenotypic patterns of TS by performing cluster analysis on TS patients [22] and identified two distinct clusters: one with predominantly simple tics (cluster 1), and the other with multiple complex tics (cluster 2). The study also found that cluster 2 membership correlated with increased tic severity, overall impairment, medication treatment, and the presence of comorbid obsessive-compulsive symptoms [22]. In addition, studies using latent class analyses and hierarchical clustering have uncovered multiple TS subphenotypes with different comorbidities and heritabilities, suggesting distinct etiologies within TS [74, 75]. These findings collectively emphasize the need for more homogeneous phenotypes in genetic research and clinical management of TS. Few studies have investigated the comorbidities of TD as clinical features of TD itself to explore the biological characteristics of TD diseases [74]. In our study, we not only included all traditional subtypes of TD but also

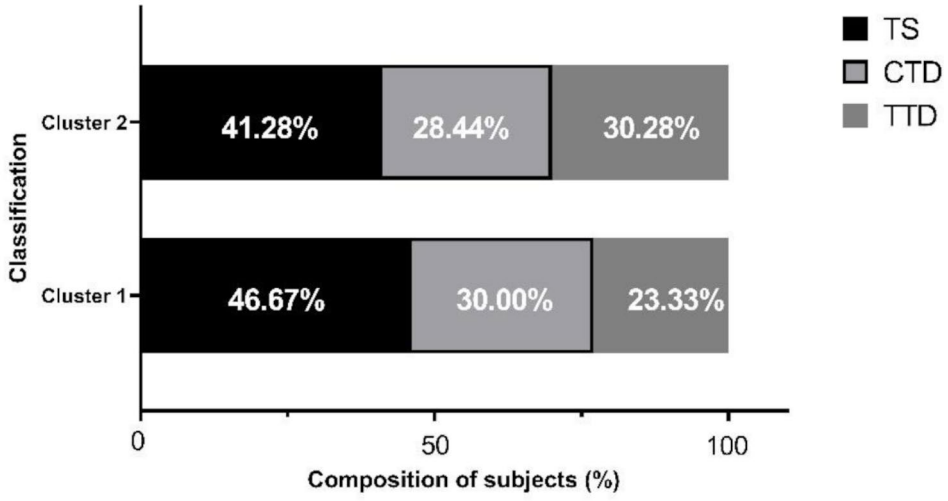

Fig. 4 Comparison between two new TD subtypes and DSM-5 TD classifications. **Abbreviation**: TS: Tourette syndrome; CTD: Chronic tic disorder; TTD: Transient tic disorder

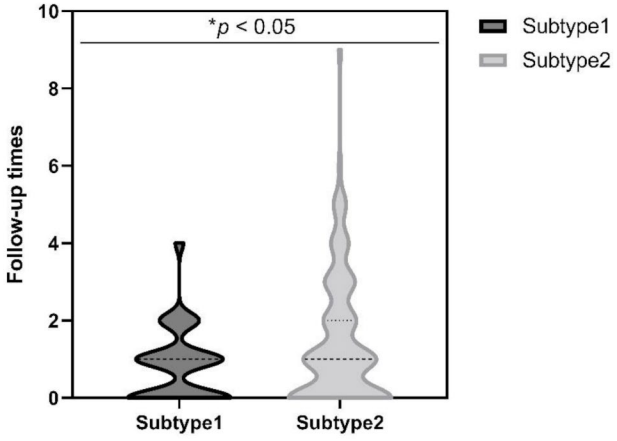

Fig. 5 Comparison of average number of follow-up visits between two new subtypes. *, $p < 0.05$

incorporated two major comorbidities, OCD and ADHD, for data-driven subtype analysis. This approach allows for a better exploration of the heterogeneity of TD.

Furthermore, through network analysis, we found that the core symptoms of the two subtypes were different, further supporting the existence of different underlying pathophysiological mechanisms. Subtype 1 showed greater effects on hyperactivity and life activities, whereas subtype 2 showed greater impact in attention deficit, hyperactivity disorder, and conduct. In the top 10 feature values of the entire EI ranking, most of the important network nodes of subtypes 1 and 2 are ADHD-related parts, a few are TD-related parts, and OCD is not important in the whole network. Studies have reported that adolescents with both TD and ADHD do not differ from adolescents with TD alone on measures of tic severity, but they do experience greater psychosocial distress and poorer overall functioning [61]. Therefore, the two new subtypes of TD identified in this study may be the two new subtypes that are more highly correlated with ADHD.

In this study, we identified statistically significant differences between the two newly identified TD subtypes across 43 clinical characteristics and follow-up frequency. Importantly, effect size analysis confirmed the practical importance of these differences. Interestingly, despite having milder tic symptoms, patients in subtype 2 had a higher frequency of follow-up visits than those in subtype 1. This seemingly paradoxical finding may be explained by factors beyond clinical severity, such as parental attitudes, dissemination of health knowledge and access to health care. A retrospective review of medical histories showed that children with subtype 1, characterized by more severe but stable symptoms, were often already on established treatment plans (most are on medication), requiring fewer adjustments and therefore fewer follow-up visits. In contrast, children in subtype 2 had less stable treatment trajectories and more frequent medication adjustments, leading to more regular follow-up schedules. Clinical observations suggest that children with mild TD or provisional TD often benefit from ongoing monitoring and early behavioral interventions, such as Habit Reversal Training (HRT) or Comprehensive Behavioral Intervention for Tic (CBIT), without necessarily initiating pharmacological treatment [76]. However, as this was not a randomized controlled trial and there was considerable heterogeneity in treatment modalities, it was not possible to conduct further comparative analysis of treatment patterns between the two subtypes.

Given that tic severity is a modifiable factor that is strongly associated with long-term prognosis, early identification and appropriate management remain critical

[61, 77]. If a patient's clinical characteristics closely match one of the identified subtypes at initial assessment, this may provide an early indication of potential risk features and allow clinicians to develop tailored follow-up schedules and intervention plans accordingly. Based on our findings, we recommend that patients in subtype 1 show more marked impairments in attention deficit, impulsivity, hyperactivity, and general functional impairment. This suggests that they may require more systematic and comprehensive intervention strategies, such as combined behavioral therapy and pharmacotherapy. In contrast, subtype 2 patients have relatively milder symptoms, and their clinical management may focus more on daily functional support and symptom monitoring. Such a subtype-based precision treatment approach holds promise for improving the long-term outcomes of patients with TD.

It is important to note that our study has some potential limitations. First, this study focuses on phenotypic classification without incorporating imaging or genetic data. The lack of multimodal information limits the biological interpretability of subtypes and may reduce the validity of our findings in capturing underlying mechanisms. More data are needed for machine learning analysis to reveal the neurobiological basis of TD [78, 79]. Second, this study used a cross-sectional design and lacked longitudinal data. Without longitudinal data, we cannot elucidate the temporal consistency of these subtypes. Third, the single-center nature of our sample may reflect site-specific referral patterns or diagnostic practices, thereby limiting the external validity of our findings. Future studies incorporating multi-center cohorts would improve generalizability to different clinical populations. Fourth, the use of K-means clustering - although repeated for stability - requires predefined cluster numbers and assumes spherical distributions. These assumptions may oversimplify the true clinical heterogeneity and reduce the internal validity of the subtype structure. Although we increased the stability of our results by repeating the clustering procedure 100 times, this limitation may still affect the broad interpretation of the clustering results, especially in the context of a relatively limited sample size [62–64]. In addition, multicollinearity among features may have biased the distance calculations and clustering. However, given the nature of our dataset and the scope of this study, we did not perform specific preprocessing steps to address multicollinearity, such as feature selection or dimensionality reduction. This limitation should be taken into consideration when interpreting the clustering results. Finally, the clinical features in this study were based on retrospective assessments, with some information reported by parents, which may introduce recall bias. In the future, objective biomarkers are expected to improve the diagnosis and classification of TD. Neurobiological and genetic studies may help to validate and refine these data-driven subtypes by identifying their underlying biological correlates [4].

Conclusion

Our study identified two new subtypes of TD based on clinical features in a sample of children and adolescents in China, thereby highlighting the heterogeneity of TD. Patients in subtype 1 had more pronounced deficits in attention, impulsivity-hyperactivity symptoms, and overall functional impairment. This suggests that they may require more systematic and comprehensive intervention strategies, such as a combination of behavioral therapy and pharmacological treatment. In contrast, patients in subtype 2 presented with relatively milder symptoms, and their clinical management may focus more on functional support in daily life and symptom monitoring. This may provide a deeper understanding of the neurobiological mechanism of TD and holds significant potential for advancing research and practice in precise treatment approaches and personalized prognosis prediction for TD. Although our findings are promising, further validation is warranted.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-025-05698-2.

Supplementary Material 1

Acknowledgements

The data collected in this study is based on the children's mental intelligence digital system Version 1.0 jointly developed and designed by Li Ying, Hong Xu and Cui Yonghua. Thanks to the three personnel who designed the system.

Author contributions

Kai Yang: Original draft, data collection, tables & figures, and review and editing; Wenyan Zhang, Ying Li, Xianbin Wang: Data collection and tables & figures; Zhongliang Jiang, Shujin Hu, JinHyun Jun, Qinghao Yang, Jingyi Li, Xu Hong: Data collection; Yonghua Cui: Conceptualization, supervision and editing; Tianyuan Lei: Conceptualization, supervision, original draft, review and editing.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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