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ORIGINAL RESEARCH

Relationship Between Anxiety Symptoms and Age-Related Differences in Tic Severity

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Purpose: Tic disorders are neurodevelopmental disorders characterized by movements or vocalizations, often accompanied by anxiety symptoms. However, the relationships between tic severity, age, and anxiety symptoms remain unclear. Here, we investigated the association between tic severity and age and examined how anxiety symptoms might influence this relationship.

Patients and Methods: Paediatric patients with tic disorders were recruited from the outpatient clinic of the in Department of Psychiatry at Beijing Children's Hospital, Capital Medical University. The final sample included 372 subjects (77 females, 295 males; mean age = 10.50 ± 2.70 years; age range: 6.33–15.92 years). Tic severity was assessed using the Yale Global Tic Severity Scale (YGTSS), while anxiety symptoms were measured using the Screen for Child Anxiety Related Emotional Disorders (SCARED).

Results: We found a significant positive correlation between both total and subscale anxiety scores and tic severity. Furthermore, anxiety symptoms, particularly separation anxiety, were found to be significantly correlated with age-related differences in tic severity. In the high anxiety group, tic severity increased significantly with age, mirroring the overall trend. Conversely, in the low anxiety group, tic severity remained relatively stable with age.

Conclusion: Our findings highlight the role of anxiety in the progression of tic disorders and emphasize the importance of addressing anxiety in the clinical management of children with tic disorders.

Keywords: tic disorders, anxiety symptom, development, children and adolescents

Introduction

Tic disorders (TD) are neurodevelopmental disorders.[1,2] The main clinical manifestations are sudden, rapid, recurrent, non-rhythmic motor movements or vocalizations.[3] Tics are common in childhood, with varying reported prevalence rates, often estimated at around 20%, and are higher in males.[1] TD is often accompanied by other psychiatric comorbidities, such as attention-deficit/hyperactivity disorder (ADHD), anxiety, and other mood disorders.[1–4] TD is associated with functional impairment in multiple domains, including physical, social, family, academic, and psychological aspects.[5] Understanding the manifestations and comorbidities is crucial for effective diagnosis and treatment of TD.

Tics usually begin around the age of 4–6 years, increase in severity around the age 10–12 years,[6,7] and often spontaneously improve during adolescence according to earlier studies.[6,7] However, some recent studies have shown that tic severity changes linearly with age.[8–10] These differing conclusions highlight the need for further research into the relationship between tic severity and age. In addition, many factors influence the variation in tic severity with age.[8,11] Importantly, coexisting neuropsychological problems place a significant burden on patients with TD,[10,12–14] and may influence the course of TD. In a large TD dataset (n = 1374), Hirschtritt et al found that the median age at onset of TD was 6 years, with anxiety disorders typically emerging within one year of the TD diagnosis.[15] This result may suggest that the course of tics is related to anxiety. However, the specific impact of anxiety symptoms on the course of TD during the vulnerable period of childhood and adolescence remains unclear.

Anxiety is characterized by excessive fear or negative emotion disproportionate to the stimulus, leading to impairment or distress.[16,17] Studies suggest that approximately 30% to 50% of people with chronic TD are diagnosed with an

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anxiety disorder.[18–20] Recent research has increasingly focused on the association between TD and anxiety disorders,[21,22] and found that anxiety symptoms may increase the severity of TD.[18,19,21,23–26] Eddy et al reported that greater severity of tics and co-occurring psychiatric conditions, including anxiety, correlated with worse quality of life.[27] Anxiety symptoms could significantly moderate the relationship between tic severity and functional impairment.[28] Specifically, there is a stronger relationship between tic severity and functional impairment in patients with higher levels of anxiety symptoms than in those with lower levels of anxiety symptoms.[28] Furthermore, a significant number of young people with TD identified anxiety reduction as an important treatment outcome, second only to tic improvement.[29] Given the variable nature of TD in childhood and adolescence, it is crucial to understand how anxiety symptoms influence the relationship between tic severity and age.

To address this issue, we investigated the impact of anxiety symptoms on the progression of tic severity. The study included 372 outpatient children (female/male = 77/295) with a diagnosis of TD, aged 6.33 to 15.92 years, from the Department of Psychiatry, Beijing Children's Hospital, Capital Medical University, between May 2022 and June 2023. We assessed tics using the Yale Global Tic Severity Scale (YGTSS) and anxiety symptoms using the Screen for Child Anxiety Related Emotional Disorders (SCARED). Our hypotheses were: (i) tic severity would be significantly positively correlated with anxiety symptom severity, and (ii) anxiety symptoms would modulate changes in tic severity with age.

Methods

Participants

Paediatric patients with a formal diagnosis of TD were enrolled from the outpatient clinic of the Department of Psychiatry, Beijing Children's Hospital, Capital Medical University, between May 2022 and June 2023. This study used cross-sectional data, and all data were collected from patients' assessments at the time of their first outpatient diagnosis. Inclusion criteria included: (1) children diagnosed with TD by child psychiatrists based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. In line with recent research,[30] TD is considered to be a spectrum, encompassing all DSM-5 defined categories, including provisional/transient tic disorder, persistent/chronic motor or vocal tic disorder, and Gilles de la Tourette's syndrome (the presence of both motor and vocal tics for a duration of at least one year); (2) children were fluent in Chinese, had age-appropriate intelligence, and were able to complete questionnaires. Exclusion criteria were: (1) because the relationship between anxiety symptoms and TD is influenced by comorbidities,[22] we excluded subjects with obsessive-compulsive disorder, autism spectrum disorder, schizophrenia, bipolar disorder, pervasive developmental disorder, somatoform disorder, severe brain injury, or other major mental and physical illnesses (except anxiety disorder and ADHD); (2) children had organic lesions causing tics; (3) children were taking medication or undergoing psycho-behavioural treatment in the two weeks prior to the assessment; (4) missing or abnormal data on the tic severity or anxiety symptom rating scales. We initially included 645 patients, and after data cleaning, the study included 372 subjects (77 females and 295 males, age range: 6.33–15.92 years; see Table 1). All the procedures were performed in accordance with the Declaration of Helsinki, and verbal informed consent was obtained from all participants and their parents/guardians (see ethics statements).

Measures

We collected demographic data, including the clinical characteristics of tic symptoms and a family history of TD. All participating children completed several assessments, including the Yale Global Tic Severity Scale (YGTSS) and the Screen for Child Anxiety Related Emotional Disorders (SCARED). Below is a brief overview of each scale and its relevance to our study:

Yale Global Tic Severity Scale

The severity of tic symptoms was assessed using the Yale Global Tic Severity Scale (YGTSS), developed by Leckman et al.[31] The YGTSS, a semi-structured clinician-rated scale, assesses five dimensions of tic symptoms: number, frequency, intensity, complexity, and interference. The YGTSS can be divided into motor tics, vocal tics, and impairment scores, and the sum of the three scores is the total YGTSS score. It provides a total tic score ranging from 0 to 100, reflecting the severity of motor and

Table 1 Demographic and Clinical Characteristics of the Participants

Variables	n = 372
Demographic characteristics	
Age (Year, Median [IQR])	10.50 [3.06]
Age subgroup, n [%]	
6–7 years	6 [1.61]
7–8 years	17 [4.57]
8–9 years	60 [16.13]
9–10 years	73 [19.62]
10–11 years	61 [16.40]
11–12 years	53 [14.25]
12–13 years	36 [9.68]
13–14 years	33 [8.87]
14–15 years	28 [7.53]
15–16 years	5 [1.34]
Sex at birth, n [%]	
Male	295 [79.30]
Female	77 [20.70]
Clinical characteristics	
Tic disorders, n [%]†	372 [100]
Provisional tic disorder	191 [51.34]
Chronic vocal tics	39 [10.48]
Chronic motor tics	97 [26.08]
Tourette's syndrome	45 [12.10]
Tic severity, Median [IQR]	
YGTSS total	22.00 [15.75]
YGTSS motor	13.00 [6.00]
YGTSS vocal	7.00 [11.00]
Anxiety disorders, n [%]†	94 [25.27]
Panic disorder	10 [2.69]
Generalized anxiety disorder	16 [4.30]
Separation anxiety	31 [8.33]
Social phobia	24 [6.45]
Agoraphobia	21 [5.65]
Anxiety Symptoms, Median [IQR]	
SCARED total	19.50 [21.00]
SCARED panic	4.00 [7.00]
SCARED generalized	5.00 [6.00]
SCARED separation	4.00 [4.00]
SCARED social	5.00 [5.00]
SCARED school	2.00 [3.00]
ADHD, n [%]†	101 [27.15]

Note: †Diagnosis according to DSM-5.

Abbreviations: IQR, interquartile range, Q3-Q1; YGTSS, Yale Global Tic Severity Scale; ADHD, Attention-deficit/hyperactive disorder; SCARED, Screen for Child Anxiety Related Emotional Disorders.

vocal tics in the previous week, with higher scores indicating greater severity. The Chinese version of the YGTSS has shown good reliability and validity in the assessment of children and adolescents with TD.[32]

Screen for Child Anxiety Related Emotional Disorders

The Screen for Child Anxiety Related Emotional Disorders (SCARED) is a widely used self-report questionnaire that screens for various anxiety disorders in children. It included five distinct domains: panic/somatic anxiety, generalized

anxiety, separation anxiety, social phobia, and school phobia.[33,34] The SCARED consists of 41 items and total score is calculated by summing all item responses, with scores ranging from 0 (no anxiety) to 82 (severe anxiety). Psychometric results suggest that SCARED is a reliable and valid tool for screening for childhood anxiety disorders, particularly in Chinese clinical settings.[35]

Statistical Analysis

To assess the relationship between tic severity and anxiety symptom severity, we calculated Spearman correlation coefficients between the total and subscale scores for all scales. We then used hierarchical regression models to understand how tic severity changes with age and whether this is influenced by anxiety symptoms. First, linear regression models were used to assess the association between tic severity and age, applying this method to YGTSS total, YGTSS motor, and YGTSS vocal scores. To investigate both linear and quadratic age effects, multiple linear regressions were performed with age and age squared as predictors, along with covariates such as sex (female 0, male 1) and ADHD diagnosis (no 0, yes 1). Specifically, the linear model was defined as follows

$$Y = \beta_0 + \beta_1 \times age + \beta_2 \times sex + \beta_3 \times ADHD + \varepsilon \quad (1)$$

The quadratic model was defined as follows

$$Y = \beta_0 + \beta_1 \times age + \beta_2 \times age^2 + \beta_3 \times sex + \beta_4 \times ADHD + \varepsilon \quad (2)$$

The Akaike Information Criterion (AIC) was used to select the model that best fit the data. Second, to determine the effect of anxiety symptoms on age-related changes in tic severity, variables representing anxiety and its interaction with age (anxiety × age) were progressively added to the regression model. These steps resulted in the following models:

$$Y = \beta_0 + \beta_1 \times age + \beta_2 \times sex + \beta_3 \times ADHD + \beta_4 \times anxiety + \beta_5 \times anxiety \times age + \varepsilon \quad (3)$$

and

$$Y = \beta_0 + \beta_1 \times age + \beta_2 \times age^2 + \beta_3 \times sex + \beta_4 \times ADHD + \beta_5 \times anxiety + \beta_6 \times anxiety \times age + \varepsilon \quad (4)$$

The AIC criterion was again used to select the most appropriate model. In cases where the interaction term proved to be significant, a simple slope analysis was conducted to clarify the moderating effect. This involved repeating the simple linear regression analysis separately for the high and low anxiety groups. Two grouping strategies are used in this study. The first strategy utilizes a widely accepted cut-off value of 15,[34] defining scores above 15 as belonging to the high anxiety group and scores below 15 as belonging to the low anxiety group. The second strategy is to divide by the quartiles of participants' scores to avoid possible bias introduced by the absolute cut-off. Subjects with a SCARED total score above the 75th percentile are classified as belonging to the high anxiety group, while those with a score below the 25th percentile are classified as belonging to the low anxiety group.

Finally, to investigate the differential impact of various anxiety factors on changes in tic severity with age, we divided the SCARED scale into its five sub-dimensions: panic/somatic, generalized anxiety, separation anxiety, social phobia, and school phobia. For significant interaction terms, we conducted simple slope analyses and repeated the linear regression for high and low anxiety groups, defined by two grouping strategies of each sub-dimension. The significance level was adjusted for multiple comparisons using the Bonferroni correction method, with a corrected p-value threshold of < 0.05. All statistical analyses were performed with MATLAB 2019b and SPSS 26.

Results

Relationship Between Anxiety Severity and Tic Severity

We found significant positive correlations within tic scales (YGTSS) and within anxiety scales (SCARED), with correlation coefficients (r) ranging from 0.19 to 0.76 and 0.32 to 0.88, respectively (Table 2). Correlations between total tic and anxiety scores and most subscale scores were also significantly positive, with coefficients ranging from 0.12 to 0.31 (Table 2).

Table 2 Correlations Matrix for Tic Severity and Anxiety Symptoms

Spearman Correlation Coefficients	YGTSS Total	YGTSS Motor	YGTSS Vocal	SCARED Total	SCARED Panic	SCARED Generalized	SCARED Separation	SCARED Social	SCARED School
YGTSS total	–	0.61***	0.76***	0.28***	0.24***	0.31***	0.17***	0.20***	0.19***
YGTSS motor		–	0.19***	0.21***	0.14**	0.20***	0.22***	0.12*	0.21***
YGTSS vocal			–	0.19***	0.16**	0.21***	0.065	0.17***	0.083
SCARED total				–	0.86***	0.88***	0.76***	0.74***	0.60***
SCARED panic					–	0.73***	0.57***	0.51***	0.48***
SCARED generalized						–	0.58***	0.56***	0.47***
SCARED separation							–	0.47***	0.46***
SCARED social								–	0.32***
SCARED school									–

Notes: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. The strength of correlations is categorized based on Cohen's guidelines: small ($r = 0.10$), medium ($r = 0.30$), and large ($r = 0.50$), to facilitate interpretation of effect sizes.
Abbreviations: YGTSS, Yale Global Tic Severity Scale; SCARED, Screen for Child Anxiety Related Emotional Disorders.

Moderating Role of Anxiety on the Changes in Tic Severity with Age

We found that the total scores of YGTSS increased significantly with age ($p < 0.001$), as detailed in Figure 1 and Table 3. We further analyzed the YGTSS scale by dividing it into motor and vocal tic scores and found a significant increase with age in vocal tic severity ($p < 0.001$), but not in motor tic severity. To explore whether anxiety influences the progression of tic severity with age, we conducted a hierarchical regression analysis, adding an interaction term between age and the anxiety score (Table 3). The results showed that anxiety significantly moderated the relationship between YGTSS total and age ($p = 0.0059$, $t = 2.77$). The adjusted R-squared value for the model was 0.169, indicating that 16.90% of the variance in tic severity was explained by the model. Anxiety was found to significantly moderate the relationship between YGTSS vocal score and age ($p = 0.037$, $t = 2.09$). However, this moderating effect did not remain significant after applying Bonferroni correction, as the p-value should be less than 0.017.

The significant interaction effect observed suggests that anxiety acts as a moderator of the relationship between tic severity and age. A simple slope analysis was used to further elucidate this interaction. We first defined the high and low anxiety groups based on the optimal cut-off score of 15 on the SCARED scale.[34] In the high anxiety group, a significant increase in YGTSS total score with age was observed ($p = 2.99 \times 10^{-6}$, $t = 4.79$), whereas in the low anxiety group, this relationship was not significant ($p = 0.68$, $t = 0.42$, Figure 2A). To avoid potential bias introduced by the absolute threshold value, we defined the high and low anxiety groups based on the 75th and 25th percentiles of the participants,

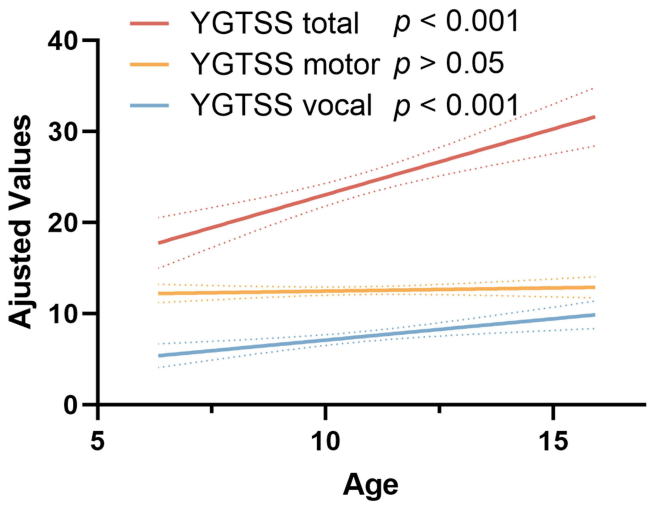

Figure 1 Age effects on the tic severity total scores. The adjusted value denotes the measure of interest corrected for sex and ADHD diagnosis.
Abbreviation: YGTSS, Yale Global Tic Severity Scale.

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Table 3 Hierarchal Regression Model for the Relationship Between Tic Severity and Age Under the Influence of Anxiety Symptoms

Variables	YGTSS Total			YGTSS Motor			YGTSS Vocal		
	p	t	*Adjusted R^2 (%)*	*p*	t	*Adjusted R^2 (%)*	*p*	t	*Adjusted R^2 (%)*
Step1			5.73			< 0.001			3.04
Age	1.42×10^{-6}***	4.90		0.51	0.66		7.96×10^{-4}***	3.38	
Sex	0.87	0.17		0.13	1.51		0.95	−0.066	
ADHD	0.51	−0.65		0.88	−0.15		0.15	−1.46	
Step2			15.40			5.35			6.38
Age	1.61×10^{-4}***	3.81		0.81	−0.24		8.34×10^{-3}**	2.65	
Sex	0.24	1.17		0.025*	2.25		0.61	0.51	
ADHD	0.36	−0.92		0.75	−0.32		0.11	−1.62	
SCARED	1.84×10^{-10}***	6.56		4.12×10^{-6}***	4.68		1.96×10^{-4}***	3.76	
Step3			16.90			5.23			7.69
Age	0.84	−0.20		0.46	−0.75		0.039*	2.07	
Sex	0.17	1.36		0.023*	2.29		0.46	0.74	
ADHD	0.50	−0.67		0.80	−0.25		0.13	−1.54	
SCARED	0.14	−1.48		0.88	0.16		0.19	−1.32	
SCARED × Age	0.0059**	2.77		0.46	0.74		0.037*	2.09	

Notes: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
Abbreviations: ADHD, Attention-deficit/hyperactive disorder; YGTSS, Yale Global Tic Severity Scale; SCARED, Screen for Child Anxiety Related Emotional Disorders.

respectively. In the high anxiety group, we observed a significant increase in the total YGTSS score with age ($p = 1.82 \times 10^{-5}$, $t = 4.55$). Conversely, this relationship was not significant in the low anxiety group ($p = 0.49$, $t = 0.69$), as shown in Figure 2B. These results suggest that high anxiety is associated with an increased in tic severity with age, whereas low anxiety is associated with a more stable tic severity that does not change significantly with age. Furthermore, the moderating effect of anxiety on the relationship between tic severity and age is independent of the grouping strategies of anxiety symptoms used.

Moderating Effects of Anxiety is Different in Each Subscale

To determine which anxiety subscales most significantly influence changes in tic severity with age, we analyzed the five dimensions of the SCARED scale. These dimensions include panic/somatic, generalized, separation, social, and school phobia anxiety symptoms. Each subscale score was independently entered into the linear regression model. We found that generalized, separation, and school phobia anxiety significantly influenced changes in tic severity with age (all *p*s < 0.05), explaining 16%, 15.6% and 10.9% of the variance, respectively. However, only the moderating effect of separation anxiety could pass Bonferroni correction ($p < 0.01$). In contrast, panic/somatic and social anxiety did not show

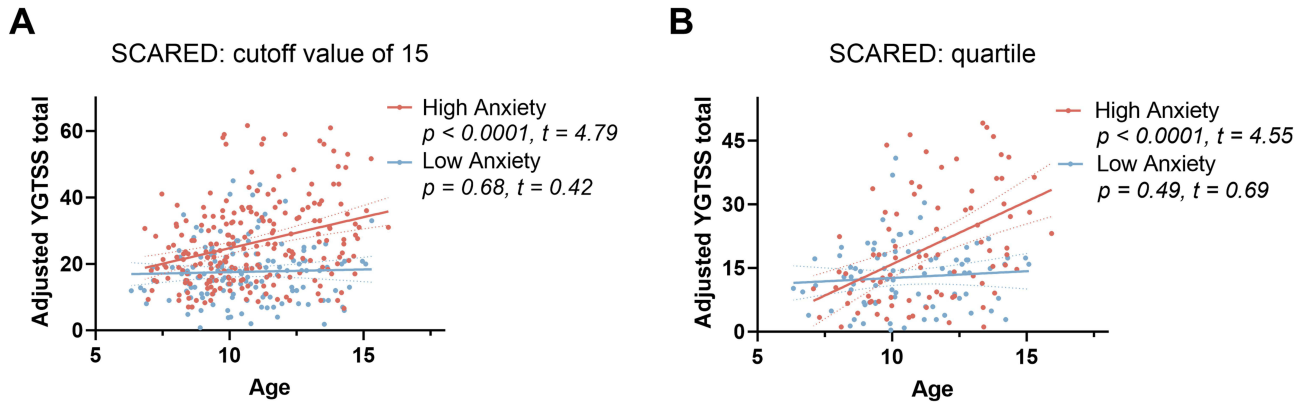

Figure 2 Anxiety symptoms moderate the relationship between tic severity and age. (**A**) Simple slope analysis for grouping with cutoff value of 15. (**B**) Simple slope analysis for grouping with 75th and 25th percentile of the participants. The adjusted value denotes the measure of interest corrected for sex and ADHD diagnosis.
Abbreviations: YGTSS, Yale Global Tic Severity Scale; SCARED, Screen for Child Anxiety Related Emotional Disorders.

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Table 4 Linear Regression Model for the Relationship Between Tic Severity and Age Under the Influence of Different Anxiety Subscales

Variables	YGTSS Total			Variables	YGTSS Total		
	p	*t*	*Adjusted R^2 (%)*		*p*	*t*	*Adjusted R^2 (%)*
Anxiety→SCARED total			16.90	Anxiety→SCARED separation			15.60
Age	0.84	−0.20		Age	0.92	−0.11	
Sex	0.17	1.36		Sex	0.39	0.85	
ADHD	0.50	−0.67		ADHD	0.44	−0.78	
Anxiety	0.14	−1.48		Anxiety	0.0015**	−3.19	
Anxiety × Age	0.0059**	2.77		Anxiety × Age	3.20×10^{-5}***	4.21	
Anxiety→SCARED panic			13.60	Anxiety→SCARED social			9.62
Age	0.17	1.38		Age	0.21	1.25	
Sex	0.38	0.89		Sex	0.37	0.90	
ADHD	0.55	−0.60		ADHD	0.63	−0.49	
Anxiety	0.52	−0.64		Anxiety	0.43	−0.78	
Anxiety × Age	0.077	1.77		Anxiety × Age	0.12	1.57	
Anxiety→SCARED generalized			16.00	Anxiety→SCARED school			10.90
Age	0.79	0.27		Age	0.19	1.32	
Sex	0.20	1.29		Sex	0.48	0.71	
ADHD	0.37	−0.90		ADHD	0.50	−0.68	
Anxiety	0.37	−0.91		Anxiety	0.095	−1.68	
Anxiety × Age	0.032*	2.16		Anxiety × Age	0.012*	2.54	

Notes: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
Abbreviations: ADHD, Attention-deficit/hyperactive disorder; YGTSS, Yale Global Tic Severity Scale; SCARED, Screen for Child Anxiety Related Emotional Disorders.

a significant effect (Table 4). Simple slope analyses for separation anxiety still considered two grouping strategies. Using a cut-off of 4,[34] we observed a significant increase in total YGTSS score with age in the high anxiety group ($p = 1.65 \times 10^{-7}$, $t = 5.48$), whereas this relationship was weaker in the low anxiety group ($p = 0.024$, $t = 2.28$, Figure 3A). Using quartiles for group participants, we found that in the high anxiety group, there was a significant increase in total YGTSS score with age ($p = 3.57 \times 10^{-7}$, $t = 5.51$), whereas in the low anxiety group the relationship was not significant ($p = 0.24$, $t = 1.18$, Figure 3B). These results suggest that the effect of anxiety on the relationship between tic severity and age varies across subscales, with separation anxiety making a notable contribution.

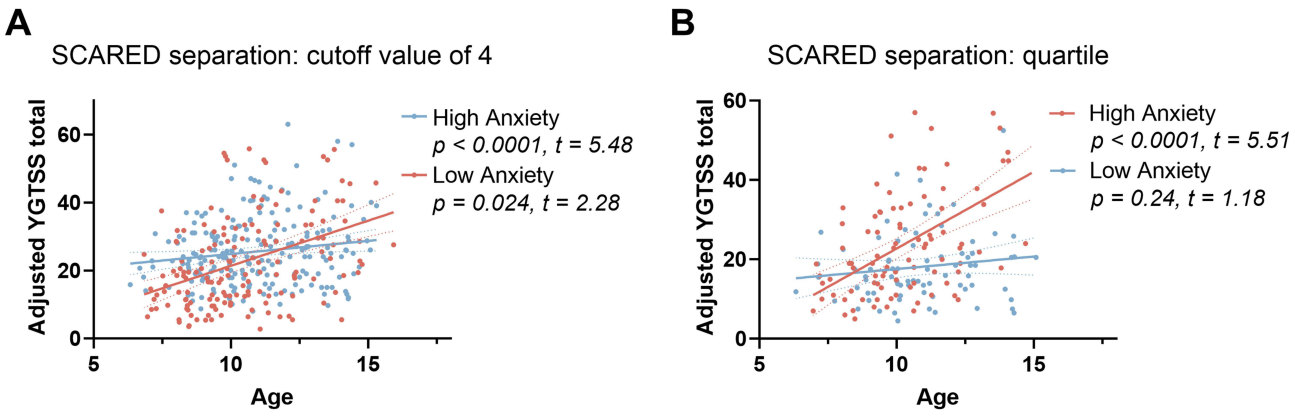

Figure 3 Separation anxiety moderate the relationship between tic severity and age. (**A**) Simple slope analysis for grouping with cutoff value of 4. (**B**) Simple slope analysis grouping with 75th and 25th percentile of the participants. The adjusted value denotes the measure of interest corrected for sex and ADHD diagnosis.
Abbreviations: YGTSS, Yale Global Tic Severity Scale; SCARED, Screen for Child Anxiety Related Emotional Disorders.

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Discussion

This study uniquely demonstrates how anxiety symptoms modulate the relationship between tic severity and age. Our analysis revealed a significant positive correlation between tic severity and anxiety severity in children and adolescents. In particular, tic severity increased linearly with age and was moderated by the presence of anxiety symptoms. In the high anxiety group, tic severity increased significantly with age, mirroring the overall trend. Conversely, in the low anxiety group, tic severity remained relatively stable regardless of age. We also found that specific anxiety sub-dimensions had varying degrees of influence on changes in tic severity with age, with separation anxiety making a notable contribution.

Our findings suggest a linear increase in tic severity with age, particularly for vocal tics. This escalation may be due to an increase in comorbidities over time, leading to greater overall impairment. Previous research suggests that tics typically begin between 4 and 6 years of age and peak in severity between 10 and 12 years of age.[6,7] In contrast to these earlier studies, our results did not show a significant quadratic relationship between tic severity and age, which is consistent with more recent findings.[8–10] However, our study does not imply that tic severity does not decrease after the age of 12 in children with anxiety. It is important to note that this is a group-level analysis, and changes at the individual level cannot be fully inferred from group-level findings. These differences in conclusions highlight the need for a larger and more diverse population to provide a more accurate picture of the course of tic severity.

In recent years, there has been increasing research into comorbid anxiety symptoms in people with TD.[21] On the one hand, anxiety disorders are more commonly diagnosed in people with TD than other emotional problems such as depression.[19,20,23,26,36] On the other hand, the anxiety of people with tics can sometimes be more distressing than the tics themselves.[29,37] Consistent with previous research,[18,19,23,24] our study found a significant positive correlation between both total and subscale anxiety scores and tic severity. However, a few studies show inconsistencies, reporting no relationship between anxiety and tic severity,[25,38] possibly due to different methodologies and small sample sizes ($n < 50$), highlighting the need for consistent research approaches and increased statistical power. Our study underscores that anxiety symptoms not only reflect the tic severity, but also significantly influence the relationship between tic severity and age. We observed that tic severity escalated significantly with age in the high anxiety group, whereas tic severity remained relatively stable in the low anxiety group. Our study is supported by the study by Kim et al, who followed 39 patients with provisional TD over 12 months and found that those with an anxiety disorder had more severe total tic scores.[39] This is consistent with our findings and further suggests a relationship between the course of TD and anxiety.

Although the precise pathophysiological mechanisms underlying the effect of anxiety on tic severity are not fully understood, preliminary evidence suggests a relationship. Behaviorally, the association between anxiety and tics may be due to efforts to suppress tics.[12,40] Patients often actively inhibit tics, and failure to adequately control them may exacerbate anxiety and lead to more severe tics. Patients with TD may also experience anxiety due to fear of social reactions, stigma and bullying from society, social isolation and bullying. Another aspect is abnormal interoceptive awareness, where patients have difficulty accurately identifying and responding to internal bodily cues, potentially exacerbating the co-occurrence of anxiety and premonitory urges in TD.[41,42] At a neurobiological level, TD and anxiety may share common brain circuits and neurochemical pathways.[43–47] This overlap, particularly in the basal ganglia and cortico-striato-thalamocortical loops, which are involved in both motor control and emotional processing, suggests a mutual influence. In addition, increased reactivity in the hypothalamic-pituitary-adrenal axis and altered levels of corticotropin-releasing factor, which have been implicated in the expression of tics,[48] may also influence anxiety symptoms.[43,44] Despite these findings, direct evidence on the neural mechanisms linking anxiety and TD is still lacking. Future research using neuroimaging[49,50] and animal models[51,52] may be crucial in elucidating this relationship.

Our study found that different anxiety subscales variably influence changes in tic severity with age. Specifically, separation anxiety, generalized anxiety, and school phobia showed relatively significant contributions, whereas panic/somatic and social anxiety did not. Separation anxiety, which assesses a preference to stay close to family or a fear of being alone, was found to be more prevalent in adolescents with TD than in participants without TD.[24] It was identified as a strong predictor of tic severity, consistent with previous studies.[18,23,26] The significant interaction of separation anxiety in our study suggests its crucial role in exacerbating tic severity with age, underscoring the need for parental support and care for children with TD. Generalized anxiety disorder, characterized by widespread worries about daily life and work, was found to significantly influence tic severity. This aligns with previous research suggesting that daily life stressors, including anxiety, can exacerbate tics.[53] School,

as the primary social and educational environment for children, can be a significant stressor. Peer ridicule and special treatment by teachers can contribute to psychological distress, leading to increased efforts to suppress tics and subsequent stress or anxiety about attending school.

Children with TD often face underdiagnosis or undertreatment of their anxiety symptoms.[23,54] Our results should alert clinicians to the critical need to manage anxiety symptoms in children with TD. First, it is essential to increase the screening for anxiety disorders, according to established practice guidelines,[55] to ensure that every child with TD is assessed for potential anxiety symptoms. Second, there is the possibility that treating anxiety first may reduce tic severity or increase the effectiveness of subsequent tic treatment. Studies have shown that the presence of an anxiety disorder may reduce the response to tic-specific treatments.[56] Improving emotion regulation has been shown to be beneficial in alleviating tics.[57] Future work needs to evaluate the effects of treating anxiety on tic symptoms.

There are several key issues and directions for further research. First, the current study is only based on cross-sectional studies only and lacks longitudinal data. We cannot further capture the dynamic relationship between anxiety and tics as a result of treatment or natural changes. Although cross-sectional data may still reflect certain longitudinal characteristics,[58] future research should aim to increase the longitudinal sample size. Second, our current subjects were drawn from clinical settings, which may limit generalizability. Future studies should include patients from community settings, such as schools or residential areas, to broaden our conclusions. Third, although our study used a moderation model to explore the relationship between anxiety and tic changes, future research should use more sophisticated approaches, such as multivariate models[59] or machine learning models,[60–62] to further elucidate these dynamics. Furthermore, due to the limitations of our data, we only assessed the relationship between a single anxiety symptom and tic severity. In the future, more attention could be paid to investigating tics in children with comorbid multiple anxiety disorders. Fourth, we have focused on children and adolescents, a critical period for the onset and treatment of most mental disorders.[63] However, the impact of anxiety symptoms on the lifespan trajectory of tic severity remains an area for future investigation. In particular, some studies suggest that TD may manifest as early as infancy,[64] but the concurrent anxiety status during this period remains unclear. The development of effective assessment tools to evaluate internalizing disorders (eg, anxiety) in younger children is of paramount importance. Finally, this study primarily considers self-reported anxiety symptoms and clinician-rated tic severity. Future research may benefit from incorporating parent-reported data to avoid bias in the rating of scales and to provide a more comprehensive understanding of anxiety and tic symptoms.

Conclusion

This study shows that anxiety, especially separation anxiety, significantly influences the relationship between tic severity and age. In the high anxiety group, tic severity increased significantly with age, mirroring the overall trend. Conversely, in the low anxiety group, tic severity remained relatively stable regardless of age. These findings highlight the importance of considering anxiety in the effective management of TD.

Ethics Statements

All the procedures were performed in accordance with the Declaration of Helsinki, and verbal informed consent was obtained from all participants and their parents/guardians. The study protocol was approved by the Ethics Committee of Beijing Children's Hospital, Capital Medical University (IEC-C-006-A04-V.07).

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Disclosure

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References

1. Ueda K, Black KJ. A comprehensive review of tic disorders in children. *J Clin Med*. 2021;10(11). doi:10.3390/jcm10112479
2. Knight T, Steeves T, Day L, Lowerison M, Jette N, Pringsheim T. Prevalence of tic disorders: a systematic review and meta-analysis. *Pediatr Neurol*. 2012;47(2):77–90. doi:10.1016/j.pediatrneurol.2012.05.002
3. Cohen SC, Leckman JF, Bloch MH. Clinical assessment of Tourette syndrome and tic disorders. *Neurosci Biobehav Rev*. 2013;37(6):997–1007. doi:10.1016/j.neubiorev.2012.11.013
4. Yan J, Deng H, Wang Y, et al. The prevalence and comorbidity of tic disorders and obsessive-compulsive disorder in Chinese school students aged 6-16: a national survey. *Brain Sci*. 2022;12(5):650. doi:10.3390/brainsci12050650
5. Conelea CA, Woods DW, Zinner SH, et al. Exploring the impact of chronic tic disorders on youth: results from the Tourette syndrome impact survey. *Child Psychiatry Hum Dev*. 2011;42(2):219–242. doi:10.1007/s10578-010-0211-4
6. Leckman JF, Zhang H, Vitale A, et al. Course of tic severity in Tourette syndrome: the first two decades. *Pediatrics*. 1998;102(1):14–19. doi:10.1542/peds.102.1.14
7. Bloch MH, Leckman JF. Clinical course of Tourette syndrome. *J Psychosom Res*. 2009;67(6):497–501. doi:10.1016/j.jpsychores.2009.09.002
8. Garcia-Delgar B, Servera M, Coffey BJ, et al. Tic disorders in children and adolescents: does the clinical presentation differ in males and females? A report by the EMTICS group. *Eur Child Adolesc Psychiatry*. 2022;31(10):1539–1548. doi:10.1007/s00787-021-01751-4
9. Girgis J, Martino D, Pringsheim T. Influence of sex on tic severity and psychiatric comorbidity profile in patients with pediatric tic disorder. *Dev Med Child Neurol*. 2022;64(4):488–494. doi:10.1111/dmcn.15088
10. Groth C, Mol Debes N, Rask CU, Lange T, Skov L. Course of Tourette syndrome and comorbidities in a large prospective clinical study. *J Am Acad Child Adolesc Psychiatry*. 2017;56(4):304–312. doi:10.1016/j.jaac.2017.01.010
11. Liu F, Fan C, Yao B, et al. Factors linked to prognosis in children with provisional tic disorder: a prospective cohort study. *Eur J Pediatr*. 2024;183(9):4009–4017. doi:10.1007/s00431-024-05651-y
12. Conelea CA, Woods DW, Brandt BC. The impact of a stress induction task on tic frequencies in youth with Tourette Syndrome. *Behav Res Ther*. 2011;49(8):492–497. doi:10.1016/j.brat.2011.05.006
13. Deeb W, Malaty IA, Mathews CA. Tourette disorder and other tic disorders. *Handb Clin Neurol*. 2019;165:123–153. doi:10.1016/B978-0-444-64012-3.00008-3
14. Iverson AM, Black KJ. Why Tic Severity Changes from Then to Now and from Here to There. *J Clin Med*. 2022;11(19):5930. doi:10.3390/jcm11195930
15. Hirschtritt ME, Lee PC, Pauls DL, et al. Lifetime prevalence, age of risk, and genetic relationships of comorbid psychiatric disorders in Tourette syndrome. *JAMA Psychiatry*. 2015;72(4):325–333. doi:10.1001/jamapsychiatry.2014.2650
16. Matsuyama S, Otsubo T, Nomoto K, Higa S, Takashio O. Prevalence of generalized anxiety disorder in Japan: a general population survey. *Neuropsychiatr Dis Treat*. 2024;20:1355–1366. doi:10.2147/NDT.S456272
17. Wang F, Yang H, Li F, et al. Prevalence and comorbidity of anxiety disorder in school-attending children and adolescents aged 6-16 years in China. *BMJ Paediatr Open*. 2024;8(1):e001967. doi:10.1136/bmjpo-2023-001967
18. Coffey BJ, Biederman J, Smoller JW, et al. Anxiety disorders and tic severity in juveniles with Tourette's disorder. *J Am Acad Child Adolesc Psychiatry*. 2000;39(5):562–568. doi:10.1097/00004583-200005000-00009
19. Kurlan R, Como PG, Miller B, et al. The behavioral spectrum of tic disorders: a community-based study. *Neurology*. 2002;59(3):414–420. doi:10.1212/wnl.59.3.414
20. Bitsko RH, Holbrook JR, Visser SN, et al. A national profile of Tourette syndrome, 2011-2012. *J Dev Behav Pediatr*. 2014;35(5):317–322. doi:10.1097/DBP.0000000000000065
21. Sapozhnikov Y, Vermilion J. Co-occurring anxiety in youth with tic disorders: a review. *J Child Adolesc Psychopharmacol*. 2023;33(10):402–408. doi:10.1089/cap.2022.0091
22. Ludlow AK, Anderson S, Hedderly T, Gutierrez R. The relationship between anxiety and tic severity in children and adolescents with Tic disorders: a scoping review. *Curr Psychol*. 2024;43(25):21808–21829. doi:10.1007/s12144-024-05975-w
23. Marwitz L, Pringsheim T. Clinical utility of screening for anxiety and depression in children with Tourette syndrome. *J Can Acad Child Adolesc Psychiatry*. 2018;27(1):15–21. doi:10.1186/s12888-015-0430-0
24. Vermilion J, Pedraza C, Augustine EF, et al. Anxiety symptoms differ in youth with and without tic disorders. *Child Psychiatry Hum Dev*. 2021;52(2):301–310. doi:10.1007/s10578-020-01012-6
25. Wattanarojjanakit P, Chuthapisith J, Khongkhatithum C. Anxiety and parenting style in children and adolescents with tic disorders. *Pediatr Neurol*. 2023;146:139–143. doi:10.1016/j.pediatrneurol.2023.06.021
26. Eaton CK, Jones AM, Gutierrez-Colina AM, et al. The influence of environmental consequences and internalizing symptoms on children's tic severity. *Child Psychiatry Hum Dev*. 2017;48(2):327–334. doi:10.1007/s10578-016-0644-5
27. Eddy CM, Rizzo R, Gulisano M, et al. Quality of life in young people with Tourette syndrome: a controlled study. *J Neurol*. 2011;258(2):291–301. doi:10.1007/s00415-010-5754-6
28. Lewin AB, Storch EA, Conelea CA, et al. The roles of anxiety and depression in connecting tic severity and functional impairment. *J Anxiety Disord*. 2011;25(2):164–168. doi:10.1016/j.janxdis.2010.08.016
29. Hollis C, Pennant M, Cuenca J, et al. Clinical effectiveness and patient perspectives of different treatment strategies for tics in children and adolescents with Tourette syndrome: a systematic review and qualitative analysis. *Health Technol Assess*. 2016;20(4):1–450,vii–viii. doi:10.3310/hta20040
30. Muller-Vahl KR, Sambrani T, Jakubovski E. Tic disorders revisited: introduction of the term "tic spectrum disorders". *Eur Child Adolesc Psychiatry*. 2019;28(8):1129–1135. doi:10.1007/s00787-018-01272-7

31. Leckman JF, Riddle MA, Hardin MT, et al. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. *J Am Acad Child Adolesc Psychiatry*. 1989;28(4):566–573. doi:10.1097/00004583-198907000-00015
32. Wen F, Gu Y, Yan J, et al. Revisiting the structure of the Yale Global Tic Severity Scale (YGTSS) in a sample of Chinese children with tic disorders. *Bmc Psychiatry*. 2021;21(1):394. doi:10.1186/s12888-021-03399-5
33. Birmaher B, Brent DA, Chiappetta L, Bridge J, Monga S, Baugher M. Psychometric properties of the Screen for Child Anxiety Related Emotional Disorders (SCARED): a replication study. *J Am Acad Child Adolesc Psychiatry*. 1999;38(10):1230–1236. doi:10.1097/00004583-199910000-00011
34. Birmaher B, Khetarpal S, Brent D, et al. The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. *J Am Acad Child Adolesc Psychiatry*. 1997;36(4):545–553. doi:10.1097/00004583-199704000-00018
35. Su L, Wang K, Fan F, Su Y, Gao X. Reliability and validity of the screen for child anxiety related emotional disorders (SCARED) in Chinese children. *J Anxiety Disord*. 2008;22(4):612–621. doi:10.1016/j.janxdis.2007.05.011
36. Sambrani T, Jakubovski E, Muller-Vahl KR. New insights into clinical characteristics of Gilles de la Tourette syndrome: findings in 1032 patients from a single German center. *Front Neurosci*. 2016;10:415. doi:10.3389/fnins.2016.00415
37. Cuenca J, Glazebrook C, Kendall T, et al. Perceptions of treatment for tics among young people with Tourette syndrome and their parents: a mixed methods study. *Bmc Psychiatry*. 2015;15(1):46. doi:10.1186/s12888-015-0430-0
38. Modafferi S, Stornelli M, Chiarotti F, Cardona F, Bruni O. Sleep, anxiety and psychiatric symptoms in children with Tourette syndrome and tic disorders. *Eur J Paediatr Neurol*. 2016;20(5):696–703. doi:10.1016/j.ejpn.2016.05.003
39. Kim S, Greene DJ, Bihun EC, et al. Provisional tic disorder is not so transient. *Sci Rep*. 2019;9(1):3951. doi:10.1038/s41598-019-40133-4
40. Bortolato M, Coffey BJ, Gabbay V, Scheggi S. Allopregnanolone: the missing link to explain the effects of stress on tic exacerbation? *J Neuroendocrinol*. 2022;34(2):e13022. doi:10.1111/jne.13022
41. Ganos C, Garrido A, Navalpotro-Gomez I, et al. Premonitory urge to tic in Tourette's is associated with interoceptive awareness. *Mov Disord*. 2015;30(9):1198–1202. doi:10.1002/mds.26228
42. Pile V, Lau JYF, Topor M, Hedderly T, Robinson S. Interoceptive accuracy in youth with tic disorders: exploring links with premonitory urge, anxiety and quality of life. *J Autism Dev Disord*. 2018;48(10):3474–3482. doi:10.1007/s10803-018-3608-8
43. Kim J, Gorman J. The psychobiology of anxiety. *Clin Neurosci Res*. 2005;4(5–6):335–347. doi:10.1016/j.cnr.2005.03.008
44. Mah L, Szabuniewicz C, Fiocco AJ. Can anxiety damage the brain? *Curr Opin Psychiatry*. 2016;29(1):56–63. doi:10.1097/YCO.0000000000000223
45. Ganos C, Roessner V, Munchau A. The functional anatomy of Gilles de la Tourette syndrome. *Neurosci Biobehav Rev*. 2013;37(6):1050–1062. doi:10.1016/j.neubiorev.2012.11.004
46. Singer HS, Minzer K. Neurobiology of Tourette's syndrome: concepts of neuroanatomic localization and neurochemical abnormalities. *Brain Dev*. 2003;25(1):S70–84. doi:10.1016/s0387-7604(03)90012-x
47. Mou S, Yan S, Shen S, et al. Prolonged disease course leads to impaired brain function in anxiety disorder: a resting state eeg study. *Neuropsychiatr Dis Treat*. 2024;20:1409–1419. doi:10.2147/NDT.S458106
48. Swain JE, Scahill L, Lombroso PJ, King RA, Leckman JF. Tourette syndrome and tic disorders: a decade of progress. *J Am Acad Child Adolesc Psychiatry*. 2007;46(8):947–968. doi:10.1097/chi.0b013e318068fbcc
49. Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. *Nat Rev Neurosci*. 2009;10(3):186–198. doi:10.1038/nrn2575
50. Zhang C, Bie L, Han S, et al. Decoding consciousness from different time-scale spatiotemporal dynamics in resting-state electroencephalogram. *J Neurorestoratol*. 2024;12(1):100095. doi:10.1016/j.jnrt.2024.100095
51. Nestler EJ, Hyman SE. Animal models of neuropsychiatric disorders. *Nat Neurosci*. 2010;13(10):1161–1169. doi:10.1038/nn.2647
52. Zhang L, Cao C, Luo C, et al. Comparison of chronic restraint stress-and lipopolysaccharide-induced mouse models of depression: behavior, c-Fos expression, and microglial and astrocytic activation. *J Neurorestoratol*. 2024;12(3):100130. doi:10.1016/j.jnrt.2024.100130
53. Conelea CA, Woods DW. The influence of contextual factors on tic expression in Tourette's syndrome: a review. *J Psychosom Res*. 2008;65(5):487–496. doi:10.1016/j.jpsychores.2008.04.010
54. Safer DJ, Rajakannan T, Burcu M, Zito JM. Trends in subthreshold psychiatric diagnoses for youth in community treatment. *JAMA Psychiatry*. 2015;72(1):75–83. doi:10.1001/jamapsychiatry.2014.1746
55. Pringsheim T, Okun MS, Muller-Vahl K, et al. Practice guideline recommendations summary: treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology*. 2019;92(19):896–906. doi:10.1212/WNL.0000000000007466
56. Sukhodolsky DG, Woods DW, Piacentini J, et al. Moderators and predictors of response to behavior therapy for tics in Tourette syndrome. *Neurology*. 2017;88(11):1029–1036. doi:10.1212/WNL.0000000000003710
57. Ruhrman D, Mikulincer M, Apter A, Benaroya-Milshtein N, Steinberg T. Emotion regulation and tic disorders in children. *Eur Child Adolesc Psychiatry*. 2023;32(5):893–902. doi:10.1007/s00787-021-01912-5
58. Kraemer HC, Yesavage JA, Taylor JL, Kupfer D. How can we learn about developmental processes from cross-sectional studies, or can we? *Am J Psychiatry*. 2000;157(2):163–171. doi:10.1176/appi.ajp.157.2.163
59. Yang X, Liu Q, Zhang H, Lu Y, Yao L. A predictive model for functionality improvement after stroke rehabilitation. *J Neurorestoratol*. 2024;100157. doi:10.1016/j.jnrt.2024.100157
60. Bzdok D, Meyer-Lindenberg A. Machine learning for precision psychiatry: opportunities and challenges. *Biol Psychiatry Cogn Neurosci Neuroimag*. 2018;3(3):223–230. doi:10.1016/j.bpsc.2017.11.007
61. Dwyer DB, Falkai P, Koutsouleris N. Machine learning approaches for clinical psychology and psychiatry. *Annu Rev Clin Psychol*. 2018;14(1):91–118. doi:10.1146/annurev-clinpsy-032816-045037
62. Gupta A, Mishra N, Jatana N, et al. Predicting stroke risk: an effective stroke prediction model based on neural networks. *J Neurorestoratol*. 2024:100156. doi:10.1016/j.jnrt.2024.100156
63. Marin O. Developmental timing and critical windows for the treatment of psychiatric disorders. *Nat Med*. 2016;22(11):1229–1238. doi:10.1038/nm.4225
64. Zinner SH. Tourette syndrome in infancy and early childhood. *Infants Young Children*. 2006;19(4):353–370. doi:10.1097/00001163-200610000-00007

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