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Fine Motor Skills in Children with Tourette Syndrome and their Unaffected First-degree Siblings

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Abstract

Background: The exact etiology of Tourette Syndrome (TS) remains unclear, making the search for impaired neuropsychological functions possibly connected to the underlying cause of TS as important as it is challenging. One neuropsychological domain of interest is fine motor skills.

Method: This study compared fine motor skill performance on the Purdue Pegboard Task (PPT) in 18 children with TS, 24 unaffected first-degree siblings and 20 controls. A set of screening questionnaires was administered to determine comorbid psychiatric illness.

Results: Children with TS, their siblings and controls did not differ significantly in fine motor skills as measured with the PPT. Performance on the PPT was not correlated with tic severity; however, we found an inverse correlation with severity of attention-deficit/hyperactivity disorder (ADHD) symptoms, as assessed by parent reported ADHD symptoms. Children with TS were found to have significantly higher parent reported ADHD symptoms compared to controls, yet only two out of the 18 participants had been diagnosed with ADHD.

Conclusion: This study suggests that fine motor skill impairment in children with TS may be more strongly correlated with comorbid ADHD than to TS and tics.

Keywords: Tourette Syndrome; fine motor skills; ADHD; neurodevelopment

Introduction

Tourette syndrome (TS) is a childhood-onset neurodevelopmental disorder, characterized by the presence of multiple motor tics and at least one vocal tic, persisting for more than one year (1). Tics are defined as rapid, recurrent, non-rhythmic, semi-(in)voluntary, stereotyped movements (motor tics) or vocalizations (vocal tics), which are usually preceded by a premonitory urge (2). They typically occur in bouts throughout the day and wax and wane over the course of months (3). A systematic review and meta-analysis estimated the prevalence of TS in children to be 0.3% to 0.9%, with the true population prevalence likely being towards the higher end, and a male/female ratio of approximately 3-4:1 (4, 5). TS commonly has an onset around the age of four to six years, with symptoms peaking at the age of 10 to 14, with many experiencing significant improvements in tic severity moving towards adulthood (6, 7). A large clinical longitudinal study found that 17.7% of participants above the age of 16 had no tics, whereas 59.5% had mild to minimal tics and 22.8% had moderate to severe tics (8).

The phenotypic presentation of TS varies greatly, ranging from mild cases with simple tics to more complicated cases with severe and/or debilitating tics, such as coprolalia (inappropriate vocal tics) or copropraxia (inappropriate motor tics). These may lead to considerable social stigma and decreased quality of life (9, 10). Additionally, individuals with TS often present with comorbid disorders, such as attention-deficit/hyperactivity disorder (ADHD) or obsessive-compulsive disorder (OCD) (11, 12).

The etiology of TS is complex and multifactorial, as studies have demonstrated that TS is one of the most heritable neuropsychiatric disorders, while also involving immunological and environmental factors.

Nevertheless, the precise pathogenesis remains elusive (13-16).

Endophenotypes are described as measurable, trait-like deficits or components of neuropsychiatric illnesses along the pathway between disorder and genotype (17). Knowledge of these underlying mechanisms that may predispose individuals for developing an illness is vital for a better understanding and tailoring of effective treatments and even preventive approaches. The search for consistently impaired neuropsychological domains as endophenotypes in TS has been challenging as findings have been difficult to replicate.

One candidate for consistent neuropsychological deviations in individuals with TS may be the impairment of fine motor skills. Fine motor function is neurologically associated to the basal ganglia and the cortico-striato-thalamo-cortical (CSTC) circuitry (18). These brain regions are also assumed to be involved in tic generation, and therefore it can be hypothesized that these components could be correlated (4, 7, 19). Additionally, TS is associated with dysfunctions involving motor cortical areas, such as heightened activation of premotor cortex and supplementary motor areas, which are involved in the planning and coordination of temporal sequences of action (20-22). Reduced caudate volumes have been demonstrated in patients with TS on structural MRI and correlated to future tic severity in early adulthood (23, 24). Neuroimaging studies which suggest the involvement of primary motor structures of the brain, along with the nature of tics as motor symptoms, could implicate that impaired fine motor skill is an endophenotype for TS.

Adequate fine motor skills are crucial in the performance of almost all everyday tasks, such as self-care (brushing teeth, clothes fastening, eating), writing, opening a lunch box or social activities such as gaming or text messaging. As such, deficits in this domain of function may have a profound negative effect on a child's self-esteem and compromise their general development. This is perhaps even more true for children with TS, as experience of inadequacy in these situations could cause excess stress and cause worsened tic severity and social stigma (3). Contributing to this hypothesis of fine motor skills being an endophenotype of TS could provide a basis for offering proactive treatment in the form of relevant training and support in mastering daily tasks related to fine motor skills for patients with TS.

Several studies have reported deviations in fine motor function in children with TS. A study by Bornstein and colleagues found impaired performance on the Grooved Pegboard Test and the Tactual Performance Test time score (25). Nomura and colleagues revealed clumsiness of rapid alternating pronation-supination movements of the arm and induced rigidity of the contralateral arm in drug-naive patients with TS, suggesting hypofunction of the nigrostriatal dopamine system (26). Bloch and colleagues reported that children with TS performed one to one-half standard deviation below normative data on the Purdue Pegboard Test (PPT), and that poor fine motor skills were a predictor of future tic severity (27). Sukhodolsky and colleagues reported that boys with TS showed impairments in the dominant-hand PPT performance, while girls with TS performed within normal ranges (28). However, other reports described intact fine motor function in children with TS (29). A review on the research on motor function in TS by Kalsi and colleagues suggested that the varying results may be due to differences in study designs including in/exclusion criteria on comorbidity (30).

The present study sought to examine fine motor skills in children with TS, compared to their unaffected first-degree siblings and healthy controls, as measured with the PPT. Differences between these three groups would further strengthen the validity of deficiency in fine motor skills as an endophenotype for TS. Our hypotheses were as follows: Children with TS have significantly impaired fine motor skills compared to their unaffected first-degree siblings, as measured with the PPT. Secondly, a control group performs significantly better than both TS-children and their unaffected first-degree siblings. In other words, we expected to find a dose-response relationship between genetic load for TS and fine motor skills across the three groups.

Materials and Methods

Recruitment and Characteristics

We recruited participants with a preexisting diagnosis of TS through the national Tourette Clinic at the Pediatric Department at Herlev University Hospital in Denmark. We asked visiting families about unaffected (i.e. tic-free) first-degree siblings and invited them to participate if they met the criteria for inclusion. We assigned the pair of siblings to two separate groups: children with TS and first-degree sibling without TS.

The following inclusion criteria were applied: Participants were a pair of first-degree siblings, one sibling previously diagnosed with TS and one unaffected, both between the age of 7-14 and from the Capital Region of Denmark. Exclusion criteria were IQ +/- two standard deviations from the mean and unaffected siblings with a previous episode with transient tics.

We recorded any preexisting psychiatric comorbidity and medication. Comorbid conditions were based on clinical consensus diagnosis made prior to this study

through standard Danish diagnostic procedures by neuropediatricians and/or child psychiatrists.
The control group was randomly selected from the Danish Civil Registration System and manually matched to unaffected siblings by age and sex, permitting an age difference of no more than four months, which allowed the recruitment of a representative control sample (31).

Participants

We recruited a total of 21 children with TS (mean age 11.9 years ± 1.9) but excluded three participants from our dataset. One participant never completed the full testing course and two did not meet the full diagnostic criteria for TS. Twenty-seven unaffected siblings were recruited (mean age 10.3 years ± 1.8), three of which had to be excluded. One sibling was bilingual and did not fully understand the testing instructions as presented in Danish, while the other two were excluded on account of their siblings not meeting the diagnostic criteria for TS. We recruited 23 randomly selected controls (age 10.4 years ± 1.8) who were matched to unaffected siblings by age and sex. Three controls presented with IQ-estimate scores above 130 (+2SD) and were therefore excluded from the analysis.

Procedures

A uniform battery of neuropsychological tests, described in the following sections, was performed in a single session by the same clinician in a controlled, undisturbed environment, lasting on average 80 minutes in total per subject.

Screening Questionnaires

Parents were asked to fill out questionnaires concerning their children, to determine comorbid psychiatric illness, namely: the ADHD Rating Scale (ADHD-RS) and the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) was completed in cooperation with a clinician (32, 33).
For children with TS, assessment included a measure of current tic severity, with and without impairment (Global Severity Score and Total Tic Severity Score, respectively), using the Yale Global Tic Severity Scale (YGTSS) (34).
The choice of questionnaires reflects the general gold-standard for diagnostics in both clinical and research related settings and is also used for children with TS when diagnosing comorbidity.

Purdue Pegboard Task (PPT)

The PPT assesses manual dexterity and bimanual coordination. The task involves gross motor function of arms, hands and fingers and fine fingertip dexterity together with hand-eye coordination (35). Participants self-reported their handedness, and if in doubt were asked about which hand they favored for writing.
The test is performed with a rectangular board fitted with two parallel rows of 25 holes, aligned vertically down the middle. At the top of the board are four concave trays containing various metal bits (pegs, collars and tubes). All participants were asked to perform four different tasks once (dominant hand, non-dominant hand, bimanual and assemble), with a short practice session before each task. In the two first subtasks the subject is instructed to insert as many 1.5 cm metal pegs into the holes as possible within the allotted time (30 seconds), using their preferred and then non-preferred hand. For the third task, the subject is asked to repeat the task using both hands simultaneously. In the final subtask, the subject is instructed to use both hands alternately to construct "assemblies", which consist of four metal bits each (a peg, one collar and a tube followed by another collar). The subject has one minute to complete as many assemblies as possible. We used the standardized instruction manual, translated from English to Danish.

Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV)

We administered five subtests of the WISC-IV to acquire an estimate of Full-Scale IQ, namely: block design, similarities, vocabulary, matrix reasoning and coding. These subtests were chosen to reflect the contents of the Wechsler Abbreviated Scale of Intelligence which does not currently exist in a Danish translation (36, 37). In addition, we included the "Coding" subtest, as it measures visual-motor speed and complexity and motor coordination, which was deemed relevant for this study.
To acquire an estimate of Full Scale IQ using five subtests of the WISC-IV, we calculated Total Scale Scores (TSS) for the four main indexes (Verbal Comprehension Index (VFI), Perceptual Reasoning Index (PRI), Working Memory Index (WMI) and Processing Speed Index (PSI), by multiplying the sum of the included subtests for each index by the inverse fraction of tests performed (i.e. TSS-VFI: as two out of three included subtests were used (vocabulary and similarities), the sum of the two scale scores were multiplied by 3/2). This methodology is also established in the WISC-IV manual to achieve VFI/PRI Index Scores when only two subtests are available (38).

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 24.0.
Group variables (age, IQ-estimate, questionnaire results and distribution of sex) were examined for differences between the three groups. We tested for

TABLE 1. Demographic information of the included participants. Means ± standard deviation.

	Children w/ TS	Siblings w/o TS	Controls	p-values
N	18	24	20	n/a
Age	11.9 ± 1.9	10.3 ± 1.8	10.4 ± 1.8	0.016
Sex (M / F)	13/5	12/12	10/10	0.277
IQ[1]	103.9 ± 12.4	107.1 ± 10.1	113.5 ± 10.3	0.026
Comorbidity[2]	4 (22.2%)	2 (8.3%)	0	n/a
Medication[3]	3 (16.7%)	0	0	n/a
ADHD-RS[4]	22.4 ± 15.3	13.9 ± 9.9	9 ± 7.9	0.001
YGTSS[5]	26.1 ± 14.1	n/a	n/a	n/a
Total Tic Severity Score[6]	18.6 ± 8.8	n/a	n/a	n/a
CY-BOCS	1.0 ± 2.3	0	0	>0.05

Two-tailed p-values that represent the value across all three groups. See the text for p-values between groups. [1]IQ estimate created using five subtests of WISC-IV (see paragraph 2.5 for description); [2]Children w/ TS: 2 = ADHD, 1 = OCD, 1 = ASD. Siblings w/o TS: 1 = ADHD, 1 = ASD; [3]Anti-tic or ADHD medication: Two participants received noradrenaline reuptake inhibitors (atomoxetine) and one received neuroleptics (risperidone, aripiprazole); [4]Parent reported; [5]Global Severity Score; [6]YGTSS w/o impairment; TS: Tourette Syndrome, ADHD: Attention-deficit/hyperactivity disorder, OCD: Obsessive compulsive disorder, ASD: Autism spectrum disorder, ADHD-RS: Attention-deficit/hyperactivity disorder Rating Scale, YGTSS: Yale Global Tic Severity Scale, CY-BOCS: Children's Yale-Brown Obsessive-Compulsive Scale.

differences in age and IQ-estimates using separate ANOVA's and post hoc tests and for differences in sex with a chi-square test.

We conducted Pearson correlations to examine the relationship between PPT scores and IQ-estimates, parent reported ADHD-RS scores and tic severity (YGTSS) within the three groups.

Finally, we performed a multivariate analysis of covariance (MANCOVA) to examine differences between the three groups on PPT performance for each subtask, controlling for age and IQ-estimate. A second analysis, including ADHD-RS scores as a third covariate, was also performed. Given the low CY-BOCS scores within all three groups (TS: 1.0 ± 2.3; non-TS: 0; controls: 0), which were all within the subclinical range of 0-7, these data were not included as covariates. Statistical analysis was two-tailed and the threshold for significance was set at $p \leq 0.05$.

Results

Descriptive results

Groups differed in age ($F(2, 59) = 4.45$, $p = 0.016$), with children with TS being significantly older compared to siblings without TS ($p = 0.023$) and controls ($p = 0.037$). Non-TS siblings and controls did not differ with respect to age ($p = 0.99$). Since statistical testing yielded no significant difference in sex distribution between the groups ($\chi^2(2)$, $p = 0.277$) and due to the low number of participants, sex was not included as a covariate in the final ANCOVA analysis.

Analysis revealed a significant difference in IQ-estimate ($F(2, 59) = 3.89$, $p = 0.023$). The control group (113.5 ± 10.3) performed significantly better in cognitive testing compared to children with TS (103.9 ± 12.4, $p = 0.023$). On the other hand, we found no significant difference in IQ-estimate between non-TS siblings and controls ($p = 0.138$) or children with TS ($p = 0.609$). Demographic data, estimated IQ and questionnaire scores are presented in Table 1.

Screening questionnaire results

Thirteen children of the 18 subjects with TS had experienced clinically significant tic symptoms (YGTSS ≥ 15) within the last week prior to testing. None of the participants reported having clinically significant OCD symptoms (CY-BOCS ≥8) at testing. Three children with TS scored between 0-7 (subclinical values), although one had previously been diagnosed with OCD. Given the low CY-BOCS scores within all three groups (TS: 1.0 ± 2.3; non-TS: 0; controls: 0), these data were not included as covariates. Analysis of the parent-reported ADHD-RS screening questionnaire uncovered significantly higher ADHD-RS scores among children with TS (22.4 ± 15.3) compared to controls (8.98 ± 7.9, $p = 0.001$) and their siblings (13.9 ± 9.9, $p = 0.034$) (Table 1). Controls and non-TS siblings did not differ in their ADHD-RS parent reported scores ($p > 0.05$).

Purdue Pegboard Results

Purdue Pegboard scores did not differ significantly between the three groups, before or after controlling for age and IQ-estimates. Adding ADHD-RS as a covariate did not affect the main outcome. Although not statistically significant, controls generally had marginally higher average scores, followed by non-TS siblings and TS children who had similar scores after controlling for age and estimated IQ (Table 2).

We examined correlations between PPT scores and IQ-estimates, parent reported ADHD-RS scores and tic severity (YGTSS) within the three groups.

We did not find any correlation between tic severity and performance in any subtasks of PPT ($p > 0.05$). No participants reported or were observed to have

TABLE 2. Purdue Pegboard Task results.

Purdue Pegboard	Children w/ TS	Siblings w/o TS	Controls	*p*-value[1]	η_p^{2}[2]
Dominant hand	12.9 ± 2.2	13.5 ± 1.9	13.9 ± 2.0	0.189	0.057
Non-dominant hand	12.6 ± 2.2	12.6 ± 2.0	13.2 ± 1.8	0.345	0.037
Bimanual	10.7 ± 1.9	10.7 ± 1.4	11.0 ± 1.4	0.914	0.003
Assemble	30.7 ± 5.4	30.2 ± 5.7	33.1 ± 5.3	0.175	0.059
Total	66.9 ± 9.2	67,0 ± 9.8	71.2 ± 8,8	0.176	0.059

Purdue Pegboard Test results are presented as means ± standard deviation. Results are controlled for age and IQ-estimates. [1]Analysis of Covariance, ANCOVA. Two-tailed p-values. [2]Partial eta squared, effect size. TS: Tourette Syndrome.

TABLE 3. Correlations between parent reported ADHD-RS and Purdue Pegboard scores across all groups.

Purdue Pegboard	Pearson Correlation	p-value[1]
Dominant hand	-0.39	0.002
Non-dominant hand	-0.25	0.050
Bimanual	-0.26	0.039
Assemble	-0.36	0.004
Total	-0.39	0.002

[1]Two-tailed p-values. Degrees of freedom = 60.

hand or arm tics, which could have directly disturbed their PPT performance.

Higher IQ-estimates were positively correlated with PPT scores in almost every subtask (non-dominant hand (Pearson correlation coefficient (PCC) ($r = 0.25$, $p = 0.04$), bimanual ($r = 0.39$, $p = 0.002$), assemble ($r = 0.26$, $p = 0.045$), total score ($r = 0.32$, $p = 0.012$)). We found no significant association between PPT scores in all subtasks and CY-BOCS scores.

A statistically significant inverse correlation was found across groups between PPT performance on all subtasks and parent-reported ADHD-RS.

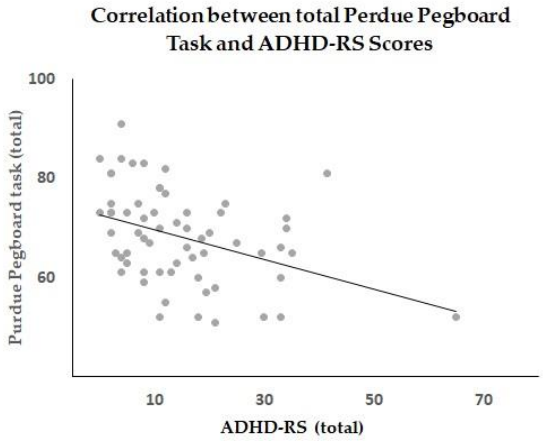

FIGURE 1. The Correlation between total Perdue Pegboard task and Attention-Deficit/Hyperactivity Disorder-Rating Scale (ADHD-RS) scores: Children with lower ADHD-RS scores performed better on the Perdue Pegboard task than children with higher scores. An inverse correlation was found across groups between total Perdue Pegboard task performance and total parent-reported ADHD-RS scores ($r(60) = -0.392$, $p = 0.002$).

The PCC's ranged from -0.25 to -0.39 which translates into a weak to moderate negative relationship between PPT and ADHD-RS scores (Table 3 and Figure 1). To ensure the correlations were not the result of confounding by indication (i.e., TS diagnosis) we performed an additional correlation analysis excluding children with TS and were able to replicate the correlation in this subsample.

Discussion

The aim of this study was to examine fine motor skills in children with TS and their unaffected siblings. We hypothesized that we would find a dose-response relationship between deficits in fine motor skills and genetic load for TS, by comparing PPT performance between children with TS, their unaffected first-degree siblings and healthy controls. We expected to find that children with TS would have significantly impaired fine motor skills compared to their tic-free, first-degree siblings, who are assumed to carry a genetic load for TS, but below the threshold for clinical phenotypic presentation. In turn, both siblings would have poorer fine motor skills than a randomly selected control group with no genetic disposition for TS.

We did not find any significant deviations in fine motor skills between the three groups within any of the four subtasks of the PPT when correcting for age and estimated IQ. We did not find any correlation between PPT performance and tic severity (YGTSS scores) at the time of assessment. An earlier study reported that poor performance on the dominant and non-dominant handed tasks were correlated with higher tic severity at time of testing, and that the dominant hand task predicted worse adulthood tic severity (27). The contradictory results may be due to variations in study design and sample size, or the fact

that tics typically wax and wane during short periods of time and are highly dependent on environmental factors such as excitement, stress, fatigue, and/or temperature, all of which are difficult to actively control in a testing environment (3, 6). Notably, we did not observe any hand/finger related tics among our participants, which could have impaired their performance.

Several previous studies have demonstrated deficits in fine motor coordination tasks such as the PPT in individuals with TS, while others have not been able to find an association (25-29). A review of the research on TS and fine motor function hypothesizes that these conflicting outcomes may be attributed to differences in approach and study design, especially regarding in-/exclusion criteria based on co-occurring comorbidity, lack of control measures, variation in studied age groups and testing methods (30).

This study found significantly higher parent reported ADHD-RS scores among participants with TS compared to siblings and controls. This was expected considering the high prevalence of co-occurring ADHD along with TS, yet notably the scores were largely below the diagnostic cut-off for the questionnaire (only two out the 18 participants with TS had a score above the cut-off). The low prevalence of comorbidity in our study group could be explained by the general practice of the Tourette's clinic, where patients with more dominant comorbidities are typically referred onwards to other, more appropriate health departments.

Interestingly, we also found a significant inverse correlation between PPT-scores and parents reported ADHD-RS scores across all groups, meaning that an increased severity of ADHD symptoms was significantly correlated to lower PPT performance for all participants. This correlation was also present when we excluded the children with TS from the analysis.

Overall, this could suggest that deficits in fine motor skills may be more strongly correlated to the severity of ADHD symptoms (even those below the diagnostic cut-off) than to tic severity. Considering the high prevalence of comorbid ADHD in the TS population, this may potentially explain the tendency for reduced fine motor skills among children with TS, and why we do not find a direct correlation to tic severity. It also may explain why previous research has produced conflicting results due to their varying study designs and in/exclusion of comorbid ADHD. In fact, several previous studies have found that co-occurring ADHD may be strongly correlated to neuropsychological deficits in children with TS (28, 29, 39). Additionally, the high prevalence of comorbid ADHD among patients with TS has previously been cited as a factor confounding our understanding of the neuropsychological profile of TS (40). This theory is supported by the fact that deficits in fine motor skills have also been linked to pure ADHD (41, 42).

A future investigation could aim to examine whether children with TS generally have more ADHD related symptoms without meeting the full diagnostic cut-off.

A strength of this study was that all procedures were performed with validated testing methods, applied by the same qualified clinician under supervision. Testing lasted only 80 minutes with a break in the middle, and no participants expressed fatigue after testing - in fact, they tended to find the PPT amusing.

The main limitation of this study was the small sample size. A plausible explanation for our primary negative findings is the relatively small sample size, which may have caused a lack of statistical power. However, the effect sizes (partial eta squared) were not representative of a meaningful difference between the groups, regardless of significance. In future studies, inclusion of a larger study group in addition to a follow-up study would be able to further investigate these and aforementioned factors.

TS children (and their siblings) were all recruited through a tertiary TS-specialized clinic at a hospital, where they received regular check-ups, psychoeducation and in some cases treatment in the form of either medication or cognitive behavioral therapy. Consequently, our TS study group was generally well treated from an early age, yet we may assume that they mainly represented a smaller part of the general TS population who required treatment in the first place, and therefore typically more severe cases of TS. The relatively small percentage of comorbidity in the TS group, while it may be considered a strength due to the assumed reduction of possible confounding effect, might also cause our study group to be less representative of the general TS population.

Earlier studies have generally demonstrated no influence from medication use on testing of fine motor function in patients with TS (25, 27, 28). Due to the small number of participants receiving medication (three out of 18), we cannot reliably test the potential modifying effect stemming from these conditions.

The lower average age among the siblings without TS can be seen as a potential confounder, even after controlling for age in the analysis, as it may be that they were too young to have their first appearance of tics. However, the mean age was 10.3 ± 1.8 which is older than the typical age of onset, but we cannot conclude that none of them could develop tics later in their lives, as we did not include a follow-up. None of the unaffected siblings in our study had experienced transient tics at the time of testing.

Estimated IQ on the WISC was notably higher in the control group compared to the siblings with TS making it a viable confounder in our analysis. The Purdue Pegboard task (PPT) is demanding of cognitive speed, and we can theorize that a higher full-scale IQ could translate into better performance on the PPT. However, to the best of our knowledge, no studies have yet examined this specific correlation (IQ and the PPT), yet we included IQ estimate as a covariate in the ANCOVA analysis due to significant differences between the groups.

Only one unaffected sibling had a clinical diagnosis of ADHD, which is comparable with the prevalence in the general population.

Normally, full ADHD-RS results consist of both a questionnaire filled out by the child's daily institution/school and parents, whereas we only included the latter due to easy availability at the time of testing. This would however be necessary in further investigations to fully confirm the results of the questionnaire.

To the best of our knowledge, no previous studies have examined unaffected first-degree siblings of children with TS as a secondary study group, when examining neuropsychological deficits related to genetic disposition for TS. We believe that the inclusion of the unaffected siblings is what makes this study unique and has the potential to add new knowledge to the current understanding of this subject, and perhaps inspire future studies to include siblings when investigating neuropsychological markers for TS. A comparison between unaffected siblings and healthy controls could provide an interesting perspective on the effect of genetic load on general neuropsychological functions.

Conclusions

In conclusion, our results did not show any statistically significant differences in fine motor skill performance between children with TS, unaffected first-degree siblings and healthy controls. When taking past studies into account, there seems to be a connection between fine motor skills and TS, yet it is difficult to discern its exact nature. This study did not find a correlation between tic severity and fine motor skill performance, but an inverse correlation between severity of ADHD symptoms (parent reported ADHD-RS) and deficits in fine motor skill performance was shown. Participants with TS were found to have significantly higher parent reported ADHD-RS scores compared to controls, although largely below the diagnostic cut-off. This might suggest that dysfunction of fine motor skills among patients with TS may be more strongly correlated to the high prevalence of comorbid ADHD and related symptoms, even when below the diagnostic cut-off on the ADHD-RS, than to TS and tics themselves. Further studies are needed to examine the exact nature of this possible correlation more thoroughly. Future studies could include a comparison between fine motor skill performance between a "pure" TS, a "pure" ADHD and a TS-ADHD group.

This preliminary study aimed to contribute to the understanding of TS and perhaps pave the way for further investigation into this avenue of interest.

Author Contributions

Conceptualization and methodology was defined by all authors; software, M.T.; formal analysis, M.T and K.M.; investigation, M.T. and J.H..; resources, K.P. and K.M.; data curation, M.T.; original draft preparation, M.T.; review and editing, all authors; visualization, M.T.; supervision, N.B. and K.P.; project administration, N.B., K.P. and M.T.; funding acquisition, K.P. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and project protocol was approved by the Danish National Committee on Health Research Ethics, Capital Region of Denmark (ref. nr.: H-15010087, Feb. 2015). All procedures were approved by Danish Data Protection Agency.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy and Danish data laws.

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Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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