Title: Association of tic disorders with poor academic performance in central Spain. A population-based study.

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Cubo E: Conception, design, acquisition of data, analysis, interpretation of data, drafting the article and final approval
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Abstract

Background: Tic disorders have been associated with impaired academic achievement, but this association has not been explored in detail. Our objective was to analyze the association of tic disorders with poor academic performance.

Methods: Cross-sectional, observational study conducted in a randomly selected sample of mainstream schoolchildren (aged 6-16 years). The sampling frame included different types of schools and educational levels. We identified pupils with poor academic performance (repeating a grade, special needs), and tic disorders (defined by DSM-IV TR criteria). Pupils with vs. those without tics, and those with vs. those without poor academic performance were compared in terms of clinical features (medical history, neurological and psychiatric comorbidities), school and environmental characteristics. Logistic regression analyses were performed using school performance (dependent variable), and tic disorders (independent variable), after adjusting for confounding variables.

Results: We included 1,867 pupils [mean age 10.9 + 2.9 years, 1,007 (53.9%) males]. Tics were present in 162 pupils (8.6%) and poor academic performance in 223 (11.9%). Overall poor academic performance was associated with age (odds ratio [OR]=1.71, p<0.0001), TV viewing (OR=5.33, p=0.04), attention deficit hyperactivity disorder (OR=1.38, p<0.0001), a family history of school dysfunction (OR=2.43, p=0.02), and negatively associated with higher intelligence quotient (OR=0.90, p<0.0001), and tic disorders (OR=0.29, p=0.01).

Conclusions: After adjusting for other covariates, tic disorders were not associated with poor academic performance. Early academic support and modification of environmental characteristics are needed for pupils at higher risk for school dysfunction, to enhance academic performance.

Key Words: tics, movement disorders, epidemiology, school dysfunction.

Background

Primary tic disorders are neurodevelopmental disorders of childhood characterized by being repetitive motor movements or sounds, which have a tendency to improve over time in most cases.[1] They are considered the most frequent movement disorder in the pediatric population, with 4% to 20% of schoolchildren experiencing tics during their lifetime,[1,2] and are frequently associated with psychiatric comorbities, especially attention-deficit disorder (ADHD), and obsessive-compulsive disorder (OCD).[3,4] According to the literature, individuals with tics, and especially those with associated ADHD, have a high prevalence of comorbid learning disabilities (LD), and these children are up to five times more likely to require special educational services than the general childhood population.[5]

There are many factors contributing to poor academic performance in children with and without tics, including the presence of LD, comorbidities such as low birth-weight, tics, ADHD, OCD, sedative effects of pharmacological treatments, below average intelligence quotient (IQ), and specific socio-cultural and home environmental characteristics such as too much television-viewing, maternal education, and lack of academic support.[6] Therefore, when evaluating children with tic disorders and poor academic performance, in order to attempt to maximize focused therapies for better performance, it is essential to distinguish the specific role of the tics relative to other individual contributing factors. Since little is known about the impact of tic disorders on poor academic performance, the aims of this study were, first, to determine the prevalence of poor academic performance and tic disorders in a mainstream school-based population, and second, to determine the association of tics with poor academic performance after adjusting for confounding variables.

PARTICIPANTS, MATERIALS AND METHODS

Setting, design, sample and procedure

This cross-sectional, population-based, case-control study was conducted between March 2007 and December 2009, in the Neurology Department, Hospital Universitario of Burgos, Spain. A previous study was conducted in 2007-2008 in two schools, in order to validate our methodology and screening procedures for tic disorders compared to the gold standard (neurological diagnosis established by the neurologist).[7] At the start of the present study, we received a computerized roster from the Burgos school district of all 31,028 pupils in primary and secondary education (aged 6 –16 years). We calculated that out of 31,028 pupils, a sample size of 1,730 (6%) pupils from mainstream schools was required and could feasibly be enrolled. This calculated sample size assumed a prevalence of 20% for tic disorders, [8] a prevalence of 7.5% for poor school performance (data obtained from the Castilla y León Government Education authorities in 2006), an estimated dropout rate of 15%, with a beta value > 99%. The Burgos school district with 98 public and 70 state-assisted schools, included 111 urban and 57 rural schools. Using a random digit table, 4 of the 168 mainstream schools were selected to participate. Educational placement (urban [defined as school situated in a city with more than 30,000 inhabitants] vs. suburban), financial support (public vs. state assisted), and educational level (elementary, middle and high school) information was taken into account for stratification. This study was carried out in 2 phases. *Phase 1* involved the application of the screening tool for tic disorders, and collection of academic data provided by the teacher responsible from each classroom. At this point, teachers were unaware of tic status information. The following information was obtained: academic scores, presence of LD, need of academic support at school and at home, and school characteristics [urban (yes, no), educational level, public vs. state-assisted (Catholic vs. non-Catholic schools), teacher/student ratio, availability of technology and academic team support at school, and teacher characteristics (gender and years of experience). *Phase 2* involved the collection sociodemographic, clinical, home and environmental characteristics data provided by trained researchers, and the ascertainment of tic disorders by the neurologist. The past medical, and family history, and environmental characteristics data were collected using structured questionnaires, included data on pregnancy, birth, perinatal and developmental problems, presence of comorbidities, need for pharmacological treatment, family history of tics and psychiatric disorders, habits and environmental characteristics (TV viewing, use of electronic games, parental education background, family history of poor academic performance, family size, and physical exercise). For operational reasons, prenatal and perinatal problems were grouped into one category, including pre-term infants, delivery problems, need of incubator, and other perinatal problems.

Data collection

<u>1 Definition of poor academic performance.</u>

Poor academic performance was operationally defined as full-time placement in special education needs, and/or current grade retention. Diagnosis of LD was based on psychoeducational assessments performed by licensed LD specialists at school using DSM-IV TR criteria, [9] and teachers information on the overall achievement of competencies (for the school year), which consisted of the same information provided to the educational board.[9] Deficits in reading, writing, and mathematical skills were assessed using 4-point scales (none, mild, moderate, severe), and subsequently dichotomized academic skills into unimpaired/ impaired (mild, moderate, severe), for the purpose of the present study. Previous work shows that teachers can provide accurate judges of impairment and their ratings concur with test result achievements.[10]

2. Screening tools for tic disorders

According to our previous validated screening procedure in our school-based population,[7] we developed a two-stage screening tool to be used in this study. First, a Proxy-Report Questionnaire was completed by parents and teachers, and second, the subjects were observed by trained raters (one psychologist, and two school teachers). In mainstream schools, based on our pilot study, the sensitivity of our screening battery for tic disorders compared to the neurological diagnosis of tics established by the neurologist was 79% (95% CI, 71.68-86.70), specificity 98% (95% CI, 94.26-99.58), positive predictive value 97% (95% CI, 91.64-99.38), and negative predictive value 98% (95% CI, 94.30-99.58).[7]

3 Ascertainment of tic diagnosis

Our diagnostic procedures for tic disorders have been previously validated and described (appendix 1, 2).[7-11] Briefly, if all essential criteria of tics were fulfilled including the presence of repetitive movements or sounds, the urgency and relief before and after, and the change and fluctuations over time of these repetitive behavior, a diagnosis of tic by history was reached. If some of the essential criteria were not fulfilled a diagnosis of possible tic disorder was established. To reduce variability, the diagnosis of tic disorder was assigned by one movement disorder neurologist [EC], who interviewed by telephone the parents of all participants with (1) poor academic performance, and (2) at least one positive screening source for tic disorders, and unaffected age-, gender-, and matched- classmates for subjects with tics or poor academic performance. Tic severity and impairment (defined as any difficulty in self-esteem, family life, social acceptance, or school functioning), were assessed by the neurologist using the Yale Global Tic Severity Scale.[12,13] Tic disorders were classified by the neurologist as Tourette syndrome [TS], chronic motor tics [CMT], chronic vocal tics [CVT], transient tics [TT], and non-specified tics [NST], with/without impairment criteria using the DSM-IV TR criteria.[9]

4 Comorbidities

Comorbidities were screened by trained raters, who were blinded to the group assignment, using validated clinical scales and semistructured questionnaires. We included comorbidities previously associated with tic disorders including: 1) Autism Spectrum Disorders (ASD), using the autism domain of the Autism-Tics, ADHD and other Comorbidities Inventory (A-TAC) scale.[14] This questionnaire has been validated in the Spanish school age-population, with a range of scores from 0 (normal) to 17 (worse), and a cut-off score of 4.5 for the ASD domain; 2) Mental disorders, using the Spanish computerized version of the Children Predictive Scales (DPS),[15] which contains 18 subscales including phobia disorders, ADHD, OCD, oppositional defiant disorder, anxiety disorders, major depressive disorders, conduct disorder, and substance abuse. For subjects aged 6-10 years, the DPS was completed by parents, and for older subjects, the DPS was self-completed. A DPS total score $\geq$ 9 indicates the presence of probable mental disorders. Also, for screening of specific mental disorders individual diagnosis, there are individual cutoff scores for each subscale;[15] 3) Restless leg syndrome (RLS), using the National Institutes of Health pediatric diagnostic criteria for RLS.[16,17] Screening estimates of verbal and non-verbal intelligence plus a composite IQ were obtained using the Kaufman Brief Intelligence test (KBIT),[18] based on a mean of 100 and standard deviation of 15, indicating very high abilities (scores > 130), high abilities (scores from 120-129), average-high abilities (scores 110-119), average abilities (90-109), and below average abilities ($\leq$ 89). In addition, structured questionnaires were administered to parents to elicit information on presence of headache, and child´ sleep complaints.

Ethical Issues

The study protocol was approved by the ethical review board of the Burgos Hospital Complex Ethics Committee and School government district (Consejeria de Educación de Castilla y León), and the local school authorities, acting as the ethical committee for each school. Written consent from a parent/guardian was requested, and if the parent declined to participate in the study, no data were collected on that child.

Data analysis

Statistical analyses were performed using IBM-SPSS Version 19.0 (SPSS, Inc., Chicago, IL). All tests were two-tailed with alpha = 0.05. Descriptive statistics (i.e. means $\pm$ standard deviations [SD], range and 95% confidence intervals (CI) were used to describe demographic and clinical data. Using a one-sample Kolmogorov–Smirnov test, we tested whether continuous variables were normally distributed. Missing observations were encoded as missing data. In order to avoid confusion, all patients diagnosed with possible tics were excluded from analysis.

In this study, the conceptual framework included an ecological perspective that recognizes the ways in which clinical and demographic characteristics, family and environment can influence school success. The goal of the statistical analyses was to obtain the most parsimonious predictive model for academic performance. To achieve this goal, we performed a series of statistical tests to narrow down the number of predictors. We began with crude comparisons, where case-control differences were compared using Mann–Whitney U or Student t tests for continuous variables, as needed, and, the $\chi 2$ or Phi and V Cramer tests for categorical variables. Logistic regression analyses were then performed to test the association of tic disorders with poor academic performance using different interactive models. Poor academic performance (yes vs. no) was used as the dependent variable, and tic disorders as the independent variable. The resulting models of performed logistic regression analyses are usually considered good predictors of the outcome variables, taking into account that 50% corresponds to chance and 100% corresponds to perfect prediction.[19] In logistic regression analysis, we included all covariates that were associated in initial bivariate analyses (p value < 0.09) with either tic disorders or school performance. To narrow down the number of predictors, we performed two blocks of analysis. In the first block, tic disorders were adjusted for different covariates, and three different domain-specific models for demographics and clinical, school and environmental variables were included. In the second block, after excluding any variable not significantly associated with poor academic performance in the first block, we combined the remaining predictors from all three domain-specific models into one regression model. The goodness of fit of the regression model was evaluated using the Hosmer-Lemeshow test, and the Nagelkerke R^2 estimates. These analyses generated odds ratios (OR) with 95% confidence intervals (CI).

RESULTS

<u>Subjects.</u> In September of 2008, letters that explained the need for the survey (i.e., explaining the lack of information on the frequency of tics in Spain), and inviting participation were mailed to 2,806 parents (9%) out of 31,028 eligible pupils from mainstream schoolchildren in the province of Burgos. In *phase 1*, 1,867 (66.5%) parents agreed to participate, and the screening survey for tics, academic, school and teacher characteristics was completed on 1,858 pupils (99.5%, 54% males, 46% females), with a mean age of 10.9 $\pm$ 2.9 years. There were no differences between participants and non participants in terms of gender (χ2 test, p=0.56), and age (Mann-

Whitney test, p=0.50). In contrast, there was a higher participation of pupils with adequate academic performance compared to those with poor academic performance (77% vs. 56%, $\chi 2$ test, p<0.0001), and with a positive screening for tics compared to those with negative screening (75% vs. 71%, $\chi 2$ test p=0.02). In *phase 2*, 799 pupils were invited to participate, and 526 pupils were evaluated with a dropout rate of 35%. There was a similar participation in terms of a positive vs. negative screening for tics ($\chi 2$ test p=0.12), and age (Mann-Whitney test, p=0.94). Furthermore, there was a higher participation of males (53% vs. 47%, $\chi 2$ test, p<0.0001), and pupils with adequate academic performance (56.5% vs. 47.5%, $\chi 2$ test, p<0.0001), from Catholic Schools (55% vs. 45%, %, $\chi 2$ test, p<0.0001) in the assessed group compared to the non assessed group.

<u>Crude prevalence of tics and poor academic performance.</u> Based on the neurologist ascertainment, 162/1,867 pupils (8.6%, 95% CI 7.3-9.9) were diagnosed with tics (68.5% males and 31.5% females, and 28% and 72% with and without impairment criterion respectively). TS was diagnosed in 59/1,867 (3.1%, 95% CI 2.3-3.9), CMT in 73/1,867 (3.9 %, 95% CI 3.0-4.8), CVT in 20/1,867 (1.0 %, 95% CI 0.5-1.5), TT in 10/1,867 (0.5 %, 95% CI 0.1-0.8). One hundred and twelve pupils were diagnosed with possible tics (5.9 %, 95% CI 4.8-7.1) and were excluded for further analysis. Poor academic performance was found in 223 of 1,867 pupils (11.9%, 95% CI 10.44-13.44), including 199 (10.7%) current grade repeaters, and 24 pupils (1.2%) with special academic needs.

<u>Comorbidities.</u> Our results for comorbidities are summarized in Table 1. Pupils without tics and with adequate academic performance had a relatively low frequency of comorbidities. In contrast, pupils with tics suffered from ADHD, and sleep complaints more often, and had higher scores for ASD screening, compared to those pupils without

tics. There was also a trend towards having a higher proportion of social and specific phobia, mania and oppositional defiant disorder in the group of pupils with tics. In the group of pupils with poor academic performance, there was also a trend towards having a higher proportion of conduct disorder compared to those with adequate school performance.

Clinical, demographic, school and teachers, and environmental characteristics of cohort stratified by tic and academic performance status. Fully computable data were obtained for 93% of the sample. The results of the comparison of pupils with vs. without tics, and pupils with poor vs. adequate performance are all summarized in Tables 2 and 3. Of note, the proportion of poor academic performance was lower in the group of pupils with tics compared to those without tics ($\chi 2$ test p=0.03, unadjusted OR=0.55, 95% CI 0.32-0.93). In terms of YGTSS scores, tic severity was similar for pupils with poor academic performance compared to those with adequate academic performance (Mann Whitney test, p=0.64). Likewise, coexistent LD, pass rate, and the need for additional academic support were also similar for pupils with tics and without tics.

Association of sociodemographic, clinical, school-teacher, and environmental characteristics with academic performance. The final regression model is within the logistic regression, and for easy of reading, we only present the variables retained in the full model (Table 4). Overall poor academic performance was associated with age (OR=1.71, 95% CI 1.42-2.06, p<0.0001), TV viewing (OR=5.33, 95% CI 1-01-28.16, p=0.04), ADHD (OR=1.38, 95% CI 1.08-1.76, p<0.0001), a family history of school dysfunction (OR=2.43, 95% CI 1.10-5.38, p=0.02), and negatively associated with higher IQ (OR=0.90, 95% CI 0.87-0.93, p<0.0001), and tic disorders (OR=0.29, p=0.01). This model classified 88.6% of this population (94.9% with adequate academic performance, and 62.3% with poor academic performance).

DISCUSSION

In contrast to previous reports,[8,21] our results indicate that tic disorders are not associated with poor academic performance, demonstrating the importance of including other confounding variables that could account for academic underachievement. To further support the robustness of our results, the pass rate, tic severity, frequency of coexistent LD, and the need for academic support were overall similar, when pupils with and without tics were compared, regardless of how academic success was defined. In fact, in contrast to previous studies, pupils with tics were less likely to be academic underachievers. Several factors may account for this discrepancy such as different study methodology and data analysis, pupils, schools, and attrition characteristics. In this regard, whereas other studies analyzing impaired academic performance were just comparing pupils with tics (with and without comorbidities) to pupils without tics,[21] we analyzed the specific role of tics relative to other individually contributing factors using an interactive model for poor academic performance.

Additionally, our results add the Spanish experience to the global prospective on scholastic function of pupils with and without tics in different parts of the world. In terms of clinical and demographic characteristics, adolescents, with below average IQ, and a family history of psychiatric disturbances, were at higher risk of having scholastic impairment. In terms of school characteristics, pupils attending rural schools and with higher frequency of school attendance, were less likely to have scholastic impairment. Finally, in terms of environmental characteristics, low frequency of physical exercise, too much television viewing, and a family history of school dysfunction, were the most significant predictors of scholastic impairment. But, overall, the most relevant factors associated with poor academic outcomes were age, below average IQ, ADHD and poor environment defined as too much television-viewing, and a family history of school dysfunction. In this model, pupils with tic disorders were less likely to have poor school performance, and predicted scholastic impairment in 62.3% of the group of pupils with poor academic performance. However, based on the cross-sectional design of this study we cannot establish the direction of these observations (whether it was the cause or the consequence for a poor academic performance in this population).

Extending the findings of previous studies, we found that poor habits and environment in terms of parental academic achievement, were strongly associated with school dysfunction most likely due to inadequate study patterns.[22,23] In this regard, the usefulness of habit modification, including reduction of the number of hours of TV viewing, enhancing physical exercise, and providing early academic support, should be considered in further longitudinal studies of interventions geared toward improving academic achievement.

In terms of comorbidities, and in agreement with other studies,[3,4] ADHD was the most frequent comorbidity of pupils with tic disorders, and strongly and independently associated with poor academic performance.[24] The coexistence of tics with ADHD can cause a bias in terms of academic underachievement, and can at least partly explain why tics were previously associated with academic problems. Ideally, screening for ADHD symptoms should be a part of the school health surveys to provide academic support to this group. Interestingly, tic disorders were also associated with a higher frequency of ASD, prenatal and perinatal problems, a family history of psychiatric disorders, and sleep complaints, as shown in the bivariate analysis. Previous studies have also found that patients with tics display low sleep efficiency with elevated arousal index in sleep, and ASD trait.[25,26] These results highlight the fact that tics may represent an observable sign of minor cerebral damage,[8] as well as the importance of assessing comorbidities in patients with tic disorders, in order to avoid misdiagnosis and guide specific treatments for this population.

A limitation of this study was the lack of ascertainment for clinical comorbidities, the possibility of increased “false positive results” given the large number of variables and analyses conducted, the lack of precision in estimates of transient tics, and comorbidities not present at the time of the study, and possible selection bias. The lack of association between tics and poor academic performance may, in part, due to the mild severity of the tics in this population, and the definition of poor academic performance used for this study. Even though our results should be viewed as exploratory, the advantages of this study included a mainstream school population with the whole spectrum of tic disorders regardless of having functional impairment, a randomized cohort of pupils from different school types, and a relatively low dropout rate. Therefore the results of this study can to some extent be applied to other mainstream school based populations. In addition, the use of multivariate analysis allowed us to select the most meaningful predictive factors associated with poor academic performance, not just bivariate comparisons, and the multivariate adjustments. There is no doubt that the use of a cross-sectional design makes us more susceptible to confounding variables, however, it also enables us to generate hypotheses. However, because attrition and therefore sample selection bias is inevitable in epidemiological studies, especially those involving youngsters, further studies are required to confirm our results.

Specific strengths of this study include an adequate coverage of children and adolescent populations, the use of a validated screening battery for tic disorders and comorbidities, the inclusion of a large number of variables associated with either academic success or tics, and a description of the main attrition variables that may affect the precision in estimates.

In conclusion, despite a higher frequency of comorbid conditions in children with tic disorders, tics were not associated with academic difficulties after adjusting for confounding variables. The results of this study provide a basis for the need to identify pupils at risk for school underachievement, and underscore the urge for longitudinal studies of the impact of modification of environmental variables in improving scholastic achievement in mainstream schoolchildren. Furthermore, larger studies should be performed to ensure the validity of these results in different school systems.

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Appendix 1.

Proxy Report Questionnaire for parents and teachers

Tics are abnormal movements with the following characteristics:

a. They are sudden, brief and rapid

b. They are repetitive

c. They can be controlled voluntarily during short periods of time

d. They can change and affect other body parts periodically

e. They improve and worsen from time to time

f. Boys are more frequently affected than girls

The most common tics are eye blinking; elevating the eyebrows; twitching the nose and the mouth, and shoulder shrugging; shaking the head; twitching the neck; touching objects, other people or body parts (hair, nose, etc.); kicking the legs; throat clearing; sniffing, barking, and verbalizations.

According to these characteristics,

-Do you believe that your son/daughter has had tics? (yes or no)

-Do you believe that your son/daughter (or pupil) has tics? (yes or no)

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Appendix 2.

To formulate a diagnosis of tic based on history, a semi-structured interview with one of the parents at school, was used with all the criteria listed in the interview based on parents' reports. Based on a prior reliability pilot study performed in 37 students,[7] the intra-rater reliability of the telephone-based interview versus in-person neurological interview showed a k coefficient of 0.83 (95% CI 77.83-88.17).

ESSENTIAL CRITERIA OF TICS

1 Does your child make repeated and short movements or sounds? To give an example: constant blinking, screwing up of the nose, continuously clearing of the throat….

Yes No

2 Do these movements/sounds, despite being repetitive, change? To give an example: one period it may be blinking and in another period head shaking movements….

Yes No

3 Do these movements/sounds fluctuate over time? To give an example: are there days/periods of time with many movements/sounds and other days/periods of time with none.

Yes No

4 Is there a sense of "urgency" before making the sound/movement? To give an example: feeling of discomfort/itching in the area of the tic, sensory symptoms….

Yes No

5 Can he/she suppress them for a short period of time? To give an example: it is normal for children to have few tics in school and have more at home. Young people can even notice this suppression

Yes No

6 Is there a feeling of relief when the tic movements are made? To give an example: those affected can often make themselves nervous when they suppress tics for a long time and afterwards, they notice a decrease in this "tension".

Yes No

Table

Table 1. Comorbidities of cohort stratified by tic and school performance status

Comorbidity	**Description** Children without tics & Adequate academic performance	**Comparison** Children with vs. without tics P value	**Comparison** Children with poor vs. adequate school performance P value
ADHD (%)	10 (6.4)	32 (23.9) vs. 17 (8.3) **<0.0001**	15 (20.3) vs. 40 (13.7) 0.20
OCD (%)	4 (2.5)	6 (4.5) vs. 6 (2.9) 0.54	3 (5.8) vs. 10 (3.6) 1.00
Social phobia (%)	8 (5.5)	12 (10.3) vs. 9 (3.7) 0.06	4 (5.3) vs. 19 (7.8) 0.61
Conduct disorder (%)	8 (5.1)	12 (9.2) vs. 13 (6.5) 0.40	10 (14.7) vs. 18 (6.6) 0.09
Mania (%)	1 (0.6)	4 (2.9) vs. 1 (0.5) 0.07	0 vs. 5 (1.8) -
Oppositional defiant disorder (%)	9 (5.5)	16 (12) vs. 13 (6) 0.07	8 (10) vs. 24 (8.6) 0.82
Depression (%)	1(0.6)	3 (2.1) vs. 2 (0.9) 0.38	4 (4.8) vs. 3 (1.0) 0.23
Eating disorder (%)	11 (7.8)	14 (12.5) vs. 18 (9.6) 0.44	11 (15.9) vs. 23 (9.7) 0.29
Specific phobia (%)	5 (3.3)	10 (8) vs. 7 (3.4) 0.07	3 (3.6) vs. 14 (5.4) 0.58
Generalized anxiety (%)	0	4 (3.1) vs. 3 (1.4) 0.43	3 (3.7) vs. 4 (1.5) 0.38
Agoraphobia (%)	7 (4.5)	5 (3.7) vs. 10 (4.8) 0.34	3 (3.6) vs. 12 (4.4) 1.00
Separation anxiety (%)	6 (3.8)	10 (7.5) vs. 10 (4.7) 0.34	5 (5.8) vs. 15 (5.5) 0.78
Panic attack (%)	3 (1.9)	4 (3.1) vs. 6 (2.9) 1.00	4 (3.2)vs. 7 (2.6) 0.50
Restless leg syndrome (%)	3 (1.7) 0.70	3 (1.9) vs. 3 (1.3) 0.68	2 (2.2) vs. 5 (1.6) 0.65
Sleep complaints (%)	6 (3.4)	17 (11) vs. 8 (3.4) **0.005**	7 (7.5) vs.21 (6.8) 0.82
ASD Mean ± SD (median)	0.1 ± 0.4 (0.0)	1.5 ± 2.1 (1.0) vs. 0.5 ± 1.0 (0) **<0.0001**	0.9 ± 1.6 (0) vs. 0.9 ± 1.6 (0.1) 0.29

In these cells, there are missing data so that the total number of participants does not add up for cases or for controls.
ADHD (attention deficit hyperactivity disorder); OCD (obsessive compulsive disorder); ASD (autism spectrum disorders).

Table 2. Comparison of students with vs. those without tics

	Children with tics N=162	Children without tics N=245	Comparison p value
	Demographic & Clinical Characteristics		
Age (years) Mean ± SD (median)	11.6 ± 3.1 (11)	12.3 ± 3.1 (13)	**0.03**
Gender (males %)	111 (68.5)	148 (60.7)	0.11
Right handed (%)	139 (89.7)	213 (91)	0.87
Race Caucasian (%)	149 (92.5)	214 (88.4)	0.91
Pupils exposure to toxics Smokers Alcohol	 6 (4.2) 9 (6.3)	 12 (5.4) 11 (4.9)	 0.80 0.63
Mother mean age at child birth Mean ± SD (median)	33.6 ± 5.1 (33.0)	39.7± 12.8 (33)	0.27
Intelligence quotient Mean ± SD (median)	96.4 ± 13.9 (97)	94.9 ± 14.9 (97)	0.30
Weight at birth (Kg) Mean ± SD (median)	3.1 ± 0.5 (3.2)	3.2 ± 0.5 (3.2)	0.46
Body Mass Index (Kg/m^2) Mean ± SD (median)	18.4 ± 4.0 (18.3)	18.8 ± 3.5 (18.9)	0.11
Need for pharmacological treatment (%)	19 (12.3)	22 (9.4)	0.40
Prenatal & Perinatal problems (%)	50 (37.9)	46 (22.3)	**0.003**
Family history of tics	53 (34.4)	35 (15)	**<0.0001**
Family history of psychiatric disorders	63 (40.9)	70 (30)	**0.02**
	School and Teacher characteristics		
Located in Elementary school (%)	60 (37)	121 (49.4)	**0.01**
Located in Urban school (%)	113 (70.2)	176 (72.7)	0.65
Located in Public school (%)	61 (37.7)	138 (57)	**<0.0001**
Located in Catholic schools (%)	101 (62.3)	105 (43.4)	**<0.0001**
Academic support at home (%)	33 (21.4)	41 (16.7)	1.00
Learning difficulties (%)	53 (32.7)	82 (33.5)	0.91
Academic support at school (%)	18 (11.3)	41 (16.7)	0.15
Poor school performance	23 (14.2)	56 (23.1)	**0.03**
Teacher. Years of experience Mean ± SD (Median) Elementary.School Middle& High.School	 17.1 ± 11.8 (15) 15.7 ± 10.3 (13)	 19.7 ± 12.9 (15) 16.0 ± 10.2 (14)	 0.18 0.80
Teacher/student ratio	23.0 ± 4.1 (24.4)	21.8 ± 4.6 (24.1)	**0.003**
Use of technology in classroom (%)	34 (21.0)	77 (32)	**0.01**
Academic support team at school (%)	158 (97.5)	233 (96.3)	0.57
Academic achievement			

Pass rate (%) over the last 3 months Elementary School Middle & High School	 74 (80.4) 9 (17.3)	 81 (71.7) 21 (18.9)	 0.19 1.00
School attendance Number of days school absences Mean $\pm$ SD (median)	 0.9 $\pm$ 4.0 (0)	 1.3 $\pm$ 3.5 (1.0)	 0.06
	Environmental characteristics		
Physical exercise (%)	97 (62.6)	132 (56.7)	0.24
Electronic games Yes (%) Number hours/day Mean $\pm$ SD (Median)	 62 (40.5) 1.3 $\pm$ 0.4 (1.0)	 121 (52.4) 1.4 $\pm$ 0.5 (1.0)	 **0.02** 0.19
TV Yes (%) Hours per day Mean $\pm$ SD (Median)	 133 (85.8) 1.3 $\pm$ 0.5 (1.0)	 208 (88.9) 1.4 $\pm$ 0.5 (1.0)	 0.43 0.18
Mother main caretaker (%)	87 (58.0)	139 (61.8)	0.12
Parents education background Father high school (%) Mother high school (%)	 16 (10.7) 22 (13.8)	 28 (11.9) 27 (11.3)	 0.94 0.73
Family history of poor school performance (%)	62 (40.8)	82 (35.3)	0.28
Household members Mean $\pm$ SD (Median)	 3.9 $\pm$ 0.7 (4.0)	 4.0 $\pm$ 0.9 (4.0)	 0.53
Number hours of study Mean $\pm$ SD (median)	 1.8 $\pm$ 0.5 (2)	 1.8 $\pm$ 0.5 (2)	 0.90

In these cells, there are missing data so that the total number of participants does not add up for cases or for controls.

Table 3 Comparison of students with poor vs. adequate academic performance

	Poor academic performance N=223	Adequate academic performance N=1,644	Comparison P value
	Demographic and Clinical characteristics		
Age (years) Mean ± SD (median)	14.7 ± 2.7 (15)	11.4 ± 3.0 (11)	**<0.0001**
Gender (males %)	133 (62.4)	210 (64.6)	**0.01**
Right handed (%)	84 (89.4)	280 (90.3)	0.91
Race Caucasian (%)	174 (79.0)	298 (91.7)	**<0.0001**
Pupils exposure to toxics Smokers Alcohol	 10 (11) 8 (8.8)	 12 (4.1) 13 (4.5)	 **0.02** 0.10
Mother mean age at child birth Mean ± SD (median)	30.7 ± 3.2 (30.5)	37.7 ± 11.2 (33)	0.58
Intelligence quotient Mean ± SD (median)	85.5 ± 13.0 (88)	97.6 ± 13.8 (99)	**<0.0001**
Weight at birth (Kg) Mean ± SD (median)	3.2 ± 0.5 (3.3)	3.2 ± 0.5 (3.2)	0.61
Body Mass Index (Kg/m^2) Mean ± SD (median)	20.3 ± 3.5 (20.3)	18.3 ± 3.8 (18.2)	**0.0001**
Need for pharmacological treatment (%)	15 (16.0)	28 (9)	**0.05**
Prenatal & Perinatal problems(%)	26 (31)	76 (28.6)	0.58
Tics Any tic disorder Tic with functional impairment	 23 (29.1) 10 (15.2)	 139 (42.8) 34 (15.4)	 **0.03** 1.00
Family history of tics (%)	18 (19.4)	75 (24.2)	0.48
Family history of psychiatric disorders (%)	35 (37.6)	100 (32.4)	0.26
	School and Teacher characteristics		
Located in Elementary school (%)	54 (24.2)	201 (61.8)	**<0.0001**
Located in Urban school (%)	180 (80.7).	223 (68.8)	**0.002**
Located in Public school (%)	176 (78.9)	135 (41.5)	**0.002**
Located in Catholic schools (%)	48 (21.5)	190 (58.5)	**0.003**
Academic support at home (%)	42 (32.6)	57 (18.2)	**0.01**
Learning difficulties (%)	82 (36.8)	86 (26.5)	**<0.0001**
Academic support at school (%)	46 (20.6)	29 (8.9)	**<0.0001**
Teacher. Years of experience Mean ± SD (Median) Elementary.School Middle&High .School	 21.2 + 14.8 (22) 16.1 ± 10.7 (14)	 17.9 + 12.1.(15) 14.1 ± 10.2 (14)	 0.39 0.61
Teacher/student ratio	20.1 ± 5.0 (21.0)	22.9 ± 4.5 (24.1)	**<0.0001**
Use of technology in classroom (%)	89 (40.3)	76 (23.4)	0.82

Academic consultant team at school (%)	213 (95.5)	1,699 (91)	**0.02**
Academic achievement Pass rate (%) over the last 3 months Elementary School Middle & High School	 6 (3.9) 4 (13.3)	 149 (96.1) 26 (87.7)	 **<0.0001** **<0.0001**
School attendance Number of days school absences Mean + SD (median)	3.3 + 7.0 (2.1)	0.6 + 1.9 (0.3)	<0.0001
	Environmental characteristics		
		192 (61.9)	
Electronic games Yes (%) Number hours/day Mean + SD (Median)	 55 (59.8) 1.3 + 0.6 (1.0)	 139 (45.3) 1.2 + 0.4 (1)	 **0.01** 0.95
TV Yes (%) Hours per day Mean + SD (Median)	 89 (94.7) 1.4 + 0.5 (1.0)	 265 (85.5) 1.4 + 0.5 (1)	 **0.02** 0.21
Mother main caretaker (%)	52 (57.1)	182 (60.9)	0.12
Parents education background Father high school (%) Mother high school (%)	 9 (7.4) 14 (12.1)	 38 (12.3) 40 (12.4)	 **<0.0001** **<0.0001**
Family history of poor school performance	47 (51.1)	105 (34.2)	**0.002**
Household members Mean + SD (Median)	3.9 + 0.9 (4.0)	4.0 + 0.8 (4)	0.92
Number hours of study Mean + SD (median)	1.7 + 0.5 (2)	1.8 + 0.5 (2)	0.80

In these cells, there are missing data so that the total number of participants does not add up for cases or for controls.

Table 4. Logistic Regression of Model of adequate vs. poor school performance (dependent variable)

	Unajusted Odds Ratio (95% CI) P value	Adjusted Odds Ratio (95% CI) P value
Demographics & Clinical characteristics [a]		
Age (each additional year)	1.47 (1.31-1.64) <0.0001	1.77 (1.42-2.21) 0.02
IQ (each additional point)	0.94 (0.92-0.96) <0.0001	0.92 (0.88-0.95) <0.0001
ADHD	1.15 (0.98-1.33) 0.06	1.37 (1.03-1.81) 0.02
Tic disorders	0.55 (0.32-0.93) 0.03	0.25 (0.09-0.71) 0.009
Model fiftness (Nagelke R^2)		0.47
School characteristics [b]		
Rural schools	0.40 (0.19-0.84) 0.01	0.16 (0.05-0.43) <0.0001
School attendance	1.20 (1.10-1.31) 0.01	1.14 (1.04-1.26) 0.003
Tic disorders	-	0.94 (0.50-1.78) 0.86
Model fiftness (Nagelke R^2)		0.30
Environmental characteristics [c]		
Physical exercise	0.56 (0.34-0.94) 0.02	0.54 (0.32-0.93) 0.03
Daily TV viewing	4.13 (1.24-13.67) 0.02	4.02 (1.17-13.76) 0.02
Family history of poor school performance	1.47 (0.87-2.14) 0.14	2.14 (1.24-3.68) 0.001
Tic disorders		0.52 (0.29-0.94) 0.03
Model fiftness (Nagelke R^2)	-	0.10
Final Regression model [d]		
Tic disorders		0.29 (0.11-0.75) 0.01
Age (each additional year).		1.71 (1.42-2.06) <0.0001
Family history of poor academic performance		2.43 (1.10-5.38) 0.02
Daily TV viewing		5.33 (1.01-28.16) 0.04
IQ (each additional point)		0.90 (0.87-0.93) <0.0001
Model fiftness (Nagelke R^2)		0.54

IQ= Intelligence quotient;. The logistic regression model included all variables with either tic disorders or school performance
a. This model was adjusted for gender, age, race, family history of tics, student tobacco exposure, family history of psychiatric disorders, pre-perinatal history, use of pharmacological treatment, body mass index, conduct disorders, attention deficit hyperactivity disorder, autism spectrum disorder, sleep disturbances, and tic disorders.
b. This model was adjusted for school location, private vs. state supported schools, Catholic vs. non Catholic schools, school attendance, ratio of student/teacher, the use of technology in the classroom, and tic disorders.
c. This model was adjusted for the use of electronic games, daily TV viewing, physical exercise, and family history of poor academic performance, and tic disorders.
d. This model was adjusted for school location, age, TV viewing, family history of poor academic performance, and psychiatric disorders and tic disorders.