

**Title:** Physical Exercise in Tourette Syndrome: A systematic review

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**Abbreviated Title:** Exercise in Tourette Syndrome

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## Summary

**Background:** Tourette Syndrome (TS) is a common neuropsychiatric disorder which, in addition to the core symptoms of motor and vocal tics, includes a high association with mental health disorders. Physical exercise is increasingly being recommended as part of management for children and young people with mental health problems. However, there is a lack of guidance regarding the role of physical exercise in the management of TS in children.

**Methods:** EMBASE, MEDLINE, PsycINFO, SportDiscus, Google scholar and Cochrane register of controlled trials (CENTRAL) databases were searched. Studies investigating interventions aimed at reducing core symptoms of TS and comorbidities and exploring the relationship between physical exercise and tic severity were included.

**Results:** Seven studies were identified. Five focused on physical exercise interventions and two were observational studies investigating the relationship between tic severity and physical activity. There was some evidence indicating that physical exercise reduces tic severity in the short term and some evidence regarding the benefit of physical exercise on associated co-occurring symptoms, such as anxiety. However, none of the intervention studies involved randomisation and interventions varied in terms of content and duration.

**Conclusion:** There was some evidence of a short term improvement in tic expression as a result of physical exercise interventions but there is a lack of methodologically robust studies. Thus conclusions about the impact of exercise on TS symptoms or comorbidities cannot be drawn at this stage. There is a clear need for well-designed methodologically robust studies including prospective observational studies and randomised controlled designs.

**Keywords:** Tourette syndrome, exercise, physical activity, children, adolescence

## Key Practitioner message

- There is limited research exploring the impact of physical exercise on children with Tourette syndrome.
- There is some evidence that exercise positively affects tic frequency and severity and associated mental health problems but there is a paucity of well-designed observational or experimental studies.
- Further large scale observational and experimental studies of physical activity based interventions in children with Tourette disorder are warranted to better understand the impact of physical exercise on both tic severity and related co-occurring psychiatric conditions.

## Introduction

Tourette Syndrome (TS) (Tourette Disorder in DSM 5) is a common neuropsychiatric disorder characterised by the presence of chronic motor and vocal/phonic tics beginning before adulthood (Leckman, King & Bloch, 2014) and lasting more than one year (American Psychological Association 2013). TS affects up to 1% of children and adolescents, with a male:female ratio of 3:1. (Robertson, 2012). It is found across most cultures and has been described almost worldwide (Robertson, Eapen & Cavanna, 2009). TS is often associated with significant psychosocial difficulties, including social isolation, stigma, lower quality of life and behavioural problems (Cutler et al., 2009; Eapen, Cavanna & Robertson, 2016; Robertson et al. 2017). Additionally, children with TS commonly have other co-existing mental health disorders, particularly obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD) (Robertson, 2012) which tend to reduce in frequency in children with TS as they mature (Groth et al., 2017). For moderate to severe TS, drug therapies are the most frequently used forms of treatment (Piacentini et al. 2010). However, these treatments often either lack efficacy, or are associated with intolerable side effects (Roessner et al. 2013). In addition, parents and affected children and adolescents often prefer evidence based behavioural therapy, such as habit reversal training and exposure with response prevention (Verdellen et al., 2011; Cuenca et al., 2015). Clinically, parents often report that physical exercise is beneficial in reducing tics and improving symptoms of co-occurring disorders (Tourette Association of America <https://www.tourette.org/resource/exercise-sports-tourette-syndrome/> accessed August 3<sup>rd</sup> 2017).

The benefits of physical activity/exercise for school aged children are well documented with respect to physical health (Janssen & Le Blanc 2010). Physical exercise interventions have also shown promise for children with mental health disorders (Biddel & Asare, 2011) and a meta-analysis suggesting that although improvements in mental health were small, they were significant (Ahn & Fedewa, 2013). A recent review of physical exercise interventions in ADHD suggested that physical exercise represents a promising alternative or additional treatment option for children and adults with ADHD with beneficial effects reported with regard to several cognitive, behavioural, and socio-emotional functions (Den Heijer et al. 2017). A pilot exercise intervention with adults with OCD showed promising results in terms of OCD symptom severity and overall wellbeing (Brown et al. 2007).

As a result of the beneficial effects on symptoms of psychiatric disorders, physical exercise is increasingly being recommended as part of interventions for children with mental health problems. For example, the UK National Institute For Health and Clinical Excellence (NICE) recommends that healthcare professionals should emphasise the value of regular exercise for children, young people and adults with ADHD in their care (NICE, 2016 <https://www.nice.org.uk/guidance/cg72> accessed July 7<sup>th</sup> 2017). Despite the increasing research suggesting the beneficial therapeutic effects of exercise on children with mental health difficulties including ADHD, a condition frequently co-occurring in young people with TS, no reviews to date have examined the literature regarding the effect of exercise for children with TS and the effects of exercise on tics is not well understood (Leckman & Swain, 2005). It is possible that physical exercise may impact on

TS through reducing their motor and vocal tics or may be beneficial in treating the commonly associated comorbidities. There may be a common pathway of efficacy between exercise and TD and related disorders. The potential positive effects could have thus a direct impact on the severity of tics or emotional function, or an indirect effect on quality of life.

The aim of the present paper was to review studies which have evaluated physical exercise interventions and observational studies which have focussed on physical exercise in children with TD. The aim of the review was thus to assess whether physical exercise based treatment have been seen to affect the core symptoms of motor and phonic tics and associated mental health symptoms. The second aim was to explore whether observational studies have noted a significant relationship between physical exercise and Tourette syndrome

## **Method**

The PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines (Moher, Liberati, Tetzlaff et al. 2009) were followed in order to undertake the systematic review of the literature and to present the results. The protocol was registered with the Centre for Reviews and Dissemination (ID: CRD42015029561).

## **Search Methods**

Electronic searches of the literature were performed by MG in MEDLINE, EMBASE, PsychINFO, SportDiscus Google scholar and Cochrane register of controlled trials (CENTRAL) databases from inception to 26<sup>th</sup> June 2017. Broadly, the search terms were categorised into two main areas; (1) Tourette Syndrome and (2) Exercise. The Key words and MeSH terms used were (“Tourette” OR “tic” OR “involuntary movement” OR “involuntary sound” OR “gilles de la Tourette”) AND (“exercise” OR “exercising” OR “aerobic exercise” OR “anaerobic exercise” OR “physical activity”). Additional literature was found through personal contact with researchers in this area.

Data was extracted on the following: (i) characteristics of the child participants (n, age and sex); ii) features of the exercise intervention (type, duration, frequency, intensity of exercise, adherence, drop out and any adverse effects); (iii) methods used to evaluate the intervention (questionnaires, video measurement); (iv) results of outcomes.

## **Inclusion criteria**

(1) Studies of any level of evidence including randomised controlled trials, controlled trials, cohort studies, cases control studies and baseline studies; (2) Majority (>50%) of study participants aged between 0 to 17 with a diagnosis of Tourette Syndrome; (3) Participants who have received a physical exercise based intervention or provided information on their exercise activity. There was no requirement for the exercise based activity to be of a particular duration or frequency over time. 4) Studies in English.

## Results

The results of the initial search identified 351 papers. 233 independent papers were then screened after duplicates were removed. Following screening of abstracts, 19 papers remained and their abstracts were examined and assessed for eligibility. Seven studies were found to fit with the criteria of the review. Table 1 shows the results of seven studies on children and young people diagnosed Tourette Syndrome.

The children and young people in the studies were aged between 2 and 20 years of age. All participants were diagnosed with TS by a psychiatrist or a clinical psychologist. The total number of children across all of the studies was 138 with 103 being males (75%) and 35 females (25%), which is consistent with male:female ratio of TS in epidemiological studies (e.g Robertson, 2012). Recruitment for the studies was primarily from clinics/hospitals or TS support groups.

Due to the wide variability in study design, it was considered that a formal measure of study quality would not be appropriate. However, the Effective Public Health Practice Project tool quality rating tool ([http://www.ehphp.ca/PDF/Quality%20Assessment%20Tool\\_2010\\_2.pdf](http://www.ehphp.ca/PDF/Quality%20Assessment%20Tool_2010_2.pdf) accessed June 3<sup>rd</sup> 2017) was referred to when considering the overall quality of the studies. The EPHPP headings used were: Selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop outs and intervention integrity. In addition feasibility and acceptability was also considered where reported on.

### Studies with a physical exercise intervention

Five studies investigated an exercise intervention. Three used experimental designs with more than one participant (Nixon et al. 2014; Packer-Hopke & Motta, 2014; Simms, 2006). and two were case studies (Wang et al 2011; Liu et al. 2011)

Regarding the nature of the physical exercise intervention, one of the studies focused on a once off 2.5 hour intervention (Nixon et al. 2014) whereas the other two experimental designs involved regular exercise sessions on a weekly, bi-weekly, or tri-weekly basis, for 6 weeks and 3 months, respectively (Packer-Hopke & Motta, 2014; Simms, 2006). The interventions included a kickboxing exercise routine (Nixon et al. 2014)), a 30 minute aerobic exercise session (Packer-Hopke & Motta, 2014) and a group aerobic exercise class (Simms, 2006)). In one of the studies which involved a number of sessions, support was provided via Skype (Packer-Hopke & Motta, 2014), whilst in another a certified physical trainer was present during the sessions (Simms, 2006). In the two case studies the exercise intervention was not described in any detail (Wang et al 2011; Liu et al. 2011).

With respect to measurement of tics in the intervention studies, tic frequency and severity pre and post intervention were measured via observation in three studies (Nixon et al. 2014; Packer-Hopke & Motta, 2014; Simms, 2006) and via a standardised rating scale in four of the studies (Packer-Hopke & Motta, 2014; Wang et al. 2011; Liu et al. 2011; Simms, 2006). Reliability between raters on the video assessment was reported in one of the studies where video observation was used (Nixon et al. 2014). With respect to

outcomes in the interventions studies, improvements in tic frequency were reported by participants in the three experimental designs and in the one study where tic severity was recorded, a reduction was also noted (Packer-Hopke & Motta, 2014; Simms, 2006; Nixon et al. 2014). However, in the one study with control participants, some participants also recorded a reduction in tic severity but not tic frequency (Simms, 2006). Tic frequency was measured at 4 week follow up in this study and had returned to baseline for three of five participants suggesting gains may not be long lasting.

The measurement of related neuropsychiatric conditions was considered in three of the five intervention studies. One study included a standardised measure of anxiety and a standardised measure of OCD symptoms (Packer-Hopke & Motta, 2014) and a reduction in symptoms of both disorders were noted (Packer-Hopke & Motta, 2014). A measure of mood using two Likert scale items focussing on cheerfulness and anxiety was employed in another study (Nixon et al. 2014) and significantly improved functioning was reported after exercise. In one of the case studies a measure of paediatric quality of life was used (Liu et al. 2011). Simms (2006) reported that parents reported a positive influence on self-esteem as a result of participation in the exercise intervention but this was based on qualitative report and not standardised measures.

With respect to acceptability and feasibility of interventions one study reported qualitative data indicating that the intervention was well received by participants (Packer-Hopke & Motta, 2014).

### *Study quality*

With respect to selection bias, none of the studies could be considered truly representative of the TS population with recruitment primarily relying on hospital based or support group referrals. None of the studies involved randomization to the intervention/non-intervention arm. Assessors of outcome, as far as could be ascertained, were not blind to intervention status of participants. Both observational methods and standardised measures of tics were used and in one study reliability between rates between video assessors was reported (Nixon et al. 2014). Inter-rater agreement in this study was reported to be 87%. Withdrawals and drop outs were not reported systematically in any of the studies. There was no systematic reporting of intervention integrity in any of the studies.

### Observational studies examining TS expression and physical exercise

Two studies consisted of bespoke surveys focussing on the impact of environmental factors, including physical activity ('sports activities' - Silvia et al., 1995; 'playing sports and other leisure activities'; Caurin et al., 2014), on tic expression.. In the two studies, the percentage of respondents endorsing physical exercise as playing a role in tic expression was noted but no further statistical analysis was undertaken regarding the relationship between tics and physical exercise. In both studies, more participants reported a reduction in tic frequency than reported an increase, but in both studies the majority reported no difference in tic expression as a result of participation in physical activity.

## Discussion

This review indicates that there are some reports of reductions in tic severity and frequency associated with engaging in physical exercise in children and young people with Tourette syndrome. However, there is not enough high quality evidence to state with any certainty whether physical exercise interventions or engaging on physical activity has an impact on tic expression or the symptoms of associated mental health comorbidities, such as OCD and ADHD.

While this review indicates that there is some preliminary evidence that tic frequency and tic severity reduces as a result of participation in physical exercise, it is possible that these improvements are short lived, as both studies which had a follow up evaluation indicating that reported improvements were not sustained (Simms, 2006; Packer-Hopke & Motta 2014). In addition the design of the studies and reporting of outcome limits our capacity to understand if the short-term changes were clinically significant. Regarding the impact on comorbid psychological conditions, it would appear that improvements are more durable but not all studies investigating comorbid conditions included a follow up assessment.

One of the key limitations in the studies to date is study design, which has not been robust enough to provide the quality of evidence needed to evaluate whether physical exercise has benefits in children with TS. Studies to date have included a small number of participants with potentially biased recruitment. There is thus a need for larger, more representative samples and a need to clearly describe and consider the characteristics of the participants (age, SES, education, comorbid mental health conditions). There is also a need for randomised controlled trials with clear description of method of randomisation. Study samples to date have been too small to make any comment with respect to possible factors associated with outcome or indeed any mechanism of why such as change may have occurred based on a biological or psychological model. With respect to outcome measures, it is likely that the use of structured observation, including a consideration of measurement reliability, as well as use of standardised measures, will yield most valid data with respect to tic frequency and tic severity. In relation to mental health outcomes, none of the studies to date have considered symptoms of ADHD despite ADHD being one of the most common comorbidities (Freeman et al. 2007) and evidence that exercise can impact positively on ADHD symptoms (Den Heijer et al 2017). Studies should also include measures of quality of life to acknowledge the wide ranging impact TS can have on child functioning.

There is also a need to consider which interventions are likely to be most feasible with respect to frequency, intensity and duration. Whilst there are many current interventions aimed at increasing physical activity in children, very few are being targeted or tailored for specific populations including children with mental health and medical conditions. Measures of intervention fidelity are also important whether the intervention is delivered in person or remotely. None of the studies have included economic cost and there is thus a lack of clarity over the cost and feasibility of such interventions compared to evidence-based behavioural interventions used routinely in everyday clinical practice.

## Conclusion

There is not enough quality research evidence to draw conclusions about the impact of physical exercise on tic expression or associated mental health conditions in children with TS. This review has highlighted the research findings to date and suggestions for future directions with respect to developing an evidence base via observational and experimental studies.

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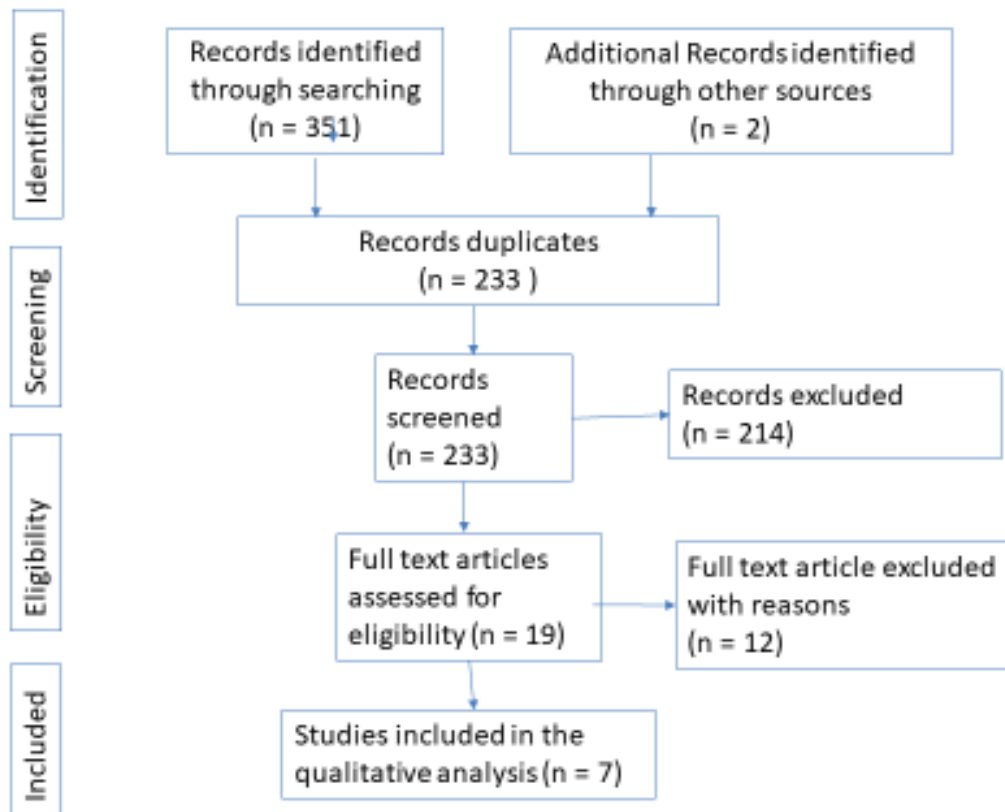
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Figure 1: Search process for studies focussing on exercise in Tourette Syndrome



**Table 1:** Studies focussing on physical exercise in Tourette Syndrome

Authors	Gender (m/f)	Age in years (range/mean)	Recruitment	Inclusion/Exclusion criteria	Study design	Exercise Intervention/ Measures	Measures of TS and comorbidities	Main Findings
Nixon et al. 2014)	13m/5f:	10-20/14.5	Through TS UK Charity	Clinical diagnosis of TS in absence of comorbid psychiatric disorder, serious physical illness or mental disorder. Aged between 10 and 20 years. A minimum of 1 discernible tic per minute.	<b>Experimental</b> Before/during/after measures of Tics. Before after mood and anxiety	One 2.5 hour session. Xbox Kinect Kickboxing exercise based routine	Video based measurement of Tic frequency. Mood (Anxiety and cheerfulness) based on a 10 point Likert scale.	Tic rates were lowest in exercise condition (hard or easy exercise), followed by post exercise and highest in pre exercise condition. Significantly improved self-rated mood and anxiety reported after exercise.
Packer-Hopke and Motta 2014)	5m/0f:	9-13/NR	Psychiatrist, support group and internet in US.	Had to have a professional diagnosis of TS and OCD.	<b>Experimental</b> Before/during/after measures of Tics, mood and anxiety.	30 minute aerobic exercise DVD Twice per week for 6 weeks. Participants had to be achieving 60-80% of max heart rate during the exercise.	Tic measurement based on scores on YGTSS, TODS-PR, 5 minute observation of tic frequency (most prominent tic focus of observation).  BAI-Y used for anxiety CY-BOCS for OCD symptoms All measured at baseline, 2, 4 and 6 weeks.	All 5 children had a reduced tic frequency measured through self and parental report, clinician rated interview and behavioural observation during the intervention. Children also had reduced OCD and Anxiety levels. However, at 4 week follow-up symptoms on TODS-P scales returned to baseline level for two children and observed tic frequency returned to the baseline level for 3 of 5 participants.

Caurin et al. 2014)	67m/25f	2-17/9	Recruited from a tertiary level hospital in Spain,	Patients with ASD and psychosis excluded from study. 52 has TS, 22 chronic tics and 18 tics of less than 12 months duration.	<b>Observational</b> Parents completed a range of standardised questionnaires including one that focussed on what might be associated with Tic occurrence	No exercise intervention. Participants reported on role of sporting activity on Tic expression.	A non - standardised questionnaire focussed on environmental factors that might influence tic expression.	32% of children reported a reduction in tic frequency while playing sports and other leisure activities. 17% reported an increase in tic frequency. 51% noticed no difference.
Wang et al. 2011	1m/Of TS	11/11	<b>NR. China</b>	Diagnosis based on DSM IV-TR	<b>Case report</b>	Reported that child played table tennis for 6 hours every weekday for six months.	YGTSS	YGTSS when boy was diagnosed at 4 years was 36. Two years after end of exercise intervention YGTSS was 5 and 'his TS no longer affects him'.
Liu et al. 2011	1m/Of	12/12	Referred by paediatric neurologist in China	NR	<b>Case report</b>	2 hours training session once a week for 3 months. Aerobic, stretch and strength, balance and coordination based.	YGTSS CHQ-PF50	Self-reported reduction in the frequency of tics. YGTSS score reduced from 37 to 28. Increased CHQ-PF50 score (i.e. better functioning). Reduced overall severity of tics.
Simms 2006	6m/1f	8-14/10.6	Recruited from the Pennsylvania Tourette Syndrome Association in the US.	6 had received a diagnosis of TS and 1 had a diagnosis of Chronic motor tic disorder.	<b>Experimental Case and control study</b>  <b>4 in fitness group and 3 in control group</b>  Measures at baseline and at 8 weeks.	Group aerobic exercise class three times a week for 8 weeks. Exercise ball toss, obstacle course, sit ups and push ups, stretch an relaxation	YGTSS and RVBTRS Weekly exercise activity logs	All participants in the exercise group reported a reduction in the severity of tics of at least 10% (mean reduction 13.85%) but 2 of the 3 participants in the control group also reported a reduction in tic severity. With respect to symptom

						over 46 minutes.		frequency 2 of three in experimental group demonstrated a decrease in tic frequency while one of the participants reported an increase in tic frequency. 2 of the 3 control group participants demonstrated an increase in tic frequency and a third did not demonstrate any change in frequency. 6 month follow up: Parents reported positive influence on self-esteem (qualitative report) but tic frequency and severity appeared to have returned to baseline levels
Silvia et al. 1995	10m/4f*	6 –14/10.3	A subset (14) of 53 patients consecutively referred to a Tourette's clinic.	All met DSM-III-R criteria for TS. Had never been medicated for TS	<b>Observational</b> Parent and young person completed TS questionnaire# focussed on environmental factors associated with TS.	No exercise intervention. Sport activity in the last year reported by questionnaire.	YGTSS in 8/14.	2 found sport activities reduced their tics, 6 noticed no difference and 3 noticed an increase in their tics.

TS= Tourette syndrome, m=male, f=female, NR=Not reported, OCD=Obsessive Compulsive Disorder, ASD= Autism Spectrum Disorder, DSM-III-R = Diagnostic and Statistical Manual of Mental Health Disorders –third edition revised (American Psychiatric Association, 1987), RVBTRS= Rush Video-Based Tic Rating Scale (Goetz et al. 1987), DSM IV-TR= Diagnostic and Statistrtical Manual of mental disorders, fourth edition – Text revision. American Psychiatric Association, & American Psychiatric Association. (2000). Task Force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. Washington, DC: American Psychiatric Association. YGTSS= Yale Global Tic Severity Sccle (Leckman et al. 1989), TODS-PR= Tourette's Disorder Scale –Parent Rated (Shytle et al. 2003), BAI-Y =Beck Youth Inventories- Second edition- Anxiety

Inventory (Beck 2005), CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale (Scahill et al. 1997), CHQ PF-50 = Child Health Questionnaire, Parent-Form 50 (Landgraf et al. 1996).



