Psychiatric comorbidity is common in dystonia and other movement disorders

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Abstract

Objective: To determine rates of psychiatric comorbidity in a clinical sample of childhood movement disorders.

Design: Cohort study.

Setting: Tertiary children's Hospital Movement disorder clinics in Sydney, Australia and London, UK.

Patients: Cases were children with tic movement disorders (n=158) and non-tic movement disorders (MD) (n=102), including 66 children with dystonia. Comparison was made with emergency department controls (n=100), neurology controls with peripheral neuropathy or epilepsy (n=37), and community controls (n=10,438).

Interventions: On-line Development and Wellbeing Assessment (DAWBA) which was additionally clinically rated by experienced child psychiatrists.

Main outcome measures: DSM-5 criteria for psychiatric diagnoses.

Results: Psychiatric comorbidity in the non-tic MD cohort (39.2%) was comparable to the tic cohort (41.8%) (not significant). Psychiatric comorbidity in the non-tic MD cohort was greater than the emergency control group (18%, ($p<0.0001$) and the community cohort (9.5%, $p<0.00001$), but not the neurology controls (29.7%, $p=0.31$). Almost half of the patients within the tic cohort with psychiatric comorbidity were receiving medical psychiatric treatment (45.5%) or psychology interventions (43.9%), compared to only 22.5% and 15.0% respectively of the non-tic MD cohort with psychiatric comorbidity.

Conclusions: Psychiatric comorbidity is common in non-tic movement disorders such as dystonia. These psychiatric comorbidities appear to be under-recognised and under-treated.

Introduction

Psychiatric co-morbidities have been well described in adults with movement disorders such as Huntington's Disease and Wilson's Disease[1]. Psychiatric comorbidity in children with tics and Tourette syndrome (TS) is also well described and is often more impairing than the tics themselves. However the investigation of psychiatric comorbidity in children with a broader range of movement disorders such as dystonia and chorea is limited to case reports and small case series.[2, 3] Studies have consistently shown that children with long-term health conditions, especially neurological disorders such as epilepsy have elevated rates of psychiatric illness.[4] In addition, common psychiatric disorders are increased in populations of physically unwell children, which can be effectively treated with well-established evidence-based treatments. [5, 6]

In Tourette's syndrome and tic disorders, there is better awareness of the high rates of psychiatric comorbidity and the impairment these cause, and national guidelines for the treatments of tics increasingly emphasise the importance of detection and treatment of comorbid mental health conditions. [7] However there is no such emphasis for non-tic movement disorders.

In this study a comparison was made between the rate of psychiatric comorbidity in children with non-tic movement disorders to children with tics and TS, as well as other control groups. We found that children with non-tic movement disorders have a similar rate of psychiatric comorbidity to children with tics and Tourette syndrome. We also established that, similar to children with other neurological disorders such as epilepsy, these children with non-tic movement disorders were much less likely to have their mental health needs detected and treated.[8]

Method

Patients: Patients were recruited according to inclusion criteria as follows: (1) age between 5 and 16 years (2) ability to speak in minimum of 5-word sentences, and (3) parental ability to speak English to allow for informed consent and questionnaire completion. Patients were recruited from The Children's Hospital at Westmead, Australia and Great Ormond Street Hospital, United Kingdom. We

recruited all eligible and sequential patients to avoid recruitment bias. Table 1 shows the baseline demographic data across all cohorts.

The tic movement disorder cohort consisted of patients with tics and Tourette Syndrome (n=158, including n=136 with TS). Within the non-tic movement disorder (MD) cohort (n=102), patients were diagnosed with either neurotransmitter disorders (n=13, GTP-cyclohydrolase deficiency, tyrosine hydroxylase deficiency and 6-PTPS deficiency), a proven genetic disorder (n=24, including KMT2B dystonia, TBC1D24 dystonia, SCGE myoclonus dystonia, GNB1 dystonia, glutaric aciduria type 1, paroxysmal kinesiogenic dystonia, benign hereditary chorea, Wilsons disease and Juvenile Huntington's disease), suspected genetic disorders (clinical course, imaging and/or family history compatible a genetic diagnosis however genetic testing negative, n=18), immune mediated movement disorders (n=11, including Sydenham's Chorea, antiphospholipid chorea, basal ganglia encephalitis, Rasmussen encephalitis, opsoclonus myoclonus syndrome and acute immune akinetic psychotic syndrome), dyskinetic cerebral palsy (n=22), developmental conditions such as stereotypy (n=11) or functional movement disorders (n=3). Further information of movement disorder phenomenology in the non-tic MD cohort is presented in Table 2.

To compare the findings in the movement disorder patients, we recruited an additional 137 patients from The Children's Hospital at Westmead, Australia to establish two clinical control groups: (1) an Emergency control cohort consisting of patients without neurological disease presenting to the Emergency Department for acute paediatric care (n=100), and (2) a Neurological disorder control cohort (n=37) consisting of patients without movement disorders but affected by peripheral neuropathy (n=25) or epilepsy without movement disorder (n=12). In addition, for further comparison, data from 10438 British children, who had completed the British Child and Mental Health Survey in 1999 using the same diagnostic tool (DAWBA- described below), were included as a community control group [9]. Detailed intellectual assessment was not performed however school support was recorded. There was a low rate of special school needs in all of the cohorts, although

there was a slightly elevated requirement for support in mainstream class for the non-tic group (Supplementary table 1).

Psychiatric assessment: All patients from all study groups were screened for psychiatric comorbidities using parental completion of the Development and Wellbeing Assessment Tool (DAWBA), an on-line self-completed questionnaire that has been validated previously, [9, 10] and generates DSM-5 diagnoses from a computer algorithm. The DAWBA questionnaires were additionally clinically rated by experienced child psychiatrists. The community cohort of 10438 children from the UK had been assessed with the same DAWBA tool in 1999 [9].

Statistics: Chi square probabilities were calculated to determine statistical validity of prevalence rates between groups.

Ethics and Data-sharing statement: Anonymized data will be shared by request from any qualified investigator. Ethical approval was received from the institutional review board (11CHW14).

Results

The rate of any DSM-5 psychiatric diagnosis in the tic cohort was 41.8% (n=66/158), compared with 39.2% (n=40/102) in the non-tic MD cohort (no statistically significant difference, p=0.68). The rate of psychiatric comorbidity in the non-tic MD cohort was significantly higher than the Emergency cohort (39.2% vs 18%, p<0.0001), and those in the UK community cohort (39.2% v. 9.5%, p<0.00001), but not higher than the neurology control group (39.2% v. 29.7%, p=0.31). Table 3 provides all DSM-5 psychiatric diagnoses according to the different cohorts. Figure 1 depicts the statistical differences between the non-tic MD cohort and other cohorts in terms of any psychiatric DSM-5 disorder, any anxiety disorder, any disruptive disorder, and any oppositional/conduct disorder. Supplementary Table 2 presents the number of DSM-5 diagnoses (1, 2, 3, 4, or more diagnoses). Table 4 details the psychiatric comorbidity in the non-tic cohort according to movement disorder phenotype, and Table 5 presents psychiatric comorbidity according to aetiology. Anxiety disorders were the most frequent psychiatric diagnoses in the non-tic cohort.

Of the patients with tics who had a psychiatric comorbidity, 45.5% had received psychiatric medications, and 43.9% had received psychological therapy. By comparison, despite the fact the psychiatric comorbidity was similar in the non-tic MD cohort, 22.5% of the non-tic MD patients with psychiatric comorbidity had received psychiatric medications, and 15.0% had received psychological therapy.

Discussion

This study demonstrates that children with movement disorders are four times as likely to have a psychiatric diagnosis than children in the general community. We show that children with non-tic movement disorders, including dystonia and chorea, have similar rates of psychiatric comorbidity as children with tics. Specifically, of the 66 patients with primary or secondary dystonia, 33.3% had a psychiatric comorbidity. Emotional disorders such as anxiety were the most dominant psychiatric comorbidity in all movement disorder patients.

An interesting finding in this study related to therapies provided to the tic and non-tic MD cohorts. Despite the similar psychiatric comorbidity in the tic and non-tic MD cohort, the rate of psychiatric medical or psychological therapies was significantly lower in the non-tic MD group. Although we cannot determine if the level of impairment in the tic and non-tic MD cohorts were identical, this does suggest that psychiatric comorbidity in non-tic MD patients is currently under-recognised and potentially under-treated. This heterogeneous group of movement disorders provides an additional example of groups of children with physical ill-health who should receive timely access to appropriate mental health interventions where needed [11].

One of the strengths of the study was the recruitment of control groups and the use of the same standardised diagnostic tool for all patient and control groups. The large community study in the UK found a rate of 9% psychiatric disorder. We found higher psychiatric comorbidity in our hospital controls (emergency and neurology controls) compared to the community controls. The 'emergency' control cohort (n=100) found a higher rate of psychiatric comorbidity than the UK community control group ($p<0.0001$), which may be due to the fact children with acute injuries may have inherently more psychiatric comorbidity such as ADHD. Although the neurology control group was not the focus of this work, the elevated psychiatric comorbidity (29.7%) supports the need for further research and larger cohorts. Table 3 highlights the details of the psychiatric comorbidity in the neurology control group, with high rates of anxiety, depression, ADHD and social deficits,

whereas by contrast, obsessive-compulsive disorder and oppositional defiant disorder were not elevated in the neurology control group. The high rate of psychiatric comorbidity in the neurology control group raises the question of whether raised psychiatric comorbidity is a common feature of childhood neurological disease in general, rather than specific to movement disorders. Furthermore, the study methodology cannot determine if the elevated psychiatric comorbidity in the movement disorder patients is due to specific neural circuit disruption, or due to the burden of chronic impairing disease. Indeed, it is well described that adolescents with chronic disease such as diabetes, inflammatory bowel disease and asthma have increased psychiatric outcomes [12].

A further confounder was the slightly elevated rate of educational adaptations in the non-tic cohort compared to the tic cohort and control groups, as it is recognised that intellectual disability is a risk factor for psychiatric comorbidity, however it should be noted that only 3 of the whole recruited patients required special school (2 in the tic group) (supplementary Table 2).

Overall the rates of psychiatric comorbidities in children with tic movement disorders children were lower than other studies, where comorbidities have been described in up to 90% [13]. The DAWBA has been described as more conservative than other psychiatric screening tools such as the DISC and CAPA; in one study the DAWBA detected 1 or more diagnoses in 17.7% of patients in paediatric care clinics, whilst the DISC and CAPA diagnosed disorders in 47.1% and 32.4% respectively. [14] Several papers have suggested that the DAWBA tends to under-diagnose emotional disorders [15, 16], and we observed an under-diagnosis of OCD in our cohorts. Therefore, we suspect that our cohort data should be considered a conservative approximation of psychiatric comorbidity in paediatric movement disorder cohorts.

The strengths of the study were the use of a standardized and validated tool to diagnose psychiatric comorbidity in patients and controls, and the recruitment of sequential patients therefore reducing selection bias. Weaknesses of the study were that despite the fact the non-tic cohort was moderately

large (n=102), the individual phenotypic and aetiological subgroups within the non-tic cohort were sometimes small, making subgroup conclusions difficult regarding the risk of psychiatric comorbidity. A further limitation was that the cohorts were recruited from two different centres in Australia and UK, although there was no psychiatric comorbidity difference between the patients recruited from the two countries (data not shown).

In conclusion, this study recognises that children with non-tic movement disorders are just as vulnerable to psychiatric comorbidities as children with tics and TS. Findings such as this add support to the increasing emphasis on developing services which fully integrate physical and mental health care. [17] This new evidence should encourage clinicians to screen for psychiatric comorbidities in all movement disorder (and all neurology) patients, therefore allowing earlier diagnosis and treatment. Although there are a number of tools available to the clinician, the Strengths and Difficulties Questionnaire (SDQ) is a validated screening tool, is quick to complete and assess, comes in 80 languages, and has no cost[18]. For patients that have identified problems using the SDQ, further assessment and treatment would depend on the services available in the patient's region, and experience of the screening clinician.

What is already known on this topic:

1. Psychiatric comorbidity is common in children with chronic diseases.
2. Psychiatric comorbidity is common in children with tic disorders and Tourette syndrome.

What this study adds:

1. Psychiatric comorbidity is not isolated to children with Tourette, but also with other non-tic movement disorders such as dystonia.
2. Psychiatric comorbidity is less likely to be recognised, diagnosed and treated in children with non-tic movement disorders compared to Tourette syndrome.

Competing interests: None of the authors report a competing interest apart from Robert Goodman. Robert Goodman and his family are the owners of Youthinmind Limited, which provides no-cost and low-cost measures of child mental health, including the Strengths and Difficulties Questionnaire (SDQ) and the Development and Well-Being Assessment (DAWBA).

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Table 1: Demographic data across all cohorts in the study

	Tic cohort	**Non-tic MD cohort**	**Emergency control**	**Neurology control**	**Community control [4]**
Total (n=)	**158**	**102**	**100**	**37**	**10438**
Australian (n=)	83	97	100	37	0
UK (n=)	75	5	0	0	10.438
Gender Male	127 (80.4%)	47 (46.1%)	56 (56.0%)	19 (51.3%)	5212 (49.9%)
Age range	5-16y	5-16y	5-16y	5-16y	5-15y
Mean age	10.6y	10.9y	9.8y	12.3y	11y

Table 2. Non-tic MD cohort by primary and secondary movement phenomenon, with demographic data.

Primary movement phenomenon	**n =**	**Secondary movement phenomenon**	**n =**	**Gender (male)**	**Mean age at onset (y)**	**Mean age at DAWBA (y)**
Dystonia	66	Chorea	4	2 M	4.5	9.3
		Myoclonus	3	1 M	2.5	14. 3
		Tremor	6	3 M	6	11.3
		Bradykinesia	4	1 M	4.2	10
		Stereotypy	2	0 M	2	12
		none	47	19 M	3.5	10.8
Chorea	12	Myoclonus	2	1 M	2.7	8
		none	10	5 M	5.5	12.5
Stereotypy	11	none	11	7 M	2.5	8.5
Myoclonus	6	Dystonia	3	2M	1.7	8
		none	3	3 M	4	10. 3
Tremor	5	none	5	2 M	10	12.4
Bradykinesia	1	none	1	0M	15	15
Other (functional)	1	none	1	0 M	1	16
Total	**102**			**46 M**		**10.9**

Table 3. All psychiatric disorder groups and subgroups (DSM-5) in all cohorts

	Tic cohort	Non-tic MD cohort	Emergency control	Neurology control	Community healthy control
Total (n=)	**158.0**	**102.0**	**100.0**	**37.0**	**10 438**
Any psychiatric disorder (%)	**41.8**	**39.2**	**18.0**	**29.7**	**9.5**
Any Anxiety disorder (%)	**32.3**	**28.4**	**11.0**	**27.0**	**3.8**
Sep Anxiety	11.4	7.8	3.0	2.7	1.2
Social phobia	1.3	4.9	2.0	5.4	0.3
Agoraphobia	0.6	0.0	0.0	0.0	0.1
OCD	8.9	0.0	0.0	0.0	0.3
Gen anxiety	3.2	5.9	0.0	8.1	0.7
Specific phobia	3.8	3.9	4.0	2.7	1.0
Panic disorder	2.5	1.0	1.0	2.1	0.1
PTSD	0.0	1.0	1.0	0.0	0.1
Other anxiety	1.9	3.9	0.0	5.4	0.9
Depressive disorder (%)	**3.2**	**4.9**	**1.0**	**2.7**	**0.9**
Major depression	3.2	4.0	0.0	2.7	0.7
Other depression		0.0	0.0	0.0	0.2
Disruptive disorder (%)	**8.8**	**13.7**	**5.0**	**13.5**	**5.9**
ADHD combined	0.0	3.9	4.0	5.4	1.4
ADHD hyperactive	5.1	1.0	1.0	8.1	0.2
ADHD inattentive	3.8	9.8	0.0	0.0	0.7
Oppositional/conduct disorder (%)	**17.7**	**2.9**	**4.0**	**2.7**	**3.8**
ODD	17.7	6.9	4.0	2.7	2.3
Conduct	1.3	2.9	0.0	0.0	1.5
Social (%)	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Selective mutism	0.0	0.0	0.0	0.0	0.0
Attachment disorder	0.0	0.0	0.0	0.0	0.0

PDD/Autism (%)	**3.8**	**2.0**	**0.0**	**5.4**	**0.3**
Eating disorders (%)	**0.0**	**0.0**	**0.0**	**0.0**	**0.1**

OCD: Obsessive-compulsive disorder, PTSD: post-traumatic stress disorder, ADHD: attention deficit hyperactivity disorder, ODD: oppositional defiant disorder, PDD: pervasive developmental disorder.

Table 4: Rates and types of DSM-5 diagnoses in the non-tic movement cohort (n=102) by movement disorder phenotype

Primary movement disorder	**n =**	**Patients with DSM-5 psychiatry (%)**	**Specific diagnoses present**
All dystonia	66	22 (33%)	Separation anxiety (5), social phobia (5), specific phobia (4), ADHD combined (3), ADHD inattentive (3), ODD (3), generalised anxiety (2), other anxiety (1), Major depression (1), ADHD hyperactive (1)
All chorea	12	8 (66.7%)	Separation anxiety (1), other anxiety (1) bipolar/mania (1), major depression (2), ADHD inattentive (1), ODD (3) conduct disorder (1
All myoclonus	6	1 (16.7%)	ADHD combined (1)
All tremor	5	3 (60.0%)	Generalised anxiety (1), panic disorder (1), major depression (1)
All bradykinesia	1	0 (0%)	-
All stereotypy	11	5 (45.5%)	Generalised anxiety (1), ADHD inattentive (3), ODD (1) PDD/Autism (2)
All other (functional)	1	1 (100%)	Generalised anxiety (1), PTSD (1), major depression (1) ADHD, conduct disorder
All clinical phenomena	**102**	**40 (39.2%)**	

Table 5. Rate of psychiatry and specific psychiatric diagnoses presented by movement disorder aetiology

Aetiology	n =	Patients with psychiatry (%)	Specific diagnoses present
All neurotransmitter	**13**	**3 (23.1%)**	**Generalised anxiety disorder (2), separation anxiety (1), conduct disorder (1)**
Dopa responsive dystonia (GTP cyclohydrolase deficiency)	4	0	
Dopa responsive dystonia (gene negative)	3	2	Generalised anxiety (2), conduct disorder (1)
Tyrosine hydroxylase deficiency	3	1	Separation anxiety (1)
6 PTPS deficiency	3	0	-
All proven genetic	**24**	**13 (45.1%)**	**Separation anxiety (4), ADHD inattentive (3), ODD (3), other anxiety (2), social phobia (1), specific phobia (1), major depression (1), ADHD combined (1), ODD (1)**
KMT2B dystonia	2	2	Separation anxiety (1), social phobia (1), ADHD combined (1), ADHD inattentive (1)
TBC1D24 dystonia	1	0	-
Myoclonus dystonia (SCGE)	7	3	Specific phobia (1), other anxiety (1), ADHD inattentive (1)
GNB1 dystonia	1	0	
Glutaric acidura type 1	2	1	Separation anxiety (1)
Paroxysmal kinesiogenic dystonia (PRRT2)	4	2	Major depression (1), ODD (1)
Benign hereditary chorea	5	4	Separation anxiety, (1) other anxiety (1), ADHD inattentive (1), ODD (2)
Wilsons disease	1		
Juvenile huntingtins disease	1	1	Separation anxiety (1)

All suspected genetic	**18**	**9(50%)**	**Separation anxiety (2), generalised anxiety (2), social phobia, (1), , specific phobia (1), major depression (1), panic disorder (1), ADHD combined (2), ADHD hyperactive (1), ODD (1)**
Dystonia - gene negative	11	6	Separation anxiety (2), generalised anxiety (1), social phobia, (1), generalised anxiety (1), specific phobia (1), ADHD combined (1), ADHD hyperactive (1), ODD (1)
Chorea - gene negative	1	0	
Myoclonus - gene negative	2	1	ADHD combined (1)
Tremor gene negative	4	2	Generalised anxiety (1) panic disorder (1), major depression (1)
All immune	**11**	**4(36.4%)**	**Social phobia (2), major depression (2), Bipolar/mania (1) ADHD combined (1), ODD (1)**
Sydenham's chorea	2	2	Bipolar/mania (1), major depression (2)
Antiphospholipid chorea	1	0	
Basal ganglia encephalitis (Dopamine 2 Receptor Antibody positive)	4	2	Social phobia (2) ADHD combined (1), ODD (1)
Rasmussen encephalitis with hemidystonia	1	0	-
Opsoclonus myoclonus syndrome	2	0	-
Acute immune akinetc psychotic syndrome	1	0	-
All multifactorial (dyskinetic CP group)	**22**	**6 (27.3%)**	**ADHD inattentive (2), specific phobia (2), separation anxiety (1), generalised anxiety (1), social phobia (1)**
Prematurity defined as cause	7	4	Separation anxiety (1), social phobia (1), specific phobia (1), ADHD inattentive (2)
Vascular event (in utero or neonatal)	4	0	
Kernicterus	3	1	Generalised anxiety (1)

Hypoxic ischaemic encephalopathy or traumatic delivery	4	1	ADHD inattentive (1), specific phobia (1)
Unknown	4	0	-
Stereotypy (All developmental)	**11**	**4(36.4%)**	**Generalised anxiety (1), ADHD, inattentive (2) ODD (1), PDD/autism (2)**
Functional movement disorder	**3**	**1(33.3%)**	**Generalised anxiety (1), PTSD, (1), major depression (1), ADHD inattentive (1), conduct disorder (1)**
	102	**40 (39.2%)**	

Figure 1: The percentage of patients from each group who had any DSM-5 psychiatric diagnosis, any anxiety disorder, any disruptive disorder or any oppositional disorder. Significant statistical associations are highlighted (*)