PATIENT'S CHOICE

REVIEW

Relationship between movement disorders and obsessive–compulsive disorder: beyond the obsessive–compulsive–tic phenotype. A systematic review

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ABSTRACT

Background Obsessive–compulsive disorder (OCD) and symptoms (OC symptoms) are associated with tic disorders and share an aetiological relationship. The extent to which OCD/OC symptoms are correlated with other hyperkinetic movement disorders is unclear. The aim of this review was to investigate this co-occurrence and the extent to which OCD/OC symptoms and hyperkinetic movement disorders share a neurobiological basis.

Methods A systematic review was performed, specifically searching for OCD/OC symptom comorbidity in hyperkinetic movement disorders using case control studies, longitudinal studies and family based studies. The literature search was conducted using PubMed and PsycINFO databases.

Results Heterogeneity of measurement instruments to detect OCD diagnosis and OC symptoms decreased comparability between studies. The most convincing evidence for a relationship was found between the choreas (Huntington's disease and Sydenham's chorea) and OCD/OC symptoms. Furthermore, elevated frequencies of OC symptoms were found in small case control series of dystonias. Small family based studies in dystonia subtypes modestly suggest shared familial/genetic relationships between OC symptoms and dystonia.

Conclusion Current data indicate a relationship between OCD/OC symptoms and the choreas. As OCD and the choreas have been associated with dysfunctional frontal–striatal circuits, the observed relationships might converge at the level of dysfunctions of these circuits. However, paucity of longitudinal and family studies hampers strong conclusions on the nature of the relationship.

Implications The relationship between OCD and movement disorders needs further elaboration using larger family based longitudinal studies and sound instruments to characterise OC symptomatology. This could lead to better understanding of the shared pathology between OCD and hyperkinetic movement disorders.

INTRODUCTION

Obsessive–compulsive disorder (OCD) is a heterogeneous disorder characterised by intrusive obsessions producing anxiety or tension, and compulsions aimed at stress or anxiety reduction. The lifetime prevalence of OCD is between 2% and 3%.[1] OCD has a variety of phenotypic presentations.[2 3] Attempts have been made to create more homogenous subgroups using factor analytic strategies with obsessive–compulsive (OC) symptoms. At least four symptom dimensions are currently recognised: (1) contamination/cleaning, (2) hoarding, (3) symmetry/ordering and (4) obsessions/checking.[4 5] Furthermore, age at onset and gender are also likely to affect the phenotypic presentation of OCD.[3 6–8]

Another method to obtain more homogeneity among OCD is to study its comorbidity pattern. The most common movement disorders comorbid with OCD are the tic disorders.[2 9] Family studies on the relationship between OCD and tic disorders indicate a familial tic related OCD subtype which is associated with characteristics such as early age at onset, male gender and tic-like compulsions besides the 'classical' compulsions.[10] Goal directed behaviour, such as compulsions, is orchestrated by the basal ganglia, through parallel but interconnected frontal–striatal circuits.[11 12] Dysfunction of these frontal–striatal circuits is known to play a role in the pathogenesis of tic-disorders[13] and may also underlie OCD.[14 15] Other hyperkinetic movement disorders (from now on referred to as 'non-tic movement disorders'), in which frontal–striatal impairments are documented, are also hypothesised to be associated with OCD but have been largely understudied in relation to OCD in comparison with tic disorders.

This review aims to investigate the relationship between OCD and these other hyperkinetic movement disorders. We have aimed to investigate: (1) whether OCD/OC symptoms occur more often than expected by chance in patients with various (non-tic) hyperkinetic movement disorders and (2) whether increased co-occurrence between these non-tic movement disorders and OCD/OC symptoms reflects an aetiological relationship.

METHODS

Literature search and data sources

The literature search was done in accordance with the preferred reporting items for systematic review and meta analyses guidelines.[16] Articles were identified through searches in the databases PubMed and PsycINFO. The following search terms were used: OCD, obsessive–compulsive symptoms,

movement disorder, hyperkinesia, chorea, Huntington's disease, myoclonus dystonia, generalised dystonia, idiopathic focal dystonia, idiopathic spasmodic torticollis, blepharospasm, dystonia, tremor, ballism.

Inclusion and exclusion criteria

All articles published in English up to December 2010 were included. Epidemiological, case control, longitudinal cohort and family based studies were included. Those articles were selected that (1) reported on non-tic movement disorder comorbidity with OCD/OC symptoms and (2) used some form of standard assessment or self-report of OCD diagnoses according to DSM-IV criteria,[17] and/or assessed OC symptomatology using validated rating scales. In all studies detected, the following scales were used to assess OC symptoms: the Yale–Brown Obsessive–Compulsive Severity Scale (Y-BOCS),[18 19] the Problem Behaviour Assessment for Huntington's Disease,[20] the Leyton Obsessional Inventory,[21] the Unified Huntington's Disease Rating Scale (UHDRS),[22] the Schedule of Compulsions, Obsessions and Pathological Impulses,[23] the Maudsley Obsessional–Compulsive Inventory[24] and the Hamburg Obsession/Compulsion Inventory.[25]

As repetitive behaviour is often termed inconsistently—for example, perseveration behaviour, repetitive behaviour or impulse control disorder—and since it was unclear how these behaviours were defined or assessed, only articles in which the presence of 'obsessive–compulsive symptoms' according to well defined rating scales were included. Finally, to limit false positive chance findings due to small sample size, while taking into account the rare population prevalence of some of the movement disorders studied, studies with a sample size of <15 subjects were excluded.

Data extraction

Two authors (LAF and AJLMvB) assessed the eligibility of the studies by independently reviewing the selected studies on sample size, study design, type of movement disorder under investigation, diagnostic instruments used to assess severity and symptom characteristics of the movement disorder, OC symptoms and OCD diagnosis, and finally, results of the studies. After the studies were coded twice, discrepancies between the coding forms were resolved by the authors by reviewing the data of the original article and reaching consensus on a final form.

RESULTS

The initial search yielded 3910 hits in PubMed and PsycINFO. Based on title and abstract, 3836 articles were excluded as they did not contain a report on comorbidity between OCD/OC symptoms and movement disorders. In addition, 36 articles encompassing reviews, letters, comments or duplicate publications were excluded. Nine articles were excluded because of a sample size <15 (n=4), paucity of study (n=1) or did not use standardised measurement instruments (n=4). As a result, 27 articles from PubMed and two articles from PsycINFO were included (see figure 1). The articles included covered the period between February 1992 and October 2010.

The selected articles include 16 case control studies, eight cohort studies and five family studies. The movement disorders

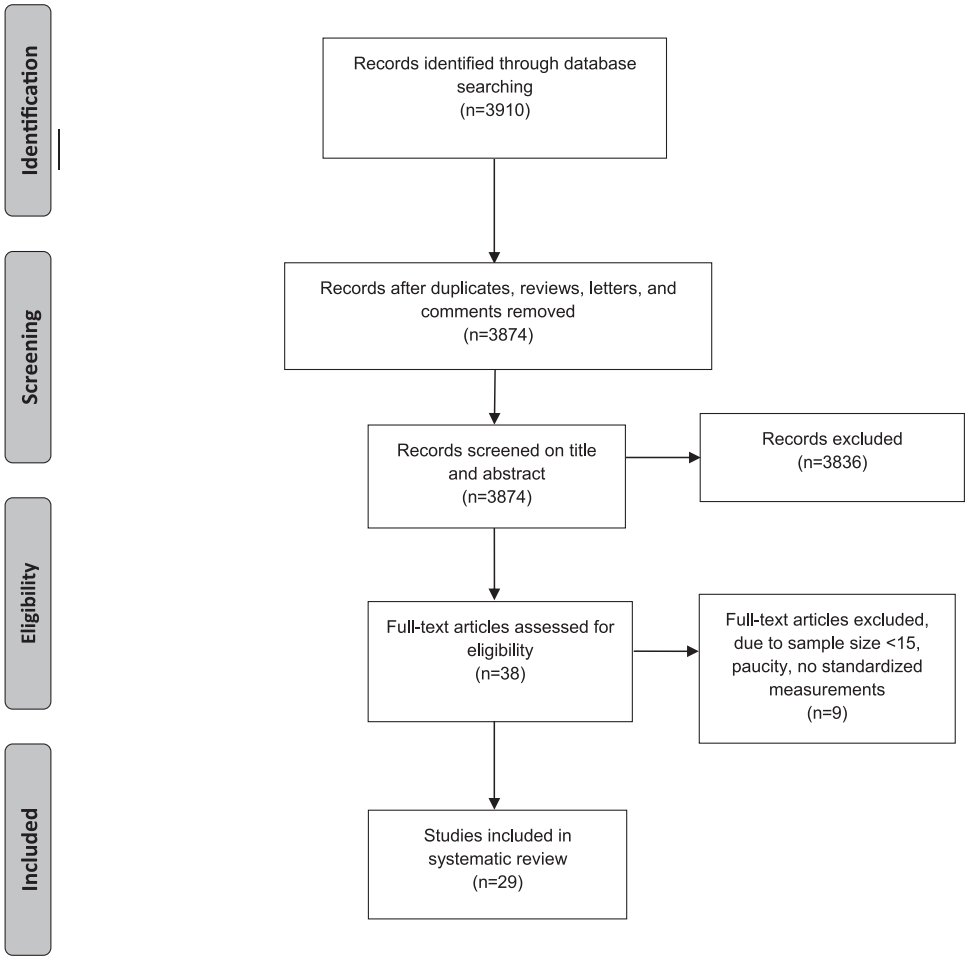

Figure 1 Flow diagram of study selection.

described were: chorea (Sydenham's chorea and Huntington's disease) and dystonia (myoclonus dystonia, generalised dystonia and focal dystonias (blepharospasm, idiopathic spasmodic torticollis, idiopathic focal dystonia)). No articles were found on tremor or ballism. The characteristics of the studies are presented in table 1.

Chorea

Huntington's disease

In Huntington's disease, seven studies (five cohort studies and two case control studies) investigated the presence of comorbid OCD/OC symptoms.[20 26–31] No family studies on comorbidity between Huntington's disease and OCD/OC symptoms were identified. In all studies, only OC symptoms were investigated, with the exception of van Duijn *et al*[30] who studied the presence of OCD diagnosis as well as OC symptoms in manifest and non-manifest gene carriers of Huntington's disease. In the van Duijn *et al* study,[30] three out of 55 (5.5%) presymptomatic mutation carriers and three out of 85 (3.5%) symptomatic mutation carriers had an OCD diagnosis, which was not significantly elevated compared with non-carriers (n=56) but was increased compared with the general population. Craufurd *et al*[20] and Murgod *et al*[31] studied patients with Huntington's disease for the rates of OC symptoms, without the use of control groups. Craufurd *et al*[20] found that 5% of 134 patients with Huntington's disease showed obsessions and 10% compulsions. Murgod *et al*[31] found increased frequencies of obsessions (n=4) and compulsions (n=3) in 26 patients with Huntington's disease. In three controlled studies with 1959 patients with Huntington's disease,[26 27 29] increased rates of OC symptoms were found both in non-manifest and manifest carriers compared with the general population (27%, 52% and 24%, respectively). Beglinger *et al*[28] studied a large cohort of 3964 subjects with Huntington's disease with either manifest symptoms (n=3255) or prior to symptom onset (n=709), for the presence of OC symptoms. The subjects showed a maximum of 24.0% obsessions and 12.0% compulsions at stage 4 of the disease according, to Shoulson and Fahn criteria (stage 0 indicating no functional impairment and stage 5 indicating the highest level of disability[54]), compared with a proportion of 7% for obsessions and 3.5% for compulsions in stage 0. Beglinger *et al*[29] subsequently studied 300 patients with expansion of the CAG repeats who were not yet manifesting, in comparison with 108 expansion negative family member controls. They were grouped according to different times to onset periods (>15 years vs 9–15 years vs <9 years prior to onset[55]). Interestingly, patients with 9–15 years prior to onset showed the most OC symptoms compared with controls (p=0.02), whereas patients with <9 years before onset showed less OC symptoms compared with patients with 9–15 years prior to onset, but OC symptom rates were increased compared with controls. Anderson *et al*[27] found a longer duration of illness to be associated with more severe OC symptoms, and severity of OC symptoms was associated with increased executive dysfunction (measured using the Total Functional Capacity Scale, assessing motor and cognitive functioning, behavioural abnormalities and overall functional capacity). Whether these OC symptoms decreased at the most severe stage of Huntington's disease was not reported. These data suggest a complex aetiological relationship between Huntington's disease and OC symptoms which depends on a time window in disease progress.[28] Of note, in those studies investigating OC symptom severity, severity remained at a sub-threshold level at all stages of disease progression (<1 h daily spent on OC behaviour, and only mild distress from OC symptoms).[26–31]

Two studies[26 29] investigated the content of the OC symptoms associated with Huntington's disease. Anderson[26] found that aggressive obsessions (26%), contamination obsessions (22%) and checking compulsions (19%) were most frequently reported by patients with Huntington's disease. Unfortunately, no control group was used. Beglinger[29] reported more checking and pathological impulses in expansion positive patients compared with expansion negative controls.

Sydenham's chorea

Six case control studies, one cohort study and one family study have investigated the occurrence of OCD/OC symptoms in patients with Sydenham's chorea with or without rheumatic fever.[32–39] Five studies found a significant increase in OC symptoms in cases versus controls in both Sydenham's chorea with and without rheumatic fever.[32 33 37–39] With respect to OCD diagnosis, one out of six studies found a significant increase compared with controls.[38]

Asbahr *et al*[33] investigated the time course between the onset of Sydenham's chorea and development of OC symptoms in 21 patients with rheumatic fever with and without Sydenham's chorea. Six patients (29.0%) developed OC symptoms before the onset of rheumatic fever, seven (33.0%) developed OC symptoms concomitantly with the onset of Sydenham's chorea and eight (38.0%) developed OC symptoms after the onset of Sydenham's chorea. The OC symptoms peaked in all patients <2 months after the onset of the rheumatic fever with chorea, with significantly more symptoms in patients with the combination of rheumatic fever and chorea compared with patients with rheumatic fever alone (p=0.007). Four months after the onset of rheumatic fever with chorea, OC symptoms had subsided in most patients but from these reports, the severity and extent of symptoms of rheumatic fever after 4 months are unclear.

Hounie *et al*,[37] using a controlled family based approach, investigated the occurrence of obsessive–compulsive spectrum disorders (OCSD) in 98 probands with rheumatic fever, of whom 31 had rheumatic fever without Sydenham's chorea, 28 had rheumatic fever with Sydenham's chorea and 39 were control subjects. Two out of the 98 probands had an OCD diagnosis, which was not increased compared with the control group. In the first degree relatives of the 98 probands, the occurrence of OCSD was significantly increased compared with the first degree relatives of the control group. Furthermore, the occurrence of Sydenham's chorea among probands with OCSD was associated with an increased rate of OCSD among their first degree relatives. The latter suggests that not only mechanisms associated with infectious disease but also genetic vulnerability to OC symptomatology are operant in the relationship between OCD and rheumatic fever, either with or without Sydenham's chorea.

Two studies[32 34] reported the characteristics of the OC symptoms in patients with Sydenham's chorea. Alvarenga *et al*[32] found that aggressive obsessions and ordering–arranging compulsions were significantly increased in patients with a history of rheumatic fever (n=3/51) compared with controls (n=0/46). Asbahr[34] reported increased rates of aggressive obsessions (63%), contamination obsessions (34%), checking compulsions (53%) and cleaning compulsions (42%). Unfortunately, no control group was included.

Dystonia

Both generalised dystonia, with a deletion in the DYT1 gene, and myoclonus dystonia, with a deletion in the DYT11 gene, have been studied with regard to comorbidity with OCD/OC symptoms. In three family studies, the comorbidity of OCD/OC

Table 1 Studies of obsessive–compulsive disorder comorbid with hyperkinetic (non-tic) movement disorders

Author	n	Study design	Measurement instrument OC symptom	OC symptom severity*† ‡	Measurement instrument OCD diagnosis	OCD diagnosis† ‡
Chorea						
Huntington's disease						
Anderson *et al*[26]	27	Cohort	Y-BOCS	–¶	–	–
Anderson *et al*[27]	1642	Cohort	UHDRS	–¶	–	–
Beglinger *et al*[28]	3964	Cohort	UHDRS	–¶	–	–
Beglinger *et al*[29]	300§	Case control	SCOPI	Far to onset† Mid to onset‡ Near to onset†	–	–
Craufurd *et al*[20]	134	Cohort	PBA-HD	–¶	–	–
van Duijn *et al*[30]	140§	Case control	–	–	CIDI	‡
Murgod *et al*[31]	26	Cohort	UHDRS	–¶	–	–
Sydenham's chorea						
Alvarenga *et al*[32]	51§	Case control	Y-BOCS	‡	–	†
Asbahr *et al*[33]	50	Case control	LOI (resistance) LOI (interference)	Month 1+2‡ Month 3+4† Month 5+6† Month 1+2‡ Month 3+4† Month 5+6†	K-SADS	†
Asbahr *et al*[34]	73	Cohort	Y-BOCS	–¶	–	–
Asbahr *et al*[35]	38§	Case control	Y-BOCS	†	–	–
Hounie *et al*[36]	59§	Case control	Y-BOCS	†	SCID	†
Hounie *et al*[37]	50§	Family study**	Y-BOCS	‡	SCID, K-SADS	†
Maia *et al*[38]	106§	Case control	LOI (median) Y-BOCS (median)	‡ ‡	K-SADS	‡
Mercadante *et al*[39]	42§	Case control	Y-BOCS	†	K-SADS	†
Dystonia						
Myoclonus dystonia						
Foncke *et al*[40]	27§	Family study**	Y-BOCS	†	SCID	NMC† MMC†
Saunders-Pullman *et al*,[41] Hess *et al*[42]	30§	Family study**	–	–	CIDI	NMC† MMC‡
Generalised dystonia						
Heiman *et al*[43]	27§	Case control	MOCI	NMC† MMC†	CIDI	NMC† MMC†
Blepharospasm						
Bihari *et al*[44]	21§	Case control	MOCI	‡	–	–
Broocks *et al*[45]	13§	Case control	SCL-90-R HOCI	† ‡	–	–
Hall *et al*[46]	159§	Case control	HOCI	†	–	–
Munhoz *et al*[47]	30§	Case control	Y-BOCS	†	–	†
Wenzel *et al*[48]	31	Cohort	–	–	SCID	†
Idiopathic focal dystonia						
Cavallaro *et al*[49]	76§	Family study**	Y-BOCS	–¶	–	‡
Fabbrini *et al*[50]	86§	Case control	Y-BOCS	†	–	–
Lencer *et al*[51]	86§	Case control	–	–	SCID	‡
Idiopathic spasmodic torticollis						
Bihari *et al*[52]	22§	Case control	Y-BOCS MOCI SCL-90-R	‡ † ‡	–	–
Focal hand dystonia						
Voon *et al*[53]	39	Cohort	–	–	SCID	–¶

Characteristics of the 29 included studies regarding patients with movement disorders and comorbidity with OCD.
*OC symptom severity in study group compared with control group.
†No difference between case and controls.
‡Significant difference between case and controls.
§Only the case group is listed.
¶No information available or study design not suitable for comparison.
**Only the probands of the family studies are presented.
CIDI, Composite International Diagnostic Interview; HOCI, Hamburg Obsession/Compulsion Inventory; K-SADS, Schedule for Affective Disorders and Schizophrenia for School Aged Children; LOI, Leyton Obsessional Inventory-child version; MMC, manifest mutation carrier; MOCI, Maudsley Obsessive–Compulsive Inventory; NMC, non-manifest mutation carrier; OCD, obsessive–compulsive disorder; PBA-HD, Problem Behaviours Assessment for Huntington's Disease; PD, Parkinson's disease; SCID, Structured Clinical Interview for DSM-IV Axis I Disorders; SCL-90-R, Symptom Check-List-90-revised; SCOPI, Schedule of Compulsions; UHDRS, Unified Huntington's Disease Rating Scale; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

symptoms in patients with myoclonus dystonia and their family members was investigated.[40–42] To examine whether similar underlying genetic influences might be operant in the manifestation of OCD/OC symptoms and this hyperkinetic movement disorder, patients with myoclonus dystonia were divided into manifest and non-manifest mutation carriers. In the

Foncke *et al* study,[40] who investigated 69 subjects within one family, two (14.3%) manifest mutation carriers (n=14) and one (8.3%) non-manifest mutation carrier (n=12) had a comorbid diagnosis of OCD which was not significantly elevated compared with the healthy family members (one (2.4%) of 42). Both non-manifest and manifest mutation carriers had low OC symptom severity ratings (mean score of 1 as, assessed using the Y-BOCS). In contrast with this study, the Saunders–Pullman study,[41] investigating three families with a total of 55 participants, reported elevated rates of OCD in manifest myoclonus dystonia (four out of 16 (25.0%)) compared with non-carrier family members (0 out of 28). Non-manifest mutation carriers did not show elevated frequencies of OCD compared with controls. Hess *et al* (2007)[42] added two more families to the Saunders–Pullman data and corroborated the original findings of OCD comorbidity in the manifest mutation carriers compared with controls.

One study[43] investigated OCD comorbidity in 156 generalised dystonia patients with a DYT1 mutation, of whom 96 were manifest mutation carriers and 60 were non-manifest mutation carriers. The control group consisted of 65 non-carriers. Of the manifest mutation carriers, three (3.1%) had OCD. Of the 60 non-mutation carriers, one (1.7%) had OCD. Of the 65 controls, three (4.6%) had OCD. No differences were found between carriers and non-carriers on OC symptoms. Thus frequencies of OCD/OC symptoms in both manifest and non-manifest carriers were not significantly elevated compared with controls, arguing against a relationship between generalised DYT1 dystonia and OCD/OC symptoms. Both manifest and non-manifest mutation carriers showed no difference in symptom characteristics compared with non-carriers.

Four case control studies and one cohort study have investigated the presence of comorbid OCD/OC symptoms in a total of 254 patients with blepharospasm and 153 controls.[44–48] Two studies found significantly elevated frequencies of OC symptoms in patients with blepharospasm.[44 45] Bihari *et al*[44] administered the Maudsley Obsessional–Compulsive Inventory Questionnaire to 21 patients with blepharospasm and 19 controls. The blepharospasm patients scored significantly higher compared with controls ($p<0.01$). Broocks *et al*[45] compared 13 patients with blepharospasm with 13 patients with hemifacial spasm. Patients with blepharospasm had significantly increased OC symptoms compared with controls, as indicated by the Hamburg Obsession/Compulsion Inventory. Munhoz *et al*[47] found 3.3% comorbid OCD in 30 blepharospasm patients, which was not significantly increased compared with patients with hemifacial spasm (3 out of 30 (10%); $p=0.61$), or compared with the general population. Hall *et al*[46] investigated a large sample of patients with blepharospasm (n=159) compared with 91 controls. The authors found that 60 (37.7%) of the 159 blepharospasm patients had OC symptoms, which was not significantly increased compared with controls (28 out of 91 (30.1%)). Wenzel *et al*[48] also found no increase in OCD in 31 patients with blepharospasm but unfortunately did not include any controls.

One family study[49] and two case control studies[50 51] have investigated comorbid OCD/OC symptoms in patients with idiopathic focal dystonia, which includes blepharospasm diagnosis. Lencer *et al*[51] studied 86 patients with idiopathic focal dystonia, of whom 70 (81.4%) suffered from cervical dystonia and 16 (18.6%) from blepharospasm. Their control group consisted of a population based sample (n=3932). Compared with the population based sample, OC symptoms were increased in patients with idiopathic focal dystonia, with an OR of 8.4. Patients with increased OC symptoms were found to have an earlier age at onset of OC symptoms than the onset of idiopathic focal dystonia (18 vs 31 years, respectively). Fabbrini *et al*[50] studied the comorbidity of OCD in 34 patients with cervical dystonia, 28 patients with blepharospasm, 16 patients with laryngeal dystonia and 11 patients with arm dystonia compared with 62 healthy controls. OCD was found in one patient with cervical dystonia (2.9%), one patient with blepharospasm (3.6%) and one patient with arm dystonia (9.1%). These rates were not significantly increased compared with controls. Cavallaro *et al*[49] investigated 76 patients with idiopathic focal dystonia, of whom 50% (n=38) suffered from blepharospasm, 36.8% (n=28) from torticollis, 9.2% (n=7) from dysphonia, 2.7% (n=2) from focal hand dystonia and 1.3% (n=1) from oromandibular dystonia in comparison with a control group (n=129). Overall, 15 (19.7%) out of 76 patients were diagnosed with OCD, which was significantly increased compared with the control group. No further details were provided regarding the association between OCD and the various types of idiopathic focal dystonias. The morbidity risk for OCD was evaluated in family members of patients with idiopathic focal dystonia versus controls. A family morbidity risk of 13.8% was found in the family members of patients with idiopathic focal dystonia, which was significantly increased compared with controls.[49] These data suggest a shared familial/genetic background between focal dystonias and OCD.

One study[53] investigated the comorbidity of OCD in 39 patients with focal hand dystonia, of whom four (10.3%) suffered from OCD. Although no control group was included, similar to the previous investigations, this proportion of OCD thus appears to be increased compared with the general population.

Finally, one study[52] has been conducted investigating OC symptoms in idiopathic spasmodic torticollis, using 22 patients and 29 controls. These patients scored, on average, significantly higher on the Y-BOCS symptom checklist compared with controls.

DISCUSSION

This review focused on non-tic hyperkinetic movement disorders and their relationship with OCD/OC symptoms. Elevated frequencies of OCD/OC symptoms were most evident for the choreatic movement disorders, such as Huntington's disease and rheumatic fever with Sydenham's chorea. As for types of dystonia, the available evidence, although pointing in the direction of shared aetiologies, is scarcer and less straightforward.

Chorea

Huntington's disease was found to be associated with increased rates of OC symptoms, in manifest as well as non-manifest gene carriers, and with the whole range of OC symptom dimensions present, as found in 'classical' OCD, except for hoarding. The finding that OC symptoms were more prevalent in Huntington's disease independent of the presence of movement disorder symptomatology may suggest that OC symptoms share gene effects with this movement disorder. Interestingly, OC symptoms were found to increase with disease severity, with a tendency to decrease at the most severe stage of the disease. Apparently, at this end stage of the disease, cognitive decline results in both a lower accuracy in reporting OC symptoms and a decrease in the cognitively driven obsessions that motivate OC behaviour in these patients.[28] The finding that OC symptoms are already present in the pre-manifest stage of Huntington's

disease, coupled with the U shape of OC symptom severity related to time to disease onset, suggests that the motor and OC symptoms in Huntington's disease share similar aetiological mechanisms which might be based on similarities in basal ganglia dysfunction coupled with decreased frontal–striatal control.

In Sydenham's chorea, environmental (infectious) factors appear to be a prerequisite to obtain the disease, as indicated by the time course of onset and a resolution of OC and motor symptoms after successful antibiotic treatment for group A streptococcal infection.[56] This is strongly suggestive of a shared (environmental) aetiology for these comorbid disorders. However, family study data by Hounie *et al*[37] suggest that this is only part of the story. Streptococcal infections may increase vulnerability for both Sydenham's chorea and OC symptoms in genetically susceptible persons, which is in line with current concepts of paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) origins of the disease.[57] PANDAS encompasses the phenomenon of a subset of children in whom symptoms of OCD and/or tic disorders exacerbate or worsen after group A streptococcal infection. One study including first degree relatives of patients with group A streptococcal infection and comorbid movement disorders showed that the relatives had an increased frequency of mood and anxiety disorders, including OCD.[58] Furthermore, patients with OCSD have been found to have more first degree relatives with rheumatic fever with and without Sydenham's chorea compared with normal controls.[37] Moreover, Sydenham's chorea, as well as tics and OCD, often begin in early childhood and share common dysfunctional neuroanatomical areas—that is, cortico-striatal circuit dysfunction—supporting the possibility that subgroups of patients with these disorders share common immunological and/or genetic vulnerabilities. Currently, it is being hypothesised that immunological mechanisms operant in PANDAS, Sydenham's choreas and subforms of OCD (and tic disorders) might directly interact with striatal D2 receptors, producing—depending on which exact site of action within the striatal circuits—movement disorders, OC symptoms or a combination.[59] However, although it is likely that some OCD cases are true PANDAS cases, the PANDAS concept has yet to be addressed further in future studies, particularly in light of the equivocal or negative prospective longitudinal studies showing no clear exacerbation of OC symptoms after a streptococcal infection in both children with and without PANDAS.[59–61] Alternatively, in some forms of OCD there might be a shared genetic risk for developing OC complaints and immune reactions between streptococcal antibodies and basal ganglia tissue, both leading to dopaminergic imbalance within the frontal–striatal circuitry.

Dystonia

In myoclonus dystonia, a possible association with OCD was found in manifest mutation carriers only, suggesting that OC symptomatology is secondary to the movement disorder rather than reflecting an alternative expression of the same aetiological factors. Mostly, idiopathic focal dystonia was associated with increased frequencies of OCD,[49 51] with one study reporting an OR of 8.4.[51] However, these studies did not make a distinction between the different dystonias. Future research must indicate which focal dystonias are specifically associated with increased frequencies of OCD/OC symptoms. One family study on focal dystonia confirmed shared familial/genetic relationships between OC symptoms and dystonia,[42] but larger scale family based studies are warranted to confirm this finding across the various dystonias.

In summary, to date, due to the paucity of studies in other movement disorders, most convincing evidence has been found for the association of OCD and choreatic movement disorders. Chorea as well as OCD have been associated with dysfunctional frontal–striatal circuits.[62 63] Chorea is characterised by disinhibited frontal–striatal circuitry due to deficient inhibitory input from the internal part of the globus pallidus to the thalamus, resulting in excessive thalamocortical facilitation.[64] This mechanism, in combination with hypofunctional dorsolateral prefrontal cognitive control, as found in OCD, seems to underlie the disinhibited repetitive behaviour in both conditions.[15 65] Altered cortico-subcortical connectivity appears to underlie motor symptoms as well as emotional and cognitive impairments found in chorea, the latter occurring often before the onset of motor symptoms.[66] Cognitive impairments in chorea mainly pertain to higher order executive functions, such as working memory and response inhibition,[65 67] cognitive domains that rely on proper functioning of the frontal–striatal circuits, which are also dysfunctional in OCD.[68–70] The neuroanatomical model of chorea is in line with proposed neuroanatomical models of OCD. Specifically, OCD is likely to be characterised by an excess tone in the direct relative to the indirect pathway of the ventromedial frontal–striatal circuit.[15] Thus OCD and chorea are both characterised by frontal–striatal dysfunctions, which may result in overlapping obsessive and compulsive symptoms.

In OCD, distinct frontal–striatal circuits have been found to be associated with separate OCD and OC symptom dimensions.[15 71] Which OC symptom dimensions are predominant in Huntington's disease and Sydenham's chorea, and whether they are likewise bound to distinct neurobiological pathways, has not been studied extensively. A few studies reported on OC symptomatology. These studies found an increase in aggressive obsessions, contamination obsessions and checking compulsions.[26 29 32 34] This seems to be an important issue that might improve our knowledge across disorders on the relationship between repetitive behaviour and the underlying neuronal circuits. For instance, OC symptoms in patients with tic related disorders are more prominently associated with symmetry behaviour than the more anxiety driven washing and checking behaviours, as seen in OCD without comorbid tic disorders.[72] OC symptoms co-occurring with choreas might also be associated with a clinically distinct presentation (and associated cortico-striatal circuitry).

Limitations

To address the occurrence of OCD diagnosis, in general, appropriate diagnostic instruments have been used (Structured Clinical Interview for DSM-IV Axis I Disorders, Composite International Diagnostic Interview, Schedule for Affective Disorders and Schizophrenia for School Aged Children; see table 2 for an overview). However, less than half of the studies of this review have systematically assessed the occurrence of OCD diagnosis. With respect to rating scales used to assess OC symptoms and characteristics, only five studies included in this review[26 29 33 34 43] have described OC symptom characteristics. Most studies used the scales for measuring either proportion of patients reporting on symptoms or symptom severity. Furthermore, scales differ widely with respect to psychometric quality for measuring OC symptom severity or presence of symptoms, leading to clear differences in study outcome between studies. For instance, the PBS-HD has only one single screening item on

Table 2 Overview of scale properties measuring obsessive–compulsive symptoms

	No of items measuring OC symptoms	Severity scale	Total severity score	Subscales
Y-BOCS symptom checklist	64	y/n	0–64	1. Contamination and cleaning 2. Hoarding and collecting 3. Symmetry, ordering, counting and arranging 4. Harm due to injury, violence, aggression, natural disasters and related compulsions 5. Sexual and religious 6. Miscellaneous
Y-BOCS severity scale	10	0–4	0–40	1. Obsessions: time spent, suffering, interference, resistance, control 2. Compulsions: time spent, suffering, interference, resistance, control
UHDRS	2	0–4	0–8	–
SCOPI	47	1–5	0–32	1. Checking 2. Cleanliness 3. Compulsive rituals 4. Hoarding 5. Pathological impulses
PBA-HD	1	0–4	0–4	–
LOI				
Obsessions	44	y/n	0–44	1. Thoughts
Resistance	44	0–3	0–44	2. Checking
Interference	44	0–3	0–44	3. Dirt and contamination 4. Dangerous objects 5. Cleanliness and tidiness 6. Order and routine 7. Repetition 8. Overconscientious 9. Indecision 10. Hoarding 11. Meanness 12. Magic games
HOCI	72	y/n	0–72	1. Checking 2. Cleaning 3. Arranging/hoarding 4. Obsessional thoughts of words/pictures 5. Counting/touching/speaking 6. Obsessional thoughts about harming self/others
MOCI	30	y/n	0–30	1. Washing 2. Checking 3. Doubting 4. Slowness
SCL-90-R	10	0–4	0–40	–

HOCI, Hamburg Obsession/Compulsion Inventory; LOI, Leyton Obsessional Inventory-child version; MOCI, Maudsley Obsessive–Compulsive Inventory; OC, obsessive–compulsive; PBA-HD, Problem Behaviours Assessment for Huntington Disease; SCL-90-R, Symptom Check-List-90-revised; SCOPI, Schedule of Compulsions Obsessions and Pathologic Impulses; UHDRS, Unified Huntington's Disease Rating Scale; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

OC symptoms, and the UHDRS behavioural section (28 items) contains only two items to assess severity of obsessions and compulsions in a 0–4 range. These screening instruments have been used in three studies on Huntington's disease, including two large cohorts, and the negative results of these studies might be the consequence of a lack of sensitivity of the UHDRS and PBA-HD to pick up OC symptomatology. The other studies on Huntington's disease, using more elaborate and refined screeners on OC symptoms, are likely to have been more informative. To this end, the Y-BOCS symptom checklist with the severity scale has superior quality over all other scales as it contains elaborate symptom data coupled with a 10 item scale specifically designed to measure OC symptom severity, addressing various aspects (ie, time per day, distress and interference) of obsession and compulsion severity separately. Another limitation is that, in general, none of the OC symptom scales used are able to differentiate between perseveration/stereotypies and impulsive behaviours on the one hand and OC symptoms on the other. Furthermore, only clinical studies have been reported. Population based studies may provide more accurate estimates of frequencies of movement disorders and their comorbid OCD/OC symptoms. Thus confirmation bias may have led to an overestimation of OCD comorbidity in these clinical groups compared with a population sample of movement disorder subjects. Further limitations are: small sample sizes and—in some studies—lack of information regarding the time course between onset of the movement disorders and of OCD/OC symptoms, and paucity of family study information (in Huntington's chorea) on the prevalence of OCD/OC symptoms in their family members.

In conclusion, the choreas were most consistently, and presumably aetiologically, associated with an increased incidence of comorbid OCD/OC symptoms. Chorea shares an aetiological basis with OCD which probably converges at the level of the frontal–striatal circuitry. The elevated frequencies of OC symptoms in focal dystonias point to a similar direction but need further exploration. Additional research, including MR studies comparing OCD/OC symptoms and non-tic movement disorders, studies on the time course of the movement disorders and OCD/OC symptoms, and family based approaches, are warranted to gain further insight into the nature of the observed relationships.

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