Neurological soft signs in obsessive compulsive disorder: standardised assessment and comparison with schizophrenia

D. Bolton[a,*], W. Gibb[b], A. Lees[c], P. Raven[d], J.A. Gray[a], E. Chen[e] and R. Shafran[f,1]
[a]*Psychology Department, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK*
[b]*Wessex Neurological Centre, Southampton General Hospital, Southampton, UK*
[c]*National Hospital for Neurology and Neurosurgery, Queen Square, London, UK*
[d]*Department of Psychological Medicine, Royal Free Hospital, London, UK*
[e]*Department of Psychiatry, University of Hong Kong, Hong Kong*
[f]*Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, UK*

While several studies have detected raised levels of neurological soft signs in patients with obsessive compulsive disorder (OCD), the specificity of these abnormalities remains uncertain. This study used a new standardised measure, the Cambridge Neurological Inventory (CNI), to assess soft signs in 51 subjects with OCD. Comparison was made with data on patients with schizophrenia and a non-clinical control group from a previously reported study. Individuals with OCD showed raised levels of soft signs compared with non-clinical controls in many categories of the CNI: Motor Coordination, Sensory Integration, Primitive Reflexes, Extrapyramidal Signs, and Failure of Suppression. Compared with patients with schizophrenia, the OCD group had lower levels of neurological signs in some CNI categories: Hard Signs, Motor Co-ordination, Tardive Dyskinesia, Catatonic Signs, and Extrapyramidal Signs. However, levels of soft signs in the OCD group did not significantly differ from those in the schizophrenia group in other CNI categories: Sensory Integration, Primitive Reflexes and Failure of Suppression. The significance of these patterns of findings is discussed.

Keywords: Obsessive-compulsive disorder, neurological soft signs, schizophrenia, specificity

*Corresponding author: Tel.: +44 171 919 3255; Fax: +44 171 919 3772; E-mail: d.bolton@hkcl.bpmf.ac.uk.

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1. Introduction

Obsessive compulsive disorder (OCD) has traditionally been regarded as a functional neurosis, and this is reflected in its classification as an anxiety disorder in current standard diagnostic systems such as DSM IV [4]. In recent years, however, an alternative view has become prominent, in which OCD is seen as primarily a neurological motor disorder [31, 52, 53, 55, 76]. Various kinds of evidence support models of OCD implicating neurological deficit. There is association between obsessive-compulsive symptomatology and cerebral disease, e.g. encephalitis lethargica [72], and Sydenham's Chorea [24, 69], and focal brain lesions [7, 44, 45]. There is also association between obsessive-compulsive symptomatology and suspected signs of cerebral disorder, specifically tics [48, 58]. OCD sometimes responds to psychosurgery [27, 41]. The most direct evidence of abnormal structural neurological involvement in OCD is structural abnormalities detected by computerised tomographic or magnetic resonance imaging. Some studies have reported volumetric abnormalities in the caudate nuclei, though few consistent findings have emerged [6, 29, 35, 49, 54, 59]. Functional neuroimaging studies in OCD have generally produced more uniform findings, showing involvement particularly of the orbito-frontal cortex and basal ganglia (e.g. [11, 15, 56, 59]).

Further important evidence of abnormal neurological involvement in OCD is above normal frequency of neurological soft signs in this population [17, 30, 33, 37, 60]. A neurological soft sign is a motor, sensory or integrative deviation detected by clinical neurological examination, found in the absence of features of a fixed or transient neurological lesion or disorder, and assumed not to localise the site of a putative central nervous system lesion [51, 65]. It

is generally supposed that neurological soft signs reflect impairments in several functional systems, with the relationship between a given sign and a particular cerebral location likely to be complex [13, 36]. Neurological soft signs associated with mental disorders are significant insofar as they implicate a central nervous system factor which may be relevant to aetiology or prognosis. There is evidence that neurological soft signs may be relevant to treatment outcome in schizophrenia [28, 66], though more negative results have been reported in the case of treatment of OCD [10, 32, 70].

In children and adolescents with OCD, Denckla found soft neurological abnormalities such as choreiform movements and miscellaneous neuro-developmental abnormalities [17]. Neurological soft signs have been found to be more common in patients with medication-free OCD than normal controls [30], and in patients with obsessional slowness [33]. It has been proposed that the neurological impairment found in patients with OCD should be compared with that of other psychiatric populations [30]. Specificity is a crucial issue, since this determines which feature of a particular mental disorder is associated with the neurological soft signs. In the case of OCD, questions arise as to whether the associated signs are also correlated with psychiatric disorder generally, or with other anxiety disorders, or with some other major disorder. Schizophrenia is one relevant disorder, since its association with neurological soft signs is well established (e.g. [13, 28, 34, 42, 46, 62, 73]). There is also some comorbidity between schizophrenia and OCD [19], and some overlap in symptomatology [77]. Studies of neurological soft signs associated with OCD have generally used non-clinical control groups. The present study, in contrast, aims to test specificity with a psychiatric control, specifically patients with schizophrenia, and is the first study to compare neurological soft signs in these two major disorders.

Comparisons are more reliable to the extent that assessments are standardised [5]. The present study makes use of a new standardised assessment of neurological soft signs, the Cambridge Neurological Inventory (CNI) [13]. The CNI has similarities to several soft signs assessments reported previously [12, 30, 38, 39, 51, 62]. Advantages of the CNI for the present project include that it is generally more comprehensive than previous assessments, that it was developed in application to patients with schizophrenia but was designed for use with other psychiatric disorders including OCD, and it has specified methods of eliciting and rating signs, giving high interrater reliability, with Kendall's w ranging from 0.82 to 0.97 [13].

The present study had two main aims. Firstly, to replicate using a standardised assessment, the CNI, previous studies that have found raised levels of neurological soft signs in individuals with OCD compared with non-clinical controls. Secondly, to compare using the same standardised assessment soft signs associated with OCD with those associated with schizophrenia. Approval for the study was given by the Ethical Committee (Research) of the Institute of Psychiatry and Bethlem Royal and Maudsley NHS Trust Hospitals.

2. Method

2.1. Participants

54 individuals with OCD were recruited from two sources: 24 from the community by advertisements, and 30 from a specialist clinic for the behavioural treatment of OCD. All participants were assessed by structured clinical interview as meeting diagnostic criteria for OCD according to both DSM-III-R [3] and DSM-IV [4]. None of the participants had received a neurological diagnosis. 31 were female and 23 female. Mean age was 37.9 years (s.d. 10.16, range 18–70 years). 30 were taking psychotropic medication at the time of the study. Mean I.Q. estimated by the National Adult reading Test (NART) [47] was 107.9 (s.d.10.85, range 81–125).

Neurological soft signs in this group as measured by the CNI were compared with those in groups of patients with schizophrenia and healthy controls reported previously by Chen and his colleagues in their original paper on the CNI [13]. Patients with schizophrenia were aged 18-65, selected from inpatient and outpatients services, met criteria for diagnosis of schizophrenia according to DSM-III-R, had no diagnosed neurological or serious medical illness, and no history of substance abuse. All patients were receiving neuroleptic medication, with mean daily dosage, converted to chlorpromazine-equivalent dosage according to Davis [16], of 1224 mg (s.d. = 1540 mg). The control participants were paid volunteers, with exclusion criteria being history of psychotic illness, neurological disorder, or substance abuse, assessed using a brief questionnaire.

Chen and his colleagues reported that levels of some categories of soft signs increased with age in the patient and groups under study [13], and it was noted

Table 1
Characteristics of the groups of participants: mean age and standard deviations, gender ratios, and IQ estimates means and standard deviations

	OCD ($n = 51$)	Schizophrenia ($n = 47$)	Non-clinical control ($n = 67$)
Age	36.9 (8.84)	36.7 (10.03)	38.2 (11.5)
Gender ratio: % female[a]	58.8%	31.9%	17.9%
IQ estimates	108 (11.2)	–	111 (14.1)

[a]OCD group differs from both other groups, $p < 0.05$.

that the mean ages of groups of those groups were significantly higher than that of the OCD group recruited as above. This implied that age would be confounded with diagnostic status, and to overcome this problem individuals in all groups were excluded whose age was two standard deviations or more above the mean age of the OCD group. This had the effect of excluding all subjects over the age 55, including three from the OCD group itself. The resulting groups were then well matched for age, as shown in Table 1. It can also be seen in Table 1 that the group with OCD were not matched with the comparison groups with respect to gender ratio, and that mean IQ estimated by the NART in the OCD and non-clinical groups were similar; IQ was not estimated for the patients with schizophrenia. 54% ($n = 51$) of the subjects with OCD, and 100% ($n = 47$) of the patients with schizophrenia, were taking psychotropic medication at the time of assessment.

2.2. Measures

The Cambridge Neurological Inventory The Inventory is a standardised clinical examination of neurological soft signs described by Chen et al. [13]. It takes approximately 30 to 45 minutes to administer, and begins with a screening for 'hard' neurological signs, plantar reflexes, power and reflexes in extremities. The categories into which soft signs are classified, and the individual tasks relating to them, are as follows:

Motor Co-ordination: Finger-nose test, finger-thumb tapping, finger-thumb opposition, dysdiadochokinesia, fist-edge-palm test, Oseretsky test.

Sensory Integration: extinction, finger agnosia, stereoagnosia, agraphesthesia, left-right orientation.

Primitive Reflexes: snout reflex, grasp reflex, palmomental reflex.

Tardive Dyskinesia: simple, complex and dyskinetic abnormal involuntary movements in the face, trunk and limbs.

Catatonic Signs: gait mannerism, *gegenhalten* (resistance to passive movement which increases with the force exerted), *mitgehen* ('Anglepoise lamp' raising of arm in response to light pressure), imposed posture, abrupt and/or exaggerated spontaneous movements, iterative movements, automatic obedience and echopraxia.

Extrapyramidal Signs: increased tone in limbs, decreased associated movements in walking, shuffling gait, arm dropping, tremor, rigidity in neck.

Failure of Suppression: Blinking in saccadic eye movement; head movement in saccadic eye movements; winking with one eye.

Ratings on the CNI are standardised to indicate 'normal response' (0), 'equivocal response' (0.5), 'abnormal response' (1) or 'grossly abnormal response' (2). CNI examination and rating was carried out by one of three of the investigators: WG and AL, both neurologists, and PR, trained in neurology as well as psychiatry.

2.3. Analysis

The Mann-Whitney-U statistic, appropriate for non-parametric distributions, was used to test between groups differences in CNI ratings. Statistical analyses were performed using SPSS for Windows, Release 8.0. [67].

3. Results

Preliminary analyses of the OCD group CNI data indicated that a far outlier, with a total soft sign score over 3 standard deviations above the mean, was significantly affecting the distribution, and this participant was excluded from the main analyses (reducing N from 51 to 50). Comparison of CNI scores for subjects with OCD from the two sources of recruitment (clinic and community) showed a statistically significant difference in the *Dyskinesia* category. Inspection of the data, however, revealed that all subjects were rated 0 in this category except 4 who were rated 1 in the community sample, and this difference was judged

Table 2
Median and mean scores and standard deviations for CNI categories for three groups: patients with OCD and schizophrenia and non-clinical controls; Mann-Whitney U statistics and p-values for between group differences: OCD vs. Non-clinical, OCD vs. Schizophrenia

CNI Subcategories and total	Groups									Mann-Whitney U tests			
	OCD ($n = 50$)			Schizophrenia ($n = 47$)			Non-clinical control ($n = 67$)			OCD vs. Non-clinical		OCD vs. Schizophrenia	
	Median	Mean	s.d.	Median	Mean	s.d.	Median	Mean	s.d.	z	p	z	p
Hard Signs	0.00	0.20	0.57	0.00	0.59	0.86	0.0	0.31	0.60	−1.560	0.119	−2.756	0.006
Motor Co-ordination	2.75	3.46	3.19	5.00	5.21	3.90	0.0	0.86	1.48	−5.744	<0.001	−2.184	0.029
Sensory Integration	5.00	5.11	2.07	3.00	4.47	3.84	1.0	1.73	1.98	−6.907	<0.001	−0.155	0.120
Primitive Reflexes	0.00	0.44	0.64	0.00	0.30	0.50	0.0	0.01	0.12	−5.156	<0.001	−1.011	0.312
Tardive Dyskinesia	0.00	0.08	0.27	0.00	0.71	0.93	0.0	0.02	0.10	−0.871	0.384	−4.248	<0.001
Catatonic	0.00	0.10	0.45	0.00	0.68	0.95	0.0	0.05	0.15	−0.370	0.711	−4.493	<0.001
Extrapyramidal	0.25	0.73	1.06	1.00	1.49	1.69	0.0	0.08	0.31	−5.100	<0.001	−2.209	0.027
Failure of Suppression	0.75	0.95	0.94	1.00	1.50	1.53	0.0	0.30	0.62	−4.890	<0.001	−1.419	0.156

not to have clinical significance. The scores in all other CNI categories showed no differences between the two cohorts of OCD subjects that were statistically different at the 5% level, and data from these two sources were combined for the main analyses. Comparison of medicated vs. unmedicated subjects in the OCD group also showed no differences in CNI category scores at or approaching statistical significance at the 5% level, and these subgroups were therefore also combined for the main analyses.

Median and mean CNI category scores with standard deviations for the three groups of participants with OCD, with schizophrenia, and non-clinical controls, are shown in Table 2, with statistical and probability values of differences between the OCD group and the other two groups, are shown in Table 2.

Regarding comparison between the group with schizophrenia and the non-clinical controls, the patient group had higher levels of soft signs in all categories, at probability levels below 1%. This result simply replicates on a subset of the original data set the findings previously reported by Chen and his colleagues [13]. Regarding comparisons between the OCD group and the other two, it can be seen in Table 2 that the OCD group showed raised levels of soft signs compared with the non-clinical group in the following categories of the CNI: *Motor Co-ordination*, *Sensory Integration*, *Primitive Reflexes*, *Extrapyramidal Signs*, and *Failure of Suppression*. Regarding comparison between OCD and schizophrenia, it can be seen in Table 2 that there were no statistically significant differences between these groups in the categories of *Sensory Integration*, *Primitive Reflexes*, and *Failure of Suppression*, while lower levels of signs were found in OCD compared with schizophrenia in other CNI categories: *Hard Signs*, *Motor Co-ordination*, *Dyskinesia*, *Catatonic and Extrapyramidal Signs*.

4. Discussion

The first aim of the study was to replicate previous studies which have found raised levels of neurological soft signs in individuals with OCD compared with non-clinical controls, using a standardised assessment, the CNI. The results indicate that individuals with OCD, compared with a non-psychiatric population, show raised levels of soft signs in many CNI categories: *Motor Coordination*, *Sensory Integration*, *Primitive Reflexes*, *Extrapyramidal Signs*, and *Failure of Suppression*. These findings are consistent with previous reports. Hollander and colleagues [30] found that patients with OCD had abnormalities in fine motor co-ordination, involuntary and mirror movements, and visuo-spatial function. Hymas and colleagues [33] found that a group of patients with OCD and significant slowness, compared with healthy controls, showed

loss of motor fluency, hesitancy of initiation of limb movements, speech and gait abnormalities, cogwheel rigidity, complex repetitive movements and tics.

The OCD group was matched with the non-clinical group for age and IQ, though not for gender ratio, or medication. One study of female patients with OCD failed to find raised levels of soft signs compared with female healthy controls [68], but a study of a mixed male and female group found no gender effects on levels of soft signs [30], and further analysis revealed no such effect in the present OCD group. In the non-clinical group, there were no gender effects except in *Reflexes* where females ($n = 12$) had a higher mean rating than males ($n = 55$) ($z = -2.141$, $p = 0.032$). However, as can be seen in Table 2, the mean rate in this category of soft signs, as in others, was low in the non-clinical group, and the statistical significance was due to the males being rated all 0, while the females were rated all 0 except one rated 1. It cannot be assumed that this statistically significant difference has any clinical significance. Moreover, the ratio of females in the non-clinical group was higher than in the OCD group, so the finding of raised levels of *Reflex* signs in the OCD group would remain robust given this possible gender effect. Generally, the absence of gender effects within the OCD and non-clinical groups suggests that the gender ratio differences between them are not contributing to the differences in levels of soft signs. Regarding medication, no differences in levels of soft signs were apparent within the OCD group between medication and non-medicated individuals, consistent with previous findings [8]. It is therefore unlikely that medication effects in the OCD group account for the higher levels of soft signs relative to the non-clinical control group.

The second aim of the study was to compare soft signs associated with OCD with those associated with schizophrenia. The present findings of soft signs associated with schizophrenia, which simply replicate on a subset of the original data set the findings previously reported by Chen and his colleagues [13], are consistent with other studies which have shown abnormalities notably in motor coordination, sequencing, and higher order sensory function [25, 28, 57]. Heinrichs and Buchanan [28] in their review of neurological signs in schizophrenia, which did not include studies of OCD, concluded that 'the preponderance of data suggest that schizophrenic patients have more neurological abnormalities than patients with mixed psychiatric disorders and affective disorders.' The present findings are consistent with this overall quantitative statement, but the details behind it warrant attention. Use of the same standardised examination for both disorders in the present study allows for some precision in the comparison of the kinds and extent of soft signs associated with schizophrenia and OCD. The schizophrenia group compared with the OCD group had raised levels of neurological signs in particular CNI categories: *Hard Signs*, *Motor Co-ordination*, *Tardive Dyskinesia*, *Catatonic Signs*, and *Extrapyramidal Signs*. By contrast, in certain categories of neurological soft signs the levels in the schizophrenia group did not significantly exceed those in the OCD group, these being *Sensory Integration*, *Primitive Reflexes* and *Failure of Suppression*. The present results suggest that impairments relating to these areas in individuals with OCD are no less severe than in individuals with schizophrenia.

Issues of matching also arise in comparing these two diagnostically defined groups: they were matched for age, though not for gender ratio, medication, or IQ. As noted above, there was no gender effect on levels of soft signs in the OCD group, and further analysis also revealed no such effect in the group of patients with schizophrenia. This absence of gender effects suggests that the gender ratio differences between the two groups are not contributing to the differences in levels of soft signs. Regarding medication, no medication effects were apparent within the OCD group. It is, however, impossible to assess the effects of being on as opposed to off medication within the group with schizophrenia, since all patients were receiving neuroleptic medication at the time. Many studies comparing schizophrenic patients taking neuroleptic medication to patients drug free at the time of examination have shown no difference in the prevalence of soft signs between groups [28], and several studies have reported no correlation between levels of soft signs and current dosage of neuroleptic medication [13, 39, 40]. However, one study found that neuroleptic-naive patients had lower levels of soft signs than patients on medication, though still raised levels compared with non-clinical controls [25]. It remains possible that medication effects in the group of patients with schizophrenia might explain some detected differences in levels of soft signs compared with the OCD group. Regarding intelligence, there is evidence to show that neurological soft signs are negatively associated with intelligence in childhood psychiatric disorder [61, 65] and in schizophrenia [18, 46, 51]. Studies of soft signs have generally not reported intelligence levels or interactions with levels of soft signs in OCD [30, 33]. The present OCD cohort showed no correlations at or

approaching the 5% level between soft signs and estimated IQ, except in Catatonic signs ($\rho = -0.343$, $p = 0.023$). However, the clinical significance of this positive finding is questionable in the context of low scores in this CNI category and multiple testing. It is in any case not possible to assess the possible confounding effects of IQ in the comparisons between the two diagnostically defined groups, because IQ of the patients with schizophrenia was not assessed. It remains possible that the group with schizophrenia had lower IQ than the OCD group, and that such difference might explain to some extent detected differences in levels of soft signs. Thus, replication of the present findings with groups matched for intelligence as well as age would be desirable.

A further limitation of the present design was that different examiners assessed soft signs in the three groups. As previously noted, however, the interrater reliability of CNI has been found to be high [13]. Also, because only subjects with OCD were being assessed in the present study, the neurologists who carried out the examinations were not blind to diagnosis. A further study not only matching for intelligence as well as age, but also making blind assessments would be required to address these threats to validity.

Concerning the specificity of neurological soft signs associated with OCD, the implication is that deficits compared with the non-clinical population, for example in motor co-ordination and sensory integrative functions, are not specific to OCD, but are similar to those associated with schizophrenia. This conclusion suggests in turn that the critical factor associated with these neurological soft signs is not specifically obsessive-compulsive symptomatology, nor schizophrenia, but some factor common to both. It has been suggested that neurological soft signs in schizophrenia reflect deficits in motor speed, coordination, and sequencing [20], and in working memory [43, 64]. Similar or related functional deficits may be implicated also in OCD [1, 21, 50]. Basic functions of these kinds involve frontal- subcortical circuitry [2, 78], and there is evidence that these circuits are involved in schizophrenia and in OCD. In the case of both disorders neuroimaging and neuropsychological investigations have suggested involvement of the basal ganglia, with connections to the dorso-lateral-prefrontal cortex in schizophrenia [1, 74, 75], and to the orbito-frontal cortex in OCD (e.g. [1, 11, 15, 56, 59]).

Finally, there may be subtypes associated with differing levels of neurological soft signs both in schizophrenia [22, 28, 42, 63, 64] and in OCD [9, 23, 55]. The present study, the first of its kind, was not designed to address these more complex and to some extent speculative issues, but they should be considered in future comparisons of soft signs in these two major disorders.

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