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Functional Cognitive Disorders: Can Sleep Disturbance Contribute to a Positive Diagnosis?

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Abstract

Study background: Sleep disturbance may contribute to subjective memory complaints which are frequently encountered in cognitive disorders clinics. Identification of sleep disturbance may contribute to a positive diagnosis of functional cognitive disorders (FCD) compared to dementia or mild cognitive impairment.

Methods: Jenkins Sleep Scale (JSS), a validated sleep scale, was administered to consecutive new patients attending a dedicated cognitive disorders clinic based in a regional neuroscience Centre.

Results: Sleep disturbance identified using JSS was more frequent in patients with functional cognitive disorders ($p<0.001$). Dichotomised JSS showed reasonable sensitivity (>0.8) for FCD when used as a diagnostic test.

Conclusion: Identifying sleep disturbance using a simple sleep screening scale may contribute to a positive diagnosis of functional cognitive disorders in a dedicated cognitive disorders clinic. This may have pragmatic implications for the treatment of subjective memory complaints.

Keywords: Diagnosis; Functional cognitive disorders; Memory clinic; Sleep screening

Introduction

Many patients referred to dedicated cognitive disorders clinics with complaints of cognitive impairment, chiefly of memory, are found on assessment and investigation not to harbour evidence of a neurodegenerative or cognitive neurological disorder. In our clinic such patients account for between 50-60% of referrals [1]. Whereas previously these individuals were variously labelled as being "Worried well" or "Memory complainers", or having subjective memory impairment, mild cognitive dysfunction, or functional memory disorder [2,3], more recently Stone, et al. have proposed the category of "Functional cognitive disorders"(FCD) [4].

Analogous to other functional disorders (e.g. movement, epilepsy), FCD should be a positive diagnosis, based on inconsistency or incongruence of symptoms, rather than a diagnosis of exclusion. Factors which may be more commonly observed in patients with FCD compared to patients with dementia/MCI have been suggested [1,4,5] which if confirmed may facilitate positive diagnosis of FCD. We have previously suggested that bringing a symptom list (handwritten or typed on an ipad), the phenomenon known as la maladie du petit papier, may be helpful in diagnosis of FCD [6].

Previously, it has been shown that impaired sleep quality, as measured using the Pittsburgh Sleep Quality Index (PSQI) [7], was worse in patients attending a dedicated cognitive disorders clinic whose eventual diagnosis was "Not dementia" [8]. It is possible that many of these non-demented patients may have qualified for a diagnosis of FCD.

The aim of the current study was to administer a simple sleep questionnaire to patients attending a dedicated cognitive disorders clinic to examine whether sleep impairment was more common in FCD patients and hence a possible marker for a positive diagnosis of FCD.

Methods

As part of an ongoing study of FCD in a dedicated cognitive disorders clinic, consecutive new patient referrals seen over a 6-month period (November 2017-April 2018) were assessed for sleep disturbance by administration of the Jenkins Sleep Scale (JSS) or Questionnaire which addresses four sleep-related symptoms over the previous four week period (Table 1) [9]. The scale was chosen for its brevity (administration time ca. 1 m), and because a dichotomous index may be easily computed based on the presence of any one of the four symptoms occurring on 15 or more nights during the four week period under consideration (JSS+, JSS-) [10]. JSS is considerably quicker and easier to administer, score and categorize than PSQI.

During the previous 4 weeks have you experienced:
Difficulty falling asleep?
Waking up several times per night?
Difficulty staying asleep (including waking up too early)?
Waking up feeling tired and worn out after usual amount of sleep?
If yes to any one of these, ask frequency question: 15 or more nights?
A dichotomous index was computed and coded as JSS+ if the respondents reported that any of the above sleep disturbances occurred 15 or more nights during the previous 4 weeks or as JSS-, if not.

Table 1: Jenkins Sleep Scale (JSS) or Questionnaire and its dichotomisation (after Jenkins et al.; Lallukka et al.).

Because inadequate sleep, even a mild insufficiency, may be linked to mood disturbance [11], both of which may impact on memory function, a two question screener for depression (M2Q) was also administered (Table 2) [12]. Again this scale was chosen for its brevity (administration time ca. 1 m), and because a dichotomous index may be easily computed based on the presence of either one of the two symptoms occurring ($M2Q^+$, $M2Q^-$) [12]. M2Q is considerably quicker and easier to administer, score and categorise than other mood screeners, such as the Patient Health Questionnaire 9 (PHQ^{-9}) which has previously been examined in a dedicated cognitive disorders clinic [13].

During the past month:
Have you often been bothered by feeling down, depressed, or hopeless?
Have you often been bothered by little interest or pleasure in doing things?
If yes to either one of these, coded as $M2Q^+$

Table 2: Mood 2 Question screener (M2Q) and its dichotomisation (after Arroll et al.).

Reference standard diagnosis of cognitive impairment (dementia, mild cognitive impairment) was by judgment of an experienced clinician based on standard diagnostic criteria (DSM-IV, Petersen, respectively) but did not use JSS or M2Q scores in order to avoid review bias. Reference standard diagnosis relied on clinical interview, informant interview (where possible), neuropsychological testing (bedside +/- formal as required) and structural neuroimaging (CT +/- MRI as required).

FCD was diagnosed on the basis of a typical profile of clinical features, including, but not limited to, the ability to describe in detail memory symptoms despite assertions of having a poor or terrible memory (often contrasted with a previously "Brilliant" memory); being more aware of the problems than others; variability of symptoms on a day to day basis and a relative lack of impact on social and/or occupational function [4].

Pragmatic diagnostic test accuracy study of both dichotomised instruments was undertaken. Results of the index tests and the reference standard diagnoses were cross-classified in a 2 × 2 contingency table, from which standard measures of discrimination with 95% confidence intervals were calculated, both paired (sensitivity and specificity; positive and negative predictive values [PPV, NPV], likelihood ratios [LR^+, LR^-] and clinical utility indexes [CUI^+, CUI^-]) and unitary measures (correct classification accuracy [CCA], Youden index [Y], predictive summary index [PSI], diagnostic odds ratio [DOR], area under the receiver operating characteristic curve [AUC ROC]) [14]. Dichotomised JSS and M2Q results were also combined either in series (both tests required to be positive before diagnosis of cognitive impairment is made: the "And" rule) or in parallel (either test positive sufficient for diagnosis to be made: "Or" rule) [15].

Results

Of 89 consecutive new referrals seen over the study period (F:M=43:46, 48% female; age range 22-88 years, median 62), 38 (=43%) were diagnosed with a cognitive disorder: 9 dementia (DSM-IV-TR criteria), 26 with MCI (Petersen criteria), and 3 with cognitive disorder without current cognitive impairment (e.g. transient global amnesia, transient epileptic amnesia). The remainder (51; =57%) were diagnosed with FCD.

Comparing JSS outcomes in the groups with cognitive disorders and with FCD, a higher percentage of FCD patients had markers of disturbed sleep on the dichotomised JSS (83% JSS+, *vs.* 50% of the cognitive disorders group) and this was statistically significant (chi square=11.2; $p<0.001$). JSS was negatively correlated with patient age ($r=-0.30$).

Comparing M2Q outcomes in the groups with cognitive disorders and with FCD, a higher percentage of FCD patients had markers of disturbed mood on the dichotomised M2Q (80% $M2Q^+$, *vs.* 47% of the cognitive disorders group) and this was statistically significant (chi square=10.9; $p<0.001$). M2Q was negatively correlated with patient age ($r=-0.38$).

Using either JSS or M2Q as a screening instrument for the diagnosis of FCD (Table 3), both showed a similar profile of reasonable sensitivity (≥ 0.8) but poor specificity (around 0.5) and positive predictive value (<0.7). Clinical utility indexes suggested both tests might be adequate to rule in a diagnosis of FCD, but very poor for ruling out the diagnosis.

Combining JSS and M2Q either in series or in parallel (Table 4) produced the anticipated changes [14], namely increased specificity, NPV, and LR- in series, and increased sensitivity, PPV, and LR+ in parallel. None of these changes was dramatic. JSS and M2Q were positively correlated ($r=0.33$).

Test	JSS+	M2Q+
Sens	0.83	0.8
	(0.73-0.94)	(0.68-0.92)
Spec	0.5	0.53
	(0.34-0.66)	(0.36-0.69)
Y	0.33	0.33
CCA	0.69	0.68
	(0.59-0.79)	(0.58-0.78)
PPV	0.69	0.68
	(0.57-0.81)	(0.55-0.80)
NPV	0.69	0.68
	(0.51-0.87)	(0.51-0.85)
PSI	0.38	0.36
LR+	1.67=unimportant	1.69=unimportant
	(1.17-2.37)	(1.16-2.46)
LR-	0.33=small	0.38=small
	(0.23-0.47)	(0.26-0.55)
DOR	5	4.47
	(3.52-7.10)	(3.07-6.50)
CUI+ (rule in)	0.57=adequate	0.54=adequate
CUI- (rule out)	0.35=very poor	0.358=very poor
AUC ROC	0.67 (0.62-0.72)	0.66 (0.61-0.72)

Table 3: Measures of discrimination for diagnosis of FCD using dichotomised JSS or M2Q (with 95% confidence intervals).

Test	JSS+/M2Q+ series	JSS+/M2Q+ parallel
Sens	0.69	0.93
	(0.55-0.82)	(0.86-1.00)
Spec	0.69	0.33
	(0.54-0.84)	(0.18-0.49)
Y	0.38	0.26
CCA	0.69	0.67
	(0.59-0.79)	(0.56-0.77)
PPV	0.74	0.64
	(0.61-0.87)	(0.52-0.75)
NPV	0.64	0.8
	(0.49-0.79)	(0.60-1.00)
PSI	0.38	0.44
LR+	2.25=small	1.40=unimportant
	(1.33-3.83)	(1.10-1.79)
LR-	0.45=small	0.20=small
	(0.26-0.76)	(0.16-0.26)
DOR	5.03	7
	(2.96-8.55)	(5.49-8.93)
CUI+ (rule in)	0.51=adequate	0.59=adequate
CUI- (rule out)	0.45=poor	0.27=very poor

Table 4: Measures of discrimination for diagnosis of FCD using dichotomised JSS or M2Q in series or parallel (with 95% confidence intervals).

Discussion

This study has shown that sleep disturbance and mood disturbance are associated with a diagnosis of functional cognitive disorders in a dedicated cognitive disorders clinic. The findings suggest that in clinical practice enquiries for sleep and mood disturbance may facilitate a positive diagnosis of FCD.

Study shortcomings include the small size of the cohort (lower than anticipated for the study period, due to local changes in clinic scheduling outside the authors' control). Other issues may relate to the index tests and the reference diagnosis.

The limitations of JSS are recognised: the four items cannot address the spectrum of sleep disorders and hence this can only be used as a preliminary screener [16]. Moreover, dichotomising any test results in loss of statistical power, although clinicians generally prefer tests which can be easily categorised in practice.

Reference diagnoses are hampered by the lack of diagnostic criteria for FCD, with the possibility of incorrect diagnoses (e.g. MCI might be mistaken for FCD, since neither impact on activities of daily living). Moreover this was a cross sectional study with potential for diagnostic errors in the absence of longitudinal patient follow up. However, the observed frequency of FCD was very similar to that recorded in a previous series from this clinic [1] suggesting consistency in diagnostic approach. FCD is a heterogeneous group, with various suggested typologies (e.g: mood disorder, other functional disorders, medication effects, dementia health anxiety, normal cognitive experience, dissociative amnesia, malingering, or combinations thereof). The cognitive disorders group is also heterogeneous, including dementia, MCI, and occasional patients without cognitive impairment (e.g. patients seen after an episode of transient global amnesia).

Enquiries about sleep should be a routine component of health assessment in patients with memory complaints since these may represent a pragmatic treatment target [8]. The study suggests that screening for sleep disturbance may contribute to a positive diagnosis of FCD, as may other demographic and clinical parameters [1,5,6]. This finding will need to be corroborated in larger, independent, patient cohorts and by using other, more comprehensive, sleep screeners.

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