Illness-related cognition, distress and adjustment in functional stroke symptoms, vascular stroke, and chronic fatigue syndrome.

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Conflicts of Interest and Source of Funding

Authors have no conflicts of interest. This research was funded by King's Health Partners R&D Challenge Fund (RE13522). ASD is supported by the UCLH National Institute of Health Research Biomedical Research Centre. AH and TC are supported by the Department of Health via the National Institute for Health Research (NIHR) Specialist Biomedical Research Centre for Mental Health award to the South London and Maudsley NHS Foundation Trust (SLaM) and the Institute of Psychiatry at King's College London.

Cover title: Functional stroke symptoms: a case control paper.

ABSTRACT

Background: High rates of psychological distress are reported in functional conditions and vascular stroke but there is limited understanding of how patients with functional neurological symptoms in stroke settings respond to symptoms.

Aims: This study compared patients with functional stroke symptoms to those with vascular stroke and chronic fatigue syndrome (CFS).

Methods: A prospective cohort of fifty-six patients with functional stroke symptoms were age-sex matched to patients with vascular stroke and CFS. Analysis of variance compared groups on cognitive and behavioural responses to symptoms, psychological distress and functioning. Sensitivity analyses controlled for known confounders. The proportions of clinical anxiety and depression were compared between groups.

Results: The functional stroke symptom group had a higher proportion of clinical anxiety cases compared to the CFS group, and a higher proportion of clinical depression cases compared to the vascular stroke group. Patients with functional stroke symptoms reported the highest rate of 'damage beliefs' and 'all-or-nothing' behaviours and greater symptom focussing and resting behaviour than patients with vascular stroke.

Limitations: Larger cohorts and a longitudinal design would strengthen study findings.

Conclusion: Compared to patients with vascular stroke or CFS, patients with functional stroke symptoms show a somewhat distinct profile of illness-related beliefs, behaviours, and cognitions, as well as higher rates of clinical anxiety . Understanding such group differences provides some insights into aetiology and cognitive-behavioural responses. Appropriate support and referrals should be available to patients with functional stroke symptoms to address distress and reduce likelihood of severe impairment.

Keywords: functional neurological conditions, stroke, case-control, cognition, psychology.

INTRODUCTION

Functional neurological symptoms (FNS) can be identified as apparently involuntary motor, sensory or cognitive symptoms, inconsistent with normal neurological functioning and unexplainable by recognised disease mechanisms (Stone, 2014). FNS are an established and common presentation in neurology outpatient clinics (Nimmuan et al., 2001). However, there is also evidence that a proportion of patients presenting to acute neurology settings (i.e. stroke services) have FNS, with no accompanying organic brain pathology. Some of these patients will meet criteria DSM-5 diagnostic criteria for Functional Neurological Symptom Disorder (DSM-5 300.11) or an ICD-11 criteria for Dissociative neurological symptom disorder (6B60), though it is likely they may not receive these diagnoses in UK stroke settings. Although FNS can occur in the context of organic symptoms (Factor et al., 1995), the incidence of comorbidity with vascular stroke has not been established. A large retrospective study reported approximately 8% patients in hyperacute stroke services had FNS (Gargalas et al., 2015) and meta-analyses have estimated 15% of 'stroke mimics' have FNS (Jones, O'Connell, & David, 2019). Despite increasing evidence for effective treatment approaches (Espay, 2018; Nicholson & 2020), services for FNS are generally limited, with many patients experiencing substantial delays receiving diagnoses and treatment (Herzog et al., 2018). In stroke settings, there is no clear onward referral pathway for patients with functional symptoms. It is not known how patients with functional stroke-like symptoms compare to patients with vascular stroke alone, or patients experiencing other functional or 'medically unexplained' conditions, in their levels of distress, disability, or response to symptoms. Establishing differences between these groups is important to increase understanding of functional presentations in stroke settings and improve decision making around best care pathways.

Cognitive and behavioural response to symptoms

Biases in illness-related cognitions and behaviours are central to the current understanding of functional symptom onset and maintenance (Deary et al., 2007; Henningsen et al., 2018; Jones, O'Connell, David, et al., 2019). Models of functional motor symptoms suggest that introspective

attention biases, symptom expectations and a low sense of personal agency are key to symptom maintenance (Jones, O'Connell, David, et al., 2019). Similar biases are described in other 'medically unexplained' syndromes such as chronic fatigue syndrome (CFS) (Deary et al., 2007). Health behaviours, such as help-seeking and resting, can negatively impact symptom reduction and recovery (Fobian & Elliott, 2018; Moss-Morris et al., 2018). Determining the cognitive and behavioural patterns in functional stroke-like symptoms could indicate treatment targets and provide a rationale for a clear care pathway.

Stroke survivors report negative perceptions of the duration and impact of post-stroke symptoms but rate their understanding of symptoms and the helpfulness of treatment more positively (Groeneveld et al., 2019). Nevertheless, negative illness-related beliefs are associated with worse mood, while perceptions of personal control are associated with better recovery from stroke (Aujla et al., 2018; Johnston et al., 1999).

Compared to patients with 'organic' neurological diagnoses, patients with FNS express more negative illness-related cognitions, specifically reporting lower levels of personal control (Binzer, 1997) and are less likely to link symptoms with life events/stress (Stone et al., 2010). Additionally, reluctance from clinicians to discuss functional symptoms (Monzoni et al., 2011) can leave patients with low levels of understanding and little hope of recovery (Gelauff et al., 2014; Nettleton et al., 2004). Whether such differences exist between patients with functional versus vascular presentations in stroke settings is unknown.

Psychological distress

Stroke survivors experience high levels of psychological distress linked to significant cognitive, motor and language disabilities. Meta-analyses report rates of 9.3% for any anxiety and 33.5% for depressive disorder in stroke survivors across settings (Mitchell et al., 2017). Consequently, there is increased access to psychological treatments available to vascular stroke patients (Gillham & Clark, 2011). Given that functional stroke symptoms can be as physically disabling as vascular stroke

symptoms, levels of distress may be comparable across these patient groups. Depressive or anxiety disorders have been associated with worse physical and social functioning in patients with functional motor symptoms compared to those with organic motor disorders, even when levels of psychiatric symptoms are similar (Stone et al., 2010; van der Hoeven et al., 2015).

Aims and rationale

Given the low accessibility of specialist services for patients with FNS, it is important clinicians draw on research to provide a good understanding of functional stroke symptoms and the best possible care and advice (Dworzynski et al., 2013). This paper compares a consecutive sample of patients with FNS in acute stroke settings (herein referred to as functional stroke symptoms) to a matched group of patients with vascular stroke and a second group of patients with chronic fatigue syndrome (CFS). CFS was chosen as a comparator as, like FNS, it is a contentious, disabling illness often requiring the input of specialist services. Though the similarities between FNS and CFS can be debated, there is recognition that patients with both conditions share subjective symptoms and aetiological factors (Teodoro, 2018; Wessely et al., 1999). Groups were compared on demographic and clinical characteristics, cognitive and behavioural responses to symptoms, levels of psychological distress and health-related functioning.

METHODS

Functional stroke cases

Functional stroke cases were prospectively recruited between 4th January-31st May 2019 from hyperacute stroke units (HASUs) across four hospital sites in South London and Kent: King's College Hospital, St George's Hospital, St Thomas' Hospital and Princess Royal University Hospital. Cases were identified by stroke clinicians following clinical investigations, examination for positive signs of FNS, and consideration given to any necessary imaging results and patients' medical history. All recruited participants received a diagnosis and explanation of their symptoms from a medical professional prior to being recruited into the study. A thorough and detailed description of data

collection for this sample can be found elsewhere (Jones et al., 2020). Participants completed measures on the ward within 24 hours of admission or over the phone within a week of referral from a stroke clinician. Patients with FNS and current or previous 'organic' stroke were not excluded as evidence supports the importance of recognising comorbid conditions due to the impact multimorbidity has on patient outcomes (McPhail, 2016). As such, FNS could impact the future symptom burden and healthcare use. The decision was made to recruit participants in the acute phase of symptom onset because the care pathway for these patients is not established. This means that many are not invited to a follow-up clinic or referred on to another service and would therefore be 'lost to follow-up' unless captured shortly after admission.

Inclusion Criteria:

a) Admitted to a stroke unit with suspected stroke
b) No stroke aetiology but possible functional presentation; or stroke aetiology with functional symptoms
c) Aged ≥18 years
d) Able to communicate in English

Comparison groups

Two comparison groups were selected by individual case matching. Criteria for case control samples were: i) aged >18 years when recruited ii) completed at least one of the self-report measures.

Chronic fatigue cases

The first comparison group was patients who experience a different category of functional/'medically-unexplained' symptoms: chronic fatigue syndrome (CFS). The cohort was 406 such patients who attended the Persistent Physical Symptom Research and Treatment Centre, a specialist tertiary service, between January 2013-October 2018. Patients were diagnosed by NICE criteria, which requires fatigue to be present for more than 4 months and all other possible

diagnoses to be excluded (NICE, 2021). CFS cases completed measures at baseline before treatment commenced.

Vascular stroke cases

Stroke cases provided a comparison group of patients with 'organic' stroke symptoms. Patients attending neurology clinics for post-stroke follow-ups at King's College London, Royal Berkshire or Sussex Hospital were approached as part of the Trans-diagnostic Approaches to Persistent Physical Symptoms (TAPPS) project, providing a cohort of 68 patients diagnosed with ischemic stroke, haemorrhagic stroke or transient ischemic attack. Measures were completed between January 2017-May 2019.

Measures

Demographic and clinical information

Age, sex, ethnicity, educational attainment, occupational and marital status were collected for all participants. Clinical information included duration of symptoms and diagnosis for which the participant was seeking help. Ethnicity and education were dichotomised for inferential analysis due to limited sample sizes. Ethnicity was dichotomised into 'White ethnic background' vs 'Racialised communities'. Education level was divided into 'Education up to 18 years old' vs 'Further education beyond school'.

Cognitive Behavioural Responses Questionnaire – short version (CBRQ)

The CBRQ measures responses to symptoms. Eighteen items are rated from 0 (strongly disagree) to 4 (strongly agree), with some reverse scored. There are six subscales consisting of 3 items each: Fear avoidance (e.g. Physical activity makes my symptoms worse), Damage beliefs (e.g. When I experience symptoms my body is telling me that there is something seriously wrong), Embarrassment (e.g. I am embarrassed about my symptoms), Symptom focusing (I think a great deal about my symptoms), All-or-nothing behaviour (I find myself rushing to get things done before I crash) and Resting behaviour (I stay in bed to control my symptoms). The CBRQ has been applied

across two chronic fatigue symptom cohorts, showing good validity, internal reliability (Cronbach's α = 0.67-0.88) and high factor loadings (Ryan et al., 2018).

Hospital Anxiety and Depression Scale (HADS)

HADS is a 14-item, brief self-report measure consisting of two subscales, developed to identify anxiety (HADS-A) and depression (HADS-D) in hospital or outpatient settings (Zigmond & Snaith, 1983). Both subscales show good discriminant validity and internal reliability across several settings (Bjelland et al., 2002) with mean Cronbach's alpha .83 for HADS-A and .82 for HADS-D. Scores of ≤7 for each subscale are considered in normal range, scores of 8-10 are possible cases and scores of ≥11 are probable cases (Zigmond & Snaith, 1983).

Work and Social Adjustment Scale (WSAS)

The WSAS is a simple 5-item scale with each item indicating the impact of symptoms on work, home, social activities, and relationships. Each item is scored from 0 (not at all impaired) to 8 (very severely impaired). It has good validity, test-retest reliability and internal consistency as a self-report measure (Cronbach's α≥ 0.90), and correlates with psychiatric symptom severity (Mundt et al., 2002). Psychometric properties of WSAS have been established in CFS cohorts (Cella, 2011).

Ethics statement

All data were de-identified. Ethical approval for collection of the functional stroke symptom data was granted as part of a feasibility study by the Health and Research Authority on 10th December 2019 (IRAS reference: 245303) following approval from Riverside Research Ethics Committee on 8th December 2018 (REC reference: 18/LO/1878). The Persistent Physical Treatment Centre collects measures from all patients for ongoing service audits and clinical evaluations. Approval for data collection was given by the Department of Psychological Medicine Audit and Clinical Outcomes Committee. The TAPPS project has ethical approval from the South East London Research Ethics Committee (REC: 10/H0808/135). All participants provided written consent. All data was anonymised.

Statistical analysis

Case matching

Matching criteria were age (+/- 10 years) and sex (exact match). One control was generated for each functional stroke symptom case at random using the 'fuzzy' command in SPSS with priority given to exact matches. The CFS group produced a matched case for all 56 functional stroke symptom cases from 42 exact matches and 14 non-exact/approximate matches (termed 'fuzzy'). Stroke cases produced 9 exact matches and 30 'fuzzy' matches, leading to a total of 39 matched cases.

Matched case control analyses

McNemar's tests compared the proportion of cases classified as potential anxiety or depression between patients with functional stroke symptoms, CFS cases and Stroke cases (Riffenburgh, 2006). Multivariate analysis of variance (MANOVA) compared groups on the CBRQ and HADS. Univariate analysis of variance (ANOVA) compared groups on WSAS scores. Type III sum of squares were calculated to account for uneven sample sizes. Pillai's trace (V) examined group effects; this measure is considered the most reliable and appropriate to use with smaller sample sizes (Tabachnik & Fidell, 2013). Where statistically significant group effects were observed, post-hoc comparisons were calculated using the conservative Bonferroni method appropriate for unequal sample sizes (Lee & Lee, 2018). If homogeneity assumptions were violated then Games-Howell comparisons were applied (Ruxton & Beauchamp, 2008). Sensitivity analyses for group comparisons on CBRQ, HADS and WSAS scales controlled for potential covariates of age, sex, and duration of symptoms. An additional covariate, occupational status, was used in the sensitivity analysis for WSAS comparisons.

Missing data

Three cases had not completed the HADS and were excluded from this specific analysis. One case had two missing HADS items, and two cases had one missing item. These three cases remained in the analysis. Even small amounts of missing data threaten the validity of short measures where summary scores are calculated from a small number of items. The summary scores for CBRQ

subscales and the WSAS are calculated from only 1 or 5 items. Therefore, participants with missing items on CBRQ subscales and WSAS were excluded from analyses of these measures.

RESULTS

Matched case cohort characteristics

There were 56 functional stroke cases aged between 21-78 years; 56 matched CFS cases aged 26-73 years and 39 matched Stroke cases aged 20-79 years. Within the functional stroke group, 40 (71·4%) had functional symptoms in isolation and 16 had functional symptoms as well as vascular stroke. Cohort characteristics can be seen in Table 1. Univariate analyses of variance with age as the dependent variable confirmed matched case groups did not differ statistically in age. McNemar's tests confirmed groups did not differ in proportions of males/females. Compared to the CFS group, the functional stroke group had a higher proportion of cases identifying as belonging to a racialised community (50% vs 13%, p=·037) and a higher proportion of cases who had engaged in higher education beyond 18 years old (48·2% vs 17·9%, p=·034).

Case control analysis

Between-group anxiety and depression cases

The stroke group had the highest proportion of possible anxiety cases (Table 2). The CFS group had the highest proportion of probable depression cases. The proportion of probable anxiety cases in the functional stroke group was higher than in the CFS group (p=·027). The proportion of probable depression cases in the functional stroke group was higher than in the stroke group (p<·001) but lower than in the CFS group (p<·001) (Table 2).

Analysis of Variance

HADS

We compared groups on the HADS anxiety and depression subscales separately. Multivariate ANOVA compared groups on the HADS anxiety and depression scales (F(4, 290)=6·13, V=·156, *p*<·001, η2=·78). There were significant group differences in HADS anxiety and depression scores (Table 3). Games-Howell post-hoc contrasts showed the functional stroke cohort to have lower mean HADS depression scores than the CFS group (*p*=·003, 95% CIs: -4·06, -·69). The functional stroke symptom group did not differ statistically from the two comparison groups on anxiety scores; group effects on anxiety resulted from higher anxiety scores in the stroke compared to the CFS group. Sensitivity analyses controlling for age, sex, and symptom duration did not affect the group effects and statistically significant group effects were not found for either covariates.

CBRQ

Multivariate tests indicated a statistically significant group effect (F(12, 274)= 12·61, V=·712, *p*<·001) on CBRQ subscale scores. Effect size calculations (partial η2) suggested a 35·6% variance in CBRQ sub-scale values. Group effects were significant for all CBRQ sub-scales to an alpha level of <.001, except for Embarrassment avoidance (Table 3).

Bonferroni post-hoc comparisons indicated that compared to CFS, the functional stroke group reported lower mean Fear Avoidance scores (*p*<·001, 95% CIs: -4·96, -2·04) but scored higher on Damage Beliefs (*p*<·001, 95% CIs: ·72, 2·56) and All-or-nothing Behaviour (*p*<·001, 95% CIs: 1·47, 4·42). Compared to the Stroke group, the functional stroke group reported higher mean scores on Damage Beliefs (*p*<·001, 95% CIs: 1·41, 3·47), Symptom focusing (*p*<·001, 95% CIs: 1·19, 4·32), All-or-nothing Behaviours (*p*<·001, 95% CIs: 2·90, 6·19) and Resting Behaviours (*p*<·001, 95% CIs: 1·16, 4·48) (Figure 1). Sensitivity analyses controlling for age, sex, and symptom duration did not affect the group effects and statistically significant effects were not found for covariates.

WSAS

One-way ANOVA estimates indicated a statistically significant group effect on mean total WSAS scores (F(2)=19·28, *p*<·001, partial η2=·212)· Homogeneity of variance assumptions were violated according to Brown-Forsythe and Levene's Tests. Subsequently, Games-Howell post-hoc contrasts were calculated; the mean WSAS scores of the functional stroke group were higher (worse) than those of the vascular stroke group (*p*=·004, 95% CIs: 2·33, 13·97) and lower than the CFS group (*p*=·012, 95% CIs: -9·89, -1·03).

Exploratory factor analysis of WSAS has previously suggested responses to items can differ across diagnostic groups and therefore may not be valid for between-group comparisons (Thandi et al., 2017). We therefore carried out a sensitivity analysis without item 1 and 5. In this analysis, there was no longer a group difference between the functional stroke and CFS groups. However, given that removing items effects the content validity (Thandi et al., 2017), we have retained the original ANOVA results. A further sensitivity analysis controlling for occupational status, age, sex, and symptom duration did not alter group effects, but occupational status was a statistically significant covariate (F(1)=5·61, *p*=·020, partial η2=·046).

DISCUSSION

Patients with functional stroke show a pattern of psychological distress and cognitive behavioural responses to symptoms discernible from that of age-sex matched patients with vascular stroke and CFS. Approximately 40% of patients with functional stroke symptoms were probable anxiety cases. This was greater than the proportion of anxiety cases in patients with CFS. A fifth were probable depression cases, greater than the proportion of probable cases within the vascular stroke group. Compared to both case-control groups, functional stroke patients reported stronger damage beliefs and greater use of 'all-or-nothing' behaviours. The functional stroke group also had the highest rates of symptom focussing and resting behaviours for coping with symptoms, compared to the vascular stroke group. Finally, the functional group reported that symptoms interfered with social functioning

to a greater extent than the vascular stroke group but less than the CFS group. These differences have implications for symptom onset and maintenance, as well as clinical interventions.

Findings relating to demographic variables of age and sex corresponded to previous research. In line with a previous meta-analysis (Jones, O'Connell, & David, 2019), a higher proportion of functional stroke cases were female than male. This meta-analysis also reported that patients with functional stroke symptoms were on average younger than patients with vascular stroke. In the present study, the functional stroke group were somewhat younger than the vascular stroke group, but not to a statistically significant level. Given evidence that marginalised groups may be at greater risk of medically unexplained syndromes and have more severe symptoms but benefit equally from specialist interventions, ethnicity-based disparities in referral and access to services should be explored, (Ingman, 2016). Functional symptoms have historically been associated with ethnic minority status, though evidence reliability is compromised by differences in sampling and study methods (Brown & Lewis-Fernández, 2011). In this study, a higher proportion of patients with functional stroke identified as belonging to a racialised community compared to patients with CFS. In contrast to our findings, a study of patients with functional motor disorder in community or outpatient settings reported higher rates of White British identity compared to a psychiatric control group (O'Connell, 2019). These divergent findings may result from disparities in access to healthcare services but also higher rates of cardiovascular risk factors, such as diabetes and hypertension, in racialised compared to non-racialised communities (Cooper et al., 2013; Hinton, 2018).

Patients with functional stroke had mean depression scores that were lower than the CFS group but comparable to the vascular stroke group. Mean anxiety scores in the functional stroke group were not statistically different to either comparison group. Consistent with previous research (Mitchell et al., 2017), the vascular stroke group demonstrated high levels of psychological distress, in particular anxiety. However, when applying clinical cut-off scores, a higher proportion of patients with functional stroke symptoms had probable depression compared to patients with vascular stroke,

corresponding with previous data comparing functional and organic weakness (Stone et al., 2012). Similarly, the greater proportion of probable anxiety cases in the functional stroke group compared to CFS points to a possible role for anxiety in the aetiology of functional stroke symptoms. These findings indicate a need for psychological input at least on par with that offered to patients with vascular stroke, starting with assessment and referral to appropriate services (Gillham & Clark, 2011).

The functional stroke group had the highest mean scores on CBRQ subscales of damage beliefs and all-or-nothing behaviour compared to both the CFS and vascular stroke group. This finding supports suggestions that unhelpful cognitive and behavioural responses are important in the maintenance of functional symptoms (Deary et al., 2007). Patients with functional stroke symptoms had scores on symptom focussing that were comparable to the CFS group but higher than the vascular stroke group. This finding supports a model of functional stroke symptoms which indicates attentional biases are perpetuating factors (Jones, O'Connell, David, et al., 2019). The vascular stroke group demonstrated the least maladaptive cognitive and behavioural responses to symptoms, despite experiencing the highest levels of anxiety. This contrasts with previous research which found an association between illness-related beliefs and mood in stroke samples (Aujla et al., 2018). However, patients with vascular stroke may have a greater understanding of symptoms, experience less uncertainty, and feel more supported by medical interventions. This is likely to influence their coping, leading them to not engage in unhelpful coping behaviours, despite high anxiety levels (Groeneveld et al., 2019). High reports of resting behaviours from patients with functional stroke symptoms may be partly explained by patients responding to an acute illness and being encouraged to take rest during their inpatient hospital admission. Fatigue was not measured in this study but given the prevalence of post-stroke fatigue (Acciarresi, 2014) and the centrality of fatigue in CFS, this could be an pertinent confounder to explore. Controlling for symptom duration did not influence any group differences in CBRQ subscales suggesting differences were not attributable to the timing of patients completing the measures. We have some confidence that differences in symptom

responses, such as those reported here, may be clinically relevant in stroke settings, as illness-related cognitions have been previously associated with prognosis in FND (Gelauff & Stone, 2016)

Impairment in work and social activities was highest in the CFS group. The disabling impact of CFS is well recognised (Dickson, 2009) and would be expected in those attending a specialist service. More surprising was the higher rate of work and social disability reported by the patients with functional stroke symptoms compared to those with vascular stroke, given the potentially devastating and long-lasting effects of stroke lesions (Wilkinson et al., 1997). However, findings should be interpreted with caution given that the functional stroke group completed measures shortly after symptom onset whilst the vascular stroke group completed measures at outpatient follow-up appointment, some months after the occurrence of their stroke. The vascular stroke group may have experienced recovery from their stroke or adjusted to residual stroke symptoms. It is possible that the high impairment ratings reported by the functional stroke symptom group reflect catastrophising predictions about the impact of symptoms, also indicated by the strong damage beliefs and uncertainty about prognosis.

Implications

In our recent conceptual model of functional stroke symptoms (Jones, O'Connell, David, et al., 2019), we hypothesised that the symptoms were driven by physical manifestations of anxiety. The similar mean rates of anxiety between patients with functional and vascular stroke may suggest the phenomenological experiences of patients with stroke-like symptoms are similar, but that coping strategies and underlying beliefs separate the groups. Physiological arousal resulting from high levels of anxiety may be interpreted by patients with functional symptoms as evidence of an ongoing threatening health event.

Interesting to note was the high degree of damage beliefs in the functional stroke group, despite most of these patients having no new structural brain pathology and receiving reassurance from clinicians. This supports previous findings that patients with functional symptoms are not provided

with clear, explanatory models about their symptoms (Nettleton et al., 2004). This potentially fuels anxiety and propagates further symptoms. High levels of symptom focussing, and functional impairment further suggest that patients with functional stroke symptoms are concerned and have a bleak outlook on recovery. All-or-nothing behaviour in functional stroke is consistent with other work reporting this as a risk factor for functional symptoms (Spence & Moss-Morris, 2007), tending to be prevalent in acute, as opposed to chronic phases of functional illness (De Gucht et al., 2016). Comparing the pattern of responses from patients with functional symptoms to the other groups may give insight to aetiology of these symptoms: high levels of pre-existing anxiety leads to physiological arousal which triggers threat perceptions and attention towards symptoms. Such cognitive distortions will be associated with patients engaging in behavioural responses (i.e. resting or boom and bust cycles of activity) to improve or prevent symptoms but which restrict social and occupational functioning, exacerbating anxiety – and so on in a vicious cycle.

Study strengths and limitations

Strengths of this study included having two well-matched comparison groups, allowing comparisons to be drawn between patients with functional stroke-like symptoms, another functional condition and patients in a stroke setting with vascular strokes. Samples were collected at comparable time periods from similar geographical regions. A larger sample of vascular stroke patients would have provided equal group sizes and greater power. Patients with functional stroke completed measures shortly after the onset of symptoms whilst the comparison groups completed measures in outpatient/specialist clinics. This may have influenced patients' illness-related cognitions and how patients approached questions, particularly those in the 'adjustment' phase. Effort was made to control for this potential confounder in sensitivity analyses controlling for duration of symptoms. Future studies may seek to compare patients in the acute stage of 'organic' stroke with those in acute stroke services with FNS. The acute onset of functional stroke-like symptoms separates them from other functional neurological presentations (e.g. functional tremor), which often have a more insidious onset. However, future studies could consider recruiting patients presenting to A&E with

e.g. functional seizures which could provide a comparison group where outcomes can be assessed within a shorter timescale. Despite the HADS questionnaire referring to mood in the past week, the cross-sectional design of this study means we cannot conclude that high rates of anxiety reported by the functional stroke group reflect psychiatric comorbidity or a reactionary response to distressing symptoms. Assessing anxiety and depression using diagnostic criteria, as opposed to a screening measure, would improve the strength of our conclusions. Longitudinal research would be useful to identify if the anxiety is a predisposing factor for functional stroke symptoms.

Summary/Conclusions

Patients with functional stroke symptoms show higher rates of anxiety than patients experiencing CFS. Additionally, the pattern of cognitive and behavioural responses to symptoms demonstrated by patients with functional stroke was discernible, and in some domains more dysfunctional, than in patients with vascular stroke or CFS. This finding could inform explanatory models of the functional syndrome and indicate treatment targets in an adapted intervention. The distress and disability experienced by patients with functional symptoms in stroke settings should lead to referrals for appropriate support.

Figure 1. **Bar chart of mean CBRQ subscale totals across functional stroke symptom, CFS and stroke groups.**

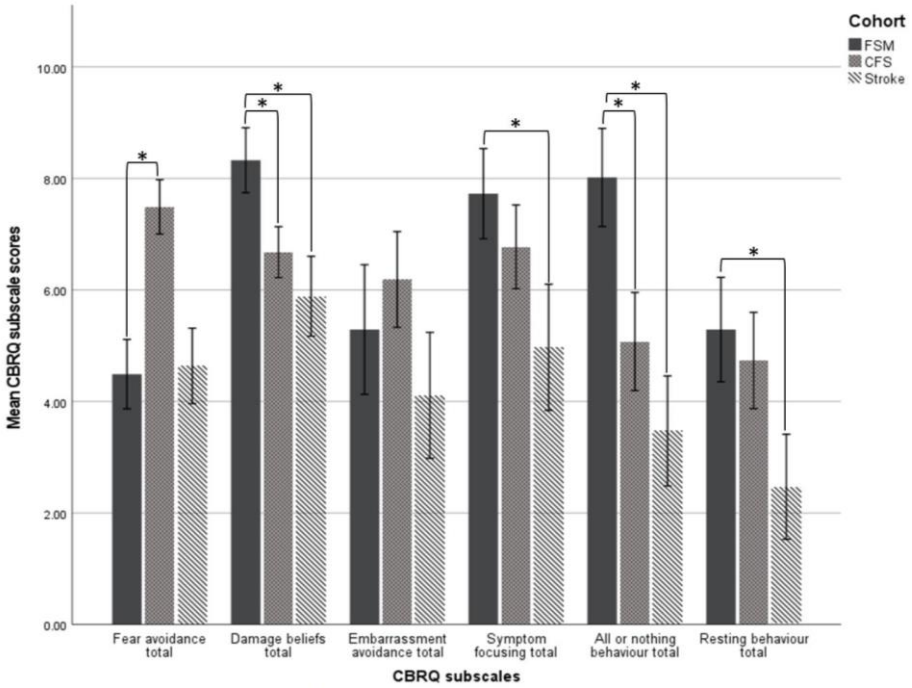

Figure 1. **Bar chart of mean CBRQ subscale totals across functional stroke symptom, CFS and stroke groups with standard error bars (+/- 2 SE).**

Footnote: * p<.001

Table 1. Demographic information and symptom duration of functional stroke symptom cases and age-sex matched CFS cases and stroke cases.

	Functional stroke (n=56)	CFS (n=56)	Stroke (n=39)
Age years (mean (SD))	50·9 (13·7)	49·5 (12·0)	55·6 (15·1)
Symptom duration (median, (range))	7 days (0·5 days-11 years)	4 years (10 months-32 years)[†]	16 day (>1day-10 months)
Sex (n (%))			
Female	35 (62·5)	36 (64·3)	19 (48·7)
Ethnicity (n (%))			
White	28 (50)	47 (83·9)	31 (79·5)
Black/ African/ Caribbean/ Black British	21 (37·5)	3 (5·4)	4 (10·3)
Mixed/ Multiple ethnic groups/ Other	4 (7·1)	2 (3·6)	4 (10·3)
Asian or Asian British	3 (5·4)	2 (3·6)	0
Marital status (n (%))			
Single	18 (32·1)	22 (39·3)	16 (41·0)
Married/ Cohabiting	21 (37·5)	26 (46·4)	19 (48·7)
Divorced/ Separated	12 (21·4)	7 (12·5)	3 (7·7)
Widowed	5 (8·9)	1 (1·8)	1 (2·6)
Occupational status (n (%))			
Employed full-time	21 (37·5)	11 (19·6)	9 (23·1)
Employed part-time	6 (10·7)	6 (10·7)	5 (12·8)
Unemployed	11 (19·6)	5 (8·9)	2 (5·1)

Student	1 (1·8)	1 (1·8)	1 (2·6)
Retired	9 (16·1)	6 (10·7)	8 (20·5)
Sick leave or disabled	2 (3·6)	14 (25·0)	7 (17·9)
Other	3 (5·4)	1 (1·8)	4 (10·3)
Self-employed	2 (3·6)	1 (1·8)	0
Carer	1 (1·8)	0	0
Highest education (n (%))			
No formal education	10 (17·9)	2 (3·6)	3 (7·7)
GCSE/O Level Equivalent/<16yo	11 (19·6)	2 (3·6)	7 (17·9)
A Level or equivalent/<18yo	6 (10·7)	6 (10·7)	5 (12·8)
Degree or other higher education	19 (33·9)	36 (64·3)	21 (53·9)
NVQ/ work-based qualification/ Other	10 (17·9)	10 (17·9)	2 (5·1)

†CFS cases had symptom duration available only in months not days, therefore cases with symptom duration of less than a month had missing data.

Table 2. Proportion of probable anxiety and depression cases and mean scores on the HADS in functional stroke, chronic fatigue, and stroke cohorts.

	Functional stroke sx (n=55)	CFS (n=54)	Stroke (n=39)
Probable anxiety cases (HADS-A≥11) n(%)	21 (38·2)	15 (27·8)	23 (59·0)
Probable depression cases (HADS-D≥11) n(%)	10 (18·2)	15 (27·8)	2 (5·1)
Mean (SD)HADS-A	9·24 (4·91)	9·20 (2·97)	11·08 (2·88)
Mean (SD) HADS-D	6·42 (4·22)	8·80 (3·10)	7·72 (1·87)

Note: 8·8% of cases across all cohorts had scores ≥11 on both HADS-A and HADS-D subscales.

Table 3. Means of CBRQ, WSAS and HADS scales across functional stroke, CFS and stroke cohorts with ANOVA between-subject effect estimates.

	Cohort means			Between-Subject Effects					
	Functional stroke mean	CFS mean	Stroke mean	Sum of Squares	df	Mean Square	F	Sig.	Partial η2
CBRQ-subscales									
Fear avoidance total	4·49	7·50	4·90	290·20	2	145·10	34·37	*p<·001	·328
Damage beliefs total	8·33	6·73	5·81	145·01	2	72·51	18·35	*p<·001	·207
Embarrassment avoidance total	5·29	6·05	4·00	92·65	2	46·32	3·41	†·036	·046
Symptom focusing total	7·73	6·73	5·05	165·77	2	82·89	9·15	*p<·001	·115
All-or-nothing behaviour total	8·02	5·16	3·74	493·51	2	246·75	24·58	*p<·001	·258
Resting behaviour total	5·29	4·73	2·74	183·37	2	91·69	8·97	*p<·001	·113
WSAS									
Total	22·15	27·60	14·00	4161·17	2	2080·59	19·28	*p<·001	·212

*p<.001, †p<.05

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