NeuroRehabilitation 42 (2018) 235–246
DOI:10.3233/NRE-172245
IOS Press

Balance deficits in Chronic Fatigue Syndrome with and without fibromyalgia

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Abstract.
OBJECTIVE: Chronic Fatigue Syndrome (CFS) is a disorder of unknown etiology associated with debilitating fatigue. One symptom commonly reported is disequilibrium. The goal of this study was to determine if CFS patients demonstrated verified balance deficits and if this was effected by comorbid fibromyalgia (FM).
METHODS: Twenty-seven patients with CFS (12 with comorbid FM) and 22 age and gender matched controls performed posturography.
RESULTS: Balance scores were significantly correlated with physical functional status in the CFS group ($R^2 = 0.43$, $P < 0.001$), which was not found for mental functional status ($R^2 = 0.06$, $P > 0.5$). CFS patients (regardless of FM) had significantly higher anxiety subscale of the vertigo symptom scale scores. CFS patients, regardless of FM status, demonstrated significantly lower overall composite balance scores (Controls - 78.8 ± 1.5; CFS – 69.0 ± 1.4, $P < 0.005$) even when controlling for anxiety and also had worse preference scores, indicating they relied on visual information preferentially even when visual information was incorrect. Interestingly, the CFS+FM group, not CFS only, demonstrated significantly worse vestibular scores (Controls – 70.2 ± 2.4; CFS only - 67.9 ± 3.8; CFS with FM - 55.4 ± 4.6, $P = 0.013$).
INTERPRETATION: The major findings are that poor balance may be associated with poorer self-reported physical health. In addition, CFS patients seemed to rely preferentially on visual inputs, regardless of whether it was correct. The finding that vestibular function may be impaired in patients with CFS+FM but not in those with CFS alone suggests that the pathophysiology of CFS+FM may differ as has been suggested by some.

Keywords: Chronic Fatigue Syndrome, fibromyalgia, posturography, vestibular function

1. Introduction

Chronic Fatigue Syndrome (CFS) is a disorder of unknown etiology that is associated with debilitating fatigue that persists for six months or more and presents with various rheumatological, infectious, and neuropsychiatric symptoms (Fukuda et al., 1994). No pathogenic mechanism has been consistently identified by physical or laboratory tests, and therefore the diagnosis of CFS relies on the exclusion of other medical explanations. One symptom commonly reported by those with CFS is disequilibrium (Komaroff & Buchwald, 1991), which can manifest as dizziness,

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blurred vision and vertigo (Carruthers et al., 2003; Komaroff, 1993). Indeed, some subtle alterations in balance (Ash-Bernal et al., 1995; Furman, 1991; Paul, Wood, & Maclaren, 2001) and gait (Boda, Natelson, Sisto, & Tapp, 1995; Paul et al., 2001; Saggini, Pizzigallo, Vecchiet, Macellari, & Giacomozzi, 1998) have been documented in a few, small-sample studies of CFS patients. Moreover, one of us [BHN] has noted that CFS patients often sway on clinical Romberg testing with eyes closed – suggesting a problem with balance in some. Altered balance, if a feature of CFS, suggests a potentially important potential treatment avenue whereby balance could be corrected using rehabilitative procedures like those used with other patients with disequilibrium.

A relationship has been reported to exist between balance and health-related quality of life. For example, community-dwelling older women with osteoporosis showed significant relations between their scores on a dynamic test of balance, the Neurocom Sensory Organization Test (SOT) and both knee extensor strength (Carter et al., 2002). Similarly, Marsh et al. found that the balance (forward leaning) of older adults with knee pain was significantly associated with self-reported disability, even when adjusted for knee strength (Marsh, Rejeski, Lang, Miller, & Messier, 2003).

In two previous studies of balance in CFS subjects, those with CFS had abnormal balance responses in sway-referenced tests where visual and/or proprioceptive information was distorted (Ash-Bernal et al., 1995; Furman, 1991). In addition, some CFS patients had abnormal responses in rotational tests, or showed positional nystagmus (Ash-Bernal et al., 1995; Furman, 1991). These previous studies also revealed potential problems in balance using the Neurocom SOT. These dynamic posturography tests also have good specificity for balance problems; specifically, few people without balance problems are incorrectly identified as impaired, and when several tests are considered together, these have relatively good sensitivity for identifying vestibular problems (Di Fabio, 1995). Another assessment of balance in CFS patients showed no differences between CFS patients and controls; however, this study used only static sway tests (Paul et al., 2001) which have considerably poorer reliability than dynamic tests (Brouwer, Culham, Liston, & Grant, 1998; Liston & Brouwer, 1996). As a whole, these studies suggest possible alterations in balance function in patients with CFS. However, these studies suffer from small sample sizes, lack of a control group, and it is difficult to compare results across these studies because different balance assessments were used across studies.

The purpose of this study was to compare participants with CFS and healthy, sedentary controls on static and dynamic balance parameters. We hypothesized that subjects with CFS would have poorer balance than healthy control subjects (HEA). In addition, we assessed whether there was a relationship between poorer functional status and poorer balance in those with CFS. Finally, because of evidence indicating differences between CFS and fibromyalgia (FM) (Abbi & Natelson, 2013), a medically unexplained illness characterized by widespread pain which can co-occur in patients with CFS, we also compared the balance of patients with CFS alone to those with CFS plus FM (CFS+FM).

2. Methods

2.1. Participants

We initially compared two groups of participants, those with CFS (N = 27) and an age- and gender-matched group of healthy controls (N = 22) who were sedentary and did not exercise regularly. Participants with CFS were drawn from the NJ CFS Cooperative Research Center and the protocol for the study was approved by the VA NJ Institutional Review Board, and informed consent was obtained from each subject. As part of their intake into this center, participants were diagnosed with CFS according to the 1994 CDC criteria (Fukuda et al., 1994). The diagnosis required chronic fatigue lasting 6 consecutive months or longer, that was of new or definite onset, not due to exertion, not substantially reduced by rest, and resulting in a substantial reduction from previous levels of activity. In addition, the fatigue must have been accompanied by at least 4 of the following symptoms: (a) short-term memory or concentration problems severe enough to restrict activities, (b) sore throat, (c) tender cervical or axillary lymph nodes, (d) muscle pain, (e) multijoint pain without swelling or redness, (f) headaches of a new type or pattern, (g) unrefreshing sleep or (h) postexertional malaise lasting more than 24 hours. All CFS participants met these criteria and no alternative explanations could be found for their fatigue. Participants were also evaluated to determine if they had the widespread pain and tenderness diagnostic of FM (Wolfe et al., 1990). Based on these criteria, twelve of the 27 CFS patients had comorbid FM. It should be noted that a subset of these participants' data was previously published as a comparison of SOT scores derived from the Neurocom to a novel measure of postural stability (Chaudhry et al., 2004; Chaudhry et al., 2005).

2.2. Balance variables

We used the Neurocom SOT along with several other dynamic posturography tests, including the Adaptation Test (ADT), the Motor Control test (MCT) and the Rhythmic Weight Shift (RWS) test to assess multiple features of balance function.

The Neurocom SOT compares a participant's sway across 6 conditions (see Fig. 1, panel A): (1) eyes open, platform and visual surround stable, (2) eyes closed, platform and visual surround stable, (3) eyes open, platform stable, visual surround sway-referenced to the participant's motion, (4) eyes open, platform sway-referenced, visual surround stable, (5) eyes closed, platform sway-referenced, and (6) eyes open, both platform and visual surround sway-referenced. The SOT composite score is the overall balance score derived from the SOT. The SOT visual score (ratio of performance on Condition 4 which uses a sway-referenced platform to performance on Condition 1 which uses a stable platform) indicates the degree to which a participant does not appropriately use visual cues to maintain upright posture, particularly when somatosensory cues are inaccurate. The SOT visual preference score (ratio of performance on Conditions 3 + 6, i.e., both conditions where eyes are open, and the surround is sway-referenced, but in 6 the platform is also sway-referenced, to the performance on Conditions 2 + 5, i.e., both conditions where eyes are closed, and in 5 the platform is sway-referenced) indicates the extent to which a participant relies on visual cues, even when they are inaccurate. The SOT somatosensory score (ratio of performance on Condition 2 in which eyes are closed and the platform is stable to performance on Condition 1 in which the eyes are open and the platform stable) indicates the extent to which a participant can use somatosensory information to maintain balance. The SOT vestibular score (ratio of performance on Condition 5 in which the eyes are closed, and the platform is sway-referenced to performance on Condition 1 in which the eyes are open and the platform is stable) indicates the extent to which a participant can use vestibular information to maintain balance without visual or accurate somatosensory information. The Neurocom Equitest system also provides a strategy score that indicates the extent of horizontal shear force, which tends to be low when most of the movement occurs about the ankles (as occurs in those with normal balance), and high when most of the movement occurs about the hips or when the arms are moved (as more often occurs in those with poorer balance).

In the Neurocom ADT, sway energy is measured for the first 2 seconds after fast, dynamic platform rotation in either the "toes up" or "toes down" direction (with an average taken over 5 trials). Sway energy is calculated by the NeuroCom Equitest system using differentiation of the Y axis vertical force position trace and a weighting constant to give dimensionless sway energy values.

In the Neurocom MCT, the platform shifts quickly and horizontally in either the forward or backward direction. Trials of small, medium and large translations of the force plate in both directions permit deriving response latency scores reflecting the speed with which a person restores their center of gravity after the force plate shifts. The MCT composite score is derived from the mean latency in msec for the medium and large forward and backward platform displacements.

In the Neurocom rhythmic weight shift (RWS) test, participants rhythmically shift their center of gravity from side to side or forward to backward following an on-screen target. On-screen targets move at three speeds: slow (3 seconds from peak to peak), medium (2 seconds peak to peak) and fast (1 second peak to peak). Directional control was calculated (per the NeuroCom Equitest manual: NeuroCom, 1991) as: (Amount of intended movement-Amount of extraneous movement)/Amount of intended movement. On-axis velocity is calculated by Neurocom by creating a variance measure across all speeds of weight shift. The calculation (effectively an average squared deviation) is $((\text{Ideal velocity} - \text{Actual velocity}_{\text{slow}})^2 + (\text{Ideal velocity} - \text{Actual velocity}_{\text{medium}})^2 + (\text{Ideal velocity} - \text{Actual velocity}_{\text{fast}})^2) / 3$. This measure provides an average deviation from ideal velocity across the slow, medium and fast speeds of weight shift.

2.3. Functional status

The Physical Component Summary Score (PCS) and Mental Component Summary Score (MCS) from the Medical Outcomes Survey Short-Form-36 (SF-36) (J. E. Ware, Jr. & Sherbourne, 1992; J. E. Ware, Kosinski, & Keller, 1994) were used as measures of physical and mental functional status, respectively.

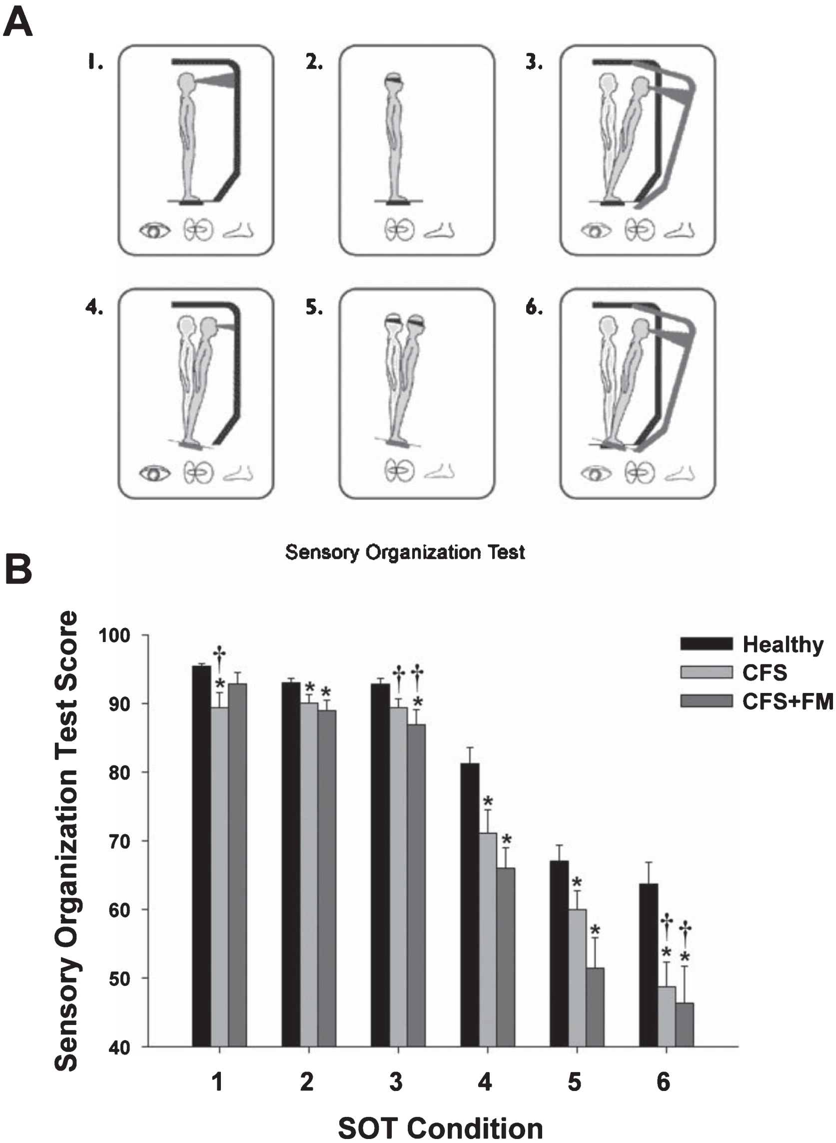

Fig. 1. Panel A: The 6 test conditions comprising the SOT (description in methods). Panel B: Change in SOT scores by condition in three groups, Healthy, Chronic Fatigue Syndrome (CFS) and CFS with fibromyalgia (CFS+FM). *indicates significant difference from healthy group using height and age as a covariate ($P < 0.05$). †indicates a significant difference from healthy with the addition of anxiety as a covariate ($P < 0.05$). Note that there were no significant differences between CFS and CFS+FM in any comparison.

Higher physical and mental functional status scores indicate better function, and these normed scores range from 0–100.

2.4. Other self-report measures

Physical activity was measured using the Godin Questionnaire (Godin & Shephard, 1985). Fatigue was measured using the Multidimensional Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995), a 20 item measure of fatigue. Physical symptoms were measured using the Patient Health Questionaire-15 (Kroenke, Spitzer, & Williams, 2002), a brief measure of physical symptom severity. The Vertigo Symptom Scale (VSS) (Yardley, Masson, Verschuur, Haacke, & Luxon, 1992) was used to measure self-reported anxiety and both brief and prolonged vertigo.

2.5. Data analysis

Data were examined for outliers (none exceeded 3 SD from the mean and all data points were retained) and normality. Variables that were non-normally distributed were transformed where possible using a square root transformation, and where not possible, non-parametric statistics were performed. Because of the hypothesis that CFS and FM may be discrete and different illnesses, balance was also evaluated for those with CFS alone and those with CFS plus FM. Statistical significance was assumed at $P < 0.05$, and all tests were two-tailed.

3. Results

3.1. CFS and Healthy group characteristics

There were no significant differences between CFS and HEA groups on sex or age (matching variables) or on height or weight (all P's > 0.05; see Table 1). The CFS and HEA groups differed in the expected directions on variables previously shown to distinguish these groups. For example, despite our use of sedentary controls, CFS patients still had lower self-reported physical activity levels on the Godin (Godin & Shephard, 1985) than did controls (Mann-Whitney U = 150.0, $P < 0.05$). Compared to HEA, CFS patients also had poorer functional status (PCS: $t = 12.45$, $P < 0.0001$; MCS: $t = 5.54$, $P < 0.0001$), had more fatigue (Mann-Whitney U = 0, $P < 0.0001$), greater non-specific physical symptom severity ($t = 11.46$, $P < 0.0001$), and more anxiety ($t = 10.26$, $P < 0.0001$). Finally, CFS patients had more brief and prolonged vertigo symptoms than did HEA (both t's > 6.0, P's < 0.0001).

3.2. Balance differences between groups

To assess CFS subjects for balance dysfunction across a range of sensory inputs, we chose 4 tests (sensory organization test or SOT, motor control test or MCT, adaptation test or ADT & rhythmic weight shift or RWS) (Nashner & Peters, 1990). Furthermore, because balance is related to anxiety and because our groups differed in self-reported anxiety, we wanted to test whether there were any differences in balance parameters between the 2 groups that were not simply attributable to anxiety (see Table 2 for descriptive statistics). Finally, because we were interested in the physical and mental functional status of the CFS and healthy groups, and because prior literature has suggested a positive relationship between balance and functional status (both physical and mental), we also assessed these relationships using Pearson's correlations.

3.3. Performance on the SOT

CFS patients had lower SOT composite scores than healthy controls ($P < 0.001$), indicating that they had worse overall balance (See Table 2). Because there were group differences in the SOT composite score, we also examined what aspects

Table 1
Demographic and Group Characteristics

	Range	CFS	HEA	Significance
N		27	22	
Sex				
Female (%)		77.8%	77.3%	NS
Ethnicity		100 % white	86 % white, 9% black, 5% Asian	NS
Age (yrs)		40.3 (2.0)	38.6 (2.4)	NS
Height (cm)		165.9 (1.8)	165.5 (2.1)	NS
Weight (kg)		69.2 (2.0)	70.2 (3.7)	NS
Physical Activity		24.0 (4.8)	38.4 (4.5)	$P = 0.038$
SF36 – PCS	0–100	30.2 (1.9)	55.5 (0.7)	$P < 0.001$
SF36 – MCS	0–100	39.4 (2.3)	53.7 (1.2)	$P < 0.001$
General fatigue (from MFI-20)	5–20	18.4 (0.3)	7.2 (0.5)	$P < 0.001$
PHQ-15 (Symptoms)	0–48	22.0 (1.7)	3.5 (0.6)	$P < 0.001$
Anxiety (from VSS)	0–60	36.2 (2.1)	11.2 (1.2)	$P < 0.001$
Brief vertigo (from VSS)	0–36	11.4 (1.4)	1.9 (0.3)	$P < 0.001$
Prolonged vertigo (from VSS)	0–44	8.0 (1.0)	2.1 (0.4)	$P < 0.001$

Notes. Means (SEM) shown except where indicated. Physical activity is derived from the Godin questionnaire. PCS is the Physical Component Summary score from the Short Form 36 version of the Medical Outcomes Study, and MCS is the Mental Component Summary score. MFI-20 is the Multidimensional Fatigue Scale. PHQ-15 is the 15 item physical symptom severity scale. VSS is the Vertigo Symptom Scale.

Table 2
Balance test parameters for the SOT, MCT, ADT and RWS tests

	Range	CFS	HEA	Significance	Significance Controlled for Anxiety
SOT					
Composite	0–100	69.0 (1.4)*	78.8 (1.5)	$P < 0.001$	$P = 0.003$
Visual	0–100	76.4 (3.0)*	85.1 (2.4)	$P = 0.033$	NS
Vestibular	0–100	62.4 (3.1)	70.2 (2.4)	$P = 0.061$	NS
Visual preference	0–100	93.3 (1.8)	97.8 (1.5)	$P = 0.065$	$P = 0.001$
Somatosensory	0–100	99.2 (2.2)	97.5 (0.4)	NS	NS
Strategy score	0–100	85.8 (0.8)	89.5 (0.7)	$P = 0.001$	NS
MCT					
Composite (ms)		129.0 (2.1)	129.1 (1.9)	NS	NS
ADT					
Toes Up		60.3 (2.2)	64.0 (3.2)	NS	NS
Toes Down		50.3 (2.1)	45.7 (2.6)	NS	NS
RWS					
Directional control – L/R	0–100	86.8 (0.7)	87.1 (0.8)	NS	NS
Directional control – A/P	0–100	83.6 (1.0)	84.3 (2.0)	NS	NS
On-axis velocity – L/R		0.91 (0.22)	1.21 (0.35)	NS	NS
On-axis velocity – A/P		0.61 (0.13)	0.46 (0.12)	NS	NS

Notes. SOT is the sensory organization test, MCT is the motor control test, ADT is the adaptation test and RWS is the rhythmic weight shift test. MCT composite is the mean latency in msec for the medium and large forward and backward platform displacements. ADT Toes Up and Toes Down measures are dimensionless measures of sway energy. Directional control measures indicate the amount of movement in the intended direction relative to the amount of extraneous movement with higher scores indicating less extraneous movement. The on-axis velocity measures here represent average squared deviations of actual velocity compared with ideal velocity of weight shift movement.

of SOT performance might be influencing the results.

We found that subjects with CFS had poorer scores on the SOT visual score ($P = 0.033$). Low scores on this visual assessment indicate that CFS patients were unable to use visual information accurately, particularly when somatosensory cues were inaccurate. There were also trends toward CFS subjects having poorer SOT vestibular score ($P = 0.061$) and SOT visual preference scores ($P = 0.065$). The SOT vestibular score indicates that subjects with CFS have a reduced tendency to correctly use vestibular cues when vision is not available and when somatosensory cues are not accurate. The SOT visual preference score indicates that the CFS subjects have a greater tendency to use visual cues even when they are not accurate than do HEA participants. There were no differences between the CFS and HEA groups on the SOT somatosensory measure; ($P > 0.4$).

Finally, we examined whether CFS and HEA participants differed in their use of movement about the hips versus ankles to maintain posture. The NeuroCom Equitest system provides a strategy score that reflects the degree of horizontal shear. This will be near zero if the subject mostly moves about the ankles (low shear) and high if the subject moves mostly about the hips (or otherwise causes high horizontal shear such as by moving the arms). CFS subjects had a lower strategy score (i.e., more non-ankle movement) than did the HEA subjects (i.e., relatively more movement about the ankles; $P = 0.001$).

3.4. *Performance on the ADT*

There were no group differences on mean ADT in the toes up or down conditions (both ts > 0.9, and ps > 0.15), indicating that the groups were equally good at responding to a sudden tilt of the platform either with the toes up or down. In the ADT, lower scores indicate faster response to the tilting platform. In addition, these scores were very similar to the mean ADT toes up and toes down scores of 64.2 (toes up) and 46.8 (toes down) for a normative group aged 20–59 (See Table 2; NeuroCom Equitest manual; NeuroCom, 1991).

3.5. *Performance on the MCT*

There were no group differences on the MCT composite scores ($t < 1.0$, $P > 0.9$), indicating that the groups did not differ in their overall response latency (using the mean of the medium and large forward and backward platform displacement trials). In addition, these scores were virtually identical to the mean

MCT composite score (129.8 ms) for a normative group between 20 and 59 years old (NeuroCom Equitest manual; Jacobson, Newman, & Kartush, 1997; NeuroCom, 1991).

3.6. *Performance on the RWS*

There were no differences between the CFS and HEA groups on either of the directional control variables (left/right or anterior/posterior; both t's < 0.5, P's > 0.7) or either of the on-axis velocity variables (left/right or anterior/posterior; both t's < 1.0, P's > 0.4).

3.7. *Assessment of the role of anxiety in the balance deficiencies in CFS*

Because there were group differences in anxiety, which is known to alter balance (e.g., Bolmont, Gangloff, Vouriot, & Perrin, 2002) we wanted to know whether the group difference in balance (SOT composite scores, SOT visual scores, and SOT strategy scores) were attributable simply to anxiety or whether these effects were still present after controlling for anxiety. In addition, because age and height can influence balance scores, these factors were also controlled in this analysis. We first conducted a univariate analysis of the effects of group (CFS vs. HEA) on SOT composite scores using age, height as covariates (see Table 2). We then repeated the analysis including the autonomic anxiety subscale from the VSS as a covariate. This model revealed that there was still a significant effect of CFS on SOT Composite scores even after accounting for the effects of age, height, and anxiety ($P = 0.003$). Of the covariates in this model, only height had a significant relationship with SOT scores ($P < 0.02$). Thus, these results demonstrate that although the two diagnostic groups differed in anxiety, the group differences in overall balance (i.e., composite balance score) were not attributable to the differences in anxiety. However, anxiety did play a role in the differences in scores during conditions 2, 4 and 5, since these conditions were no longer significantly different.

Examining the other ratios derived from the SOT, only visual preference scores remained significantly different between groups ($P = 0.001$) once anxiety was used as a covariate. In this analysis, the covariates that were significantly different across groups were height ($P < 0.05$) and anxiety score from the VSS ($P < 0.01$).

3.8. *The relationship between balance and functional status in CFS*

As noted above, evidence from elderly individuals has suggested a relationship between poor balance and lower self-reported functional status. We assessed whether a similar relationship held in either the CFS or HEA groups. Pearson's correlations were used to assess the relationship between SOT composite scores and functional status (self-reported physical and mental functional status). There were no significant relationships between SOT and mental or physical functional status in the HEA group. However, there was a significant positive correlation between SOT scores and physical functional status (PCS) in the CFS group ($R^2 = 0.43$, $P < 0.001$), but not between SOT scores and mental functional status (MCS; $R^2 = 0.06$, $P > 0.5$). Examination of the data revealed that there was a restriction of range on functional status scores in the HEA group that was not true of the CFS group. Thus, the lack of a relationship in the HEA group should be viewed in light of this limitation.

3.9. *Exploratory analysis of individuals with both CFS and fibromyalgia*

Given recent evidence suggesting that we should consider possible differences between CFS and CFS+FM (Abbi & Natelson, 2013), an analysis of these 2 sub-groups of CFS subjects was done to see if differences existed between these groups. We conducted an ancillary analysis to examine whether the balance of those with CFS+FM differed from those with CFS only. Examination of the SOT composite scores (Fig. 1) demonstrated that both groups had significantly lower scores ($P < 0.05$) during all conditions with the exception of condition 1 in which subjects stand with eyes open on a fixed surface. In this case only the CFS group had significantly lower scores than healthy ($P = 0.002$), with no differences for the CFS+FM group. Also during condition 3, in which the visual field sways with the participant thereby making visual field information inaccurate, CFS subjects were not significantly worse than controls, but CFS+FM were significantly worse ($P = 0.003$). Controlling for anxiety, we found that only the differences during conditions 1, 3 and 6 remained significant; these are all conditions dependent on visual input where participants had eyes open. Examination of anxiety scores in these groups demonstrated that CFS patients had higher scores

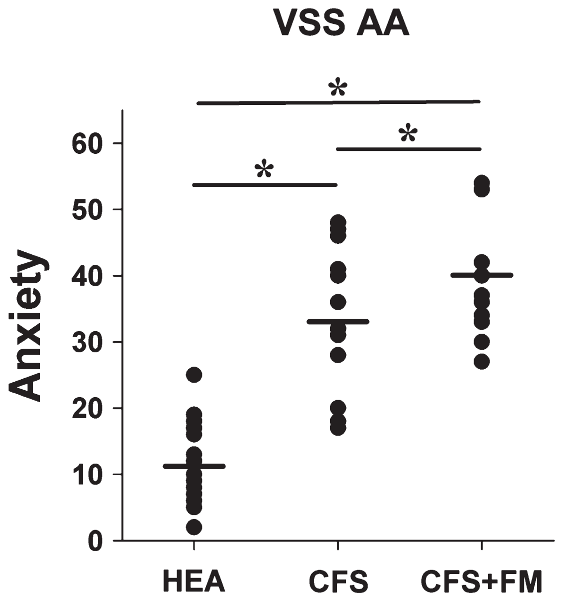

Fig. 2. Autonomic anxiety subscale scores calculated from Vertigo Symptom Scale. *indicates a significant difference between mean levels ($P < 0.001$). As can be seen, anxiety was significantly higher in the CFS group ($P < 0.001$) and was higher still in the CFS+FM group ($P < 0.001$). However, the difference between the CFS and CFS+FM groups was not as great ($P = 0.043$).

than healthy participants, but anxiety was even higher in the CFS+FM participants ($P < 0.001$; Fig. 2).

Examination of the ratios derived from the SOT found that CFS+FM patients had a significantly lower vestibular score ($P = 0.004$), even when controlling for anxiety ($P = 0.033$). Similarly, after controlling for anxiety, preference scores were lower in the CFS+FM ($P = 0.007$) as well as the CFS patients ($P = 0.002$). In contrast, only CFS+FM had lower visual ratios ($P = 0.012$). There was no difference in somatosensory scores, consistent with the previous findings.

4. Discussion

Our data document a balance deficit in individuals with chronic fatigue syndrome (CFS) relative to an age- and gender-matched group of healthy individuals. Moreover, despite having significantly more anxiety, which in other studies has been shown to be related to poorer balance, CFS subjects had balance which remained impaired compared to controls when adjusted for self-reported anxiety. Finally, within the CFS patient group, we also observed a significant positive relationship between balance and self-reported physical health. These data raise the interesting speculation that poor balance may be contributing to poorer self-reported physical health, although a confirmation of that idea awaits non-correlational data that would permit a causal interpretation.

The underlying cause of the balance deficit in CFS patients remains unclear. The balance system is complex, relying on integration of multiple sensory systems (i.e., visual, vestibular, somatosensory), and has been shown to correlate with muscle strength in the elderly (Wolfson, Judge, Whipple, & King, 1995). Our finding of impaired visual scores would suggest that CFS patients are relying on vision rather than somatosensory cues for balance. Thus, when visual cues are incorrect or missing, they are unable to instead rely on somatosensory or vestibular cues to compensate for these deficits. One explanation could be that the somatosensory and/or vestibular systems are impaired. However, there was no difference in somatosensory ratio derived from the balance data, suggesting that somatosensory function was intact.

Examining vestibular function we find that the vestibular score tended to be lower in the CFS group. However, if we consider comorbid fibromyalgia, the CFS+FM group had much lower values than the CFS only patients (Fig. 3). This suggests that CFS+FM patients may, in fact, have impaired vestibular function. This is consistent with previous research which has shown that fibromyalgia patients, without considering CFS status, have increased rates of falls (Jones, Horak, Winters-Stone, Irvine, & Bennett, 2009; Meireles, Antero, Kulczycki, & Skare, 2014) and reduced balance confidence (Jones et al., 2009; Muto et al., 2015). Other work in fibromyalgia has revealed that these subjects have increased postural sway (Jones, King, Mist, Bennett, & Horak, 2011; Muto et al., 2015), especially with eyes closed. In fact, Jones et al. (Jones et al., 2011) reported lower vestibular scores in a fibromyalgia group, similar to what we found in our CFS+FM group. However, in their group of patients, all scores were impaired including the composite, visual and somatosensory. In contrast we did not see any impairment in the somatosensory ratio in our CFS+FM group. There is, however, a difference between this study and the earlier one. Here, subjects with FM also fulfilled criteria for CFS; Jones et al. did not determine whether their FM subjects also fulfilled diagnostic criteria for CFS. The common overlap between these diagnoses make it likely that some of their patients had CFS as well as FM.

These findings suggest that FM and not CFS may be associated with some kind of vestibular impairment.

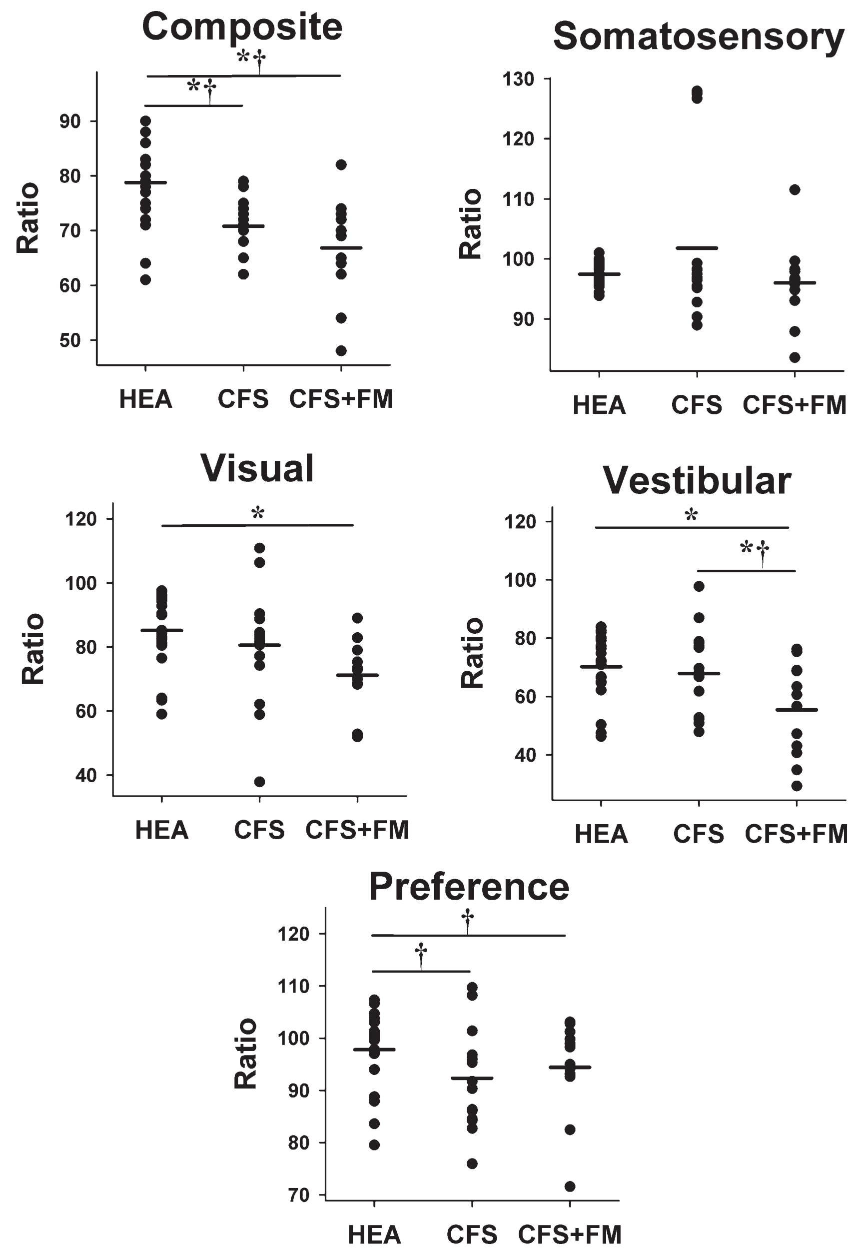

Fig. 3. Sensory Organization Test (SOT) scores (composite and subscale) as a function of group status [healthy (HEA), Chronic Fatigue Syndrome (CFS) and CFS+Fibromyalgia (CFS+FM)]. Although there was no group difference in somatosensory scores the CFS and CFS+FM groups had significantly lower composite scores. This was also true for vestibular and preference scores. Visual ratios were only significantly lower in the CFS+FM group. *indicates significant difference from healthy group using height and age as a covariate. †indicates a significant difference with the addition of anxiety as a covariate.

However, we did not perform direct vestibular assessments on these subjects and so cannot definitively characterize their vestibular function. Bayazit et al. (Bayazit et al., 2010) assessed vestibular-evoked myogenic potentials in a group of subjects with FM and found that they showed an impairment of otolith function. Since otoliths provide information as to our head location relative to gravity, impairment in otolith function would be expected to be associated with worse posture and increased sway. We have previously shown that ocular torsion (another measure of otolith function) is highly correlated with mediolateral sway, so that the lower the ocular torsion (worse otolith function) the greater the sway (Serrador, Lipsitz, Gopalakrishnan, Black, & Wood, 2009). These data would suggest that the CFS+FM group may have had impaired otolith function. Future research to directly test otolith function in this population is necessary to confirm this possibility. The mechanism of possible vestibular loss in the CFS+FM group remains unclear but is important. Finding basic neurophysiological differences between the two illness groups would be evidence against the hypothesis that the two illnesses are variants of one another – a position taken by some investigators (Barsky & Borus, 1999; Wessely, Nimnuan, & Sharpe, 1999).

The impaired balance in the CFS group did not appear to be of vestibular origin since the vestibular ratios were not significantly different from the healthy controls. Similarly somatosensory ratio was also not different. This suggests that the origin of the poor balance is due to another mechanism. One possibility is that central sensory integration was affected. So the ability of CFS patients to re-weight sensory inputs based on conditions may have been impaired, resulting in poorer balance during all conditions.

Another possibility may relate to muscle weakness which is also associated with worse balance. However, data regarding muscle strength in CFS is unclear. Some studies reported reduced peak handgrip strength compared to controls (Neu et al., 2014; Nijs et al., 2011) while others found no difference (Ickmans, Meeus, De Kooning, Lambrecht, & Nijs, 2014; Staud, Mokthech, Price, & Robinson, 2015). Another study in FM subjects without fatigue revealed them to have both reduced handgrip and leg strength (Sener et al., 2016). In contrast, another study of subjects with both CFS and FM did not demonstrate impaired handgrip strength (Ickmans et al., 2014). These conflicting data highlight the necessity of subgrouping subjects into CFS and/or FM groups in future studies to determine the relation of muscle strength, specifically in the legs, and balance impairment.

Both anxiety and physical functional status were related to balance functioning. However, factoring in anxiety did not influence the overall finding of reduced balance in CFS compared to healthy controls, but did influence the significance of some of the SOT subscores. Thus, overall balance impairment in CFS is independent of anxiety. We also found that those with better physical functional status has better balance function, consistent with prior findings in older individual that poorer balance can be associated with poorer health. The existence of a strong correlation between these two variables suggests that clinicians might use balance testing as an objective measure of improvement after therapeutic interventions.

Since CFS is a medically unexplained illness, it should not be diagnosed when another medical diagnosis exists that can produce fatigue. We have operationalized this to mean that a CFS patient must have a normal neurological examination. However, clinical evaluation often finds patients who sway on Romberg testing and who cannot maintain posture when they are asked to stand in a heel-toe posture with eyes shut. This study confirms that clinical impression in demonstrating that CFS patients have worse balance then sedentary healthy controls. In addition, subjects with both CFS and FM may have underlying impaired vestibular function. Future work in subjects with FM without CFS is needed to understand the relation between FM and impaired vestibular function.

Acknowledgments

We gratefully acknowledge helpful comments on an earlier draft of this manuscript by Christine Hartmann, Gemmae Fix, Tana Lugar, and Chris Gillespie. This work was funded by a pilot grant mechanism to K. Quigley under NIH AI-32247 (B. Natelson, PI).

Author contributions

BN and KQ conceived and designed the study, performed acquisition and analysis of data, and drafted the manuscript. CZ performed acquisition and analysis of data. TF performed analysis of data and assisted in drafting of manuscript. JS performed data analysis and drafted the manuscript. All authors approved final manuscript version.

Conflict of interest

Nothing to report.

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