

What is brain fog? An evaluation of the symptom in postural tachycardia syndrome

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Abstract

Purpose Adolescents with postural tachycardia syndrome (POTS) often experience ill-defined cognitive impairment referred to by patients as “brain fog.” The objective of this study was to evaluate the symptom of brain fog as a means of gaining further insight into its etiology and potential palliative interventions.

Methods Eligible subjects who reported having been diagnosed with POTS were recruited from social media web sites. Subjects were asked to complete a 38-item questionnaire designed for this study, and the Wood mental fatigue inventory (WMFI).

Results Responses were received from 138 subjects with POTS (88 % female), ranging in age from 14 to 29 years; 132 subjects reported brain fog. WMFI scores correlated with brain fog frequency and severity ($P < 0.001$). The top ranked descriptors of brain fog were “forgetful,” “cloudy,” and “difficulty focusing, thinking and communicating.” The most frequently reported brain fog triggers were fatigue (91 %), lack of sleep (90 %), prolonged

standing (87 %), dehydration (86 %), and feeling faint (85 %). Although aggravated by upright posture, brain fog was reported to persist after assuming a recumbent posture. The most frequently reported interventions for the treatment of brain fog were intravenous saline (77 %), stimulant medications (67 %), salt tablets (54 %), intra-muscular vitamin B-12 injections (48 %), and midodrine (45 %).

Conclusions Descriptors for “brain fog” are most consistent with it being a cognitive complaint. Factors other than upright posture may play a role in the persistence of this symptom. Subjects reported a number of therapeutic interventions for brain fog not typically used in the treatment of POTS that may warrant further investigation.

Keywords Postural tachycardia syndrome · Orthostatic intolerance · Cognition

Introduction

Postural tachycardia syndrome (POTS) is a chronic form of orthostatic intolerance (OI) defined by the onset of orthostatic symptoms associated with an increase in heart rate (HR) of at least 40 bpm in adolescents, 30 bpm in adults, or a HR >120 bpm within 5 min of 70° head up tilt (HUT) [1]. Physiologic studies in those with POTS have identified an excessive reduction in cardiac output and cerebral blood flow in the upright position [2, 3]. Patients with POTS experience a variety of symptoms suggesting central nervous system impairment ranging from prolonged fatigue and lightheadedness to overt neurocognitive deficits [2–6]. Cognitive impairment is commonly listed among the top complaints of adolescents with POTS and is typically referred to as “brain fog” by patients [3, 6]. Yet, the term “brain fog” is imprecise, and to date the cause of this

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symptom is unknown. The purposes of this study were to (1) generate a list of descriptors for the term brain fog, (2) evaluate symptoms and triggers of brain fog that could provide insight into the physiological mechanism of the symptom, and (3) assess the perceived effectiveness of treatments to identify targets for further study.

Methods

Subjects

Subjects, age 14–29, previously diagnosed with POTS were eligible to participate. Subjects were recruited through an advertisement posted in support groups for POTS patients on facebook.com as well as the Dysautonomia International research announcements. All subjects had been previously diagnosed with POTS by their physician either with a tilt table test or standing test, the two common and validated diagnostic techniques [7].

Study protocol

Informed consent was obtained from subjects or, for those under age 16, from their parents. The experimental protocol was approved by the Committee for the Protection of Human Subjects (Institutional Review Board) of New York Medical College and by the Institutional Review Board of Johns Hopkins Medical Institutions. The study protocol was modeled after the “Nausea Profile,” an effort to describe the symptom of nausea [8]. To define and evaluate brain fog, open-ended questions were first proposed to a focus group of 25 patients with POTS. The terms were evaluated and the most popular answers were used to generate terms for the final cognitive symptom questionnaire, which contained 38 questions specifically designed for this study. The Wood Mental Fatigue Inventory (WMFI) was also administered. The WMFI asked subjects to rate the frequency of nine mental fatigue symptoms and has been previously validated in patients with chronic fatigue syndrome (CFS) and OI [9, 10].

Study questionnaire

The first 19 items of the questionnaire gathered demographic and diagnostic information. The remaining 19 items were scaled questions that evaluated frequency, severity, descriptors, triggers, and treatments of brain fog. Brain fog frequency was reported on a scale from 0 to 4 with higher numbers indicating greater frequency. Subjects with daily brain fog also reported its frequency during the day. Subjects rated the severity of their brain fog on a scale from 0 to 100 in 10-point intervals with higher numbers

indicating increased severity. Subjects marked their level of agreement (strongly agree, agree, neutral, disagree, and strongly disagree) with each term in a list of descriptors of brain fog generated by our focus group. Brain fog triggers were evaluated by frequency and the posture in which they occurred. Common treatments for POTS were also evaluated for their reported effects on brain fog.

Data analysis

Wood mental fatigue inventory was scored on a scale from 0 to 36 in 1-point increments with higher numbers representing greater mental fatigue. A two-tailed Spearman’s correlation was used to compare brain fog severity ratings to scores on the WMFI. We compared the logs of WMFI scores between subjects with sleep disorders and those without using a two-tailed student’s *t* test for independent samples. Mean values were calculated from scaled questions and percentages were calculated for nominal answers. All data are reported as % (*n*) for the number of subjects who agree or disagree with a term or as the mean (*M*) ± standard deviation (SD) for numerical values.

Results

The characteristics of the study group are shown in Table 1. In all, 138 POTS patients (88 % female) responded by completing a questionnaire. The age of the subjects was 20.4 ± 4.5 years, range 14–29. Subjects had developed POTS symptoms 5.8 ± 4.6 years before study enrollment and were diagnosed with POTS 2.8 ± 2.3 years prior to enrolling in this study. Fifty-one percent of the subjects reported fainting due to OI and 14 % reported that they spent the majority of the day lying down. As shown in Table 2, 96 % of the subjects experienced brain fog and 67 % experienced brain fog on a daily basis. Subjects reported that brain fog impaired their ability to complete schoolwork (86 %), be productive at work (80 %), and participate in social activities (67 %). The severity of brain fog and mental fatigue varied greatly between subjects. Yet, as shown in Fig. 1, brain fog severity ratings correlated with WMFI scores ($\rho = 0.512$, $P < 0.0001$). Subjects with sleep disorders had higher scores on the WMFI than subjects without sleep disorders ($P < 0.01$) as shown in Table 2.

Descriptors of brain fog

As shown in Table 3, the top ranked descriptors of brain fog were “forgetful” (91 %), “difficulty thinking” (89 %), “difficulty focusing” (88 %), “cloudy” (88 %), and “difficulty finding the right words or communicating” (88 %). The least commonly reported descriptors were “thoughts

Table 1 Demographic and diagnostic data (*n* = 138)

Age, M ± SD (years)	
Age at study enrollment	20.4 ± 4.5
Age at POTS diagnosis	17.5 ± 4.6
Age at onset of POTS symptoms	14.7 ± 5.3
	% (<i>n</i>)
Female	88 (122)
Caucasian	99 (137)
Hispanic	4 (5)
POTS diagnosis method	
Tilt table test	80 (111)
Standing test	40 (55)
Serum catecholamines	6 (8)
Sleep disorder diagnoses	
Sleep apnea	6 (8)
Insomnia	13 (18)
Restless leg syndrome	3 (4)
Other	4 (6)
Frequency of fainting	
Never	49 (67)
Yearly	29 (41)
Monthly	8 (11)
Weekly	12 (16)
Daily	1 (1)
Multiple times/day	1 (2)
Spend most of the day supine	14 (19)

moving too quickly” (40 %), “detached” (60 %), “lost” (64 %), “sleepy” (69 %), and “annoying” (70 %).

Brain fog triggers

As depicted in Fig. 2, the most frequent reported triggers of brain fog were physical fatigue (91 %), lack of sleep (90 %), prolonged standing (87 %), dehydration (86 %), and feeling faint (85 %). While supine, physical fatigue triggered brain fog in 72 % of subjects, lack of sleep in 70 %, dehydration in 60 %, and feeling faint in 57 %.

Reported interventions for brain fog

Non-pharmacological interventions

Over 75 % of subjects had tried each of the non-pharmacological agents for POTS in this questionnaire with the exception of cooling vests (18 %), physical therapy (48 %), and compression stockings (63 %). As shown in Fig. 3a, subjects reported the following as helpful for improving brain fog: lying down (81 %), avoiding heat (68 %), high fluid intake (66 %), acute ingestion of at least 16 oz of water in <5 min (63 %), and high salt diet (60 %).

Table 2 Brain fog frequency and severity (*n* = 138)

	% (<i>n</i>)
Subjects who experience brain fog	96 (132)
Frequency of brain fog	
Never	4 (6)
1/month	2 (3)
1/week	6 (8)
2–3/week	20 (28)
Daily	67 (93)
Once a day	2 (3)
A few hours each day	32 (45)
Most of the day	17 (24)
All day	15 (21)
Brain fog fluctuates throughout the day	86 (119)
When brain fog is most severe	
Morning	25 (34)
Afternoon	15 (21)
Evening	13 (18)
Night	2 (3)
No pattern	36 (50)
Activities impaired by brain fog	
Schoolwork (<i>n</i> = 111)	86 (96)
Work productivity (<i>n</i> = 82)	80 (66)
Social activities (<i>n</i> = 138)	67 (92)
Higher score indicates worse impairment	M ± SD
Brain fog severity (0–100)	55.3 ± 24.9
WMFI (0–36)	
All subjects	23.9 ± 8.7
Subjects without sleep disorders (<i>n</i> = 102)	21.9 ± 9.5
Subjects with sleep disorders (<i>n</i> = 36)	24.9 ± 6.7

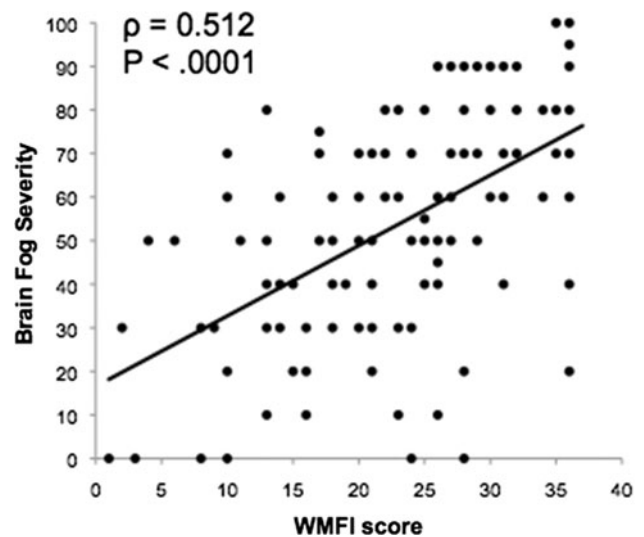


Fig. 1 Correlation between Wood mental fatigue inventory (WMFI) scores and brain fog severity. WMFI is scored on a scale from 0 to 36 in 1-point increments with higher numbers representing greater mental fatigue. Brain fog severity is ranked from 0 to 100 in 10-point increments with higher numbers representing greater severity

Table 3 Descriptors of brain fog ($n = 138$)

	Agree % (n)	Disagree % (n)
1. Forgetful	91 (125)	1 (1)
2. Difficulty thinking	89 (123)	1 (2)
3. Difficulty focusing	88 (122)	2 (3)
4. Cloudy	88 (122)	3 (4)
5. Difficulty finding the right words/communicating	88 (121)	3 (4)
6. Mental fatigue	86 (119)	2 (3)
7. Slow	86 (118)	2 (3)
8. Mind went blank	85 (117)	4 (5)
9. Spacey	83 (114)	4 (6)
10. Difficulty processing what others say	80 (110)	4 (6)
11. Exhausted	80 (110)	7 (9)
12. Easily distracted	77 (106)	7 (10)
13. Difficulty processing words read	75 (104)	10 (14)
14. Confusion	71 (99)	8 (11)
15. Annoying	70 (96)	9 (13)
16. Sleepy	69 (95)	8 (11)
17. Lost	64 (89)	14 (19)
18. Detached	60 (84)	14 (20)
19. Thoughts moving too quickly	40 (55)	37 (51)

The interventions that were reported to make brain fog worse were showering (61 %), exercise (56 %), walking (47 %), and ingestion of caffeinated beverages (33 %).

Pharmacological interventions

The POTS treatments most commonly tried by study subjects were fludrocortisone (59 %), midodrine (56 %), salt tablets (51 %), selective serotonin reuptake inhibitors

(SSRIs) (50 %), and β 1 antagonists (49 %). As shown in Fig. 3b, the pharmacological agents reported to improve brain fog were intravenous (IV) saline (77 %), stimulant medications (67 %), salt tablets (54 %), intramuscular (IM) vitamin B-12 injections (48 %), and midodrine (45 %). The interventions most commonly reported to make brain fog worse were serotonin–norepinephrine reuptake inhibitors or SNRIs (30 %), tricyclic antidepressants (25 %), β 1 antagonists (22 %), non-selective β antagonists (20 %), and fludrocortisone (17 %).

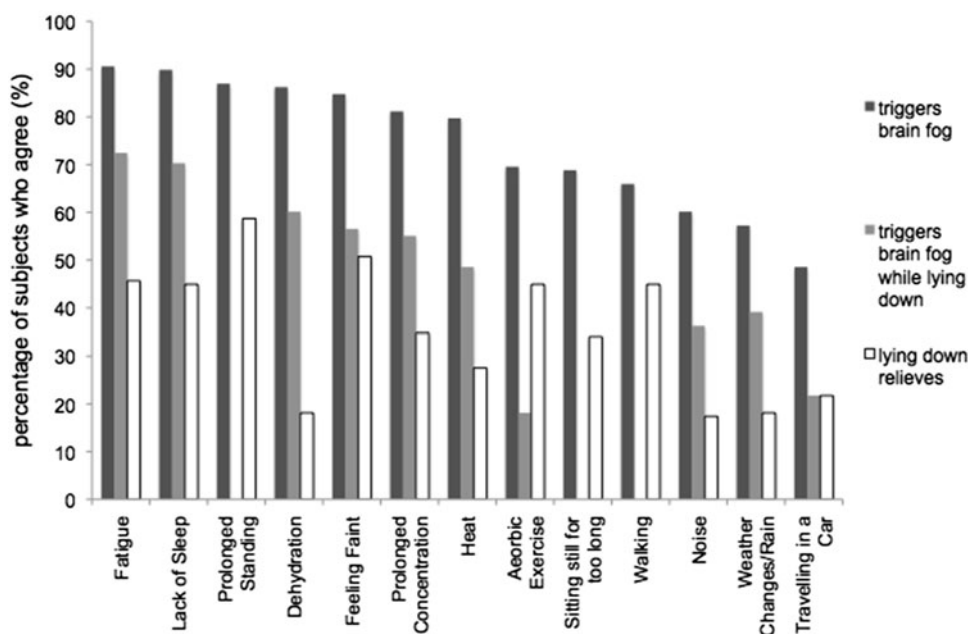
Conclusions

This paper is the first to survey POTS patients to evaluate the symptom of “brain fog.” We found that: (1) brain fog is a prevalent cognitive complaint similar to mental fatigue, (2) there are many triggers and modulators of brain fog that may explain the symptom’s physiology, and (3) there are many treatment targets that may be effective for improving brain fog in POTS including some that are not typically recommended for POTS.

What is brain fog?

Our findings suggest that brain fog is a cognitive complaint similar to mental fatigue. The top ranked descriptors of brain fog (forgetful, cloudy, and difficulty focusing, thinking and communicating) relate to impaired cognition and performance on cognitive tasks. In contrast, the least common descriptors (thoughts moving too quickly, detached, lost, sleepy) were more indicative of general fatigue, anxiety, and depression [11].

Fig. 2 Reported brain fog triggers. *Dark grey bars* represent the percentage of subjects that reported the condition to trigger brain fog. *Light grey bars* signify the percentage of subjects that reported the condition to trigger brain fog while lying supine. *White bars* represent the percentage of subjects who claimed that lying down relieved brain fog that was triggered by each condition



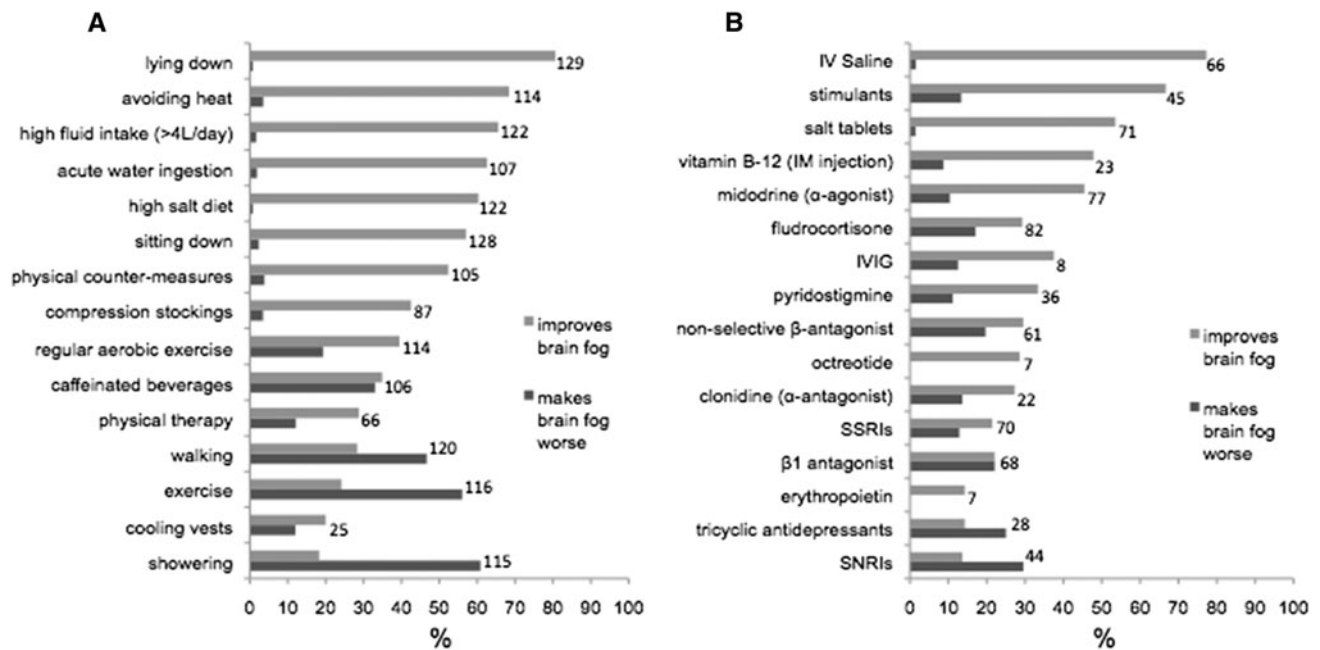


Fig. 3 Effects of non-pharmacologic (a) and pharmacologic (b) interventions for POTS on brain fog. The length of the bars shows the percentage of subjects who reported that the intervention improved

brain fog (light grey bars) or made brain fog worse (dark grey bars). The percentages are out of the number of subjects who had tried each intervention, which is indicated by the numbers next to the bars

Brain fog is not limited to the upright posture

In this study, 87 % of subjects reported prolonged standing to trigger their brain fog and 81 % recommended lying down to improve brain fog. Since orthostatic intolerance is defined by the onset of symptoms with upright posture that are relieved by recumbence, we had previously assumed that brain fog was posturally driven. In contrast to this, subjects did not agree that lying down relieved brain fog and felt that brain fog could be triggered in the supine position.

Ocon et al. [4] showed that POTS patients did not have impaired performance on an N-back memory task while supine but their performance was progressively worsened with incremental orthostatic stress. Yet, the study did not measure cognition in these patients after returning them to the supine position. Our finding that brain fog can be triggered by upright posture but not relieved by recumbence is consistent with a carry-over effect from a physiological provocation. One possible explanation for this is that brain fog could be triggered by excessive reductions in cerebral blood flow that often occurs in POTS subjects when upright [3].

Alternatively, brain fog may have a multifactorial etiology with factors not restricted solely to prolonged upright posture. 81 % subjects reported prolonged concentration to trigger brain fog, 68 % of which agreed that prolonged concentration triggered their brain fog while supine.

Manyari et al. [12] found that some patients with neurally mediated syncope had a paradoxical vasodilatory response to mental stress while seated. Although similar studies have not been performed in POTS, the lack of an appropriate peripheral vasoconstrictive response to mental stress may be present in young people with POTS and this may obstruct their ability to perform cognitive tasks.

Sleep quality may affect brain fog

The top two reported brain fog triggers were fatigue and lack of sleep. This finding made us question the sleep quality in these subjects. Our survey data showed that 32 % of subjects reported having a diagnosed sleep disorder, most commonly insomnia, sleep apnea, or restless leg syndrome. The rate of sleep disorders among subjects in this study is much higher than the prevalence among older adolescents [13]. Furthermore, subjects who reported having a sleep disorder had higher scores on the WMFI indicating worse mental fatigue compared to the study subjects without sleep disorders. Previous studies have shown decreased sleep efficiency as well as more sleep disturbances and daytime sleepiness in adults with POTS [14, 15]. Decreased sleep time and sleep quality have been shown to impair performance on various cognitive tasks [16]. How sleep efficiency affects cognition in POTS patients is unknown but, we can postulate that sleep quality is a major contributor to brain fog in POTS.

Potential interventions for brain fog

Non-pharmacologic interventions

Respondents described a variety of non-pharmacological and pharmacological interventions that improved brain fog. Most common were non-pharmacologic interventions for POTS, such as increased fluid and salt intake, which is generally the first step in treating POTS [2]. Claydon et al. [17] found 2 months of salt supplementation to improve cerebral auto-regulation in older syncope patients. A similar process may occur in younger POTS patients on a high salt diet and may explain its reported efficacy for improving brain fog.

Although 35 % of POTS subjects reported that caffeine improves brain fog, 33 % stated that it made their brain fog worse, despite the finding that epidemiological studies have shown that caffeinated beverages can improve cognitive abilities [18]. Yet, the adverse effects of caffeine, diuresis and tachycardia could exacerbate POTS symptoms in some subjects, outweighing its beneficial effects.

Pharmacologic interventions

IV saline was the pharmacologic intervention most commonly reported (51/66 subjects) to improve brain fog. Previous studies have shown that acute IV saline reduces tachycardia and symptoms in POTS [19, 20]. Yet, these studies did not investigate the effect of IV saline on cognition. Given that 86 % of subjects reported dehydration as a trigger of their brain fog, it seems likely that IV saline treatment would improve brain fog. Further studies are needed to determine whether brain fog is due to hypovolemia and if IV saline can have acute or lasting effects on cognitive performance.

In addition, some treatments commonly used to treat POTS, such as β -antagonists, SSRIs, and SNRIs were felt to have made brain fog worse. The reason behind the deleterious effects of these medications on brain fog is unknown. Raj et al. [21] found that low-dose propranolol improved symptoms in POTS subjects, but the symptom profile they used did not include cognition. Other studies have described mild cognitive impairment in healthy subjects following short-term SSRI, but not SNRI treatment [22]. The negative effects of SNRIs on brain fog could be due to high levels of synaptic norepinephrine in the hyperadrenergic POTS variant [2]. Other pharmacological interventions that are not commonly mentioned as methods of treating POTS [2, 6], such as stimulant medications and IM vitamin B-12 injections, deserve further investigation.

Exercise: both a trigger and treatment for brain fog

Of additional interest was that acute exercise was reported to make brain fog worse yet regular aerobic exercise was

reported to improve brain fog. Many POTS patients become physically deconditioned due to the debilitating nature of the disorder [23]. Exercise often worsens POTS symptoms, especially fatigue, which in turn could trigger brain fog. Fu et al. [24] found a regular cardiovascular exercise program to have profound physiological and clinical benefits in POTS patients. Yet, the study did not investigate the effects of exercise on cognitive performance in these subjects. Epidemiological studies have found positive correlations between cognitive performance and physical activity in healthy adolescents [25]. Although the reason is unknown, regular aerobic exercise may improve cognition among other symptoms in adolescents with POTS.

Summary and practical significance

We generated a list of descriptors for brain fog, a common symptom of POTS. We also determined possible triggers and treatments of brain fog that may suggest further investigations on this topic.

Limitations

The main limitation of this study is that all data were self-reported. Formal reviews of medical records and laboratory testing were not performed to validate these reports. Since to date, there are no standard methods to evaluate the subjective complaint of brain fog, dependence on self-reporting was necessary. To assure the fidelity of this information, we used the WMFI, a standard method for evaluating cognitive complaints in CFS and POTS [9], to validate our questionnaire. It is also possible that variable definitions and testing methods were used in the diagnosis of POTS in our sample, but the high percentage of reported orthostatic symptoms make it unlikely that subjects were entirely free of OI. Our recruitment method, via an advertisement, may have generated a response bias for subjects that were more affected by POTS. Yet, the reported frequency of fainting and reliance of bed rest suggests that the majority of subjects are not incapacitated. Some patients with POTS are hypervigilant [26] which may have led to overreporting of symptoms and affected our data. While we cannot make definitive claims about the nature of POTS due to a lack of objective data, we described brain fog symptoms according to subjective responses from a large sample of subjects. This study must be viewed as a first step towards understanding brain fog. Results of this study may serve as an impetus for further research on the physiological mechanism and treatment of brain fog.

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Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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