ORIGINAL ARTICLE

Does sexual functioning improve with migraine improvements and/or weight loss?—A post hoc analysis in the Women's Health and Migraine (WHAM) trial

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Summary

Background: Despite plausibility of migraine headaches contributing to impaired sexual function among women, data are inconsistent and point to obesity as a potential confounder. Prospective studies that assess the relative importance of migraine improvements and weight loss in relation to sexual function could help elucidate associations among migraine, obesity and female sexual dysfunction (FSD).

Objective: To evaluate sexual function changes and predictors of improvement after behavioural weight loss (BWL) intervention for migraine or migraine education (ME).

Methods: Women with migraine and overweight/obesity were randomized to 16 weeks of BWL (*n* = 54) or ME (*n* = 56). Participants completed a 4-week smartphone headache diary and the Female Sexual Function Index (FSFI) at pre- and post-treatment. A validated FSFI total cut-off score defined FSD. We compared changes in FSFI scores and FSD rates between conditions and evaluated migraine improvements and weight loss as predictors of sexual functioning in the full sample.

Results: Among treatment completers (*n* = 85), 56 (65.9%) participants who reported sexual activity at pre- and post-treatment were analysed. Migraine improvements were similar between conditions, whereas BWL had greater weight losses compared with ME. FSD rates did not change overall (48.2% to 44.6%, *p* = .66) or by condition (BWL: 56.0% to 40.0% vs. ME: 41.9% to 48.4%, *p* = .17). Similar patterns were observed for changes in FSFI total and subscale scores. Across conditions, larger weight losses predicted greater improvements in FSFI total and arousal subscale scores, whereas larger migraine headache frequency reductions predicted greater improvements in FSFI satisfaction subscale scores.

Conclusion: Sexual functioning did not improve with either BWL or ME despite migraine headache improvements in both conditions and weight loss after BWL. However, weight loss related to improvements in physiological components of the sexual response (i.e., arousal) and overall sexual functioning, whereas reduced

headache frequency related to improved sexual satisfaction. Additional research with larger samples is needed.

KEYWORDS

female sexual dysfunction, migraine, obesity, women's health

1 | INTRODUCTION

Female sexual dysfunction (FSD) is a condition characterized by difficulties in at least one of the following areas of sexual functioning that cause clinically significant distress or strained relationships: desire, arousal, orgasm and pain.[1-3] FSD is prevalent, with 40%–45% of women reporting impairment in at least one of the above sexual function domains.[4,5] FSD rates tend to be even higher among women who also have comorbid health conditions,[6-8] including migraine and obesity.[9-13] Women may also report impairments in sexual functioning that do not meet the threshold for a diagnosed sexual function disorder, hereafter referred to as sexual functioning impairments.

Migraine is a neurological disease characterized by moderate-to-severe headache and accompanying autonomic, affective and sensory features that affect 1 billion people globally and women disproportionately.[14] Sexual functioning impairments are common among women with migraine, with 57%–90% of participants across studies indicating some level of impairment in sexual functioning.[10-12,15-17] However, evidence is less consistent regarding whether more frequent and severe migraine attacks contribute to greater sexual functioning impairments. Specifically, although some studies have found that indices of greater migraine severity (e.g., more frequent attacks and use of abortive medications) are related to greater sexual functioning impairments among women,[10,18,19] other studies have not observed these relationships; instead, finding that migraine severity is unrelated to degree of impairments.[11,12,15,17] Thus, it is unclear whether migraine directly contributes to sexual functioning impairments and increased risk for FSD or if these relationships are influenced by a third variable.

Obesity is a likely factor that could influence sexual functioning among women with migraine. Obesity is both a risk and exacerbating factor for migraine, especially in reproductive-aged women.[20-22] Obesity is also an established risk factor for sexual functioning impairments and FSD[9,13,23-25]; conversely, weight loss can improve sexual functioning.[13,26,27] Thus, it is possible that excess weight is partially responsible for sexual functioning impairments among many women with migraine and that obesity may have been a confounding factor in past research on migraine and sexual functioning. Our group recently reported results from the first study to assess FSD rates among reproductive-aged women who had both migraine and severe obesity (n = 37) compared with a control group matched on BMI, age and reported sexual activity in the past month (n = 37).[12] Both groups completed the Female

Sexual Function Index (FSFI),[28] a brief questionnaire that assesses sexual functioning on a continuous scale and provides a validated FSFI total cut-off score for defining FSD.[29] FSD rates were similar between the participants with obesity who had migraine and those with obesity who served as controls (57% vs. 54%, p = .82). Moreover, in another analysis within this same study among a larger sample (n = 105) of women with migraine and overweight/obesity, migraine attack frequency, pain intensity and attack duration were not associated with risk of FSD.[12]

Taken together, these studies suggest that the presence of migraine and severity of migraine symptoms are not associated with FSD in women with comorbid obesity and raise the possibility that excess weight is an important contributor to sexual functioning impairments in this population. However, these studies had limitations. Given that the relationship between migraine and FSD was assessed at only time point, we cannot draw causal inferences about directionality of this relationship. Thus, it is unclear if improvements in migraine could improve FSD. Second, the prior analyses were restricted to women with migraine who had an elevated BMI. It is thus unknown how changes in weight might impact sexual functioning among women with migraine. Prospective studies involving treatment of migraine, obesity or both among women with both of these conditions would allow for determination of the relative contributions of migraine improvements and weight loss to changes in FSD and sexual functioning domains. This would aid in clarifying the relationships of migraine, obesity and FSD and improve understanding of potential targets for improving sexual functioning.

The Women's Health and Migraine (WHAM) study was a randomized controlled trial that examined the efficacy of a 16-week behavioural weight loss (BWL) intervention versus a migraine education (ME) control for treatment of migraine among reproductive-aged women with comorbid obesity and migraine. As previously reported,[30] women in both conditions experienced similar significant reductions in migraine attack frequency and several indices of severity (i.e., pain intensity, duration and impact on daily life). BWL participants achieved an average 4-kg weight loss, whereas those in ME gained 1 kg on average. Given that the WHAM trial compared treatment of both migraine and obesity (BWL) versus treatment of migraine only (ME), it offers a unique opportunity to[1] compare how targeting weight loss (which also improves migraine) versus targeting only migraine symptoms affects FSD and sexual functioning among women with comorbid obesity and migraine and[2] evaluate whether improvements in migraine or weight loss hold greater importance in relation to changes in FSD and sexual functioning across all participants.

The present study was a secondary analysis of data from the WHAM trial that sought to evaluate[1] treatment-related changes in sexual functioning and[2] the overall relationships between migraine, weight loss and sexual functioning among all participants. Given that migraine symptoms improved in both BWL and ME[30] and some past work suggesting that migraine severity relates to degree of sexual functioning impairments,[10,18,19] we hypothesized that participants in both conditions would report reduced sexual functioning impairments. We also hypothesized that the magnitude of these reductions would be larger in the BWL condition, as reductions in excess weight have been shown to improve sexual functioning in general samples of adults with obesity[13,26,27]; BWL among women with comorbid migraine and obesity may thus improve sexual functioning by targeting mechanisms underlying both obesity–sexual function-ing[9,30,31] and obesity–migraine[30] relationships. Additionally, we hypothesized that, across conditions, greater weight loss and greater reductions in migraine would each be independently associated with greater improvements in sexual functioning. Although the primary focus was on changes in rates of FSD and in overall sexual functioning (i.e., total FSFI scores), we also explored whether changes in specific domains of sexual functioning (e.g., arousal) related to changes in migraine and weight.

2 | METHODS

2.1 | Participants

Eligibility for the WHAM trial required that participants identify as biological female, be 18–50 years of age, have a BMI between 25.0 and 49.9 kg/m^2 and have migraine with or without aura, as specified by International Classification of Headache Disorders 3 criteria and as confirmed by the study neurologist, with ≥3 migraine attacks and four to 20 migraine headache days per month for the past 3 months. Participants were allowed to continue use of preventative and abortive pharmacological migraine treatments, as well as medications for depression and contraception, as long as they had been on a stable regimen for ≥2 months and agreed not to adjust their medication regimen during the study. Participants were excluded if they had a headache disorder other than migraine or migraine with tension type; had undergone bariatric surgery; were already participating in a weight loss programme; had lost ≥5% of their body weight within the past 6 months; were currently using prescription weight loss medication; had a cancer diagnosis within the past year; were pregnant, breastfeeding, or planning to become pregnant during the course of the trial; were unable to read or comprehend study materials or had another condition that the investigators judged would preclude adherence to the study protocol (e.g., plans to geographically relocate and presence of an untreated substance use disorder). For the present secondary anal-ysis, we only retained eligible participants who reported being sex-ually active at both pre- and post-treatment, as including sexually

inactive participants would artificially lower sexual functioning scores because of the way in which the FSFI is scored for individ-uals who are sexually inactive (see details below).

2.2 | Procedures

Participants were recruited from community and clinical settings between November 2012 and June 2016 via numerous methods, including direct mailing, Internet and social media postings and newspaper advertisements. Recruitment materials specified that the study was recruiting women between the ages of 18 and 50 with comorbid migraine and overweight/obesity with interest in behav-ioural headache management. Interested individuals contacted the research centre by phone and completed a brief phone screening of eligibility. Individuals appearing to be eligible were then invited to an in-person orientation session during which they were provided with details about the study, provided written informed consent, had their migraine diagnosis confirmed by the study neurologist, had their height and weight measured by research staff, and com-pleted questionnaires, including the FSFI. Participants also received a smartphone equipped with an electronic diary for daily monitoring of headaches over the subsequent 28 days (see below for details). Following this 28-day pre-treatment headache monitoring period, participants returned the smartphone to research staff and were randomized to either BWL or ME. Following completion of the 16-week intervention (i.e., at post-treatment), participants were provided with a smartphone equipped with the same headache diary for 28 days of post-treatment headache monitoring, their weight was measured in-clinic and they completed post-treatment questionnaires, including the FSFI.

Both interventions consisted of 16 weekly group meetings, which were led by one of three behavioural interventionists, who led groups across both conditions to control for therapist effects. The BWL inter-vention was modelled after the Diabetes Prevention Program and Look AHEAD trials[32,33] and encouraged individuals to lose 1–2 lb/week to achieve a ≥7% weight loss. Participants were taught behavioural modification skills (e.g., self-monitoring and stimulus control), prescribed a calorie- and fat-restricted diet (i.e., 1,200–1,500 kcal/day with ≤25% of kcal from fat) and provided with a physical activity prescription that gradually increased to 250 min of moderate-to-vigorous physical activity per week. The BWL intervention did not include content specific to migraine or its management.

The ME intervention provided education about migraine, treat-ment options (pharmacological and nonpharmacological) and evidence-based self-management strategies (e.g., relaxation tech-niques and cognitive restructuring). Sessions were structured as group lectures and did not involve active skill practice. Participants were also not explicitly instructed to practice skills outside of session. The ME intervention contained no content specific to weight management. Additional details about the interventions are available in the main

outcomes paper.[30] This study was approved by the institutional review board at The Miriam Hospital.

2.3 | Measures

2.3.1 | Headache frequency and pain intensity

Migraine headache characteristics were assessed for 28-days pre- and post-treatment via a Web-based headache diary that was designed by the research team and that was accessed by participants on their study smartphones. Each night prior to bed, participants reported migraine headache occurrence (Y/N), which was used to determine number of migraine headache days per month. Each night, participants also reported maximum intensity of headache pain (0 = *no pain*, 10 = *pain as bad as you can imagine*), which was averaged to create an average pain intensity rating. Study staff verified diary completion each day and contacted participants by telephone to obtain any missing data.

2.3.2 | Sexual activity and functioning

Current sexual activity status (i.e., sexually active or not) was determined at pre- and post-treatment via the FSFI,[28] which is a validated 19-item measure of sexual functioning. The FSFI was also used at pre- and post-treatment to assess presence of FSD and sexual functioning, both overall and in each of the following six domains: desire (2 items), arousal (4 items), lubrication (4 items), orgasm (3 items), satisfaction (3 items) and pain (3 items). Aspects of sexual functioning such as frequency, satisfaction and confidence are assessed across the various domains (i.e., desire: frequency and level; arousal: frequency, level, confidence and satisfaction; lubrication: frequency, difficulty, frequency of maintaining and difficulty in maintaining; orgasm: frequency, difficulty and satisfaction; satisfaction: with closeness with partner, with sexual relationship and with overall sex life; pain: frequency during vaginal penetration, frequency following vaginal penetration and level during or following vaginal penetration). Responses are provided using a scale ranging from either 0–5 or 1–5 (with zero reserved for those with no sexual activity). Scores for each subscale are summed and multiplied by a domain factor, resulting in potential domain scores as follows: 0–6 (arousal, lubrication, orgasm and pain), 0.8–6 (satisfaction) and 1.2–6 (desire). A total score is computed by adding the six subscales (potential range: 2–36). Higher overall and domain-specific scores indicate better sexual functioning. A validated cut-off score of ≤26.55 was used to identify presence of FSD.[28,29] Given that assigning scores of zero to individuals who are sexually inactive may artificially lower their scores and reflect greater impairment than what is truly present (e.g., for the question assessing difficulty with sexual stimulation during intercourse, 0 [*no sexual activity*] is scored less favourably than 1 [*extremely difficult or impossible*]), only sexually active participants were included in analyses.

2.3.3 | Sociodemographic characteristics and weight loss

Participants' height (in centimetre) and weight (in kilogram) were measured by research staff using a wall-mounted Harpenden stadiometer and a Tanita® digital scale, respectively, at pre-treatment to determine BMI. Participant weight was also measured at post-treatment. Percent weight loss was calculated such that more positive values indicate greater weight loss. At pre-treatment, participants completed a sociodemographic questionnaire that assessed age, race and ethnicity.

2.4 | Analytic approach

Data were analysed in SPSS version 25, and significance was set at α = .05. The number of participants who reported being sexually active versus sexually inactive at pre- and post-treatment was reported as the number and percent of participants in each category. A Chi-square test of independence was used to assess whether the number of participants identifying as sexually active at both time points differed by treatment condition. One-way analysis of variance (ANOVA) and chi-square were used to compare sociodemographic characteristics by treatment condition. A Chi-square test of independence was used to evaluate pre- to post-treatment change in the rate of FSD across the full sample, and a generalized linear mixed effects model was used to assess change in rate of FSD from pre- to post-treatment by treatment condition. Analysis of covariance was used to assess treatment condition effects on pre- to post-treatment change (difference score) in migraine headache days and average pain intensity, weight and sexual functioning (total and domain-specific scores), when controlling for pre-treatment values. Repeated measure ANOVA was used to assess change over time in sexual functioning (total and domain-specific) across all participants.

Effect sizes were calculated for condition-related and overall changes in sexual functioning. Hedges' *g* (due to the small *n* for each condition and unequal group sizes) or Glass's delta (if unequal standard deviations) were used to quantify effect size for change in sexual functioning by condition, whereas Cohen's *d* was used to quantify effect size for overall change in sexual functioning for the combined sample. For all three indices of effect size, values of 0.20 indicate a small effect, 0.50 indicate a medium effect and 0.80 indicate a large effect. Because of the limited sample size, effect sizes for these models were considered in conjunction with statistical significance, with effects that were at least medium sized deemed suggestive of a potentially meaningful effect.

Multiple linear regression was used to assess whether change in headache characteristics (days, pain intensity) or in weight related to changes in sexual functioning across the full sample. Separate models were used to predict change in each aspect of sexual functioning (total and domain-specific scores). Each model included change variables (i.e., differences scores) for headache characteristics (days and pain intensity) and weight as predictors and controlled for baseline

values for headache days, headache pain intensity, weight and the aspect of sexual functioning of interest.

All change variables were scored such that positive values indicate greater improvements. Models were tested both controlling and not controlling for any sociodemographic variables that differed between treatment conditions. As results were similar, results from models without sociodemographic covariates are reported for clearer interpretation. As only participants who identified as sexually active at both pre- and post-treatment were included in analyses; all measures had complete data.

3 | RESULTS

3.1 | Participant sample characteristics and change in migraine headache and weight from pre- to post-treatment

Of the 110 participants randomized in the WHAM trial, 85 (77.3%) completed pre- and post-treatment assessments. Of these 85 participants, 13 (15.3%) reported being sexually inactive at both pre- and post-treatment, eight (9.4%) reported becoming sexually inactive from pre- to post-treatment, eight (9.4%) reported becoming sexually active from pre- to post-treatment and 56 (65.9%) reported being sexually active at both time points. Only the 56 participants who identified as sexually active at both time points were included in analyses. The number of participants identifying as sexually active at both time points (25 participants in BWL and 31 in ME) did not differ between conditions, x^2 (1, N = 85) = 2.32, p = .13. Participants identifying as sexually active at both time points (n = 56) also did not differ from those identifying as sexually inactive at one or both time points who were excluded (n = 29) on BMI, average headache pain intensity or number of migraine headache days per month (p's > .10).

Table 1 displays sociodemographic characteristics for the full sample (n = 56) and by condition. On average, participants were

approximately 40 years old with a BMI in the obese range (M ± SD: 34.0 ± 7.1 kg/m^2). Most participants identified as White and non-Hispanic. Treatment conditions did not differ on age, baseline BMI or race. However, significantly more participants in the ME condition identified as Hispanic relative to the BWL condition.

At baseline, participants reported an average of 8.7 ±4.2 migraine headache days per month, with seven participants (12.5%) reporting chronic migraine (≥15 migraine headache days per month). Average maximum intensity of migraine pain at baseline was 5.6 ± 1.3 on a 0–10 scale. As shown in Table 2, change in number of headache days per month and in average pain intensity was similar between groups. Participants in BWL had greater weight loss than participants in ME.

3.2 | Changes in FSD and general sexual functioning by condition and overall

Change in rates of FSD from pre- to- post-treatment was not statistically significant across the full sample (48.2% to 44.6%, p = .66). Change in rates of FSD was also not statistically different between treatment conditions (see Figure 1; BWL: 56.0% to 40.0% vs. ME: 41.9% to 48.4%; p = .17). As shown in Tables 2 and 3, sexual functioning, as indicated by both FSFI total and domain-specific scores, also did not change significantly from pre- to post-treatment among the full sample nor did it differ by treatment condition (p's > .05). However, medium-to-large between-condition effects were observed for total FSFI scores (large effect) and orgasm subscale scores (medium effect) in favour of BWL.

3.3 | Relationships between change in migraine headache, weight and sexual functioning

The full regression models containing change in headache frequency, pain intensity and weight as predictors and controlling for

TABLE 1 Sociodemographic/anthropometric characteristics for the full sample and by treatment condition

		Comparisons between conditions			
	Full sample (n = 56)	BWL (n = 25)	ME (n = 31)	F or X^2	p
Age, M (SD)	39.5 (7.8)	38.9 (7.2)	40.0 (8.3)	0.30	.59
Pre-treatment BMI, M (SD)	34.0 (7.1)	35.1 (7.6)	33.3 (6.6)	0.94	.34
Race, n (%)				1.42	.70
White	47 (83.9%)	20 (80.0%)	27 (87.1%)		
African American/Black	3 (5.4%)	2 (8.0%)	1 (3.2%)		
Mixed	3 (5.4%)	2 (8.0%)	1 (3.2%)		
Other	3 (5.4%)	1 (4.0%)	2 (6.5%)		
Ethnicity, n (%)				15.05	<.001
Non-Hispanic	42 (75.0%)	25 (100.0%)	17 (54.8%)		
Hispanic	14 (25.0%)	0 (0.0%)	14 (45.2%)		

Abbreviations: BMI, body mass index; BWL, behavioural weight loss; ME, migraine education; SD, standard deviation.

TABLE 2 Changes in headache characteristics, weight and sexual functioning by treatment condition

	Pre- to post-treatment change by condition				
	BWL (*n* = 25)	ME (*n* = 31)	F	p	Effect size
Headache days/month	2.24 (4.47)	4.45 (4.19)	3.38	.07	0.51
Average pain intensity	0.86 (2.47)	1.31 (2.54)	0.43	.52	0.18
Weight loss	3.22 (4.23)	−0.96 (2.53)	21.54	<.001	1.65[a]
Sexual functioning					
Total FSFI score	2.53 (7.39)	−0.17 (2.47)	2.61	.11	1.09[a]
Desire	0.36 (1.57)	0.02 (0.72)	0.36	.55	0.29
Arousal	0.59 (1.59)	0.08 (0.73)	1.11	.30	0.43
Lubrication	0.35 (1.50)	−0.12 (0.89)	1.46	.23	0.39
Orgasm	0.72 (1.53)	−0.05 (0.81)	3.75	.06	0.65
Satisfaction	0.16 (1.62)	−0.03 (1.07)	0.01	.92	0.14
Pain	0.35 (1.39)	−0.08 (1.52)	2.50	.12	0.29

Note: All difference variables were scored such that positive values indicate improvements. All models controlled for baseline values.

Abbreviation: FSFI, Female Sexual Function Index.

[a]Glass's Δ, which used only the ME group's standard deviation, was used as the measure of effect size due to unequal standard deviations between conditions. Other effect sizes represent Hedges' *g*.
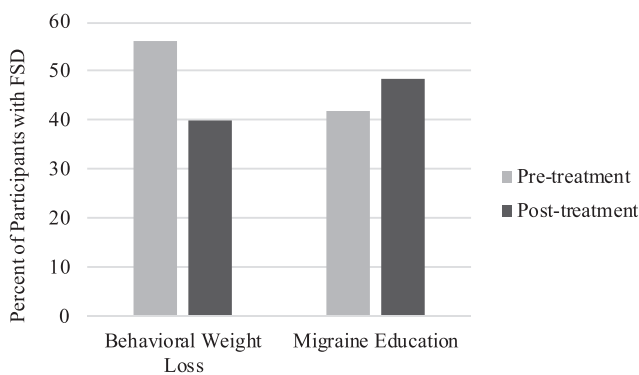

FIGURE 1 Change in rates of female sexual dysfunction (FSD) from pre- to post-treatment was not significantly different by treatment condition (*p* = .17)

relevant baseline values significantly predicted change in total FSFI scores (*p* = .001), and in the individual domains of desire (*p* < .001), arousal (*p* < .001), orgasm (*p* = .005), satisfaction (*p* < .001) and pain (*p* = .01), but not lubrication (*p* = .06). Table 4

displays standardized coefficients for change in headache characteristics and weight as predictors of each aspect of sexual functioning. As shown, greater weight loss predicted greater improvements in overall sexual functioning and in arousal, whereas greater reduction in migraine headache days per month predicted greater improvements in sexual satisfaction.

4 | DISCUSSION

This is the first study to assess treatment-related changes in FSD rates, sexual functioning and overall relationships between migraine, weight loss and sexual functioning among women with comorbid obesity and migraine. Statistically significant changes in FSD and sexual functioning were not observed with either BWL or ME treatment, despite mean improvements in headache frequency and pain intensity in both conditions and greater mean weight loss in the BWL condition. When examining the relationships between change in migraine, weight and sexual functioning across all participants, reductions in

TABLE 3 Change in sexual functioning among the full sample

	Pre-treatment	Post-treatment	F	p	Cohen's d
Total FSFI score	25.35 (7.48)	26.39 (7.09)	2.06	.16	0.14
Desire	3.16 (1.42)	3.33 (1.17)	1.19	.28	0.13
Arousal	4.06 (1.54)	4.37 (1.35)	3.57	.06	0.21
Lubrication	4.75 (1.43)	4.84 (1.49)	0.32	.58	0.06
Orgasm	4.23 (1.63)	4.52 (1.57)	3.13	.08	0.18
Satisfaction	4.34 (1.52)	4.39 (1.39)	0.10	.75	0.03
Pain	4.82 (1.88)	4.94 (1.75)	0.34	.56	0.07

Abbreviation: FSFI, Female Sexual Function Index.

TABLE 4 Pre- to post-treatment change in migraine characteristics and body weight as predictors of change in sexual functioning

Predictors of interest	Total FSFI score (β)	Specific domain of sexual functioning (β)					
		Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain
Δ Headache days	0.18	0.19	0.005	0.04	0.05	0.32[*]	0.15
Δ Headache pain intensity	0.16	0.10	0.16	0.19	0.13	0.07	−0.01
Δ Body weight (kg)	0.28[*]	0.18	0.26[*]	0.20	0.23	0.07	0.22

Note: Change variables were scored such that more positive values indicate greater improvement. All three predictors of interests were entered into a single model. Each model controlled for pre-treatment headache days, headache pain intensity and body weight, as well as baseline values for the sexual functioning variable of interest. All full models were significant at $p < .05$ except for lubrication, which was non-significant ($p = .06$).

Abbreviation: FSFI, Female Sexual Function Index.

[*]$p < .05$.

both body weight and headache frequency independently contributed to improvements in unique aspects of sexual functioning.

The statistically non-significant effect of BWL treatment on FSD rates and sexual functioning was inconsistent with both our hypothesis and findings from several previous studies suggesting that weight loss intervention improves sexual functioning.[9,13,34] It is possible that the observed modest weight loss among BWL participants was insufficient to produce larger improvements in sexual functioning. Mean weight loss in the BWL intervention was 3.8 kg, and only a subset (23%) of participants in the BWL intervention achieved the ≥7% weight loss goal, which represents a somewhat lower percentage of participants obtaining clinically significant weight loss than has been observed in previous BWL trials involving samples without migraine.[35] Particularly given that several prior studies of the impact of weight loss on sexual function have been conducted in the context of bariatric surgery[26,27,36–40] or in behavioural treatments[34] with larger observed weight losses, further research is warranted that examines whether greater changes in weight, perhaps achieved with longer or more intensive treatment, can improve sexual functioning in this population. It is also possible that our sample size limited our ability to detect effects. Although the magnitude of change in rates of FSD and in sexual functioning did not statistically differ between BWL and ME, the pattern of findings for FSD rates indicated that rates increased in ME and decreased in BWL at magnitudes that may indicate clinically significant differences between conditions. We also observed large treatment condition effects for overall sexual functioning and medium-sized effects for sexual functioning specific to orgasm in favour of greater improvements in sexual functioning in BWL. Thus, additional research involving larger samples that tests the effects of BWL and other weight loss treatments on sexual functioning in women with migraine is warranted.

Across conditions, reductions in body weight and headache frequency independently related to improvements in distinct aspects of sexual functioning. Participants who lost more weight, regardless of their treatment condition, reported greater improvements in overall sexual functioning. These improvements were observed independent of the effects of reductions in migraine frequency and pain intensity, indicating that weight loss in and of itself can improve sexual functioning among women who have comorbid migraine and obesity. These findings align with and extend results from previous studies

with individuals with obesity, but not specifically comorbid migraine, that have revealed benefits of weight loss on sexual functioning among women.[9,13,26,27,36–40] Consistent with some prior work,[37–40] weight loss also improved sexual arousal, in particular. As arousal reflects several physiological aspects of sexual functioning, such as feelings of warmth or tingling in the genitals and muscle contractions, these findings suggest that the benefits of weight loss on sexual functioning may occur largely via improvements in physiological sexual responsivity. In contrast, after accounting for weight loss, we found that reductions in migraine frequency were associated specifically with increased feelings of sexual intimacy, as reflected by perceived emotional closeness during sexual activities and satisfaction with both one's sexual relationship and overall sexual life. Thus, it appears that reductions in body weight and headache frequency might target distinct domains of sexual functioning among women with migraine and overweight/obesity and that weight loss also predicts overall sexual functioning improvement.

We did not observe any statistically significant or medium- to large-sized effects to suggest ME improved FSD or sexual functioning. These findings suggest that this migraine-specific intervention, although effective in reducing migraine frequency and severity, did not have a robust or broad effect on sexual functioning. These findings add to the mixed literature on the direct relationship between migraine severity and degree of impairment in sexual functioning[11,12,15–19] and highlight the multifactorial aetiology of FSD.[41] Rates of FSD in this sample were also lower compared with several previous estimates of FSD among individuals with migraine,[10,11,17] perhaps partially owing to our sample being limited to younger, reproductive-aged women, who tend to have lower rates of FSD compared with older women.[42] Additionally, we limited our analyses to women who reported being sexually active at both pre- and post-treatment to obtain the most accurate FSD estimates and ratings of sexual functioning; it is unclear whether previous studies that used the FSFI included participants who did not report being sexually active, resulting in artificially high FSD rates. Further study of rates of FSD among reproductive-aged women with both migraine and obesity and of treatment-related changes in sexual functioning in other samples of women with comorbid migraine and obesity is thus warranted. Consistent with prior work that has failed to observe relationships between migraine headache pain intensity and sexual

functioning,[11,12,15,17] we also found that migraine headache pain intensity was unrelated to sexual functioning when examined across all participants. It may be that the intensity of migraine headache pain simply has less bearing on sexual activity (e.g., women do not have interest in sexual activities if pain is present, regardless of its intensity). It is also possible that individuals' reactivity to their pain, such as their acceptance versus catastrophizing of it, is more influential than pain severity itself on functioning.[43–45]

Strengths of the current study include recruitment of women with comorbid obesity and neurologist-confirmed migraine, assessment of sexual functioning using a validated measure and of headache characteristics using daily surveys, and examination of the relationships between migraine, obesity and sexual functioning in a trial that enabled prospective assessment of the independent effect of headache improvement versus the combined effect of headache improvement plus weight loss on sexual functioning. Study limitations include a limited sample size, which may have been a cause of non-significant results, a demographically homogenous sample and failure to assess either sexual distress, which is a clinically and diagnostically important aspect of FSD, or relationship satisfaction, which may impact sexual functioning. We also only included women who reported sexual activity at both time points. Although we made this decision to obtain the most accurate FSD estimates and evaluations of sexual functioning, future studies may wish to examine how treatment of migraine and/or obesity may influence initiation (or avoidance) of sexual activity.

There are several important directions for future research. First, larger, fully powered trials are needed to clarify the nature and magnitude of the effects of BWL and ME on sexual functioning among women with comorbid migraine and obesity, particularly given that the effect sizes observed in the present study signalled potential benefits of BWL. Future studies should also seek to further disentangle the effects of obesity and migraine on sexual functioning through prospective examination of their unique and contributing influences on sexual functioning in interventions with greater treatment duration and/or dose (e.g., a randomized trial examining the effects of ME vs. BWL vs. ME + BWL). In addition, as physiological responsivity during sexual interactions reflects both physical and mental excitement and can be influenced by multiple biopsychosocial factors (e.g., biology and body image), further research is needed to clarify the underlying mechanisms by which weight loss improves sexual functioning and arousal, in particular.

In conclusion, although neither ME or BWL treatment significantly improved sexual functioning among women with obesity and migraine, greater weight loss and larger reductions in migraine headache frequency both related to improvements in unique aspects of sexual functioning across intervention conditions. Specifically, women who lost more weight experienced greater improvements in overall and in physiological aspects of sexual functioning (i.e., arousal), whereas reduced migraine headache frequency related to improved sexual satisfaction. Future studies that further investigate the independent and combined effects of weight change and migraine improvements on sexual functioning, as well as mechanisms of action, with larger samples are warranted.

AUTHOR CONTRIBUTIONS

All authors contributed to conception and design. DSB and JGT acquired the data. DSB, JGT and LMS analysed and interpreted the data. LMS and DSB drafted the manuscript. All authors revised it for intellectual content. All authors approved the final version of the completed manuscript.

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