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Fluoxetine-Induced Changes in Tactile Sensation and Sexual Functioning among Clinically Depressed Women

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Sexual side effects resulting from serotonin specific reuptake inhibitors (SSRIs) use may be mediated by a number of peripheral mechanisms, including alterations in tactile sensitivity. It was hypothesized that sexual difficulties resulting from SSRI use arise in part from an over-sensitivity or under-sensitivity of tactile sensation. Tactile sensitivity was examined on the index finger and lower lip in clinically depressed women at baseline (pre-medication), week 1, week 4, and week 8 of drug treatment (fluoxetine group n = 12, control n = 13). Analyses indicated that fluoxetine treatment resulted in decreased orgasm functioning. Fluoxetine-induced sexual changes were not mediated by tactile sensation. An independent association was found between sexual arousal functioning and finger sensation. Novel to this study, an independent association was found between sexual desire and finger sensation.

It is well established that antidepressant medications such as the serotonin specific reuptake inhibitors (SSRIs) often produce sexual side effects (Clayton et al., 2002; King & Horowitz, 1993; Michael & Andrews, 2002; Waldinger & Olivier, 1998), but the underlying mechanisms are poorly understood. Our current knowledge of how SSRIs impact sexual functioning suggests a

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combination of central and peripheral serotonergic mechanisms, and receptor subtypes 5-HT_2 and 5-HT_3 have been specifically implicated (Gelenberg et al., 2000; Preskorn, 1995; Robinson et al., 1996). Only 1%–2% of serotonin is located in the central nervous system (Cooper, Bloom, & Roth, 2003), suggesting that the peripheral effets of serotonin may play an important role in SSRI-induced sexual dysfunction.

SSRI-induced fluctuations in peripheral serotonin may be of sufficient magnitude to influence cutaneous sensation. Animal studies show that serotonin receptors are located in the nerves that innervate sexual organs (Amenta, Vega, Ricci, & Collier, 1992; Berkley, Robbins, & Sato, 1993), on 32% of the axons in the glabrous (hairless) skin of the rat, and in free nerve endings and in the Pc corpuscle (Carlton & Coggeshall, 1997). In the cat, serotonin excited cutaneous afferent fibers of slowly adapting pressure receptors produced a weak response in free nerve cells and thermoreceptors, and produced no response in hair receptors (Fjallbrant & Iggo, 1961). In rodents, peripheral alterations of serotonin may produce either hyperalgesia (Dirksen, Van Luijtelaar, & Van Rijn, 1998; Fasmer, Post, & Hole, 1987) or hypoalgesia (Hong & Abbott, 1994; Taiwo & Levin, 1992). In humans, it has been suggested that serotonin antagonists may be useful in the treatment of pain (Hong & Abbott, 1994; Taiwo & Levin, 1992), and some anecdotal reports indicate vaginal anesthesia resulting from SSRI use (Ellison & DeLuca, 1998; King & Horowitz, 1993). SSRIs increase the incidence of paresthesias as compared to placebo controls (Preskorn, 1995) and fluoxetine use was associated with changes in vibrotactile sensation in men (Yilmaz, Tatlisen, Turan, Arman, & Ekmenkcioglu, 1999). Anesthesia resulting from excessive vaginal stimulation is associated with heightened 5-HT activity in the spinal cord (Crowley, Rodriguez-Sierra, & Komisaruk, 1977; Steinman, Komisaruk, Yaksh, & Tyce, 1983; Whipple & Komisaruk, 1985). 5-HT receptor adaptations resulting from chronic SSRI use may amplify analgesia from vaginal stimulation to inhibit sexual function.

This study was designed to examine whether sexual difficulties secondary to SSRI use arise in part from an over-sensitivity or under-sensitivity of tactile receptors. If peripheral serotonin activity changes with SSRI use, it is possible that individuals who previously experienced normal sexual functioning experience changes in tactile sensitivity that may adversely impact sexual function (Frohlich & Meston, 2000).

METHOD

Design

The outcome variable was sexual functioning (sexual desire, orgasm), and the predictor variables were, within subject, tactile sensation (finger tactile sensation threshold [FT], lip tactile sensation threshold [LT], and between

subject, medication group (fluoxetine, control). This was a repeated measures design. Data were collected at baseline, week 1, week 4, and week 8 of drug treatment.

Participants

Participants were females (18–35 years of age), who met *DSM-IV-TR* (American Psychiatric Association [APA], 2000) criteria for a mood disorder (excluded for manic or hypomanic episodes). Fluoxetine participants ($n = 12$) were referred by psychiatrists at the University of Texas Counseling Center as good candidates for a fluoxetine treatment study. Control participants ($n = 13$) were students in Introduction to Psychology classes at the University of Texas at Austin who indicated on an Internet prescreening that they were female, sexually active, and potentially experiencing a clinically significant mood disorder (Beck Depression Inventory [BDI] score > 10). To determine eligibility for the study, all potential participants were interviewed by a Masters level clinical psychology student (control participants indicated on interview that they were not interested in receiving antidepressant medication). Participants were excluded if they had received antidepressant treatment within the past six months, and for sexual difficulties not better accounted for by depression. Three fluoxetine participants and one control participant withdrew after the first visit and thus were not included in later statistical analysis. Five of 12 (38%) fluoxetine and eight of 13 (42%) control participants reported using oral contraceptives.

Medication

Fluoxetine participants received 20 mg of fluoxetine daily for two months, as prescribed by their psychiatrists (donated by Eli Lilly, Inc.).

Measures

Beck depression inventory (BDI)

The BDI is a brief, 21-item, measure of depressive symptomology and was used to compare degree of depressive symptomology across groups (Beck & Beamesderfer, 1974).

Derogatis sexual functioning inventory (DSFI)

On the DSFI Experience subtest participants indicate (yes/no) whether they have ever engaged in 24 activities including petting, oral sex, intercourse, and masturbation (Derogatis, 1978). Validity and reliability coefficients are within acceptable ranges (please see Andersen & Broffitt, 1988; Derogatis & Melisaratos, 1979). The Experience subtest of the DSFI was used to ensure that all participants were sexually experienced, and that the two groups do not differ significantly in sexual experience.

Female sexual functioning index (FSFI)

The FSFI is a brief 19-item measure for women that provides desire, arousal, lubrication, orgasm, satisfaction, and pain domain scores and a total score (Rosen et al., 2000). Normative data is available for normally functioning women (Rosen et al.), women with Female Sexual Arousal Disorder (FSAD) (Rosen et al.) and women with Female Orgasmic Disorder (FOD) (Meston, 2003). The FSFI was used to evaluate sexual functioning.

Tactile sensitivity

Tactile sensitivity was measured using Von Frey monofilaments on the distal portion of the index finger of the dominant hand and on the corresponding side of the lower lip (e.g., right index finger, right side of lower lip). A Von Frey monofilament is a hair-like fiber that, when pressed against the skin until the hair bends, applies a specific force that depends on the diameter and length of the hair. Monofilaments were made by gluing polypropylene suture thread (Ethicon Prolene Sutures, Med-Vet International, Illinois) to commercially produced plastic monofilament casings (a pen-like instrument; North Coast Medical, San Jose, CA) and calibrated using an analytical balance (Eliav & Gracely, 1998). Based on pilot testing, finger and lip monofilaments were 6, 8, 10, 20, 30, 40, and 80 mg and 2, 4, 6, 8, 10, 20, and 40 mg, respectively.

Procedure

Eligible participants who provided written consent participated in a baseline, week 1, week 4, and week 8 session. Fluoxetine participants received medication immediately following the baseline visit. All examiners were female and blind to participants sexual functioning status.

At each session, participants sat in a comfortable recliner. To ensure the monofilaments were accurately placed over repeated tests, a water-soluble circular ink mark 1 cm diameter was placed on the finger. On the lips, the monofilament was placed in the middle of the selected half of the lower lip. During testing, participants were asked to close their eyes, relax, place their hand palm side up, and tilt their head toward the experimenter. The monofilaments were presented using a forced choice paradigm and the method of constant stimuli, procedures previously demonstrated to provide an accurate estimate of threshold (e.g., Bell-Krotoski & Tomancik, 1987, Maaser & Farley, 1980). Specifically, the experimenter cued the participant to attend to her tactile sensations by saying “okay,” and on either the count of “one” (1.5 seconds) or “two” (1.5 seconds), the monofilament was pressed against the participant’s skin until it bent, and was held for 1.5 seconds. The participants indicated on which count they felt the stimuli, and were instructed to guess if they were not sure.

A broad range of monofilament sizes were used initially, and then based on each participant’s performance, a smaller set of monofilament sizes were

selected that best reflected the participant's range of sensation. That is, seven different monofilament sizes were applied, in semi-random order, 10 times each. Four or five of the original seven monofilaments were then applied, in semi-random order, 20 times each. Combining the data from the two stages, the selected monofilaments were applied a total of 30 trials each. Between stages, the participants filled out questionnaires.

At the end of the study, participants were debriefed and provided therapy referral information. Fluoxetine participants received two months medication and control participants received 3.5 hours of Introduction to Psychology experiment credit. Participants who completed all four visits received $50 and those who withdrew prior to the final visit received $20.

DATA REDUCTION

Raw scores for each monofilament size were converted to percent correct scores such that 100% correct indicates full tactile sensation and 50% correct indicates no tactile sensation (chance levels of perception). Perceptual sensitivity to different monofilament sizes was plotted by fitting the data to a cumulative normal distribution. Specifically, the true cumulative normal psychometric function of each participant was estimated by employing the least-squares method to calculate the curve that best fit the percent correct scores of the five monofilament sizes. Threshold was defined as the interpolated monofilament size at which the subject was 84% correct because, theoretically, this is the point at which threshold estimate variability is least (Green, 1990).

RESULTS

Group Differences at Baseline

A series of independent *t*-tests were used to verify that the fluoxetine and control groups did not differ at baseline. Due to the increased likelihood of Type I errors when multiple statistical tests are performed, only mean differences of $p < .006$ ($p < .05/9$) were considered statistically significant. Group comparisons are illustrated in Table 1.

Fluoxetine-Induced Changes in Tactile Sensation and Sexual Functioning

Hierarchical linear modeling Version 5 (HLM) was used (Bryk & Raudenbush, 1992; Bryk, Raudenbush, & Congdon, 1996) to examine changes in tactile sensation and sexual functioning over time, and whether tactile sensitivity mediated antidepressant-induced sexual dysfunction.

TABLE 1. Sexual Functioning in Fluoxetine and Control Groups at Baseline

Measure	Control ($n = 13$) mean (*SD*)	Fluoxetine ($n = 12$) mean (*SD*)	p
Depression (BDI)	23.4 (8.5)	25.1 (8.0)	>.05
DSFI sexual experience	20.7 (2.8)	19.6 (5.3)	>.05
FSFI			
Sexual desire	6.8 (2.4)	6.6 (2.3)	>.05
Arousal	13.2 (5.6)	14.6 (4.2)	>.05
Lubrication	14.9 (6.0)	16.1 (3.5)	>.05
Orgasm	8.6 (4.5)	10.8 (3.8)	>.05
Satisfaction	11.3 (2.8)	10.4 (4.8)	>.05
Pain	11.2 (4.7)	10.6 (4.3)	>.05
Total score	25.0 (8.2)	25.8 (5.5)	>.05

Fluoxetine-Induced Changes in Tactile Sensation

To evaluate fluoxetine-induced changes in finger threshold, finger threshold was entered as the outcome variable, time as a Level 1 predictor variable, and group as a Level 2 variable. Finger threshold significantly declined from baseline to week 1 ($\beta = -12.87$, $SE = 5.91$, $t = -2.18$, $p = .03$) and medication did not change the temporal pattern ($p > .30$). Finger threshold did not significantly change from baseline to weeks 4 or 8 ($p > .20$), and medication did not change the temporal pattern ($p > .20$). This indicates that practice effects may account for significant improvements in finger sensation from baseline to week 1.

To evaluate fluoxetine-induced changes in lip threshold, lip threshold was entered as the outcome variable, time as a Level 1 predictor variable, and group as a Level 2 variable. Lip threshold did not significantly decline from baseline to week 1 ($p > .9$) or baseline to week 8 ($p > .10$) and medication did not alter the temporal pattern ($p > .90$; $p > .10$). Lip threshold significantly declined from baseline to week 4 ($\beta = -4.86$, $SE = 2.14$, $t = -2.27$, $p = .02$) and medication did not alter the temporal pattern ($p > .05$). This indicates that the control group may have exhibited practice-related improvements between baseline and week 4, while the fluoxetine group tended to show declines in lip sensitivity. The correlation between finger and lip sensation was significant ($r = .32$, $p < .01$).

Tactile Sensation as a Mediator of Fluoxetine-Induced Changes in Sexual Functioning

Evaluation of the data indicated that change in sexual functioning over time was best described as a categorical variable: Categorical time was significantly better than no predictors and linear for the FSFI Desire domain (respectively, $\chi^2\,(2) = 43.17$, $p < .01$; $\chi^2\,(2) = 44.78$, $p < .01$), and the FSFI Orgasm

Domain (χ^2 (2) = 28.10, $p < .01$; χ^2 (2) = 33.61, $p < .01$). Thus, change over time was used in all models as a categorical variable (dummy coded: weeks 1, 4, and 8 were compared to the baseline visit).

First, HLM was used to evaluate if fluoxetine produced the expected sexual side effects. Sexual functioning (FSFI subscales: Desire, Lubrication, Orgasm) was entered as the outcome variable, time (baseline, week 1, 4, 8) as the Level 1 predictor variable, and medication group (fluoxetine, control) as the Level 2 predictor variable. Sexual desire, arousal, and orgasm were examined in separate models. Second, HLM was used to examine if tactile sensation mediated fluoxetine-induced sexual dysfunction. Sexual desire, arousal, and orgasm were entered as outcome variables, and time and tactile sensation were entered as Level 1 predictor variables. Fluoxetine and control groups, and finger sensation and lip sensation were entered in separate models.

Sexual desire

As illustrated in Table 2, the control group exhibited a significant decline in sexual desire from baseline to week 1, but not baseline to weeks 4 or 8. Medication did not alter the temporal changes in sexual desire from baseline to weeks 1 or 4, but significantly altered it from baseline to week 8. In the fluoxetine finger sensation mediation model, adding finger threshold did not alter the pattern of temporal change, indicating that finger threshold did not mediate antidepressant-induced declines in sexual desire. As illustrated in Figure 1 and Table 2, finger threshold had a significant independent association with sexual desire. In the fluoxetine lip sensation mediation model, adding lip threshold did not significantly alter the time slope, indicating that lip threshold did not mediate antidepressant-induced declines in sexual desire. Lip threshold did not have a significant independent association with sexual desire. In the control finger sensation mediation model, adding finger threshold strengthened the temporal change in sexual desire at week 8. Finger threshold did not have an independent association with sexual desire. In the control lip sensation mediation model, adding lip threshold strengthened the temporal change in sexual desire from baseline to week 1. Lip threshold did not have an independent association with sexual desire among the non-medicated participants.

Sexual arousal

As illustrated in Table 3, the control group did not exhibit a significant change in lubrication from baseline to weeks 1, 4, or 8. Medication did not alter the temporal changes from baseline to weeks 1, 4, or 8. In the fluoxetine finger sensation mediation model, adding finger threshold did not alter the pattern of temporal change in lubrication; that is, finger threshold did not mediate antidepressant-induced declines in lubrication. As illustrated in Figure 2 and Table 3, finger threshold had a significant independent

TABLE 2. Tactile Sensation as a Mediator of Antidepressant-Induced Problems with Sexual Desire

Model	Predictor variables		$\beta(\gamma)$**	*SE*	*t*	*p*
Manipulation check	Group	Time*				
	Control	Week 1	−1.333	.627	2.125	.033
		Week 4	−.453	.750	.604	$p > .05$
		Week 8	2.593	1.604	1.617	$p > .05$
	Fluoxetine	Week 1	(.853)	.808	1.055	$p > .05$
		Week 4	(−726)	.991	.733	$p > .05$
		Week 8	(−4.088)	1.877	2.178	.040
Fluoxetine	Tactile mediation	Time*				
	basic model	Week 1	−.519	.558	.930	$p > .05$
		Week 4	−1.220	.595	2.050	.047
		Week 8	−1.491	.953	1.564	$p > .05$
	FT in model	Week 1	−1.170	.593	1.971	$p > .05$
		Week 4	1.803	.621	2.904	.007
		Week 8	−1.938	.893	2.169	$p > .05$
		Indep. Assoc.	−.027	.007	3.859	.003
	LT in model	Week 1	−.373	.520	.717	$p > .05$
		Week 4	−.982	.580	1.692	$p > .05$
		Week 8	−1.375	1.091	1.261	$p > .05$
		Indep. Assoc.	−.070	.044	1.582	$p > .05$
Control	Tactile mediation	Time*				
	basic model	Week 1	−1.333	.678	1.967	$p > .05$
		Week 4	−.496	.691	.717	$p > .05$
		Week 8	2.625	1.586	1.655	$p > .05$
	FT in model	Week 1	−.882	.641	1.577	$p > .05$
		Week 4	.201	.680	.264	$p > .05$
		Week 8	3.400	1.635	2.216	.047
		Indep. Assoc.	.036	.023	1.973	$p > .05$
	LT in model	Week 1	−1.369	.675	2.026	.049
		Week 4	−.580	.704	.825	$p > .05$
		Week 8	2.694	1.536	1.754	$p > .05$
		Indep. Assoc.	.0004	.035	.010	$p > .05$

Note: FT: Finger Threshold; LT: Lip Threshold.

*Week 1, Week 4, and Week 8 are compared to Baseline.

**β denotes Level 1 slope coefficient change from baseline, γ denotes Level 2 slope coefficient change from baseline.

association with lubrication. In the fluoxetine lip sensation mediation model, adding lip threshold did not significantly alter the time slope; that is, lip threshold did not mediate antidepressant-induced declines in lubrication. Lip threshold did not have a significant independent association with lubrication. In the control finger sensation mediation model, adding finger threshold did not alter the temporal pattern. Finger threshold did not have an independent association with lubrication. In the control lip sensation model, adding lip

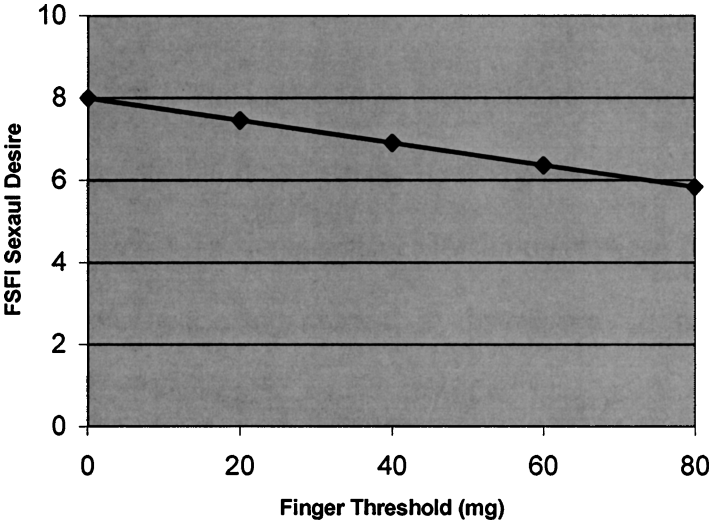

FIGURE 1. The independent association between finger sensation and sexual desire suggests that finger sensitivity decreases as sexual desire decreases.

threshold did not alter the temporal pattern. Lip threshold did not have a significant independent association with lubrication among the non-medicated participants.

Exploratory analyses indicated that changes in sexual arousal did not account for the association between sexual desire and finger thresholds. The independent association between sexual desire and finger threshold was significant with ($\beta = -.02, t = -2.47, p = .03$) and without ($\beta = -.03, t = -3.86, p < .01$) the FSFI Lubrication domain in the model, despite a strong independent association between FSFI Desire and Lubrication domain scores ($\beta = .22, t = 3.93, p < .01$).

Orgasm

As illustrated in Table 4, the control group did not exhibit any significant changes in orgasm functioning from baseline to weeks 1, 4, or 8, and medication only significantly altered temporal changes in orgasm functioning from baseline to week 8. In the fluoxetine finger sensation mediation model, adding finger threshold strengthened the temporal change in orgasm from baseline to week 1, but did not alter the temporal change in sexual desire from baseline to week 4 or week 8. That is, finger threshold did not mediate antidepressant-induced declines in orgasmic ability. Finger threshold did not have an independent association with orgasm. In the fluoxetine lip sensation mediation model, adding lip threshold did not alter the temporal change in orgasm ability. That is, lip threshold did not mediate antidepressant-induced declines in orgasmic ability. Lip threshold did not have a significant independent association with orgasm ability. In the control finger sensation mediation

TABLE 3. Tactile Sensation as a Mediator of Antidepressant-Induced Problems with Vaginal Lubrication

Model	Predictor variables		$\beta(\gamma)^{**}$	*SE*	*t*	*p*
Manipulation check	Group	Time*				
	Control	Week 1	−3.750	2.255	1.663	$p > .05$
		Week 4	.017	2.608	.007	$p > .05$
		Week 8	−.974	2.106	.462	$p > .05$
	Fluoxetine	Week 1	(.973)	2.613	.372	$p > .05$
		Week 4	(.274)	2.773	.099	$p > .05$
		Week 8	(−.370)	3.053	.121	$p > .05$
Fluoxetine	Tactile mediation	Time*				
	basic model	Week 1	−2.796	1.372	2.038	.049
		Week 4	.274	1.463	.187	$p > .05$
		Week 8	−1.442	1.658	.869	$p > .05$
	FT in model	Week 1	−2.784	1.322	2.106	.042
		Week 4	.400	1.385	.289	$p > .05$
		Week 8	−.584	1.537	.380	$p > .05$
		Indep. Assoc.	−.076	.021	3.676	.004
	LT in model	Week 1	−1.990	1.213	1.641	$p > .05$
		Week 4	1.223	1.347	.908	$p > .05$
		Week 8	−.014	1.543	.009	$p > .05$
		Indep. Assoc.	.025	.088	.286	$p > .05$
Control	Tactile mediation	Time*				
	basic model	Week 1	−3.750	2.807	1.336	$p > .05$
		Week 4	.1798	2.813	.064	$p > .05$
		Week 8	−.937	3.042	.308	$p > .05$
	FT in model	Week 1	−3.768	2.842	1.326	$p > .05$
		Week 4	.104	2.847	.037	$p > .05$
		Week 8	−.826	3.073	.269	$p > .05$
		Indep. Assoc.	−.0006	.021	.030	$p > .05$
	LT in model	Week 1	−3.739	2.803	1.334	$p > .05$
		Week 4	−.482	2.854	.169	$p > .05$
		Week 8	−1.783	3.099	.575	$p > .05$
		Indep. Assoc.	.050	.040	1.238	$p > .05$

Note: FT: Finger Threshold; LT: Lip Threshold.

*Week 1, Week 4, and Week 8 are compared to Baseline.

**β denotes Level 1 slope coefficient change from baseline, γ denotes Level 2 slope coefficient change from baseline.

model, adding finger threshold did not alter the pattern of temporal change in orgasm ability; orgasm ability did not significantly change at weeks 1, 4, or 8. Finger threshold did not have a significant independent association with orgasm. In the control lip sensation mediation model, adding lip threshold did not alter the pattern of temporal change in orgasm ability; orgasm did not significantly change at weeks 1, 4, or 8. Lip threshold did not have an independent association with orgasm.

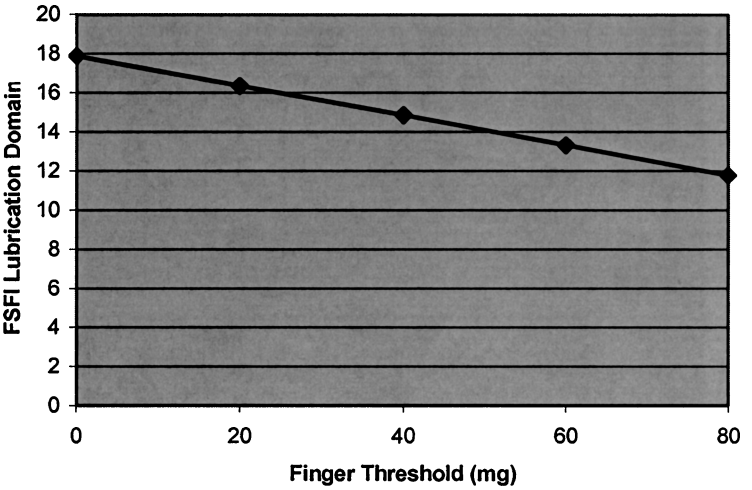

FIGURE 2. The independent association between finger sensation and sexual arousal suggests that finger sensitivity decreases as sexual arousal decreases.

DISCUSSION

This study examined tactile sensitivity and sexual functioning in depressed women receiving fluoxetine treatment, and a comparison group of depressed women who were antidepressant-medication free. In order to test the hypothesis that tactile sensation mediates fluoxetine-induced sexual dysfunction, it was critical that the participants receiving fluoxetine treatment experienced to some extent the expected sexual side effects noted with fluoxetine treatment (i.e., decreased desire, delayed or inhibited orgasm). The manipulation was successful with regard to orgasm functioning; the control group did not exhibit significant changes in orgasmic functioning, while the fluoxetine group experienced significant declines in orgasmic functioning following eight weeks of fluoxetine treatment. The control group exhibited significant improvements in sexual desire, while the fluoxetine group did not exhibit significant changes in sexual desire. No changes in arousal functioning were noted in either the control or fluoxetine groups. This finding was not surprising, however, as arousal dysfunction is not among the more commonly reported fluoxetine-induced sexual side effects (Feiger, Kiev, Shrivastava, Wisselink, & Wilcox, 1996; Meston & Gorzalka, 1992; Montejo-Gonzalez et al., 1997; Patterson, 1993; Pearlstein & Stone, 1994; Preskorn, 1995).

The hypothesis that finger or lip sensation mediated fluoxetine-induced changes in sexual functioning was not supported. These findings suggest that if tactile sensation mediates fluoxetine-induced sexual dysfunction, the changes in tactile sensation are not systemic (i.e., affecting all regions of the body), and do not involve punctate sensation. That is, it is possible that genital measures of vibrotactile sensation, temperature sensation, or pain

TABLE 4. Tactile Sensation as a Mediator of Antidepressant-Induced Problems with Orgasm

Model	Predictor variables		$\beta(\gamma)$**	*SE*	*t*	*p*
Manipulation check	Group	Time*				
	Control	Week 1	−1.821	1.323	1.376	$p > .05$
		Week 4	.318	1.514	.210	$p > .05$
		Week 8	1.460	1.321	1.105	$p > .05$
	Fluoxetine	Week 1	(.090)	1.895	.047	$p > .05$
		Week 4	(−3.880)	2.223	1.744	$p > .05$
		Week 8	(−4.180)	1.992	2.097	.036
Fluoxetine	Tactile mediation	Time*				
	basic model	Week 1	−1.732	.997	1.737	$p > .05$
		Week 4	−3.407	1.066	3.197	.003
		Week 8	−2.793	1.211	2.307	.027
	FT in model	Week 1	2.588	.965	2.683	.011
		Week 4	−4.013	1.027	3.910	.001
		Week 8	−2.555	1.143	2.235	.032
		Indep. Assoc.	−.097	.045	2.168	$p > .05$
	LT in model	Week 1	−1.742	1.014	1.717	$p > .05$
		Week 4	−2.787	1.101	3.075	.005
		Week 8	−2.787	1.243	2.243	.031
		Indep. Assoc.	−.11	.062	.176	$p > .05$
Control	Tactile mediation	Time*				
	basic model	Week 1	−1.750	1.514	1.156	$p > .05$
		Week 4	.492	2.041	.241	$p > .05$
		Week 8	1.284	1.669	.769	$p > .05$
	FT in model	Week 1	−1.729	1.444	1.198	$p > .05$
		Week 4	.161	2.034	.079	$p > .05$
		Week 8	1.599	1.622	.986	$p > .05$
		Indep. Assoc.	.017	.014	1.191	$p > .05$
	LT in model	Week 1	−1.598	1.404	1.138	$p > .05$
		Week 4	1.378	1.994	.691	$p > .05$
		Week 8	2.292	1.603	1.430	$p > .05$
		Indep. Assoc.	.052	.028	1.868	$p > .05$

Note: FT: Finger Threshold; LT: Lip Threshold.

*Week 1, Week 4, and Week 8 are compared to Baseline.

**β denotes Level 1 slope coefficient change from baseline, γ denotes Level 2 slope coefficient change from baseline.

sensation mediate antidepressant-induced sexual side effects while finger and lip punctate sensation does not. It also is possible that tactile sensation may mediate antidepressant-induced changes in sexual functioning, but not among depressed women. A placebo-controlled trial of fluoxetine as a treatment for premature ejaculation found that the fluoxetine group, but not the control group, exhibited a significant increase in penile sensory threshold and intravaginal latency following one month of medication treatment (Yilmaz et al., 1999).

Consistent with previous studies (Frohlich & Meston, 1999), an independent association was found between finger tactile sensation and arousal functioning. That is, in the fluoxetine group, as arousal functioning decreased finger thresholds increased—women reporting greater arousal problems exhibited less sensitive skin on their fingers. This indicates that the association between finger tactile sensation and arousal dysfunction is present among women with FSAD, as well as among clinically depressed women receiving fluoxetine. No significant independent associations were found between lip sensation and arousal functioning in the fluoxetine group, and between finger or lip sensation and arousal functioning in the control group.

A novel finding was that among the fluoxetine and control participants, finger threshold had a significant independent association with sexual desire, such that as sexual desire decreased, finger threshold increased. It is possible that central nervous system (CNS) processing of tactile information may account for the association between tactile sensation and sexual desire, and possibly sexual arousal, as sexual desire is likely to be controlled by CNS mechanisms. Cognitive factors such as attentional focus, performance demand, and distraction could explain the association between sexual desire and arousal, and tactile sensation (Barlow, 1986; Cranston-Cuebas & Barlow, 1990). That is, it is possible that the CNS processing of sexually relevant tactile stimuli (e.g., kissing and caressing) and non-sexually relevant tactile stimuli (e.g., tactile stimuli in the tactile examination) is altered in women who are distracted or self-focused, such that they require greater tactile stimulation before conscious perception occurs.

This study contained several limitations. First, only one type of cutaneous sensation was measured, punctate sensation. It is possible that some types of cutaneous sensation, such as vibrotactile, temperature, and pain sensation, are associated with sexual dysfunction, while others are not. Second, the behavior being examined was sexual functioning yet no measures of genital tactile sensation were obtained; only finger and lip threshold were measured in this study. Third, significant declines in sexual desire functioning among fluoxetine participants were not observed. Problems with sexual desire are a common side effect of fluoxetine treatment (Feiger et al., 1996; Meston & Gorzalka, 1992; Montejo-Gonzalez et al., 1997; Patterson, 1993; Pearlstein & Stone, 1994; Preskorn, 1995), and for the medication manipulation to be successful, the fluoxetine group would need to exhibit significant declines in sexual desire. Fourth, this study lacked placebo control, random assignment, and double-blind design. It is possible that despite efforts to find an appropriately matched control group, the two groups were not ultimately equivalent. The fluoxetine group may have had different expectations and hopes than the control group. Without a placebo control, such medication expectancies were not controlled for.

The findings from this study suggest that tactile sensation does not mediate fluoxetine-induced sexual dysfunction among depressed women; future

studies will need to consider one of two explanations for these findings. First, that tactile sensation mediates fluoxetine-induced sexual dysfunction, but measures of punctate sensation on the fingers and lips will not detect this association. Thus, it will be important that future studies conduct a comprehensive examination of tactile sensation (e.g., measures of tactile sensation, such as vibrotactile, pain, or temperature sensation, and nerve conduction velocity on genital and non-genital tissue) so that its role in fluoxetine-induced sexual dysfunction can be more clearly identified. Second, that tactile sensation does not mediate fluoxetine-induced sexual dysfunction, in which case future studies would need to consider alternative explanations for fluoxetine-induced sexual dysfunction.

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