Psychostimulant Augmentation During Treatment With Selective Serotonin Reuptake Inhibitors in Men With Paraphilias and Paraphilia-Related Disorders: A Case Series

Martin P. Kafka, M.D., and John Hennen, Ph.D.

Background: We describe an open trial of psychostimulants (primarily methylphenidate sustained release [SR]) added to selective serotonin reuptake inhibitors (SSRIs; primarily fluoxetine) during the course of pharmacologic treatment of men with paraphilias and paraphilia-related disorders (PRDs).

Method: Twenty-six men with paraphilias (N = 14) or PRDs (N = 12) were assessed for lifetime mood disorders and attention-deficit/hyperactivity disorder (ADHD) as defined by DSM-IV. All men were assessed at baseline for total sexual outlet and average time per day associated with paraphilia/PRD sexual behaviors. The indications for the addition of a psychostimulant to a stable dose of SSRI included the retrospective diagnosis of ADHD with persistent adult symptoms despite pharmacotherapy with an SSRI (N = 17); residual paraphilia/PRD fantasies, urges, and activities despite SSRI pharmacotherapy (N = 16); the persistence or presence of residual depressive symptoms despite SSRI pharmacotherapy (N = 6); relapse or loss of SSRI efficacy during the treatment of sexual impulsivity disorders (N = 4); and treatment of SSRI-induced side effects (N = 4).

Results: SSRI pharmacotherapy (mean ± SD duration = 8.8 ± 11.1 months) had statistically significant effects in diminishing paraphilia/PRD-related total sexual outlet ($p < .001$) and average time/day spent in paraphilia/PRD sexual behavior ($p < .001$). Addition of methylphenidate SR (mean dose = 40 mg/day; mean ± SD duration = 9.6 ± 8.2 months) was associated with additional statistically significant effects on paraphilia/PRD-related total sexual outlet ($p = .003$) and average time per day ($p = .04$) in addition to improvement of putative residual ADHD and depressive symptoms.

Conclusion: Methylphenidate SR can be cautiously and effectively combined with SSRI antidepressants to ameliorate paraphilias and paraphilia-related disorders for the indications listed above.

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Received Jan. 19, 2000; accepted March 15, 2000. From the Department of Psychiatry, Harvard Medical School, Boston (Dr. Kafka); and the Biostatistics Laboratory (Dr. Hennen), McLean Hospital, Belmont (Dr. Kafka), Mass.

Reprint requests to: Martin P. Kafka, M.D., McLean Hospital, 115 Mill St., Belmont, MA 02478 (e-mail: mpkafka@aol.com).

The primary pharmacologic treatment for paraphiliac disorders, especially sex offender paraphiliacs, has been the use of parenterally administered antiandrogens such as medroxyprogesterone acetate and cyproterone acetate.[1] Since 1991, however, there have been case reports,[2-5] prospective open-label clinical trials,[6–8] and retrospective chart-review reports[9,10] of the efficacy of selective serotonin reuptake inhibitors (SSRIs) for both paraphilias and paraphilia-related disorders (PRDs) in nearly 200 outpatient men.[11] Paraphiliac disorders, as recognized by our current diagnostic nomenclature, are socially deviant, persistent, highly arousing sexual fantasies, urges, or behaviors that cause personal distress and/or significant psychosocial impairment.[12] Paraphilia-related disorders, also referred to as nonparaphiliac sexual addictions or sexual compulsivity, are not included in the diagnostic nomenclature of the DSM-IV. These disorders include socially accepted forms of sexual expression that become intrusive, repetitive, and time consuming and are accompanied by personal distress and significant psychosocial impairment.[13,14] Common PRDs include compulsive masturbation, protracted promiscuity, pornography dependence, dependence on "anonymous" sexual outlets such as phone sex or Internet "cybersex," and severe sexual desire incompatibility.[15]

The rationale for the prescriptive use of SSRIs for the amelioration of paraphilias and PRDs is based on several lines of converging clinical and biological evidence. These include the sexually disinhibiting effects of low central serotonin on male mammalian appetitive sexual behavior,[16,17] the sexual dampening side effects of prescribed SSRIs in humans,[18] and the comorbid presence of depressive symptoms and dysthymic disorder in men with paraphilias and PRDs.[19,20] Despite the increasing clinical use of SSRIs for paraphilias and PRDs, there are no published placebo-controlled trials with these agents

for these disorders, and, in the available literature, outcomes after pharmacotherapy have been measured only for the short term (e.g., 12 weeks), except in 2 reports.[7,10] Overall, the published clinical data support the efficacy of SSRIs for the amelioration of both paraphilias and PRDs.

Some men with paraphilias and PRDs meet retrospective diagnostic criteria of attention-deficit/hyperactivity disorder (ADHD).[20] The concurrent treatment of ADHD in sexually impulsive men, however, has not been reported. Psychostimulant medications, the primary pharmacologic treatment for ADHD, may counteract SSRI tolerance,[21] augment the antidepressant effects of SSRIs,[22–24] and reduce or even reverse SSRI-induced sexual dysfunction[25] during the course of treatment of depressive disorders. In addition, there is some anecdotal clinical[26] and genetic evidence[27] that ADHD itself may have a disinhibiting effect on male sexual appetite and behavior. Pharmacologic tolerance to SSRIs, with loss of pharmacologic efficacy, may develop in some men prescribed such drugs for the amelioration of paraphilias and PRDs.[7] A similar loss of SSRI efficacy during depression treatment, presumably related to the development of pharmacologic tolerance, has been reported as well.[28,29] These considerations suggest that cautious augmentation with psychostimulant medications during SSRI treatment of paraphilias and PRDs may be helpful. This article reports a case series on psychostimulants prescribed to augment SSRIs in the treatment of paraphilias and PRDs.

METHOD

Twenty-six voluntary outpatient white men with current primary paraphilias or PRDs were evaluated and treated during a 3-year period with a combination of a psychostimulant added to a stable dose of an SSRI. Verbal informed consent, after discussion of the possible side effects, beneficial effects, and clinical rationale for the prescriptive use of medications, was obtained from all study participants. Nonsexual DSM-IV Axis I diagnoses were ascertained by extensive intake inventories[19,20] followed by careful psychiatric interview. For the purposes of this report, only the diagnoses of lifetime mood disorders and ADHD are reported.

The retrospective diagnosis of ADHD according to DSM-IV criteria was ascertained with the ADHD Rating Scale,[30] an operationalized checklist of the 18 different diagnostic criteria stipulated in DSM-IV, and follow-up psychiatric interview. The ADHD Rating Scale has a clinical severity component rating each symptom on a scale of 0 to 3. Individual symptoms self-rated > 2 were considered as meeting the diagnostic severity threshold for ADHD. In conformity with DSM-IV criteria, in addition to meeting the diagnostic thresholds for ADHD inattentive, hyperactive/impulsive, or combined subtype symptoms, significant psychosocial impairment associated with childhood symptoms was required for the retrospective diagnosis of ADHD to be assigned. In addition, the 26-item Wender Utah Rating Scale (WURS)[31,32] for the assessment of ADHD was administered to each patient. According to its authors, the WURS is strongly correlated with the retrospective diagnosis of ADHD combined subtype in childhood; they report that a score of > 46 is correlated (0.80) with a diagnosis of ADHD and that men retrospectively diagnosed with ADHD had a mean WURS score of 60.[31]

The diagnosis of current DSM-IV–defined paraphilias and/or paraphilia-related disorders (as operationally defined by Kafka[13–15]) was ascertained by several sexual inventories, self-report instruments employed by the senior author (M.P.K.) in several previous studies to diagnose lifetime paraphilias and PRDs.[6,7] All sexual diagnoses ascertained by the sexual inventories were confirmed by follow-up psychiatric interview.

Clinical indications for the addition of a psychostimulant to augment SSRI pharmacotherapy included treatment of presumptive current residual ADHD symptoms based on a retrospective diagnosis of ADHD (N = 17), the persistent presence of residual sexual target symptoms despite rigorous SSRI treatment (N = 16), the persistence of residual depressive symptoms despite SSRI pharmacotherapy (N = 6), relapse of sex/depressive symptoms after a period of definite improvement while taking SSRIs (N = 4), and treatment of SSRI-induced side effects, e.g., fatigue (N = 4). Many subjects conformed to more than one of these indications for combined SSRI-psychostimulant treatment.

Assessment of current paraphilia/PRD sexual behavior target symptoms was ascertained by the clinician-administered Sexual Outlet Inventory.[6,7,33,34] The target symptoms were (1) the "unconventional" total sexual outlet, operationally defined as the total number of paraphilia/PRD-associated sexual behaviors terminating in orgasms per week, and (2) average time spent (in minutes) per day in paraphilia/PRD fantasizing, urges, and explicit sexual activities during the designated week.

Paraphilia/PRD-associated total sexual outlet and average time per day spent in paraphilia/PRD-associated sexual behaviors were measured at 3 different timepoints: t_1, baseline before SSRI treatment; t_2, after SSRI treatment but immediately prior to the prescription of a psychostimulant; and t_3, at follow-up of combined SSRI plus psychostimulant treatment, defined as the most recent or last available data point. No rating scale data specifically ascertaining current ADHD symptoms at times t_1 through t_3 were obtained. Instead, subjects self-reported on target symptoms currently associated with inattentiveness/distractibility or hyperactivity/impulsivity at both t_2 and t_3.

At baseline (t_1), 19 men were prescribed fluoxetine (t_2 mean dose = 49 mg/day), 3 were prescribed sertraline

(t_2 mean dose = 110 mg/day), 2 were prescribed paroxetine (t_2 mean dose = 35 mg/day), and 2 were prescribed fluvoxamine (t_2 mean dose = 100 mg/day).

At t_2, methylphenidate sustained-release preparation (methylphenidate SR) was prescribed to 25 subjects. The 26th subject was prescribed mixed salts of dextroamphetamine because of nonsexual side effects from previously prescribed methylphenidate SR. The mean dose of methylphenidate SR was 40 mg/day (range, 20–100 mg/day). Trial completion required that subjects remain on psychostimulant treatment for at least 8 weeks in combination with SSRI treatment. Outcome data were determined at t_3, the last office visit during combined pharmacotherapy.

Statistical Analysis

As noted above, total sexual outlet and average time per day spent in paraphilia/PRD-associated behaviors were the study target symptoms (outcome variables). Total sexual outlet was analyzed as a count measure, and average time per day spent in paraphilia/PRD-associated behaviors was analyzed as an ordinal measure in 7 discrete categories: 0–1 minutes, 1–5 minutes, 5–15 minutes, 15–30 minutes, 30–60 minutes, 60–120 minutes, 120–240 minutes, and 240–480 minutes per day. Repeated measures were obtained on both variables for each subject at t_1 (baseline), t_2 (initiation of psychostimulant medication), and t_3 (last visit). For both variables, 2 sets of contrasts were carried out: between t_1 and t_2 and, separately, between t_2 and t_3. For total sexual outlet, these analyses were conducted using generalized estimating equation-based regression modeling methods, with adjustment for clustering (repeated measures) within subjects and robust estimation of standard errors.[35] For time spent per day on paraphilia/PRD-associated behaviors, the t_1 versus t_2 and t_2 versus t_3 contrasts were done using interval regression modeling methods, with adjustment for clustering within subjects.[36] Prior to doing modeling analyses, the distributional properties of the total sexual outlet variable were assessed, and logarithmic transformation was used where necessary to achieve more normal-like distributions and reduce heterogeneity of within-cell variance. Partial residual plots were used to assess goodness of model fit.

RESULTS

Twenty-one men completed the trial of SSRI plus psychostimulant augmentation as defined above. Five subjects had missing or incomplete data sets after combined pharmacotherapy owing to inadequate follow-up, i.e., failure to meet completion criteria of 8 weeks of dual therapy (N = 3); incarceration for prior offense (N = 1); or inadequate self-report at outcome (N = 1). All available treatment data in the combined psychopharmacologic treatment group (N = 26: paraphilia = 14, PRD = 12) were prospectively collected and included in the analyses.

Table 1. Demographic and Clinical Characteristics of 26 Men Cotreated With Selective Serotonin Reuptake Inhibitors (SSRIs) and Psychostimulants for Paraphilias and Paraphilia-Related Disorders[a]

Characteristic	N	%
Diagnosis		
Paraphilias	14	53.8
Paraphilia-related disorder	12	46.2
Married	14	53.8
Heterosexual	19	73.1
Mood disorder diagnosis (lifetime)	21	80.8
Retrospective ADHD diagnosis	17	65.4
Inattentive subtype	7	26.9
Combined subtype	10	38.5
Completers of SSRI/psychostimulant trial	21	80.8
Continuous variables	Mean	SD
Age, y (range, 21–52 y)	37.7	6.7
Time in SSRI treatment, mo	8.8	11.1
Time in combined treatment, mo	9.6	8.2
Total treatment time, mo	18.7	15.1
Wender Utah Rating Scale score (N = 24)	42.8	22.1

[a]Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

Characteristics of the case series subjects are summarized in Table 1. Briefly, the subjects were relatively young (mean age = 37.7 ± 6.7 years), predominantly heterosexual (N = 19), and typically married (N = 14). Eighty-one percent (21/26) reported a lifetime history of a mood disorder, most commonly dysthymic disorder, early-onset subtype. None of these subjects met lifetime diagnostic criteria for bipolar mood disorder.

Seventeen (65.4%) of 26 subjects met retrospective diagnostic criteria for ADHD, either inattentive (N = 7) or combined (N = 10) subtype. All men diagnosed with ADHD also met diagnostic criteria for a lifetime mood disorder. Twenty-four men completed the WURS. The WURS score differentiated the ADHD subjects (mean score = 56 ± 12.4) from the non-ADHD subjects (mean score = 20.5 ± 15.4; $t = 6.2$, $df = 22$, $p \leq .001$). Subjects with ADHD inattentive subtype had lower scores on the WURS (52.6. ± 7.8), on average, than subjects with ADHD combined subtype (58.4 ± 14.7), but this difference was not statistically significant.

The total sexual outlet and average time spent in paraphilia/PRD-associated sexual activities at baseline and during pharmacotherapy are described in Table 2.

Men retrospectively diagnosed with ADHD did not differ from the non-ADHD group on baseline total sexual outlet or total time per day spent in paraphilia/PRD sexual behaviors. At baseline (t_1), the mean total sexual outlet was 9.0 ± 6.0 per week (median = 8; range, 1–24) and the median time spent in problematic sexual behavior was 1 to 2 hours/day. Twenty (76.9%) of 26 men reported spending at least 1 to 2 hours/day or more in paraphiliac/PRD sexual behaviors at baseline.

At t_2, in comparison with t_1, both total sexual outlet and median time per day spent in paraphilia/PRD sexual behaviors were substantially decreased from baseline levels.

Table 2. Total Sexual Outlet and Average Time per Day Spent in Paraphilia/Paraphilia-Related Disorder Sexual Behaviors Among 26 Men at 3 Timepoints[a]

	Baseline (t_1)			SSRI Alone (t_2)			SSRI + Psychostimulant (t_3)			p Value	
Variable	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	t_1 vs t_2	t_2 vs t_3
Total sexual outlet[b]	8.0	9.0	6.0	2.5	3.3	3.4	1.0	2.0	2.3	< .001	.003
Time/day[c]	60–120	53.7	41.3	15–30	16.8	13.9	5–15	9.4	9.4	< .001	.04

[a]Abbreviation: SSRI = selective serotonin reuptake inhibitor.
[b]p Values and statistical significance determined by regression modeling, controlling for clustering within subjects. For t_1 vs. t_2, $\chi^2 = 62.2$, df = 1, $p \leq .001$; for t_2 vs. t_3, $\chi^2 = 8.5$, df = 1, p = .003. For overall model, $\chi^2 = 98.7$, df = 1, p < .001.
[c]For time/day, mean and standard deviation were estimated from midpoint values of each time interval. p Values and statistical significance are based on medians and interval regression modeling, controlling for clustering within subjects. For t_1 vs. t_2, $\chi^2 = 39.4$, df = 1, $p \leq .001$; for t_2 vs. t_3, $\chi^2 = 4.1$, df = 1, p = .04. For overall model, $\chi^2 = 51.3$, df = 1, p < .001.

Total sexual outlet decreased more than 63%, from a mean ± SD of 9.0 ± 6.0 at baseline to a mean of 3.3 ± 3.4 at time t_2. This difference is statistically significant ($\chi^2 = 62.2$, df = 1, p < .001; see Table 2). Similarly, median time per day spent in paraphilia/PRD-associated behaviors changed from 60 to 120 minutes/day at baseline to 15 to 30 minutes/day, a decrease of 75% based on change in modal category midpoints ($\chi^2 = 39.4$, df = 1, p < .001; see Table 2). Of note, the very large changes from t_1 to t_2 in these behaviors occurred despite the clinical impression that at least 13 of the men still self-reported meaningful residual sexual target symptoms at time t_2. At t_2, the subjects had been maintained with an SSRI for a mean of 8.8 ± 11.1 months (median = 4 months; range, 1.5–48 months).

Decreases in total sexual outlet and time spent in paraphilia/PRD-associated sexual behaviors continued between t_2 and t_3, the time of psychostimulant augmentation for all subjects. As noted in Table 2, the total sexual outlet measure decreased by 39%, from mean ± SD = 3.3 ± 3.4 at t_2 to 2.0 ± 2.3 at t_3 (p = .003), and time spent in paraphilia/PRD-associated behaviors decreased by 44% (p = .04).

At t_3, subjects had been maintained on treatment with psychostimulant medication with concomitant SSRIs for a mean of 9.6 ± 8.2 months (median = 7 months; range, 0–30 months), and the mean total treatment duration (since t_1) was over 18 months (mean = 18.7 ± 15.1, median = 15 months; range, 3–66 months). The mean dose of methylphenidate SR, the most commonly prescribed psychostimulant, was 40 mg/day (range, 20–100 mg/day) at t_3.

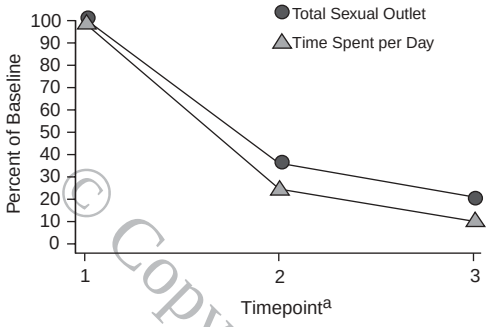
In a separate statistical analysis comparing the paraphilia and PRD groups on diagnostic and treatment-related variables, the 2 groups were statistically significantly different (greater in the paraphilia group) in the proportion of subjects with retrospective diagnosis of ADHD ($\chi^2 = 5.5$, df = 1, p = .01) and in the duration of combined SSRI/psychostimulant treatment (i.e., $t_3 - t_2$) (F = 4.0, df = 1, p = .05: paraphilia mean ± SD = 12.6 ± 7.5 months; PRD mean ± SD = 6.4 ± 7.9 months). The 2 groups did not differ, however, in mean age, mean WURS scores (F = 2.98, df = 1, p = .09), baseline (t_1) total sexual outlet, baseline (t_1) average time spent in paraphilia/PRD-related sexual behaviors, SSRI treatment duration (t_2), total sexual outlet or average time/day at t_2, combined treatment (t_3) total sexual outlet or average time/day spent in paraphilia/PRD-associated activities, or total treatment time ($t_3 - t_1$). When the duration of psychostimulant treatment ($t_3 - t_2$), age, presence/absence of a retrospective diagnosis of ADHD, and paraphilia/PRD status were added as covariates separately or together to the t_1 versus t_2 and t_2 versus t_3 contrasts of total sexual outlet and time spent per day in paraphilia/PRD-associated behaviors, the results remained the same. That is, in all contrasts the target symptoms were significantly more prominent, on average, in the earlier time period than in the later time period.

Psychostimulant-associated side effects reported were increased irritability (N = 2), upset stomach (N = 1), increased sex drive (N = 1), shallow sleep (N = 2), increased distractibility (N = 2), and mild anxiety (N = 2). Side effects were typically managed by lowering the dose of the psychostimulant. Although vital signs were not routinely measured, no self-reported cardiovascular side effects were recorded.

Changes from baseline in total sexual outlet and average time per day in paraphilia/PRD-related behaviors are shown graphically in Figure 1. On average, subjects experienced a substantial decrease in total sexual outlet and time spent per day between baseline and t_2 (while taking SSRIs alone), and then continued improvement, although at a diminished pace, between t_2 and t_3 (while taking SSRIs augmented with psychostimulants).

By both the clinician observation and subject self-report, 82.3% (14/17) of the men with retrospectively diagnosed ADHD reported definite improvement in symptoms presumptively associated with current ADHD. Of the 3 subjects in the ADHD group who did not report improvement, 1 subject reported no change, and 2 subjects were worse (increased irritability [N = 2] and/or increased distractibility [N = 1]). Of the 20 men with either residual or recurrent target sexual symptoms at t_2, 15 (75%) were clinically improved at t_3 as measured by the Sexual Outlet Inventory, and 4 reported no apparent effect. The remaining subject, whose sexual symptoms had been substantially improved with an SSRI alone, suffered a relapse of those sexual symptoms.

Figure 1. Total Sexual Outlet and Average Time Spent per Day in Paraphilia/Paraphilia-Related Disorder Behaviors in 26 Men Treated With a Selective Serotonin Reuptake Inhibitor (SSRI) and a Psychostimulant



[a]Timepoint 1 = pretreatment baseline, timepoint 2 = response to SSRI monotherapy, timepoint 3 = response to SSRI plus psychostimulant.

The clinical effects of psychostimulant augmentation of SSRIs can be further clarified with case examples from among the 26 men presented in this report.

Case Reports

Case 1: Successful psychostimulant treatment of a man with paraphilia/PRDs and ADHD following partial relapse with SSRI pharmacotherapy. Mr. A, a married heterosexual man, had been arrested for exhibitionism. Despite legal sequelae from his behavior, he continued to masturbate to pornography and had urges to expose himself. He met lifetime diagnostic criteria for dysthymic disorder, early-onset subtype; major depression, recurrent, nonpsychotic subtype; and ADHD, combined subtype. His WURS score was 62. He also had a history of polysubstance abuse, currently in remission. At t_1, Mr. A was masturbating 3 times per week, all associated with pornography use, and unconventional sexual behavior occupied a modest 15 to 30 minutes/day. After treatment with fluoxetine, gradually titrated to 60 mg/day, Mr. A's sexual impulsivity symptoms were substantially diminished. After 7 months of taking an SSRI alone, however, Mr. A reported a return of some problematic sexual ideation, but no explicit enactment of paraphiliac behavior. Total sexual outlet was 0 and time spent per day in paraphilia/PRD-associated activity had regressed to 5 to 15 minutes/day. In addition, Mr. A had been persistently and chronically distracted and disorganized at work, symptoms that were most likely related to ADHD, residual subtype. Prior to psychostimulant augmentation, Mr. A characterized himself as "depressed again" and concerned about possible relapse of paraphiliac behavior. The prescription of dextroamphetamine mixed salts, titrated to 15 mg b.i.d., produced a remission of depression, a marked and sustained decrease in time spent in paraphilia/PRD-related sexual behaviors to 0 to 1 minutes/day, and an improvement in sexual interest in his spouse. He described enhanced concentration, motivation, and energy as well as reduced anxiety. He has sustained remission of sexual, depressive, and ADHD symptoms for 2 years.

Case 2. Partial success with psychostimulant augmentation in a man with PRDs and no history of ADHD. Mr. B, a married heterosexual man, complained of compulsive masturbation and pornography dependence resistant to individual psychotherapy and 12-step self-help group treatment. He presented with recurrent major depression as well as current social phobia and had a history of dysthymic disorder, early-onset subtype. His WURS score was 1. At baseline, Mr. B was masturbating 18 times per week with pornography, having no sexual relations with his spouse, and spending 2 to 4 hours per day in PRD-associated behaviors.

Pharmacologic therapy with paroxetine, titrated to 30 mg/day, had only a modest clinical effect on sexual behaviors (with total sexual outlet reduced to 14 and no appreciable change in average time spent per day in PRD behaviors). The SSRI, however, definitely diminished depressive symptoms, but produced some fatigue. Augmentation with methylphenidate SR, 40 mg/day, reduced PRD total sexual outlet from 14 to 7 per week and average time spent per day from 2 to 4 hours to 1 to 2 hours. Fatigue was ameliorated as well, and the effects were sustained over the ensuing 3 months of follow-up.

Case 3: Reversal of SSRI-induced improvement in a man with paraphilia/PRDs and a history of ADHD. Mr. C, a single heterosexual man, was referred by his fiancée because he insisted on bondage (sexual masochism) during their sexual relations. Mr. C also acknowledged compulsive masturbation and phone sex dependence, spending over $200 per month on the latter activity. He met lifetime diagnostic criteria for dysthymic disorder, early-onset subtype; ADHD, combined subtype; and marijuana dependence. His WURS score was 80. After 2 months of pharmacotherapy with fluoxetine, 20 mg/day, total sexual outlet was reduced from a baseline of 8 per week to 2 per week, and average time spent in paraphilia/PRD-associated behaviors was reduced from 1 to 2 hours/day to 5 to 15 minutes/day. Because of residual sexual impulsivity symptoms and symptoms of distractibility, verbal impulsivity, and procrastination, he was prescribed methylphenidate SR, 20 mg/day. On treatment with that stimulant, he reported a rapid "complete reversal" of the SSRI-related gains in sexual impulse control, as well as feeling more restless and irritable.

Case 4: Successful augmentation effects of a psychostimulant in a depressed man with PRDs but no history of ADHD. Mr. D, a married heterosexual man, was self-referred because he was "sexually preoccupied with women's bodies" as well as dependent on pornography. He feared he would have an extramarital affair, but had

not done so at the time of presentation. He met Axis I criteria for current major depression and dysthymic disorder, early-onset subtype. He did not meet retrospective diagnostic criteria for ADHD, and his WURS score was 17. Despite this, he had been considered a "lazy and sloppy student" in early schooling and was currently distractible and "disorganized" at work. At baseline, PRD total sexual outlet was only 4 per week, but average time per day spent in paraphilia/PRD-associated sexual behaviors was 4 to 8 hours. He had previously experienced side effects to fluoxetine and sertraline, but reported definite improvement, maintained for 4 months, with fluvoxamine titrated to 150 mg/day. He was much less depressed, while his total sexual outlet decreased to 2 per week and average time per day decreased to 30 to 60 minutes. Because of residual sexual symptoms, methylphenidate SR, titrated to 40 mg/day, was prescribed. With fluvoxamine and methylphenidate, he was "much less distracted" by sexual thoughts involving promiscuity (5–15 minutes/day), and he no longer used pornography. PRD total sexual outlet was 0, and sexual interest in and arousal by his wife was reported to be enhanced. His concentration and organizational skills at work definitely improved. These effects have been sustained for 10 months to date.

DISCUSSION

The results of this case series suggest that when psychostimulants are cautiously added to SSRIs for specific clinical indications during the treatment of men with paraphilias and/or PRDs, the combination of these agents may synergistically mitigate sexual impulsivity disorders and concurrently diminish concomitant Axis I comorbidity. The clinical indications suggested by this case series for this combination of psychotropic medications are several.

In the present case series, the clinical effects of psychostimulant augmentation were rapid, and generally the medication combination was well tolerated. Indeed, consistent with the available literature, no unusual side effects were reported from the combination of medications. To our knowledge, no consistent clinical reports have suggested that psychostimulant augmentation of SSRIs is contraindicated on the basis of pharmacokinetic or pharmacodynamic interactions. In fact, this combination has been safely utilized for the treatment of depressive disorders[21,23] and comorbid depression and ADHD.[37]

The rationale for first prescribing a serotonergic agent and then combining it with a noradrenergic/dopaminergic drug is based on preclinical and clinical evidence that increased central serotonin, a putative effect of SSRIs, diminishes sexual appetitive behavior and arousal in some male mammals[38,39] and humans.[40] In contrast, noradrenergic/dopaminergic medications can enhance both sexual appetitive behavior and performance in humans.[41,42] Thus, at least in theory, the prescription of a psychostimulant without pretreatment with an SSRI might further disinhibit sexual behavior.[43,44] Indeed, this effect was reported in case 3 in the present case series. Of note, this disinhibiting effect was not observed in any of the other men pretreated with SSRIs in this sample, but has been observed clinically among other men with sexual impulsivity disorders (M.P.K., unpublished observations, 1999). The possibility that psychostimulants may enhance sexual arousal and performance is also suggested by some case reports that noradrenergic/dopaminergic agents can reverse SSRI-induced sexual dysfunction.[25,45]

The results of this open trial of psychostimulant augmentation of SSRI pharmacotherapy for sexual impulsivity disorders should be considered as data demonstrating preliminary effectiveness. Although not a randomized trial, this study documents a statistically significant effect of SSRIs to mitigate symptoms of sexual impulsivity disorders that is consistent with several previous reports.[6,7,10] This study also suggests the probable effectiveness of treatment with an SSRI combined with a psychostimulant for sexual impulsivity disorders. Lastly, the absence of adverse effects suggests the probable safety of this medication combination for these purposes.

Limitations of this trial include its small sample size, the absence of a rating scale to assess "residual" ADHD symptoms at all 3 timepoints, the lack of a control group, nonblinded administration of pharmacologic agents, nonrandomization of subjects, and the prescription of several different SSRIs and psychostimulants rather than a uniform pharmacologic protocol. In addition, psychosocial or psychotherapeutic ameliorative effects could not be adequately controlled. Randomized trials designed to separate the SSRI plus psychostimulant combination effects from placebo effects and develop estimates of dose/response correlations for the SSRI plus psychostimulant combination would provide valuable additional information about the usefulness of this drug combination in the treatment of paraphilia and paraphilia-related disorders.

Despite the encouraging results of this trial, caution must be advised regarding the prescription of psychostimulants because of their possible abuse potential. In this regard, a noradrenergic or dopaminergic antidepressant such as desipramine, bupropion, or venlafaxine would be a possible substitute drug for patients at risk for substance abuse relapse. In addition, as has been reported for the use of SSRIs, if one psychostimulant is ineffective or produces side effects, another drug of the same class may mitigate target ADHD and/or sexual symptoms.

In summary, the results of this case series suggest that psychostimulants can be cautiously added to SSRIs in the treatment of men with paraphilias and/or paraphilia-related disorders, and the combination of these agents may synergistically mitigate sexual impulsivity disorders.

Clinical indications for this combination of psychotropic medications include the retrospective diagnosis of ADHD with persistent adult symptoms despite pharmacotherapy with an SSRI; residual paraphilia/PRD-associated fantasies, urges, and activities despite SSRI pharmacotherapy; relapse or loss of SSRI efficacy that is sometimes reported during the treatment of both depression and sexual impulsivity disorders; the persistence or presence of residual depressive symptoms despite SSRI pharmacotherapy; and the treatment of SSRI-associated side effects. Controlled clinical trials assessing the effects of psychostimulant augmentation of SSRI treatment of paraphilias and paraphilia-related disorders are needed.

Drug names: bupropion (Wellbutrin), desipramine (Norpramin and others), dextroamphetamine (Dexedrine and others), fluoxetine (Prozac), fluvoxamine (Luvox), methylphenidate (Ritalin and others), paroxetine (Paxil), sertraline (Zoloft), venlafaxine (Effexor).

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