Assessment of Sexual Dysfunction Using the Arizona Sexual Experiences Scale (ASEX) and Implications for the Treatment of Depression

by CYNTHIA A. McGAHUEY, AA; PEDRO L. DELGADO, MD; and ALAN J. GELENBERG, MD

Up to 70% of people suffering from major depression also describe sexual dysfunction, most commonly a loss of interest in sexual activity. Although successful antidepressant treatment improves most symptoms of depression, many patients experience the emergence of new forms of sexual dysfunction during treatment. The older antidepressants such as tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) may cause erectile dysfunction, retrograde ejaculation, or anorgasmia. Although the newer selective serotonin reuptake inhibitors (SSRIs) lead to fewer side effects overall compared with TCAs or MAOIs, they have been reported to cause high rates of sexual dysfunction, including decreased libido, and anorgasmia. Whereas initial reports suggested that sexual side effects were relatively uncommon, more careful questioning suggests that up to 70% of patients may have sexual dysfunction when taking SSRIs. The initial underreporting of sexual side effects was due in part to the failure to directly ask patients about their sexual function. This poses a problem because to effectively treat sexual dysfunction, accurate measurement and quantification of the core symptoms of sexual dysfunction are necessary.

DEVELOPMENT OF THE ASEX SCALE

Many of the currently available sexual function assessment scales are lengthy, contain sexually intrusive questions, fail to assess sexual satisfaction, and lack reliability and validity data. In response to the need for a relevant, yet expedient and reliable method for assessing psychotropic drug–induced sexual dysfunction, we developed the Arizona Sexual Experiences Scale (ASEX) (Figs. 1 and 2). The ASEX is a brief 5-item scale designed to assess the core elements most commonly impaired by antidepressants: drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm. The male and female versions of the ASEX differ on the gender-specific question addressing erection/lubrication. Each item is rated in a 6-
1. How strong is your sex drive?

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<tr>
<td>extremely</td>
<td>very strong</td>
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<td>somewhat weak</td>
<td>very weak</td>
<td>no sex drive</td>
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2. How easily are you sexually aroused (turned on)?

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<tr>
<td>extremely</td>
<td>very easily</td>
<td>somewhat easily</td>
<td>somewhat easily</td>
<td>very difficult</td>
<td>never aroused</td>
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3. Can you easily get and keep an erection?

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<td>extremely</td>
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4. How easily can you reach an orgasm?

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<tr>
<td>extremely</td>
<td>very easily</td>
<td>somewhat easily</td>
<td>somewhat difficult</td>
<td>very difficult</td>
<td>never reach orgasm</td>
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5. Are your orgasms satisfying?

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<tbody>
<tr>
<td>extremely</td>
<td>very satisfying</td>
<td>somewhat satisfying</td>
<td>somewhat unsatisfying</td>
<td>very can’t reach orgasm</td>
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COMMENTS:

Figure 1. The Arizona Sexual Experiences Scale (ASEX) for men. (Copyrighted by the Arizona Board of Regents. Published with permission.)

point Likert fashion, with lower scores reflecting enhanced sexual function and higher scores reflecting impaired sexual function. Total ASEX scores range from a low of 5 to a maximum of 30. With this design, detection of the presence of overall sexual dysfunction, as well as dysfunction in specific areas, is quick and easy.

RELIABILITY AND VALIDITY OF THE ASEX

The reliability and the validity of the ASEX were determined through data obtained for 38 control subjects (nonselected hospital employees) and 58 patients (83% diagnosed with depression and 50% receiving antidepressant therapy). To determine its validity, the ASEX was compared with an existing validated sexual function scale—the Brief Index of Sexual Functioning (BISF). The ASEX scale demonstrated internal consistency (Cronbach’s alpha = .9065), and test–retest reliability significant at the .01 level (Pearson’s r was .801 for patients and .892 for control subjects). The items on the ASEX correlated with BISF factors and related items on the BISF, but not with depression score. These data support the validity of the ASEX. Mean total ASEX scores and individual item scores are shown in the table and Figure 3. Patients had higher scores than did control subjects (F = 46.983, P < .001), and women consistently scored higher than men (for patients F = 5.218, P = .026; for control subjects F = 5.050, P = .031). Overall, patients reported more dysfunction than did control subjects.

The ASEX score can be used to identify individuals suffering from sexual dysfunction. A total ASEX score of 19 or greater, or any one item with an individual score of 5 or greater; or any three items with individual scores of 4 or greater are highly correlated with the presence of clinician-diagnosed sexual dysfunction. Using the above criteria, the sensitivity and specificity of the ASEX in identifying individuals with sexual dysfunction are 82% and 90%, respectively. The positive predictive value (PPV) is 88% and...
For each item, please indicate your **OVERALL** level during the **PAST WEEK**, including **TODAY**.

1. How strong is your sex drive?

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<tr>
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<td>somewhat easily</td>
<td>somewhat difficult</td>
<td>very difficult</td>
<td>never aroused</td>
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3. How easily does your vagina become moist or wet during sex?

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5. Are your orgasms satisfying?

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<tr>
<td>extremely satisfying</td>
<td>very satisfying</td>
<td>somewhat satisfying</td>
<td>somewhat unsatisfying</td>
<td>very unsatisfying</td>
<td>can’t reach orgasm</td>
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**COMMENTS:**

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**Figure 2.** The Arizona Sexual Experiences Scale (ASEX) for women. (Copyrighted by the Arizona Board of Regents. Published with permission.)

the negative predictive value (NPV) is 85%. Receiver–operator characteristic (ROC) analysis revealed a value for the area under the curve (AUC) of .929 ± .029 (Fig. 4).\textsuperscript{16}

**DISCUSSION OF THE RESULTS**

Measurement of sexual dysfunction is greatly simplified by focusing on the core elements of the dysfunction. The high positive and negative predictive values of the ASEX, along with its internal consistency, reliability, and validity, support the use of a simplified instrument. Additionally, assessing just the core elements in a brief and nonintrusive manner reduces the discomfort that patients often feel when responding to more lengthy questionnaires.

Although effective scoring criteria have been established for the ASEX,\textsuperscript{16} the patient’s subjective view of what is or is not sexual dysfunction should be considered. For example, the criteria above imply that any individual item score of 3 or less indicates an absence of sexual dysfunction. However, if the patient is experiencing dissatisfaction with his or her sexual functioning at this level, his or her complaint should be taken seriously. The scoring criteria are to be used as a guideline, to give a general indication of the presence or absence of sexual dysfunction.

Although the ASEX allows the clinician to identify the level of sexual dysfunction, it does not establish the etiology of sexual dysfunction. Furthermore, it is our experience that if one core element is affected, it is likely that all are affected. Clinicians must use the clinical information available to them to implement one or more strategies that will provide the most benefit to the patient with the least amount of risk.
Table
Mean ASEX Scores and Demographics

<table>
<thead>
<tr>
<th></th>
<th>% College Educated</th>
<th>% Caucasian</th>
<th>ASEX 1 Drive</th>
<th>ASEX 2 Arousal</th>
<th>ASEX 3 Lubrication/Erection</th>
<th>ASEX 4 Orgasm</th>
<th>ASEX 5 Satisfaction From Orgasm</th>
<th>Total ASEX</th>
<th>HDRS/BDI</th>
<th>% With Sexual Difficulty</th>
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<tbody>
<tr>
<td>Patients</td>
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<tr>
<td>Female (N = 35)</td>
<td>45</td>
<td>49</td>
<td>66</td>
<td>4.34</td>
<td>4.09</td>
<td>3.83</td>
<td>4.43</td>
<td>3.57</td>
<td>20.26</td>
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<td>65</td>
<td>70</td>
<td>3.51</td>
<td>3.35</td>
<td>3.30</td>
<td>3.83</td>
<td>3.09</td>
<td>17.17</td>
<td>11.05</td>
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<td>Control subjects</td>
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<td></td>
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<tr>
<td>Female (N = 22)</td>
<td>38</td>
<td>68</td>
<td>91</td>
<td>2.82</td>
<td>2.68</td>
<td>2.45</td>
<td>3.27</td>
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<tr>
<td>Male (N = 16)</td>
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<td>88</td>
<td>63</td>
<td>2.25</td>
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<td>2.00</td>
<td>2.69</td>
<td>1.81</td>
<td>10.94</td>
<td>5.06</td>
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</tbody>
</table>

ASEX = Arizona Sexual Experiences Scale; HDRS/BDI = Hamilton Depression Rating Scale/Beck Depression Inventory. Values in parentheses represent standard deviation from the mean.

Figure 3. Mean individual Arizona Sexual Experiences Scale (ASEX) item scores for patients and control subjects.

OPTIONS FOR THE MANAGEMENT OF PSYCHOTROPIC DRUG-INDUCED SEXUAL DYSFUNCTION

Management of sexual dysfunction due to antidepressant therapy can include three distinct strategies: optimizing the treatment by achieving the ideal balance between therapeutic effects and side effects; providing antidotes or supplements to the existing drug therapy; and/or substituting another antidepressant with less risk of sexual dysfunction in place of the existing treatment. Lack of complete understanding of neurophysiologic aspects of sexual functioning and of the mechanisms of psychotropic drug-induced sexual dysfunction hinders the ability to know for sure which strategy provides the best efficacy.

Optimizing the Effectiveness of the Antidepressant

Reducing the dose of an antidepressant often reduces side effects. Although this strategy is often used clinically for non-sexual side effects, our clinical experience with it is that when the dose of an SSRI is lowered to try to reduce sexual side effects, there is often some loss of the antidepressant response. This strategy is most effective when a patient is taking high doses of SSRIs (e.g., 60 to 80 mg/d of fluoxetine, or 50 mg/d of paroxetine).

Abrupt discontinuation of the antidepressant for 1 or 2 days (drug holiday) has been reported to lead to the temporary return of sexual functioning in individuals with SSRI-induced sexual dysfunction.17,18 However, this strategy may induce withdrawal symptoms from SSRIs with a short half-life,19,20 and may not be effective in SSRIs with long half-lives.17

Common withdrawal symptoms may include nausea, headache, fatigue, dizziness or imbalance, insomnia, and anxiety and agitation.21-24 Withdrawal symptoms are less likely with fluoxetine because of its long half-life,19,20 but the effectiveness of the drug holiday on return of sexual functioning is minimal as well.17 For example, high rates of withdrawal symptoms have been reported for paroxetine, most likely due to its short half-life,19,20 Venlafaxine has also been reported to have high rates of withdrawal,24 with symptoms occurring within 2 days of stopping or tapering the drug. Reintroduction of the antidepressant or augmentation and/or substitution of a similar agent often relieves the withdrawal symptoms.21

Providing Antidotes to Existing Drug Therapy

The addition of another drug to ongoing antidepressant therapy has been widely used as an antidote for SSRI-induced sexual dysfunction. This strategy is hypothesized to work by either blocking a putative pharmacologic effect of the SSRI that causes sexual dysfunction or enhancing a biologic process that putatively increases sexual function. The most common approaches in this regard have involved the addition of drugs that either block serotonin or enhance dopamine neurotransmission.
Nonspecific serotonin antagonists such as cyproheptadine,25,26 or methysergide, or serotonin-2A receptor-specific antagonists such as nefazodone, or mirtazapine, have been used in this regard with some evidence for efficacy.27,28 Unfortunately, use of the nonspecific serotoninergic antagonists has led to a return of depression in some patients in whom this strategy has been applied.

Dopamine-enhancing drugs are hypothesized to either directly enhance sexual function or indirectly reduce serotonergic neuronal activity.29 The additions of amantadine, amphetamines, or methylphenidate to ongoing SSRI treatment are examples of this approach. Although these treatments have been reported to reverse sexual dysfunction, some patients may experience symptoms of anxiety.29

Yohimbine is a pharmacologically complex drug that has also been used as an antidote. Studies show some return of sexual function, but with additional side effects of nausea, anxiety, and frequency of urination.30-32 Bupropion has also shown some positive results (66% improvement in SSRI-induced sexual dysfunction),33 but causes anxiety and agitation and is associated with the potential risk of precipitating seizures in vulnerable individuals.

A recent open-label trial reported success with the addition of ginkgo biloba.34 Although the mechanism for ginkgo is unclear, it has been reported to enhance blood flow and circulation.34 Another recent strategy that is being widely used, although no published reports are available, is the addition of sildenafil for the treatment of SSRI-induced sexual dysfunction. Although sildenafil is indicated only for the treatment of erectile dysfunction in men, this strategy is being used in both men and women with SSRI-induced sexual dysfunction (personal observations of the authors).

In summary, antidote strategies may be somewhat effective in some patients. In particular, the use of mirtazapine, ginkgo biloba, and sildenafil seems promising. In general, the main disadvantages of the antidote strategy are the potential for added side effects and unexpected interactions between the two drugs, and the added costs of a multi-drug regimen.

Substituting a Different Antidepressant

Switching from an antidepressant that causes sexual dysfunction to one that does not is another viable option. This strategy provides the most favorable risk–benefit ratio of all options because it does not involve dose reduction (which can reduce antidepressant effectiveness) or combination pharmacotherapy (which can reduce antidepressant effectiveness and/or induce new adverse effects).

Several antidepressants are available that appear to have a low incidence of sexual dysfunction. These include bupropion, nefazodone, and mirtazapine.37,27,28 Although nefazodone and mirtazapine both interact with serotonergic systems in the brain, they also block serotonin-2A receptors, which is hypothesized to account for their low incidence of sexual dysfunction.

Bupropion has not only been associated with a low incidence of sexual dysfunction, but has also been hypothesized to enhance sexual function above normal in some patients.4 Bupropion has shown excellent results in some studies (94% return of orgasm function),38 but inconclusive results in others.36 Nefazodone has yet to be studied as a substitute medication for psychotropic drug–induced sexual dysfunction, although it is thought to cause lower rates of sexual dysfunction.

Mirtazapine has been studied as a substitute, with promising results. Mirtazapine enhances both noradrenergic and serotonergic neurotransmission and blocks serotonin-2A and -3 receptors.37,38 It has been reported to cause a lower incidence of sexual side effects compared with placebo.36 We recently reported the results of a trial of mirtazapine substitution in 19 patients with SSRI-induced sexual dysfunction.39 Patients who had been taking SSRIs for at least 6 months, in remission from depression,
and experiencing treatment-emergent sexual dysfunction were switched to mirtazapine for 6 weeks. Figure 5 shows a comparison of ASEX scores at screening (with SSRI) and after 6 weeks of mirtazapine treatment. ASEX scores improved significantly (F = 5.904, df = 11,7, P = .013), with 11 patients experiencing complete return to normal sexual functioning and another 2 reporting significant improvement. All individual ASEX item scores decreased significantly from screening to week 6 of mirtazapine. All 19 patients maintained their antidepressant response, but side effects (sedation, irritability, muscle soreness) were present in some patients. These results strongly support the effectiveness of mirtazapine as a substitute antidepressant for SSRI treatment-emergent sexual dysfunction.

St. John's wort is an herbal drug widely used in Germany for the treatment of depression. Although it is not currently approved by the Food and Drug Administration for the treatment of depression, it is widely used by patients throughout the United States for self-treatment of depression. European data have not specifically investigated the incidence of sexual dysfunction with St. John's wort. Several large randomized, controlled trials are under way in the United States.

CONCLUSION

Sexual dysfunction can be rapidly and accurately assessed with the use of the ASEX scale. This enables the clinician to pinpoint specific areas of sexual dysfunction resulting from either depression itself or the treatment thereof. Effective strategies for the treatment of sexual dysfunction can then be employed. Antidepressant substitution appears to be the most effective strategy with the fewest adverse side effects. When treating depression with the available antidepressants, the strategies outlined previously—optimizing, antiodal, and substitution—should be considered carefully. When this is done, patients can receive effective treatment for depression without high rates of treatment-emergent sexual dysfunction. Careful monitoring of patients' progress during the course of the treatment plan, employing effective changes in treatment strategy when needed, can produce the best results.

REFERENCES