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The ANNSERS (Antipsychotic Non-Neurological Side Effects Rating Scale): validation of sexual side-effect measurement

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***Abstract*:** Antipsychotic nonneurological side effects, such as sexual dysfunction, can adversely affect the quality of patients' relationships, their treatment adherence and their quality of life. In the UK CUtLASS (Cost Utility of the Latest Antipsychotics in Severe Schizophrenia) study, nonneurological side effects were assessed using the ANNSERSv1 (Antipsychotic Non-Neurological Side Effects Rating Scale version 1), a new scale to assess the side effects associated with both first- and second-generation antipsychotic drugs. A total of 26 participants also completed the Derogatis Interview for Sexual Functioning (self-report version, DISF-SR). A statistically significant, and specific, correlation was found between scores on the DISF-SR and the sexual side-effect section of the ANNSERS at baseline. The sexual side-effects subscale of the ANNSERS is a valid measure of sexual dysfunction in the treatment of schizophrenia.

***Keywords*:** adverse effects, antipsychotics, assessment, schizophrenia, sexual dysfunction

Introduction

Antipsychotic nonneurological side effects, such as sexual dysfunction, can adversely affect the quality of patients' relationships, their treatment adherence and their quality of life [Goff and Shader, 2003]. Sexual side effects of treatment are distressing to patients and can be experienced as worse than the symptoms of schizophrenia itself [Finn *et al.* 1990; Lambert *et al.* 2004].

Up to two thirds of treated patients report problems with sexual function in the previous month, although sexual side effects can be both underreported by patients and underdetected by clinicians [Karagianis *et al.* 2009; Yusufi *et al.* 2007]. This, together with the variety of assessment tools being used to measure sexual side effects in treated schizophrenia, means that review and synthesis of the existing literature is not straightforward.

We set out to validate the sexual side-effects section of the ANNSERS (Antipsychotic Non-Neurological Side Effects Rating Scale) by examining scores in a subgroup of participants in a large UK trial.

Methods

The CUtLASS trials

The UK CUtLASS study (Cost Utility of the Latest Antipsychotics in Severe Schizophrenia) [Jones *et al.* 2006; Lewis *et al.* 2006] comprised two multicentre randomized controlled trials. CUtLASS 1 [Jones *et al.* 2006] compared first-generation antipsychotic (FGA) with (noncloza-pine) second-generation antipsychotic (SGA) drugs in patients having a change in their treatment because of poor response or side effects. CUtLASS 2 [Lewis *et al.* 2006] compared SGAs with clozapine in patients with treatment-resistant schizophrenia. Three follow-up assessments, which were blind to treatment allocation, took place over the course of 1 year.

Participants

Participants ($N = 26$) were patients aged 18–65 years with DSM-IV schizophrenia and related (schizoaffective or delusional) disorders.

Measures

Measures used were ANNSERS version 1 (ANNSERSv1) and the Derogatis Interview for

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Table 1. Sexual side-effects subscale of the ANNSERSv1.

Instructions: This scale pertains to events over the past month. Rate each item for severity according to the following codes: 0 = absent, 1 = mild, 2 = moderate, 3 = severe				
	Absent	Mild	Moderate	Severe
Female				
Loss of libido	No change in sexual drive and/or interest	Sexual drive reduced but no significant change in activity, such as sexual intercourse or masturbation	Sexual drive reduced and sexual activity reduced	Sexual drive reduced, such that sexual activity is significantly reduced or absent
Problems of sexual arousal	No change	Patient notices occasional difficulty in ability to become aroused: subjectively and objectively (e.g. vaginal lubrication)	Patient notices regular difficulty in ability to become aroused	Patient experiences persistent difficulty in the ability to become aroused
Orgasmic difficulties	No change	Patient experiences occasional difficulty in achieving orgasm with sexual stimulation	Patient experiences frequent difficulty and/or increased delay in achieving orgasm with sexual stimulation	Patient experiences persistent difficulty and/or significant delay in achieving orgasm with sexual stimulation
Change in menstruation	No change	Minor change in frequency or duration	Menstrual periods erratic and unpredictable in frequency and/or severity, and/or dysmenorrhoea	Menstrual periods absent or very heavy, and/or severe dysmenorrhoea
Male				
Loss of libido	No change in sexual drive and/or interest	Sexual drive reduced but no significant change in activity, such as sexual intercourse or masturbation	Sexual drive reduced and sexual activity reduced	Sexual drive reduced, such that sexual activity is significantly reduced or absent
Erectile difficulties	No change	Occasional difficulty in obtaining and/or maintaining erection	Moderate difficulty in obtaining and/or maintaining erection, although may be occasionally unproblematic	Persistent difficulty in obtaining and/or maintaining erection
Delayed ejaculation	No problem	Occasional difficulty with ejaculation: time taken to achieve and/or insufficient stimulation/sensation	Frequent difficulty with ejaculation: time taken to achieve and/or insufficient stimulation/sensation	Persistently unable to ejaculate
Reduction in ejaculatory volume/intensity	No change	Patient notices modest reduction in volume of ejaculate and/or reduced intensity/force of ejaculation	Patient notices frequent/moderate reduction in volume of ejaculate and/or reduced intensity/force of ejaculation	Patient notices persistent/marked reduction in volume of ejaculate and/or reduction in intensity/force of ejaculation

Sexual Functioning (self report version; DISF-SR) [Derogatis, 1997]. The ANNSERS is a new scale to assess the side effects associated with both FGA and SGA drugs, and has good inter-rater reliability [Ohlsen *et al.* 2008; Yusufi *et al.* 2005]. The latest version of the ANNSERS (version 2) is available from Imperial Innovations Ltd., or King's College London Business. The subscales of the ANNSERS examine areas such as sleep disturbance, aversive subjective experience and cardiovascular, gastrointestinal, anticholinergic, genitourinary and sexual problems.

Table 2. Demographic data and baseline scores (ANNSERS, DISF-SR).

	Patient sample, $N=26$
Male sex (%)	15 (58%)
Age, years, mean (SD)	41.5 (12.0)
DISF-SR total score, mean, (SD)	44.2 (31.9)
ANNSERS sexual side-effects score, mean (SD)	3.4 (3.4)

The sexual side-effects subscale of the ANNSERS includes ratings for loss of libido, problems of sexual arousal, orgasmic difficulties and change in menstruation for female patients. Ratings for male patients include loss of libido, erectile difficulties, delayed ejaculation and reduction in ejaculatory volume or intensity (Table 1). Ratings cover the 4 weeks prior to assessment.

The DISF-SR is a brief, self-report, multidimensional and sex-keyed instrument designed to measure the quality of current sexual function across five key domains: sexual cognition and fantasy (five items); sexual arousal (five items); sexual behaviour and experiences (five items); orgasm (six items); and sexual drive and relationship (four items). The first three of these key domains are scored using a nine-point scale from 0 (not at all) to 8 (four or more times per day); orgasm is scored using a five-point scale from 0 (not at all) to 4 (extremely). The fifth domain, sexual drive and relationship, is scored using a combination of nine- and five-point scales. The aggregate total DISF-SR score can be used repeatedly throughout efficacy or effectiveness studies without any significant practice effects or loss of validity [Derogatis, 1997].

Procedure

We validated the sexual side-effects section of the ANNSERS using data from 26 participants who also completed the DISF-SR at baseline and 12 weeks after randomization to either an SGA or FGA drug.

Data analysis

Results were analysed using SPSS version 15 to carry out correlational analyses (Pearson's r and Spearman's rho).

Results

Demographic characteristics of the sample plus baseline scores on the DISF-SR and the sexual side effects section of the ANNSERS are shown in Table 2.

We found a statistically significant correlation between score on the DISF-SR and the sexual side-effect section of the ANNSERS at baseline, in the subsample of 26 patients with scores on both measures ($r=-0.638$, $p=0.001$). A lower score on the DISF-SR indicates greater sexual dysfunction, whereas a lower score on the ANNSERS points to fewer side effects. This correlation was specific as the other items in the ANNSERS showed no relationship with DISF-SR score (Spearman's rho $=-0.273$, $p=0.196$).

Discussion

We validated the sexual side-effects section of the ANNSERS by finding a significant and specific relationship with score on the DISF-SR in a subgroup of participants ($N=26$) with schizophrenia or related disorder in a large UK treatment trial.

One possible limitation of this study, in addition to the small sample size, is its reliance on self-reported levels of sexual dysfunction, *via* the DISF-SR. Obtaining such data with the use of direct patient interviews, however, may also result in underestimation of sexual side effects.

Recognition of sexual side effects in treated schizophrenia requires comprehensive patient reporting together with valid clinical measurement. The sexual side-effects scale of the ANNSERS provides a brief series of questions that can be completed in the busy, time-pressured psychiatric clinic, validated against one of the gold standard sexual function tools. The individual sexual side-effect items in the ANNSERS have been used successfully in recent related research, for example, to demonstrate a reduction in sexual dysfunction following a switch to aripiprazole [Mir *et al.* 2008].

Our findings provide further support for the sexual side-effects subscale of the ANNSERS as a valid measure of sexual dysfunction in the treatment of schizophrenia.

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Conflict of interest statement

All authors declare no conflict of interest.

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