Risperidone-induced hypersexuality

We report hypersexuality in three people with schizophrenia after starting risperidone, with evidence suggesting a possible link between risperidone and the hypersexuality.

Mrs X, 71 years old, married once and widowed for 20 years, with no known history of hypersexuality, was started on risperidone 25 mg intramuscular (IM) injection three times weekly. Two months later, she complained of ‘having to’ masturbate two to three times daily without being able to orgasm, lactating and losing ‘too much fluids’ vaginally. She became fixated on an imagined romantic relationship, took off her old wedding ring and attempted to hire a tourist boat for a wedding reception she planned for herself. Risperidone was stopped after 6 months and switched to pipotiazine 25 mg IM injection, three times weekly, after a washout period of 5 days. Features of hypersexuality waned and resolved 10 days later, with no recurrence.

A 53-year-old man, Mr Y, took clozapine for 14 years before it was stopped due to neutropenia. He was started on oral risperidone 2 mg twice daily and developed thoughts fixated on masturbation, erections and needing a sexual partner. Risperidone was stopped and olanzapine initiated, with no disclosed sexual content in his thoughts from the next day. Hypersexual thoughts recurred on overnight leave. During the second overnight leave, he behaved indecently towards two young women in a park and was charged with indecent assault.

A 23-year-old man, Mr Z, was re-titrated on risperidone after a period of non-adherence. From the day after oral risperidone was titrated up to 5 mg daily, when risperidone 50 mg IM injection was also administered, ten episodes of hypersexual behaviour were documented in a period of 10 days, including sexually disinhibited speech, propositioning and exhibitionism. Risperidone was tapered and stopped, and Mr Z was started on flupentixol 20 mg IM injection. There were no further episodes of hypersexual behaviour other than one episode of disinhibited speech when the risperidone was 3 mg daily. Mr Z was later readmitted and maintained on flupentixol 20 mg IM injection. No hypersexual behaviour occurred during this admission.

None of these people were hypompanic. Bipolar disorder was excluded. Prolactin levels on risperidone were 2737 IU/l for Mrs X, and 468 IU/l for Mr Y.

A review of the literature showed similar case reports.1,2 Antagonism of 5-HT2A receptors by risperidone, which increases dopamine release in the prefrontal cortex, and antagonism of alpha-2 adrenergic receptors, which disinhibits noradrenergic neurons and plays a role in genital stimulation,3,4 could explain this effect. A similar mechanism of alpha-2 adrenergic blockade has been postulated for yohimbine. The expression of these receptors in individuals may affect vulnerability. Conventional antipsychotics, by their prominent D2 blockade and hardly any affinity for alpha-2 or 5-HT2 receptors, suppress libido.

Hypersexuality as a possible side-effect of risperidone5 may need further evaluation, considering the social and medico-legal implications. However, there are limited instruments with which to score hypersexual behaviour. A special scale might have wider applications. We are therefore formulating a scale to assess hypersexual behaviour.

Avant-assisted relational therapy for persecutory voices

Concealed beneath the implausibly insentient nature of the intervention implied by Leff et al’s study title1 is in fact a highly relational therapeutic approach for voice hearers of potentially Copernican significance! An example of the kind of paradigm shift in both research and clinical practice recently advocated in the British Journal of Psychiatry (e.g. Bracken et al²).

Although only a ‘proof of concept’ study, it is predicated on a very different understanding of psychopathology than conventionally argued for in the pages of this Journal. Not only does the study shun conventional diagnosis in favour of a ‘symptom group’, as Tyrer points out in the issue’s editorial coda, but it revives the concept of psychotic symptoms as relational phenomena – both in terms of aetiology and intervention – that our group has recently further argued for.²

Although a large-scale phase III study is clearly warranted, the early impression of an evidently useful shift in the framing of psychosis potentially opens up readers of this Journal to more serious consideration of a wider range of relationally oriented aetiological factors and therapies already advocated for psychosis and psychotic symptoms in several ‘lower impact’ journals – which as Kingdon points out in his related editorial³ – have historically proved to be the principle hotbed of past game changers in psychiatric practice.

Although the Journal has itself recently published several articles acknowledging childhood maltreatment to be significant risk factors for psychosis possibly mediated by changes in the hypothalamic–pituitary–adrenal axis and downstream effects on dopamine systems, the idea that hallucinatory phenomena may themselves represent ‘echoes’ of past abuse brings us closer to dissociative concepts of such phenomena, which by definition points towards relational solutions. Indeed, outside the pages of this Journal the once confident distinction between dissociative phenomena and psychosis has been challenged on various counts, including the following.
(a) Experimental studies which have shown that psychological measures of dissociation and psychosis are highly correlated and do not have convincing differential construct validity. 4

(b) Historical analysis of changing diagnostic trends, demonstrating a waning in the popularity of multiple personality disorder at the time that the diagnosis of schizophrenia began to gain ascendance is argued to be no coincidence. 5 That childhood abuse is now suggested by some studies to have a ‘dose-dependent’ relationship with later risk of psychotic symptom development, in particular hallucinations, 6 also weakens the basis for any presumed aetiological distinction between the two.

(c) Psychological modelling of how child maltreatment and trauma may give rise to psychotic symptoms (including negative symptoms). Presumed differences between traumatic flashbacks and ‘hallucinations’ may be based more on whether insight into a link between trauma and symptom is acknowledged by the patient (and psychiatrist). 7 This becomes harder still when the hallucination is symbolic rather than simply echoic or thematic.

If such a model is correct, then we can begin to take more seriously the claims of such relational therapies as the open dialogue family therapy model for early psychosis in Finland, which claims to have reduced the transformation of new-onset psychosis to chronic schizophrenia to a remarkable degree. 8 We might also take seriously the ideas of relating therapy for voices and even the more radical, direct voice dialogue advocated by some. 9 The implications for wider practice are also substantial – after all, the difference between voice elimination/repression and integration/ transformation cannot be overstated, although clearly some patients are likely to still favour a ‘sealing off’ recovery style.

Julian Leff’s team and the editorial board of the British Journal of Psychiatry are to be congratulated for the publication of this paper. Greater insight into how the therapist learns to convincingly embody the patient’s persecutory voice, through the avatar, would however be welcome.


Specialised mood disorder clinic v. standard care for out-patients with bipolar disorder

The recent paper by Kessing et al 10 was an interesting read. However, the likelihood of the findings being useful in a setting outside Denmark could reduce the paper’s relevance to the international audience. First, the vast difference between the type of treatment received by patients in the mood disorder clinic and standard out-patient care makes it almost impossible to identify the features of the clinic that make it successful, such that they may be replicated to improve service elsewhere. Although the authors go into significant detail with regard to the type of treatment and support received by the patients in the clinic, there is very little information on the patients who went through standard care. If standard care is an appointment with a general practitioner or a private psychiatrist without any support from community mental health teams, then generalising the results to the UK might be problematic as these patients would normally be with community mental health teams with some or other type of enhanced care programme approach. Second, when refusal rates are as high as the authors mentioned in this article – out of 474 eligible patients only 158 participated in the trial – a judgement must be made as to how far the volunteers that remain can be considered representative of the target population. They might, for example, in this study be younger on average than the refusers. Is this important in relation to the study question? Third, the authors refer to psychopharmacological treatments in standard care being ‘more likely to be based on the preferences of the individual physician than on national and international guidelines’; however, they make no effort to control or correct for these factors in the analysis of results, although it has been recognised that patients from the mood disorder clinic are more likely to use mood stabilisers. Finally, the cost difference between standard care and the mood disorder clinic is mainly due to the

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Author’s reply: Dr Rodger’s view of the clinical importance of the introduction of avatar therapy is encouraging. He makes a number of important points with which I entirely agree. In particular, the frail boundary between dissociation and psychosis was brought home to me by four adolescent girls in our trial, two of whom had been sexually abused in childhood, and experienced auditory, visual and somatosensory hallucinations. One girl re-experienced the rape every night and was convinced that the rapist entered her bedroom for that purpose.

In answer to Dr Rodger’s question about the therapist’s voicing of the avatar, it is a crucial requirement that the patient accepts the avatar as a realistic representation of their persecutory voice. This is achieved by asking the patient at first contact to report on the habitual phrases they hear. The therapist’s voice is morphed into a variety of forms, from which the patient selects the one that is closest to the voice they hear. Patients assessed the closeness of the match at between 60 and 90%. In the first session of therapy the therapist, as the avatar, speaks the phrases the patient has reported hearing in order to establish the identity of the avatar as their persecutor. Of the 16 patients who experienced the full course of six sessions of therapy, only 2 failed to respond to the avatar as a convincing simulacrum of the voice they hear. Neither of them benefited from the therapy. We have discussed the possible mechanisms by which the therapy achieves its effects. 1
in-patient costs for patients on standard care. This again highlights the need for adjusting the effect of medications and this would have at the least given us some better understanding about the pharmacological treatment being offered with standard care.


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Author’s reply: First, as presented in the Results of our paper, patients in standard care were mainly treated at the local community mental health centre (56.5%), at a private psychiatrist (24.7%) or at a local psychiatrist associated with the discharging ward (15.3%). Only three patients (3.5%) were treated at the general practitioner. Further, patients could at any time, if needed, be referred to a higher level of care (e.g. a community mental health centre).

Second, it is an advantage of our study compared with most other studies that we have register-based information available on the number of non-participants and are able to compare participants and non-participants in the trial. As presented in the Results, the 158 patients who participated in the trial did not differ from the 316 other potentially eligible patients regarding gender (54.4% female compared with 48.4%; \( P = 0.2 \)) but were considerably younger (median 35.6 years (quartiles 28–47) compared with median 44.0 years (quartiles 33–57); \( P < 0.001 \)). We are rather convinced that the large proportion of non-participants in the trial is mainly due to the fact that the vast majority of these patients were simply not asked to participate in the trial (but we have register data on these as well). Clinicians may have been more observant to ask younger patients to participate (as the aim of the study was to investigate effects of interventions early in the course of bipolar disorder) and younger patients may have been more willing to participate in the trial. Nevertheless, as can be seen from the paper, the median age at inclusion in the trial was 35.6 years, very similar to findings in other studies recruiting patients following first admission to hospital\(^1,2\) (mean age 31.4 years (s.d. = 12.9) and 38.4 years (s.d. = 12.6) respectively). Thus, we believe that our findings can be generalised to patients with bipolar disorder discharged from their first psychiatric hospital admission.

Third, patients treated in the mood disorder clinic more often used a mood stabiliser (lithium or anticonvulsants) or an antipsychotic compared with patients allocated to standard care. This difference is an effect of the interventions and as medication (most likely) is an intermediary factor in relation to hospital admission as the primary outcome, adjustment for medication in the analyses would be incorrect. Finally, differences in costs were mainly due to the decreased in-patient costs for patients randomised to the mood disorder clinic, but costs to medication was included in the calculations.

Declaration of interest
L.V.K. has within the past 3 years been a consultant for Lundbeck and AstraZeneca.


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