Correspondence

Edited by Kiriakos Xenitidis and Colin Campbell

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Depression: a cultural panic attack

Mario Maj overlooks the wider importance of an evolutionary perspective in discussing when depression becomes a mental disorder.1 He rejects the contextual approach, which considers whether depression is a normal response to circumstances, because of the difficulty of being certain that it is a proportionate response to specific adverse circumstances and the consequent low reliability of the clinician’s judgement. However, the contextual approach does at least have a significant degree of validity, which is lacking in the current DSM-IV criteria. These are the equivalent of classifying any tachycardia, in excess of a particular rate or duration, as abnormal without considering whether it is occurring in the context of exercise or stress.

We recognise sadness or depression as the normal response to a range of major losses (including bereavement). There is evidence that it occurs as a consequence of evolutionary design, in view of the presence of equivalent responses in non-human primates, the response of human infants to the loss of a caregiver before socially appropriate coping mechanisms (with a degree of cultural shaping). Specific mood states may give evolutionary advantages in particular situations that have been faced recurrently over evolutionary time. The possible benefits that depressive symptoms conferred, leading to their natural selection over the course of human evolution, include protection from aggression after losses of status, attraction of social support, and promotion of disengagement from non-productive activities.2

Depressive responses probably developed within small, egalitarian, cohesive, hunter-gatherer societies on the African plains. Modern humans have moved away from the support of close relatives to function within many larger, less supportive groups. In these, they are subject to the mass media, which encourages comparison to others of higher status, motivating the pursuit of unreachable goals.3 The depressive response mechanisms may be functioning normally in environments to which our brains have not yet had sufficient time to adapt. The intensity of response to loss exists on a continuum within the population, related to the meaning of the loss for the individual and their underlying personality, and it is accepted that the precise boundary between normal and abnormal responses is unclear. Yet, it is when depression is not proportionately related to real losses that it is truly disordered, and we risk excessively pathologising depression if we fail to consider context.

A tachycardia is the normal cardiac response to exercise and stress, and a cognitive misinterpretation of the tachycardia can lead to a panic attack. Sadness or depressed mood are the normal response to loss, and our current cultural misinterpretation of the significance of these symptoms could be considered a cultural panic attack or health anxiety. This has consequences. Patients may be encouraged to consider themselves disordered and receive unnecessary treatment. Even if response to antidepressant medication is unrelated to preceding life events, this would not mean that a disorder is being treated. Psychiatric research into depression may be flawed because of the failure to distinguish normal from abnormal responses of the brain. There may also be a failure to adequately relate sadness to adverse social conditions, and a simultaneous promotion of a lack of resilience in society.

Allen Frances, the chair of DSM-IV, now believes that these flaws in research contributed to a false-positive epidemic of diagnoses of psychiatric disorder exacerbated by drug company marketing. He argues that the current DSM-5 draft will exacerbate this epidemic because of lowering of the threshold for diagnosis.4 Disconcertingly, in this draft (www.dsm5.org) the Workgroup on Mood Disorders, of which Mario Maj is a member, proposes not the encouragement of an understanding of depressive symptoms in terms of the meaning to an individual of particular adverse circumstances, but instead the removal of even the bereavement exclusion from the diagnosis of major depressive disorder, thereby removing context completely from diagnosis, exacerbating our current cultural misunderstanding and promoting the over-medicalisation of everyday life.5 Worrying times, exacerbated by the lack of an evolutionary perspective.

4 Frances A. The first draft of DSM-V. BMJ 2010; 340: c1168.

The discussion by Maj1 can be related to a recent article by Huber et al6 in the BMJ reviewing the definition of health. The authors propose a definition of health on the basis of an individual’s ability to react to perturbations in their physiological or psychological state – thus, a healthy individual can respond appropriately to the challenge of a viral infection or life event. Failure of the appropriate coping strategy, whether physiological (e.g. an inflammatory response) or psychological (e.g. a defence mechanism) leads to illness. Social health is proposed to be the ability to respond to opportunities despite limitations imposed by ill health. Huber et al suggest that health be measured through assessment of biological, psychological and social domains using instruments such as COOP/Wonca Functional Health Assessment Charts7 or World Health Organization measures.4

A similar idea is contained in DSM-IV-TR, in the Global Assessment of Functioning Scale.5 Perhaps an adaptation of this could be used to provide a unifying measure of severity and definition of mental disorder. Diagnosis could be based on the presence of symptoms and their duration, and the use of a uniform health rating scale for all disorders would allow for severity grading. Treatment would remain symptom directed, but the increased information provided by structured assessment...
would allow it to be focused on specific psychological and social domains. Overall distinction between mental health and disorder would be determined by the impact of symptoms on global assessment of health.


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Author’s reply: Dr Ganevy echoes arguments put forward for many years by Jerome Wakefield and already extensively addressed in the literature (e.g. Kendler, Murphy & Woolfolk). Indeed, the evolutionary approach may help us to understand how and why depression has developed in the human species as a response to major losses. However, the relevance of that approach to ordinary clinical practice (i.e. in helping the clinician to discern whether the depressive state of a given individual is a mental health problem deserving clinical attention) is, at the present state of knowledge, very doubtful, and the risk of ‘over-romanticizing the suffering associated with major depression’ is very high.

Wakefield himself has documented that as many as 95% of depressive episodes seen in the community are triggered by an adverse life event, according to the affected person’s report. This is not surprising, because many people with depression try to find a meaning in their current state, ascribing it to a recent event. Whether there is really a causal relationship between the event and the depressive state, what is the direction of that relationship, and whether the depressive state is ‘proportionate’ or not to the event is very difficult or even impossible to establish reliably in the vast majority of cases. This was already acknowledged by Sir Aubrey Lewis many decades ago, when he tried to apply a set of criteria aimed to distinguish ‘contextual’ from ‘non-contextual’ depression and had to conclude that almost all cases he had encountered were ‘examples of the interaction of organism and environment, i.e. personality and situation; it was impossible to say which of the factors was decidedly preponderant’.

Actually, whether there is something like a ‘normal’ or ‘proportionate’ response to a given life event is highly debatable. Even when exposed to the most extreme life event, the majority of people will not develop a depressive state. Which ‘standard’ are we going to apply when deciding whether a given depressive response is proportionate or not to a given life event? Are we aware that there are mental health professionals who do believe that every psychological and social domain are essential for that purpose. And preliminary findings.

4 Wakefield JC. Schmitz MF, First MB, Horwitz AV. Extending the bereavement exclusion for major depression to other losses: evidence from the National Comorbidity Survey. Arch Gen Psychiatry 2007; 64: 433–40.


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Psychiatric morbidity in prisoners with intellectual disabilities

Hassiotis et al describe an excess of probable psychosis in prisoners with intellectual disabilities (11.3% v. 5.7%, \(P<0.01\)). We tried to replicate this finding in a large database of 21,857 pre-trial reports of Dutch defendants.\(^3\) A diagnosis of intellectual disability (IQ < 70) was made in 609 defendants (2.8%). However, these individuals had fewer psychotic disorders than defendants without intellectual disability (5.9% v. 12.7%, \(P<0.001\)). Furthermore, fewer defendants with intellectual disabilities reported misuse of hard drugs (13.4% v. 24.6%, \(P<0.001\)) and alcohol (16.6% v. 23.1%, \(P=0.002\)) and their rate of cannabis misuse was similar to that of defendants with a normal IQ (12.9% v. 14.2%, \(P=0.51\)). This again contradicts the findings of Hassiotis et al, who found more cannabis misuse and similar misuse of hard drugs and alcohol in individuals with intellectual disability.

What could explain these opposite findings? The diagnosis of probable psychosis in the Hassiotis et al study was, in 80% of the cases, based on a lay interview, and intellectual disability was defined as a low score on the Quick Test. Diagnosis in Dutch pre-trial reports is based on: (a) multiple examinations of the defendant by a psychiatrist and/or psychologist; (b) the defendant’s judicial and psychiatric history, including previous examinations; (c) information from relatives; and (d) IQ tests in 88% of defendants with intellectual disabilities. As Hassiotis et al themselves suggest, their method may have led to an overestimation of the prevalence of intellectual disability (4%). Indeed, a systematic review in 2008 showed that the prevalence of intellectual disability in prisoners ranged from 0.0 to 2.8%.\(^4\) Moreover, low scores on the Quick Test are significantly related to the prevalence of psychosis.\(^5\) Confounding of the relationship between probable psychosis and intellectual disability is therefore probable. The conclusion reached by Hassiotis et al is premature and more studies on this topic are needed.


Authors’ reply: Vinkers et al have reported discrepant findings between their study and ours. First, their analysis is based on pre-trial reports, albeit detailed, whereas our study is based on a cross-sectional survey of current prisoners. Furthermore, additional variations that predetermine ascertainment and pathways through the criminal justice system must be taken into consideration in such comparisons. Our explanation of the higher rates of psychosis, one among a number of mental disorders we considered, is a combination of possible pre-existing morbidity and the impact of the environment on a vulnerable population. This relationship was mediated by current (defined as use while in prison) cannabis misuse. Second, our data on substance misuse are significant in terms of current use, as defined; lifelong use was similar between prisoners with and without intellectual disabilities. Third, the Quick Test may have led to over- or underestimation of the prevalence of intellectual disability, as we noted. There are additional arguments on this point, as the Quick Test has significant limitations: (a) we were quite conservative in the definition of intellectual disability, using not only a stringent cut-off for intellectual functioning but also poor educational attainment, and we excluded those not born in the UK, to avoid possible confounding by language-related problems; (b) according to Fazel et al,\(^1\) the pooled prevalence based on screening was 6.1% (95% CI 5.3–7.0%),\(^2\) therefore our calculations suggest that we have more or less identified the appropriate sample of prisoners; (c) the paper by Marjoram et al\(^5\) is, in our view, erroneously cited, as its authors discuss specifically the impact of lower IQ on participant performance in theory of mind (hinting) tasks rather than psychopathology. It should be noted that all IQ tests would be compromised if administered to acutely ill individuals. Finally, the literature suggests a common pathway between psychosis and intellectual disability, particularly in early-onset cases\(^4\) and this may be, to an extent, an underlying cause for the increased rates of psychosis. However, the cross-sectional nature of our study does not allow for further speculation on causality. In summary, prisoners with intellectual disabilities are vulnerable and may not receive adequate tailored input for their significant mental health needs. We agree that there should be further studies investigating these issues and we would like to thank Vinkers et al for their interest in pursuing this topic.


Re refurbishing the masked RCT design for psychological interventions

We would like to share some important statistical pitfalls of the randomised design in masked trials of music therapy such as that conducted by Erkkila et al.\(^3\) The randomised controlled trial (RCT) is generally considered to be the optimal design for estimating treatment efficacy in medical interventions. In a double-blind RCT, the placebo effect is equally distributed.
between treatment groups. In Erkkilä et al's trial,¹ in the music therapy arm both the patient and the therapist became aware of the treatment that the patient was receiving well before total data had been collected. Thus, masking was jeopardised. Moreover, the authors did not allow for the patients’ treatment preferences. Patients who receive their preferred treatment may experience greater improvements in the outcome because of added motivation to follow the treatment protocol than patients who do not receive their preferred treatment.

Alternatively to the RCT design could have been used in the study. One option is the randomised consent design. In this, participants are randomised to treatment groups before the informed consent stage, and informed consent is then sought only for those allocated to the experimental treatment.² Any sense of deprivation is less in the treatment as usual (TAU) group, as its members are unaware that they might have received a new treatment.

A second option is the partially randomised preference trial, in which participants without a treatment preference are randomised and those with a treatment preference are allocated to the treatment of their choice. This design has recently been used in some studies of psychological interventions for depression. The design has been recommended as it may improve both the internal and the external validity of clinical trials.³ However, it may subject some studies of psychological interventions for depression to treatment preference effects at the analysis stage and to estimate the external validity of the trial.³

A third option addresses the higher drop-out rate in the control group (11 v. 4) of the trial, which suggests the probably more demanding and careful follow-up in the experimental (music therapy) group. Here, instrumental variable methods have the advantage of allowing adjustment for non-adherence and loss to follow-up. Instrumental variables are associated with treatment choice (e.g. proximity to the music therapy clinic) but not with outcome. Had the patients’ treatment preferences been taken into account in this study, at least some of the eligible individuals would have refused to participate, especially those who lived further from the clinic. Instrumental variables provide an estimate of treatment effect that is adjusted for some of the bias associated with the patient preference design.⁴

Last, it is worth mentioning the doubly randomised preference trial.⁵ This is the most recently proposed method of estimating causal and preference effects. Patients are initially randomised to a randomisation arm, in which treatments are randomised, or to a preference arm, in which patients choose which treatment they receive.

These alternatives to the RCT, which are particularly appropriate for studies in which participants express a treatment preference or masking is less easy, are not free from biases. Nevertheless, they can ameliorate the external and internal validity of trials.

Authors’ reply: It is interesting that a methodological debate is emerging around our randomised controlled trial (RCT) of music therapy for depression.¹ Sen and colleagues could have used any RCT of a psychosocial intervention to discuss their ideas of alternative designs. In relation to our specific study, they raise the following three main points: (a) that our study was not double-blind; (b) that patients may have had a preference for music therapy; (c) that the experimental group may have been followed up more carefully than the control group. We will respond to these points in that order.

First, studies of psychosocial interventions such as music therapy can never be double-blind. Both the therapist and the patient are aware of the therapy they are providing or receiving, and active participation of the patient is necessary. Therefore, demanding a double-blind study shows a limited understanding of the nature of these therapies. We do not always agree with the opinions of Seligman,² but he has put this point very aptly: ‘Whenever you hear someone demanding the double-blind study of psychotherapy, hold onto your wallet.’ Single-blind RCTs are the most rigorous evaluation method that is possible in this field.

Second, the advertisement through which potential participants were recruited to our study did not mention music therapy. Therefore, we believe that a strong preference for music therapy was unlikely in our sample, although we are not able to completely rule out the possibility. Extensions of RCTs such as Zelen’s design³ and partly randomised designs⁴ are not new. They provide interesting options for evaluating many kinds of intervention, including music therapy. However, there are also some good reasons why they are not used more frequently. For one thing, as Sen et al note, hybrid designs may be difficult to interpret. For another, the questionable additional merits of these trials may not justify their much higher costs. Our trial was the first of its kind, and a simple randomised design therefore seemed most appropriate to us. For future trials of psychosocial interventions it may be relevant to explore the potential use of hybrid designs.

Third, in our study, the person who did the assessments, and who also scheduled the assessment interviews on their own, was masked to treatment assignment, and only very few instances of broken masking occurred. We can therefore exclude the possibility that the experimental group might have been followed up with greater care than the control group. Our conclusion remains that the differences in drop-out rates were an effect of the treatment, not an artefact of the study design.

Overall, Sen et al present interesting general thoughts for the evaluation of psychosocial interventions. Of the various suggestions made for improving study designs, we believe that assessing treatment preference and incorporating it in either the design or the analysis is the most practicable one. Hybrid designs including both randomised and non-randomised elements may be useful in certain circumstances, but because of their high costs and unclear interpretation we would not recommend them for general use.


Correspondence

Praying with patients: belief, faith and boundary conditions

The debate between Professors Poole and Cook focuses on what might be termed an epiphenomenon of faith. Poole in particular avoids any interpretation of the values he espouses for psychiatry as a belief system. In my view, this is fundamentally erroneous. The set of principles avowed by Poole find their origin in both Greek philosophy and in the Judaico-Christian system of ethics. These are essentially systems of beliefs and in that sense, particularly for the secularist, are no different from a religious doctrine. In considering this issue it is impossible to start from a position that does not invoke shared belief, and that personal position of belief that is termed faith. I would assume that Poole would take the position that psychiatrists should practise using ‘evidence-based’ techniques and therapies. If one is to take cognitive therapies as an example of this, problems of belief immediately arise, as a primary aim is to change patients’ erroneous and maladaptive belief systems. I would ask to what immediate arise, as a primary aim is to change patients’ evidence-based’ techniques and therapies. If one is to take the position that psychiatrists should practise using ‘evidence-based’ techniques and therapies. If one is to take

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A common example of the integral involvement of belief with therapy is the Alcoholics Anonymous programme. Would Poole refer a patient to this as part of his treatment or would he regard it as the unethical imposition of a belief in a ‘higher power’? More broadly, in psychotherapy there exist a number of theoretical belief systems which have some level of evidence in their favour, particularly in the belief of their proponents. Having observed successful psychotherapists with a variety of backgrounds, I am tempted to say that their theories support their therapies by providing a belief structure that supports their faith that treatment can be of benefit when progress is slow, and that this faith in the future is a key element in their success. If the argument that faith is a fundamental part of the treatment process is accepted, and I would argue that, while this is particularly so for psychiatry it also applies in other areas of medicine, then the major question is the degree to which it is synonymous with belief. If faith provides strength and purpose to both psychiatrist and patient and can be asserted a positive asset without much criticism, belief can be considered as being more problematic and potentially dangerous. In a broad sense, depressive disorders may be considered as an uncommon and unusual part of a therapeutic modality. The therapist should therefore be prepared to justify its use on a case-by-case basis and be able to demonstrate that no harm was likely to arise.

I read with interest the debate between Professors Poole and Cook in this month’s journal. I have been following the exchanges on these two highly polarised positions in the College for quite a while. Not wishing to take a position on the acceptability of praying with patients, I find myself astounded by the inability in some quarters to accept or even recognise the fact that praying with a patient may be as serious as preaching to a patient. Boundaries are set in professional practice to protect both the patient and the doctor. Would a physician feel easy taking stock market tips from their Wall Street banker patient? Or accepting racing tips from their very informed bookmaker patient? How about setting up a business venture with a venture capitalist patient with significant ‘daddy issues’?

Would it be appropriate for a doctor to tell his patient that his Church offers the best chance of redemption, or that she should divorce her cheating husband because this is what is perpetuating her depression? These are all hypothetical examples of boundary violations and are rightly proscribed in all codes of ethics worldwide. In deciding harm in a doctor–patient interaction, surely it is for the doctor to decide where the boundary lies and then to maintain it. The sexual boundary is not the only boundary we should be taught not to cross, although arguably it ought to be the first.

The fact the College has given so many column inches to the issue means that, even if there are no cogent arguments, this matter is something that has immense political clout. Matters are not being helped by letting this issue simmer. We need decisive action. Why can’t the College commission a working group representing all sides of this debate and issue a consensus statement to help believers and non-believers equally to navigate what appears not so much a moral conundrum as political posturing? When I am hauled before the GMC by a patient for inviting him (and encouraging with his ‘consent’) to give up his

system is the only basis for treatment is potentially treacherous if imposed on a patient. Even our present evidence-based structure is predicated on a belief about an organised and regular universe. Speaking as a slightly irreverent theist, I would argue that the question posed in their debate does not have a single correct answer. In judging the most appropriate manner of dealing with a particular situation, the important thing is to consider the principles to be applied. There are some behaviours that would be generally agreed to be inappropriate and damaging without recourse to argument, but others may be appropriate only in certain situations. My recommendation would be that there should not be an overall statement or conclusion that the use of prayer in therapy is either right or wrong. It would have to be considered as an uncommon and unusual part of a therapeutic programme which can only be justified in very particular circumstances. It should be accepted that there are occasions when its use is appropriate and therapeutic. Nonetheless, because of its controversial nature, and the possibility of abuse by both therapist and patient, prayer should be considered an unusual therapeutic modality. The therapist should therefore be prepared to justify its use on a case-by-case basis and be able to demonstrate that no harm was likely to arise.

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faith and join me as a fellow God-less person, where will the guidance come from?

It appears that the inequality of power in the doctor–patient relationship has been forgotten in the heat of this debate. God help me and my fellow confused brethren. It looks like we have been hit for six at this boundary.

Declaration of interest

S.P.S. is a member of the Royal College of Psychiatrists’ Special Committee for Professional Practice and Ethics and a past member of the College’s Ethics Committee.


The debate between Professors Poole and Cook appears to ignore the fact that spirituality, transcendence and individual religious beliefs expressed in prayer are historically and culturally bound to the social institution of organised religion: the first estate. Neither author acknowledges how the sociology of religion and its place in our society affects whether prayer should be shared between doctor and patient. The Christian religion has been firmly bound to the functioning of organised Western society for well over a thousand years. Consideration of the spiritual needs of patients has been part of holistic care models for decades and is present in the delivery of individualised care plans in most mental health services. However, prayer in day-to-day life does not have an individual identity that is divorced from structured religion. There is a potent social boundary here and it should not be crossed, for sociocultural reasons as well as individual professional ethics.

Poole focuses on the individual boundaries that are appropriate in the doctor–patient relationship, but we have social boundaries based on our religious history that have resulted in our modern social institutions having a broad secular base. When in the UK in 2011, religious assassination of police officers occurs within ‘the single-faith Christian tradition’, when football managers receive bullets in the post because of their particular Christian tradition, when the UK still has regions where religion is more about the fire in the belly and less about the angst between the ears, less ‘happy clappy’ and more ‘happy slappy’, it seems a little naive of Cook to view prayer as a therapeutic tool that can exclude the history of Christianity in this country and the challenges this may pose.

Within my own psychiatric service, I am happy to say that we can allow everyone the freedom to pray and express their religion as they wish, a right that has emerged from the religious history of the British Isles. I am fortunate in having a specialised team of professionals with decades of training and expertise in meeting and fulfilling the spirituality of our service users. I turn to their wisdom and guidance often when prayer and religious needs present with mental health problems. We call them the hospital chaplains. I don’t pray with the patients. They don’t give depot injections. It works.

Author’s reply: I am grateful to Dr Davies for highlighting the importance of faith and belief in psychiatry. Atheism, materialism and biological determinism are as much belief systems as are religions. Because of a mismatch between systems of belief, it will often be inappropriate for clinicians to pray with patients. But what about prayer in contexts where faith and belief are shared? In faith-based organisations, in faith communities and in other contexts where doctor and patient are brought together knowing that they share the same belief system, ‘praying with a patient’ takes on a different connotation. The psychiatrist who prays with a patient in such contexts should still be able to justify their reasons for thinking that this would be helpful, and their reasons for expecting that it would do no harm, but I do not see why it should automatically be excluded.

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as unacceptable as those situations encountered by service users who feel that they have been ‘preached at’ by their atheist psychiatrist.

Declaration of interest

C.C.H.C. is in receipt of a grant from the Guild of Health and is an Anglican priest. He is currently Chair of the Spirituality and Psychiatry Special Interest Group (SPSIG) at the Royal College of Psychiatrists. The views expressed in this article are his own.

Author’s reply: Drs Haley, Davies and Sarkar raise issues concerning religion, spirituality and clinical practice beyond the narrow question of prayer.

I am grateful to Dr Haley for setting a broader sociopolitical context. I concur with the points he makes, which underline the fact that this debate is concerned with tangible realities, not abstract differences of belief.

Dr Davies uses three rhetorical devices that have been recurrently utilised by ‘the other side’ in the broad debate. First, he argues on the basis of the fundamental philosophical fallacy of a category error. Religious faith, ethical codes, cognitive therapy and, for that matter, science may all in some way involve belief, but they are not comparable, competing belief systems. They are fundamentally dissimilar. Religious faith is concerned with transcendent, immutable truths that are outside of the realm of reason or evidence. This does not invalidate faith, but it is dissimilar to other types of belief.

Second, Davies assumes that my position is primarily determined by my atheism. However, many professionals with a strong religious faith agree with me,1 because the debate is concerned with professional boundaries, not personal convictions. In the debate with Professor Cook, I mention my participation in a meeting on ‘intolerant secularism’ at the Royal College of Psychiatrists in October 2010.3 This was addressed to the immediate past-President of the College, who did not respond. Instead, a position paper, written by Professor Cook on behalf of the SPSIG, has quietly passed through the College committee machinery, and is now Royal College of Psychiatrists policy.4

On the one hand, the College’s position paper4 emphasises that proselytisation is unacceptable, which is welcome. On the other hand, none of the key boundary issues is addressed, a scientifically controversial position has been adopted with regard to evidence, and the official position of British organised psychiatry is that ‘an understanding of religion and spirituality and their relationship to the diagnosis, aetiology and treatment of psychiatric disorders should be considered as essential components of both psychiatric training and continuing professional development’ (p. 8). This is already having an impact on services. For example, Mersey Care NHS Trust is holding a conference to promote integration of spirituality into psychiatric care5 on the basis that this is a College recommendation.

This debate has teeth, and we are already set on a course that I find extremely worrying. Those who agree with me on the importance of boundaries should make their voices heard now, as we may soon find ourselves in a very difficult place.

Declaration of interest

R.P. is an atheist.


Clozapine and bladder control

Harrison-Woolrych et al2 present an interesting exploration of the association between nocturnal enuresis and clozapine (and other atypical antipsychotic) use. They report a significantly higher rate of nocturnal enuresis with clozapine use than with the other antipsychotics assessed in the study. This suggests a possible mechanism specific to clozapine in causation of this event.

Clozapine has been shown to adversely influence bladder control.2–4 Various putative mechanisms to explain this observation include retention overflow consequent to inhibition of detrusor contraction due to anticholinergic action, reduced sphincter tone due to anti-adrenergic activity,5 sedation and lowering of the seizure threshold,6 drug-induced diabetes mellitus resulting in polyuria7 and drug-induced diabetes insipidus.7 Preclinical studies have demonstrated clozapine’s effects on urodynamics, with a centrally regulated reduction in activity of the external urethral sphincter.8

Bladder deregulation among patients with schizophrenia was described by Kraepelin, who postulated it to be an accompaniment of the ongoing ‘dementia’ process, as evident by the
neuropsychological correlates of this process.\textsuperscript{9} More recent works\textsuperscript{10,11} have also established bladder dysfunction among patients with schizophrenia. The cause was reported to be detrusor hyperreflexia in both studies based on the findings of urodynamic studies. Similarly, high rates of bladder dysfunction have been reported among patients with schizophrenia being treated with clozapine.\textsuperscript{2–4} However, the reports implicating clozapine in causation of bladder dysregulation have been criticised for concomitant use of other antipsychotics in these individuals.\textsuperscript{4} Likewise, the dose of clozapine reported in these cases has been on the higher side.

In this context, it would be interesting to make a mention of a paper reporting a possible curative role of clozapine in neurogenic bladder.\textsuperscript{12} This effect of clozapine was observed in a patient with schizophrenia. However, resolution of urinary incontinence in this case was found to be unrelated to the clinical response for schizophrenia. A high Naranjo algorithm score (\textgreater{} 9), single-photon emission computed tomography and urodynamic findings lend support to the arguments put forward by the authors. Another interesting observation in the case was a therapeutic window phenomenon. Urinary incontinence responded to a dose range of 250–300 mg/day. No response was observed at a lower dose and incontinence reappeared at doses exceeding 300 mg/day. The authors postulated a possible central mechanism for this observation. Reversal of the facilitatory role of the 5-HT\textsubscript{7} heteroreceptor on acetylcholine release by clozapine could underlie its possible role in urge incontinence.\textsuperscript{13}

There are no further reports or studies on the possible role of clozapine in correction of neurogenic bladder, nor has the dose–response effect been studied. It would be interesting to analyse the data by Harrison-Woolrych \textit{et al}\textsuperscript{1} for the effect of dose of clozapine and to see whether there is any pattern with regard to change in nocturnal enuresis.


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Psychiatric morbidity in prisoners with intellectual disabilities
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