Evidence needed for treatment strategies in refractory depression

Matthews & Eljamel (2003) lucidly describe the origin, mechanism and role of vagus nerve stimulation (VNS) in the treatment of refractory depression.

Lack of evidence for strategies to treat refractory depression and lack of perceived options necessitate a fresh look into research on the efficacy of existing treatments and development of new ones. Vagus nerve stimulation may prove to be an effective option and a major advancement, but it is too early even to speculate on recommending it for general use.

The authors state, “If any treatment for chronic, refractory depressive disorder were to offer the prospect of sustained, clinically significant changes in 20–30% of patients, this would represent a major therapeutic advancement”. However, our systematic review of treatment of refractory depression (Stimpson et al, 2002) showed an overall placebo response rate of 15% with 95% CI of 7.9–23.4%. This rate is even higher in relatively less chronic depression, reaching up to 30–40% in some trials. Hence, the response rate of 31% in open trials for VNS may largely be due to placebo response and may not result in a satisfactory ‘number needed to treat’ in randomised trials.

The need for further research in this area cannot be overemphasised. Authors have highlighted the difficulty of finding an appropriate control condition. Even if we can satisfy the need for an appropriate placebo control, these trials should not be considered sufficient. For evidence to be robust, any new treatment for refractory depression should at least be compared with the existing active treatments, such as augmentation strategies, in addition to placebo control. Non-inferiority trials without active treatment comparison are not only unethical, they do not help clarify the question of what is the next best strategy in a particular patient with refractory depression. The second half of the past century saw a number of commonly used treatment strategies based only on preliminary evidence. Let us not perpetuate the same mistake in the 21st century.


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Drug misuse in pregnancy

I read with interest the recent editorial by Johnson et al (2003) and I agree with the authors that substance misuse, including in women of reproductive age, has increased markedly over the past 20 years. In my practice of obstetrics and obstetric anaesthesia, I have provided care to many drug-misusing parturients and would like to add some comments on this timely topic.

Five million Americans are regular users of cocaine, 6000 use the drug for the first time each day and more than 30 million have tried cocaine at least once. Approximately 250 000 women in the USA meet the criteria for intravenous drug abuse. Nearly 90% of these women are of childbearing age (Kuczkowski, 2003). Psychological personality characteristics seem to predispose to, rather than result from, drug addiction. Most often, drug misuse is first suspected or diagnosed during medical management of another condition such as hepatitis, HIV/AIDS or pregnancy. Most parturients with a history of drug misuse deny it when interviewed preoperatively by primary care physicians, obstetricians or obstetric anaesthesiologists. A high index of suspicion for drug misuse in pregnancy, combined with non-judgmental questioning of every parturient, is therefore necessary (Kuczkowski, 2003). Risk factors suggesting substance misuse in pregnancy include lack of prenatal care, history of premature labour and cigarette smoking. Substances most commonly misused in pregnancy include cocaine, amphetamines, opioids, ethanol, tobacco, marijuana, caffeine and toluene-based solvents. Polysubstance misuse is very common. The diverse clinical manifestations of substance misuse, combined with the physiological changes of pregnancy and the pathophysiology of coexisting pregnancy-related disease, might lead to life-threatening complications and significantly affect the pregnancy outcome.


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The article by Johnson et al (2003) was disappointing as they failed to present a balanced view of this topic. It is, of course, important to discuss possible effects of drug misuse on pregnancy, but to emphasise them without due and thorough consideration of the many confounding factors in this area is misleading. These include smoking, alcohol use, social deprivation, poor nutrition, quality of antenatal care and drug treatment, as well as accessibility of services. Clearly, these are additional factors that drug-misusing women will have to contend with. Well-designed, unconfounded studies in this area are rare, which means that findings on the specific effects of illicit drugs are inconsistent and contradictory (Ford & Hepburn, 1997).

The article failed to reflect that much of the recent work in this area has looked at flexibility of treatment services and equity of access. Women drug users are deterred from engaging with health and social care providers because of judgmental attitudes (Klee et al, 2002). We felt that the article
had an unsympathetic tone, and had missed the point that the onus is on treatment services to make themselves accessible to women who may have chaotic lives. Our approach to care is crucial if we are to retain these women in treatment throughout their pregnancy, and this support needs to flow seamlessly into the postnatal period.

There is a relationship between maternal methadone dose and severity of neonatal abstinence syndrome, but this is not a close one (Johnstone, 1998). The onset, duration and severity of neonatal abstinence syndrome is multi-factorial and related to the infant's metabolism, gestational age and central nervous system maturity. It is essential to work with parents to prepare them for the possibility of neonatal abstinence syndrome and to try to involve them in the management of this condition.

Johnstone et al (2003) have provided us with a comprehensive list of possible unfavourable outcomes, but a more measured picture of the many difficulties that face both clients and health care professionals in this area would have better informed the Journal's readership.


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Author's reply: We thank Drs Whittaker and McIntosh for their interest in our article, but they have misinterpreted its contents. As stated, the aim of our editorial was to emphasise the importance of the topic by describing the unfavourable effects illicit substances can have on both pregnancy and infant outcome; we are therefore pleased that Whittaker and McIntosh state we have provided a comprehensive list of unfavourable outcomes. We agree that treatment services should be accessible to women, as it is important to retain them throughout pregnancy and provide support through into the postnatal period. Indeed, in the final paragraph of our editorial we described such a package of care. We are surprised that Whittaker & McIntosh feel that our article had an unsympathetic tone; careful reading of our editorial demonstrates that it emphasises the importance of optimising treatment and reducing morbidity and argues for adequate resources to be made available.

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Personality in psychiatry: what thin partitions?

In his editorial on the interpersonal domain, Hobson (2003) asserts that the analysis of intersubjective engagement in the therapeutic dyad is essential to the understanding of subjective meanings and their role in the manifestation of psychiatric disorder. In the same issue of the Journal, Lannman et al (2003) describe their attempts to determine a measure of 'fit' between individuals in a 'couple system'.

Both these papers acknowledge a fundamental fact concerning all human relationships: that they are, in their totality, the interaction between one personality and another. What is striking, however, both in these papers and in other recent literature concerning, in particular, personality disorders (Tyrer et al, 2002), is the lack of any discussion concerning the specific role the therapist's/clinician's personality plays in shaping the therapeutic relationship.

Hobson's use of Donne's metaphor ('No man is an Island, entire of itself') captures what I believe to be the sine qua non of personality disorder; namely, that personality disorders can only be understood in the context of interactions between personalities; that the construct of personality disorder cannot exist in isolation. This notion is akin to the distinction made between 'primary' and 'secondary' qualities by the philosopher John Locke. In a psychiatric context one might consider schizophrenia to be a primary phenomenon, an integral part of the individual, whereas personality disorder, being contingent on an interaction with another, is secondary.

If one can accept the notion of personality disorder as a consequence of the interaction between two personalities, then surely it behaves members of the psychiatric profession to consider how their personalities influence the therapeutic relationships that lie at the heart of the discipline. That this appears, historically, not to have been the case is revealed by Lewis & Appleby's (1988) seminal paper. While amply demonstrating psychiatrists' negative attitude towards individuals with personality disorder, the authors failed to address the possibility that this might be a function, in part, of the psychiatrists' personalities.

If we are to be 'scientific' about studying interpersonal functioning, then perhaps the first step might be to consider a systematic evaluation of both personalities involved in the therapeutic dyad. One possible method might employ a dimensional assessment of personality that would, in turn, help define how different personalities 'fit' together. For example it might be reasonable to expect a clinician, scoring highly on the 'openness' dimension of the NEO–PI–R (Costa & McCrae, 1992) to fit well with a patient scoring much lower on the same scale.

If this were shown to be the case, it could have important ramifications for resource allocation, both in psychotherapy and in the wider psychiatric field, allowing individual personalities to be fitted together in order to better facilitate the therapeutic relationship. An appreciation of the role their own personalities play in the construct known as personality disorder, might also diminish psychiatrists' negative attitudes to the disorder they appear to dislike.


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Authors’ reply: We are grateful for the opportunity to respond to Dr Calton. He challenges claims for objectivity in the diagnosis of any disorder that has an interpersonal component, taking as his example some research into the diagnosis of personality disorder. He queries why we do not consider the role of the therapist’s personality in our paper, ‘Objectivity in psychoanalytic assessment of couple relationships’ (Lanman et al, 2003). In that paper, where we show evidence of a good degree of objectivity (based on interrater reliability) for the diagnoses we discuss, we specifically refer to the fact that those making the judgments need to have had a psychoanalytically based training in order to develop their ability to make use of their emotional reactions to the patient.

Our paper deals with psychotherapeutic diagnoses, rather than with psychiatric ones, but on the basis of our work we would like to comment on Dr Calton’s position. First, there are likely to be very significant differences in what is judged to be a helpful ‘fit’ between therapist and patient, between the two different domains of general psychiatry and psychoanalytic psychotherapy. In the former, a friendly and sympathetic stance may be the crucial therapeutic vehicle for providing medication and other treatments. But in the domain of psychotherapy it is not necessarily a good thing to ‘match’ therapist to patient, if by this one means attempting to avoid prejudices or sensitive areas, because this is likely to lead to a serious evasion of the darker areas of interaction, conscious and unconscious, where the significant problems will tend to lie. If the study of the interaction ‘in the room’, between therapist and patient, is itself the treatment, then the therapist’s best equipment for this is self-knowledge, including knowledge of the darker areas of his or her own personality and knowledge of how to recognise and use the ways in which these affect him or her.

While personal psychotherapy together with detailed supervision by no means guarantees the development of such knowledge – and there will be practitioners who are unable to respond, as well as therapies which do not go far enough – these remain the best available means of acquiring the skills necessary to work with unconscious processes, enabling a therapist to understand a patient’s personality difficulties and the way these interact with their own. Outside this particular field, it may not be widely recognised that one of the principal tools of contemporary psychoanalytic therapy is the constant monitoring by practitioners of their own emotional responses to patients, not simply in order to suppress or redirect them, but in order to gain information that the therapist will then be able to employ in clinical diagnosis and engagement with patients. This is not to be confused with the self-disclosure advocated by some therapies. In our view there is no substitute for a rigorous psychotherapeutic training in this area, which includes selection of trainees, personal psychotherapy and detailed supervision.


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Creativity and mental health

After thoroughly enjoying Dr Wills’ 1988 book (Wills & Cooper, 1988) I was dismayed to see his recent article (Wills, 2003). His book detailed the real, unmitting and often unique stressors faced by those struggling to make a living from music – as opposed to the pop-psychology focus on their (allegedly) inherent psychological flaws.

Although entertaining, psychological autopsies are not valid research tools, as the author fortunately points out in the ‘limitations’ box. Further, the ‘comprehensive literature’ about the psychopathology/creativity link is shot through with badly designed studies and dramatic overstatement.

Like Wills, Jamison (1989) was the sole judge of her hand-picked sample – 47 creative artists – but few authors dig up her unreplicated original work, preferring to pass along her unscientic conclusions. For example, many introductory psychology textbooks include her contention that 50% of poets have affective disorders, without noting that she had only 18 poets in her sample and moreover diagnosed affective disorder as simply ‘seeking treatment’ for it. And while Ludwig’s book (1995) is full of charts and graphs, on close and trained inspection they are overwhelmingly meaningless; despite its subtitle, it actually resolves nothing at all.

Unfortunately, the tradition in this field is to pass along any confioratory ‘mad creative’ conclusions, regardless of any liberties taken with the scientific method.

Most of the common research blunders are detailed by Arnold Rothenberg (1990), as well as in my own work (Schlesinger, 2002a,b). Such flaws should have been fatal, but apparently the public appetite for the doomed artist is too great. It’s a shame that so many professionals continue to feed it with their invalid speculation. As Wills understands better than most, musicians don’t need anything else to worry about.


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Author’s reply: Schlesinger feels that ‘psychological autopsies are not valid research tools’, and is scathingly critical of the work of Jamison (1989) and Ludwig (1995). However, she fails to take into account the conclusions of Jamison’s later work (1993), which, as well as reporting on her own study of 47 contemporary British writers and artists, also discusses biographical material relating to 195 famous artistic creative persons, 21.5% of whom died by suicide and 33.3% of whom were hospitalised with psychiatric problems. Jamison also refers to many academic studies of creativity and mental illness stretching back over the past century.

Turning to what Schlesinger describes as Ludwig’s ‘overwhelmingly meaningless’ charts and graphs, I have to say that I find his statistics perfectly acceptable and meaningful. The use of psychological autopsies is a legitimate exercise if one follows rigorous
guidelines as laid down, for instance, in the scholarly work of Runyan (1982).

What is Schlesinger's own view of the creative person? She tells us (2002) that he/she is a heroic and mystical figure, branded as mad by the jealous and uncompromising average person. This is a straightforward reiteration of the ideas of the antipsychiatry movement of the 1960s and 1970s. We are back in the realms of the Laingian figure who is simply too insightful and too existentially aware for our society. Have we not moved on since then?


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Creativity, mental disorder and jazz

I am very happy that Poole (2003) feels that my paper (Wills, 2003) makes a significant contribution to the literature on the relationship between creativity and mental disorder. Nevertheless, I would like to comment on certain points that he makes.

First, the literature on the above topic may be flawed, but it is not small, since an abundance of references extends back at least a hundred years, and it is not inconclusive, since a regular finding is that of the connection between high artistic creativity and mood disorders.

Second, although jazz biographies are written in order to sell books, they tend to be sober, respectful and well-researched, and often are written by academics. Even the most comprehensive psychiatric assessment cannot match the time and effort expended by responsible biographers.

Poole feels that I was uncritical in my acceptance that Thelonious Monk had a dementing process caused by excessive drug usage. My information was taken from the biography by Gourse (1997).

She interviewed Dr Everett Dutil, a Monk aficionado who discussed Monk’s case with doctors who knew him, and who felt that drug-induced dementia was the likely diagnosis. Similarly, Poole feels that John Coltrane did not necessarily exhibit pathological behaviours, yet first-person accounts in six Coltrane biographies describe these, and in his acclaimed biography Porter (1998) states, ‘There is absolute agreement that Coltrane practiced maniacally…’.

Poole’s belief that ‘Even severe mental disorder is not incompatible with creativity… there is no negative association between the two’ needs clarification. It depends on the type, and the stage of development of the mental disorder. For instance, hypomania often facilitates creativity, but severe depression will extinguish it (Akiskal & Akiskal, 1988).

A better understanding of the link between creativity and mental disorder will help great artists to do what they do best – be creative.


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Flashbacks in war veterans

Jones et al (2003b) appears to have missed the point of my letter (Burges Watson, 2003). They define flashbacks as ‘a form of dissociative state’ (Jones et al, 2003a). This is the way the term flashback is used in the DSM–IV; ‘dissociative flashback episodes’ (American Psychiatric Association, 1994). They appear as an example of one of five ways in which ‘the traumatic event is persistently re-experienced’. Only one is necessary for the diagnosis. As such they are not ‘a core symptom’ of post-traumatic stress disorder. As defined in DSM–IV, flashbacks themselves are no more than ‘a recurrence of a memory, feeling or perceptual experience from the past’. This definition may well have been introduced because of the popularity of the term ‘flashback’ and necessary because its original meaning had been changed by popular usage. Jones et al are probably right when they hypothesise that this popularity was encouraged by the use of flashbacks in films and television programmes.

The changing presentation of symptoms associated with the extreme stress of war is indeed interesting. Bizarre dissociative states with physical manifestations, while very common in the First World War, were comparatively rare in the Second World War and very uncommon in Vietnam veterans. Thus, in line with the focus on physical symptoms in earlier wars, it would seem that the presentation of dissociative states has also moved from the physical to the psychological.


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Mental health and social capitals

The correspondence prompted by McKenzie et al’s (2002) editorial suggests that social capital can be the property of individuals as well as groups (Pevalin, 2003; Walkup, 2003). However, McKenzie finds this idea problematic and argues that, as the majority of health scientists conceive of social capital as an ecological concept, we should ‘consider effects at an individual level as social networks’ (McKenzie, 2003: p. 458). This restricted view rejects the potential contribution to psychiatric research of alternative sociological conceptions of social capital that are both rigorously defined and empirically tested.

One such approach is taken by Lin et al (2001) who adopt neo-Marxist notions of capital. Here, social capital is ‘investment in social relations by individuals through which they gain access to embedded resources to enhance expected returns of
Author's reply: The wealth of a country is more than the sum of the wealth of the individuals in it. When times get hard, the wealth of a person may be important but general societal infrastructure, housing, clean water, and the health and social safety net are particularly important. All these factors are linked to the wealth of the country, the distribution of wealth and the investment in a social safety net. It is clear that the health impact of the wealth of the individual is constrained by the wealth of the country – unless they are super rich or super poor. It is also clear that individual wealth is a very different animal from the wealth of a country. They are governed by different rules and indeed they have different names – an individual cannot have a gross domestic product.

Social capital is similar. There are good arguments for considering it at an ecological or an individual level. Just like the wealth of a country or an individual, the concepts of ecological and individual social capital are very different, and using the same name is confusing.

Mr Webber, Professor Huxley and I agree that social capital is the embedded resources of a society such as civic institutions. This is social capital at an ecological level. We would agree that different individuals in the same geographical area may have differential access to this social capital by way of their place in society or social relations. The sum total of social capital that they have access to is limited not only by their ability to get it, but also by the total amount that is available in that area. In addition, differential ability to get social capital is partly a function of the individual but is significantly constrained by the structure of the society that the individual lives in.

The challenge to those who consider social capital at an individual level is to answer the question: what is the added value of conceptualising and renaming social networks as social capital (McKenzie, 2003)? They also have to consider whether they are measuring what social capital is or measuring how it is acquired.

It is confusing to define social capital both as the amount of resources potentially available to anyone in society and as an individual's ability to access such resources. Moreover, linking ecological and individual variables is fraught with difficulty – classically, the ecological and atomistic fallacies.

Although I argue that another term should be used for individual social capital, I think that these arguments take energy away from what should be the focus of the endeavour which is to improve our ability to describe our social worlds.

I have used the term social capitals previously to describe different types of ecological social capital in an area (McKenzie et al., 2002). Using the plural underlines the fact that there are different dimensions of social capital in an area and that the linear scales that some use, so as to label an area high or low in social capital, do not reflect the complex nature of social capital. Areas are better considered dimensionally along the lines of their different social capitals, such as bonding, bridging, vertical, cognitive, structural or social efficacy or cohesion. Such a taxonomy of social capitals could be expanded to include varieties of individual social capital as long as the caveats above have been taken into account.

I do not suggest that the variables that some researchers call individual social capital not be measured. I have, however, suggested that they should be accurately described and named. Perhaps the way forward is to clearly state what is being measured in studies and why, rather than making a further leap to say that proxy measurements reflect social capital which is, of course, a theory that is still in development.