Correspondence
EDITED BY KIRIAKOS XENITIDIS and COLIN CAMPBELL

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Borderline personality disorder

It is refreshing to read a generally positive and optimistic editorial about borderline personality disorder and its long-term prognosis (Fonagy & Bateman, 2006). It is also reassuring to find the authors speculating about an issue long recognised by users of personality disorder services, that is, the ‘reality of iatrogenic harm’.

We feel, however, that there is a worrying element to this piece: the almost casual assertion that ‘in any case, in the vast majority of cases, borderline personality disorder naturally resolves within 6 years’. We question the validity of this rather astounding statement. One of the studies quoted by the authors as evidence of this (Zanarini et al., 2003) was a naturalistic study that assessed people at four time points (baseline and 2, 4 and 6 years) and did not document what therapy or treatment people received between assessments. It did not suggest, or even try to suggest, that borderline personality disorder ‘naturally resolves’ within 6 years.

Fonagy & Bateman also seem to imply that borderline personality disorder exists as an easily definable, distinct personality disorder, which the authors will know is very rarely, if ever, the case. People with borderline personality disorder often have other personality disorders and Axis I illnesses, as well as related alcohol and drug misuse. The idea that such complex needs will somehow spontaneously remit in 6 years is untenable.

What is particularly disturbing about this assertion is its potential political impact and the impact it may have on policy makers, coming as it does from two of the leading authorities on borderline personality disorder within the UK; indeed, from two experts who are closely involved with the development and assessment of new services for personality disorder that are currently being piloted by the Department of Health. Such a statement could be seized by a Whitehall policy advisor and taken as a perfectly adequate reason why services for people with borderline personality disorder do not need to be provided by the National Health Service, as for the vast majority of these people the problems will ‘naturally resolve’ within 6 years.

It is extremely disappointing that two such highly regarded experts in this field should perpetuate such a flagrant and dangerous simplification through the pages of this eminent Journal.

Declaration of interest

D.A. and R.H. are unpaid directors of Borderline UK Ltd.


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Authors’ reply: We thank Ashman & Haigh for their comments but are not clear why they find it ‘disturbing’ rather than heartening that current follow-up studies in the USA suggest that improvement rates associated with borderline personality disorder are far better than previously thought and that substantial numbers of those seeking treatment no longer meet diagnostic criteria on follow-up. The study by Zanarini and colleagues has, in fact, now had its 10-year follow-up (the most recent published report is Zanarini et al., 2005). The Collaborative Longitudinal Study of Personality Disorders is at present only 4 years and shows a more rapid recovery from major depressive disorder than is manifested in borderline personality disorder. We do not believe that the rapid recovery from major depressive disorder has led health experts to suggest that depression should not be treated. There is a third study, by Cohen et al. (2005), that shows similar findings in personality disorder. Why such high remission rates are observed in this population is a matter of controversy and is discussed in some detail by Livesley (2005). Issues of sampling, diagnostic criteria and interview methodology may all need to be carefully thought about before implications for clinical management and health policy are determined and this was neither the explicit nor implicit aim of our editorial. However, we feel strongly that no matter what the limitations of empirical data, systematically collected information is to be preferred to emotionally charged claims based on personal experience that for far too long have overly influenced policy in our field, to the great disadvantage of the client group.

We are sure that Ashman & Haigh will join us in hoping for a debate on the issue of remission that is well-informed by controlled trials and systematically collected follow-up data. Health policy is determined by the best currently available evidence but we make it clear that the current data are incomplete. We are not in the habit of oversimplifying complex issues and do not wish to minimise the seriousness of this disorder or the resources required for its appropriate treatment, which may indeed bring forward remission. We feel, however, that the recent follow-up data, whatever the limitations, should give hope to both families of individuals with borderline personality disorder and service providers faced with the challenge of helping these individuals, an objective that is at the core of Borderline UK’s mission.

Declaration of interest

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Psychological morbidity during pregnancy and low birth weight

Patel & Prince (2006) reported cohort data from Goa, India that showed maternal psychological morbidity to be independently associated with low birth weight (<2.5 kg) and to have an adverse impact on foetal growth. We agree with the authors’ findings and consider that low birth weight as a consequence of treatable psychological morbidity during pregnancy should be an important health priority worldwide.

Recently we investigated whether exposure to the bombing of Belgrade in 1999 during pregnancy was associated with lower birth weight of babies. Mean birth weight of infants born in 1999 in Belgrade was compared with that of those born in 1996 and 2003 (no stressful events affected the city in these years). We collated data on the number of deliveries in Belgrade, birth weight, the percentage of stillborn babies, the percentage of premature births and maternal age from information on deliveries collected annually by the Institute of Public Health, Belgrade. Secondary analysis of this data-set, despite some methodological limitations, revealed that mother’s age, percentage of stillborn babies and the percentage of premature births did not differ between the years but there was a significant decrease in mean birth weight of all babies born in 1999 compared with the other 2 years (3.111 kg v. 3.278 kg in 1996 and 3.223 kg in 2003) (P <0.05). Similarly, Lederman et al. (2004) showed that infants born at term to women who were pregnant on 11 September 2001, and who were living within 2-mile radius of the World Trade Center (New York) during the month after the bombings, showed significant decreases in birth weight and height.

Infants of low birth weight who are born at term are more likely to experience psychological distress in adulthood (Wiles et al., 2005) and to have an increased risk of affective illness (Gale & Martyn, 2004). Therefore not only is research on maternal psychological morbidity very important but a specific screening strategy and preventive plans for infants at risk of low birth weight are urgently needed worldwide.


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‘Delay’ hypothesis of onset of antidepressant action

The ‘delay’ hypothesis has had a long life and has greatly influenced the treatment of depression and research aimed at the development of new ‘more rapidly acting’ drugs. Evidence has gradually accumulated that the hypothesis is inaccurate and its entrance into the lore of clinical practice and textbooks is unwarranted. The hypothesis was derived from studies that did not test it directly and are now viewed as both conceptually and methodologically inadequate. In his editorial, Mitchell (2006) makes salient points and, after reviewing some of the current literature, comes to the correct conclusions. However, our earlier results that refuted the hypothesis (Katz et al., 1987, 1991) and a more recently published study (Katz et al., 2004), designed to definitively test the ‘delay’ notion, were not referenced. Their omission leaves important gaps.

Mitchell highlights the inadequacy of the ‘outcome’ measures used in early studies and the importance of distinguishing ‘improvement’ from ‘full response’. The central criticism of the early work (e.g. by Gelenberg & Cheson, 2000) is that most information was derived from clinical trials, not studies designed to accurately estimate onset and time course of changes. Such studies require a placebo control, sensitive measures of behavioural change (beyond the Hamilton Rating Scale for Depression) and frequent early assessment. The meta-analyses of Stassen et al. (1997) came close to achieving these aims. However, no study had met all the necessary requirements until that conducted by our group (Katz et al., 2004). This measured the major behavioural components of the disorder intensively at 3-day intervals, operationally distinguished improvement and full response and compared pharmacologically different antidepressants (a selective serotonin reuptake inhibitor and a selective noradrenaline reuptake inhibitor) with placebo. In targeting the issue directly, it used appropriate statistical methods to investigate whether algorithms could be developed to predict treatment response from early behavioural changes, problems alluded to by Mitchell. We understand that an editorial cannot provide an exhaustive review but believe the information above will contribute to the important issues addressed.


**Author’s reply:** I thank Katz et al for their insightful comments on this complex topic. I am familiar with their work but, as they suspected, unfortunately removed their 2004 reference from the final version of my editorial because of space restrictions imposed by the *Journal*. In fact, I reluctantly removed an entire section concerning the value of predicting improvement based on early response in certain psychopathological domains. Katz et al appear to be one of the few groups to examine the issue of differential response in various domains in sufficient detail (Farabaugh et al, 2005). As they recognise, the purpose of an editorial is not to provide an exhaustive review but a synopsis of studies of outstanding interest. Since submitting this editorial a year ago, colleagues and I have nearly completed a more thorough review of this topic, including the work of the San Antonio group and the parallel research that challenges the delayed onset of antipsychotics (Agid et al 2003). I would very much welcome readers’ observations regarding the rapidity and measurement of onset of action of mood stabilisers and electroconvulsive therapy, which have received relatively little attention to date.


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**Psychotropic complementary medicines**

The recent review by Wernke et al (2006) contains substantive errors and omissions regarding the *iboga* alkaloid ibogaine and its synthetic congener 18-methoxyecgoninine (18-MC). The review cites a single paper published in 1994 consisting of seven case reports and overlooks two larger studies on the use of ibogaine for the treatment of opioid withdrawal in 32 (Mash et al, 2001) and 33 patients (Alper et al, 1999). These were retrieved on Medline using the search terms stated by Wernke et al. The authors incorrectly state that clinical trials of ibogaine were abandoned because of cerebellar toxicity: this has been limited to the rat at higher doses than those that diminish drug self-administration and opioid withdrawal, and has not been evident in primates or mouse models (Alper, 2001). In 1993 the US Food and Drug Administration authorised Phase I clinical studies in which humans were given ibogaine. These studies were halted only because of a contractual dispute among the study sponsors and not because of safety issues.

**Table 6 of Wernke et al’s review states** that ‘18-MC binds to the NMDA [N-methyl-D-aspartate] receptor’ and that this is because of its putative anti-addictive mechanism of action. Mash et al (1995) is cited but this paper makes no mention of 18-MC, which lacks significant affinity for the NMDA receptor but is a potent antagonist at the z4z6 nicotinic receptor (Maisononneuve & Glick, 2003). The statement that ibogaine blocks ‘the dopamine response in general’ is inaccurate, as ibogaine does not have the properties of a dopamine receptor antagonist and does not decrease dopamine release in all brain regions (Maisononneuve et al, 1991).

Wernke et al stated that ‘All recovered papers were reviewed for further relevant references’, which would have led, among other sources, to an entire volume devoted to ibogaine of the Medline-indexed serial *The Alkaloids* (Alper & Cordell, 2001) and the additional references cited here. Systematic implementation of the stated search strategy and careful and accurate reading of the papers that were retrieved would have provided a far more credible evidence basis regarding the use of *iboga* alkaloids for the pharmacotherapy of addiction.


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The antagonism at the $\alpha_3\beta_4$ nicotinic receptor should have been highlighted as a therapeutic target for the modulation of drug seeking but this would not have changed our conclusions since we have not doubted the potential efficacy of ibogaine. However, we maintain that ibogaine and iboga extracts may not be safe and thus should not be recommended. Ibogaine derivatives with an improved therapeutic index may prove clinically useful in the future. These are likely to be synthetic, thereby leaving the realm of complementary medicine.


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One hundred years ago

The Medico-Psychological Association of Great Britain and Ireland

The quarterly general meeting of the Association was held on Thursday, May 31st, at the Medical Society’s Rooms, Chandos Street, London, W., under the presidency of Dr. Outterson Wood.

Epilepsy and changes in the blood and nervous system

Dr. John Turner read a paper entitled The Relation of Epilepsy to Changes in the Blood and Central Nervous System. He stated that epilepsy was the result of a double cause or tendency, the one an inherently-defective nervous system from a hereditarily-vicious organization, and the other some morbid condition of the blood whereby it shows a special tendency to intravascular clotting, and that the immediate cause of the fits is sudden stasis of the blood stream, resulting from the blocking of cerebral vessels by these intravascular clots. The fits he regarded as only a symptom of the general epileptic condition. Further investigations were related as to the coagulability of the blood in epileptics, which was shown to increase at the times of petit mal, grand mal, and stasis. Forms of changes in the nerve cells were shown, resembling those described as réaction à distance, and persistence of large numbers of subcortical nerve cells was shown. The author also referred to experimental work by ligature of the cerebral arteries in the dog, with acute forms of cell changes. The blood was shown to have a large number of blood plates, and specimens were shown of different forms of intravascular clotting, probably in a large measure derived from amalgamation of the blood plates. Small cortical haemorrhages were also described and shown on the screen, which could be traced to rupture of a vessel blocked up by the clots of coagulated blood referred to.

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