between sampling as widely as possible, with a consequent reduction in response rates, or sampling more narrowly and missing important pockets of data. With regard to the validity of the therapists' reports, as explained in our article, we did, in fact, tackle this issue by comparing respondents who had referred to notes with those who had not. No differences were found on any of the variables in the analyses.

In responding to our research, Drs Brandon & Boakes refer to their own experience of therapists and individuals who claim to have recovered memories. However, they do not provide any numbers or information about the source of their data. As they will be the first to acknowledge, the people who form the basis of their experiences are unlikely to be a representative sample. In contrast, our survey involved what is, to date, the largest number of observations of clients reporting recovered memories collected systematically in a sample of therapists of all theoretical persuasions.

Andrews, B., Morton, J., Bekerian, D. A., *et al* (1995) The recovery of memories in clinical practice: experiences and beliefs of British Psychological Society Practitioners. *Psychologist: Bulletin of the British Psychological Society*, **5**, 209–214.

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Ecstasy use and neuropathology

Sir: Obrocki *et al* (1999) claim to reveal long-term effects of methylenedioxymethamphetamine (MDMA) on the central nervous system in a study of seven subjects, but in fact repeat the errors of previous published studies of neurotoxicity in humans (McCann *et al*, 1998). McCann *et al* provided convincing evidence of an association between decreased serotonin (5-HT) transporter binding sites and MDMA use, and Obrocki *et al* demonstrate an association between MDMA use and altered glucose metabolic uptake in Brodmann's area 11 in particular. However, association does not imply causation, and the findings could be explained in terms of neuropathology caused by MDMA use, MDMA use caused by neuropathology, or both arising from a common denominator. Both Obrocki *et al* and McCann *et al* focus exclusively on the first hypothesis to the detriment of their otherwise convincing results. As has already been noted (Morgan, 1999), it is equally plausible that MDMA use results from pre-existing 5-HT function abnormalities; in other words, affective disturbance may lead individuals to 'self-medicate' with MDMA. Since absence of psychiatric disease constituted an exclusion criterion for Obrocki's control subjects, *P* values would be expected to be lowered further if Morgan's (1999) hypothesis were true. Future studies should consider Axis I disorder prior to MDMA use, subclinical mood disorder, and previous or current Axis II diagnoses with particular reference to impulsive behaviour in which hippocampal pathology may be involved. Since MDMA use in the community is so prevalent, prospective studies would be valuable and possible, although ethically difficult.

McCann, U. D., Szabo, Z., Scheffel, U., *et al* (1998) Positron emission tomographic evidence of toxic effect of MDMA ("Ecstasy") on brain serotonin neurons in human beings. *Lancet*, **352**, 1433–1437.

Morgan, J. F. (1999) Positron emission tomographic evidence of toxic effects of MDMA ('ecstasy') on brain serotonergic neurones in human beings: users may self-medicate for axis I and II disorders. *Lancet*, **353**, 1268–1269.

Obrocki, J., Buchert, R., Väterlein, O., *et al* (1999) Ecstasy – long-term effects on the human central nervous system revealed by positron emission tomography. *British Journal of Psychiatry*, **175**, 186–188.

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Authors' reply: We agree that there is a theoretical possibility that the alterations in glucose metabolic rates detected by positron emission tomography within the ecstasy user group might be caused by pre-existing aberrant neuronal activity. Yet, to our knowledge, conclusive neuropathological findings that are characteristic for secondary drug misuse do not exist. Putative psychopathological phenomena mediating the secondary use of ecstasy are most likely heterogeneous and too diffuse with regard to the 2-(^{18}F)-fluoro-2-deoxy-D-glucose PET method. It therefore seems more reasonable that the detection of altered glucose metabolic rates in ecstasy users is a consequence of experimentally well-documented neurotoxic serotonergic lesions caused by MDMA. In this sense, we disagree that it is equally plausible that MDMA abuse results from measurable pre-existing 5-HT function abnormalities. We have examined the relations between psychiatric disorders and PET findings mentioned by Dr Morgan in a completed study with 107 ecstasy users (Thomasius, 1998). The publication of the results is in preparation.

Thomasius, R. (1998) Ecstasy: user groups and risk levels. An empirical study based on psychiatric-, psychodynamic-, EEG-, EP-, PET and other medical diagnostics of 100 Ecstasy users. *Wiener Zeitschrift für Suchtforschung*, **21**, 9–14.

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Selective serotonin reuptake inhibitors and personality change

Sir: In Ekselius & von Knorring's (1999) study, I find it difficult to accept the assumed independence between depression and the majority of the self-rated Karolinska Scales of Personality (KSP) (e.g. somatic and psychic anxiety, muscular tension, monotony avoidance, indirect aggression, inhibition of aggression, irritability, guilt, detachment, social desirability). The authors considered the Montgomery–Åsberg Depression Rating Scale (MADRS) change (baseline – after 24 weeks) as an indicator of improvement in depression, and used this variable as a single predictor in a series of stepwise regression analyses with changes in single different KSP scores as outcome variables. The consistently low coefficient of determination R^2 values lead the authors to conclude that factors other than improvement in depression must explain their findings, and speculate that there is a direct effect of selective serotonin reuptake inhibitors (SSRIs) on the personality scales. These conclusions can be challenged. I believe that MADRS change is unsuitable for solving this problem, as it expresses magnitude of change (interval level). Suppose that in a sample of 40 improved subjects who experience change in KSP, 20 show large MADRS change values and small differences for many KSP items, and the other 20 show small MADRS change values but large differences for many KSP items. Then, the correlations between MADRS change and differences in KSP will be relatively small, despite the strong correlations between KSP changes and improvement considered at a categorical level. The Clinical Global Impression scale, also measured in this study, could address this question more

appropriately. I suspect that high R^2 values would be obtained if this category were used as the predictor variable, which would lead to rejection of the assumed independence between depression and KSP. Furthermore, the effect of SSRIs on depression would then be a more plausible explanation of the changes in personality traits during antidepressant treatment.

The 'normalising' effect of treatment on KPS requires that regression towards the mean is thoroughly evaluated. The authors dismiss it by pointing out that previous findings are in line with their results. This is an invalid argument. Two methods that can be used to detect this phenomenon come to mind. One consists of evaluating the difference between the two measures of each subject against the arithmetic mean of the measures of each subject, rather than the difference between the two measures against the initial measure as considered by Ekselius & von Knorring. This technique is neither infallible nor a substitute to the second method, that is the use of a control group. Ekselius & von Knorring do not have a control group, which means to me that the study's design is inappropriate for its secondary aim, the measurement of a treatment effect, and its conclusions lack sufficient logical support to be generalised.

Ekselius, L. & von Knorring, L. (1999) Changes in personality traits during treatment with sertraline or citalopram. *British Journal of Psychiatry*, **174**, 444–448.

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Authors' reply: Dr Marchevsky finds it difficult to accept the assumed independence between depression and the majority of the self-rated Karolinska Scales of Personality (KSP). However, the empirical data are in favour of such an assumption. In an earlier study (Perris *et al*, 1979), in-patients suffering from a moderately severe or severe depressive syndrome completed the KSP on two separate occasions. The first investigation was carried out shortly after the patients' admission to hospital when they were depressed, and the second a few months later when they were at home having recovered from the depressive illness. Most of the patients were at that time treated with tricyclic antidepressants or electroconvulsive therapy. The results of that study verified that the inventory measures traits which are fairly independent of the state of the subject. However, significant differences were seen between the two assessments for psychic anxiety, somatic anxiety and social desirability, which is why changes in these scales should be interpreted with caution.

Second, Dr Marchevsky gives an example in which patients with large MADRS changes have small KSP changes while patients with small MADRS changes have large KSP changes. In our opinion, such an example would strongly go against a relationship between the changes in depressive symptomatology and the changes in personality traits.

Finally, Dr Marchevsky raises the question concerning regression towards the mean. He discusses mathematical strategies to handle the problem but concludes that this technique is neither infallible nor a substitute to the second method – the use of a control group. We agree.

He concludes that there is not enough support to generalise the results. We agree, as is clear from the tentative wording of our Clinical Implications (Ekselius & von Knorring, 1999, p. 448).

Thus, we still believe that there is support for our conclusions, although a limitation that we pointed out (Ekselius & von Knorring, 1999, p. 448) must be borne in mind: "Although the personality inventory used has been demonstrated to be fairly independent of the clinical state of the investigated subjects, the improvement in depressive symptomatology may have influenced the results".

Ekselius, L. & von Knorring, L. (1999) Changes in personality traits during treatment with sertraline or citalopram. *British Journal of Psychiatry*, **174**, 444–448.

Perris, C., Eisemann, M., Eriksson, U., *et al* (1979) Variations in self-assessment of personality characteristics in depressed patients, with special reference to aspects of aggression. *Psychiatrica Clinica*, **12**, 209–215.

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More on amiodarone-induced depression

Sir: Ambrose & Salib (1999) assume that the depression induced in their patient by treatment with amiodarone, may not have been due to effects on thyroid functioning. Amiodarone, however, produces a variety of effects on thyroid hormone physiology.

Amiodarone reduces the conversion of thyroxine (T_4) to triiodothyronine (T_3), results in a modest decrease in T_3 serum levels, and a rise in T_4 and reverse T_3 levels. Thyroid-stimulating hormone (TSH) levels rise transiently in the first three months but thereafter return to normal. These effects are similar to the results obtained by Ambrose & Salib of raised T_4 and normal TSH levels after eight months of amiodarone treatment.

The majority of patients treated with amiodarone remain clinically euthyroid, albeit with altered thyroid indices, as in Ambrose & Salib's patient. However, occasional patients may develop overt or subclinical hypothyroidism or hyperthyroidism. In subclinical hypothyroidism clinical symptoms are generally absent, however some studies have reported somatic and psychiatric symptoms such as depressed mood, lethargy, obssessionality and impaired cognitive function. Lithium, another drug which inhibits thyroid hormone release, has been reported to cause thyroid dysfunction even when thyroid function test results remain within normal limits.

It has been suggested that hypothyroidism is a graded phenomenon with varying degrees of clinical severity and biochemical abnormality. It may well be that amiodarone-treated patients, although outside the range for overt hypothyroidism, still have subtle abnormalities in thyroid function. Observations in animal models suggest that amiodarone can antagonise thyroid hormone action at the cellular level by blocking hormone entry and receptor binding. The mildly altered biochemical indices seen in euthyroid patients on amiodarone may represent compensatory effects. Thus, the increased T_4 level may serve to overcome the blockade of T_3 production, thereby maintaining normal T_3 levels, which, in turn, may help to restore TSH levels to normal.

Ambrose & Salib's report is important as it is perhaps only the second report of psychiatric symptoms induced by amiodarone. However, they were quick to dismiss the role which may have been played by thyroid function.

Ambrose, A. & Salib, E. (1999) Amiodarone-induced depression. *British Journal of Psychiatry*, **174**, 366–367.

Figge, H. L. & Figge, J. (1990) The effects of amiodarone on thyroid hormone function: a review of the physiology and clinical manifestations. *Journal of Clinical Pharmacology*, **30**, 588–595.

Kleiner, J., Altshuler, L., Hendrick, V., *et al* (1999) Lithium induced subclinical hypothyroidism: review of the literature and guidelines for treatment. *Journal of Clinical Psychiatry*, **60**, 249–255.

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