Correspondence

EDITED BY GREG WILKINSON

Premorbid adjustment and schizophrenia

Sir: Although there had been previous evidence for premorbid social adjustment and personality being predictive for schizophrenia, Malberg *et al* (1998) are the first to show their immense impact in a cohort study. But how can premorbid functioning be measured? The Premorbid Adjustment Scale (PAS) by Cannon-Spoor *et al* (1982) covers social accessibility – isolation, peer relationships, functioning outside the nuclear family, and capacity to form intimate socio-sexual ties. Additionally, the highest level of functioning achieved before becoming ill can be estimated, as well as the time span and characteristics of the onset of illness, and general information such as education. The PAS gives a total score from 0 representing good, to 1 representing bad premorbid adjustment.

Using the PAS, we investigated a German sample of 86 unrelated patients (average age 39 years; s.d.=11.2) with a schizoaffective or schizophrenic disorder. Additionally, 38 healthy parents (average age 64 years; s.d.=12.3) were examined. DSM–IV diagnoses (American Psychiatric Association, 1994) were based on a standardised interview.

Here, we report that patients and controls differed significantly in every item of the PAS. Using a threshold between affected and healthy subjects (PAS score 0.23) an odds ratio of 27.9 (95% CI 9.39–82.89) appeared in our sample. This observation is in accordance with the findings of Malberg *et al* (1998) and supports the importance of premorbid functioning.

However, the PAS does not cover items which Malberg *et al* (1998) found to be associated with schizophrenia, such as delinquency, breach of regulations, and substance misuse. Nevertheless, the PAS can be recommended for the measurement of premorbid social adjustment. Furthermore, measuring premorbid functioning seems to be helpful in predicting the risk of developing schizophrenia. Later, it may help to estimate the course of the disorder, since high PAS values were related to an unfavourable course.

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Pindolol augmentation of antidepressant therapy

Sir: We read with interest the timely review of the augmentation of antidepressants with pindolol by McAskill *et al* (1998). They detail open studies supporting a role for pindolol in accelerating and augmenting the action of antidepressants, an effect thought to be mediated by the blockade of somatodendritic (presynaptic) 5-HT_{1A} autoreceptors. However, the controlled studies completed to date are somewhat contradictory. McAskill *et al* (1998) argue for larger-scale trials using higher doses of pindolol than those previously employed. We would suggest that such strategies require caution for interpretable results to be obtained.

McAskill *et al* (1998) imply that pindolol selectively blocks 5-HT_{1A} receptors at the somatodendritic location but not at the post-synaptic site. However, positron emission tomography (PET) imaging in man of 5-HT_{1A} binding shows that pindolol binds to both somatodendritic and post-synaptic receptors (Rabiner *et al*, 1998). Depression is thought to be associated with an impairment of post-synaptic 5-HT_{1A} function (Power & Cowen, 1992) and an increase in transmission through this receptor is hypothesised to underlie the mechanism of action of antidepressants (Blier & de Montigny, 1994). Therefore, pindolol may augment antidepressants by blocking somatodendritic 5-HT_{1A} receptors but this may be counterbalanced by a deleterious action of post-synaptic 5-HT_{1A} receptor blockade. McAskill *et al*'s (1998) suggestion of using higher doses of pindolol may compound this problem since PET studies suggest that the ratio of somatodendritic to post-synaptic blockade decreases with increasing doses (Rabiner *et al*, 1998).

The use of pindolol as a somatodendritic 5-HT_{1A} antagonist is complicated further by the possibility that pindolol may be a partial agonist at this site (Clifford *et al*, 1998). This may, together with the mixed somatodendritic and post-synaptic binding, explain the lack of a consensus in the controlled trials of pindolol augmentation of antidepressants. Rather than rushing into larger studies with higher doses of pindolol it is perhaps more sensible to first investigate whether a dose of pindolol can be found that leads to a high ratio of somatodendritic to post-synaptic binding. This may indeed be lower than the doses currently employed. Ultimately, it will only become clear if blockade of somatodendritic 5-HT_{1A} receptors is an effective means of accelerating and augmenting antidepressant actions when a pure antagonist, rather than a partial agonist like pindolol, becomes clinically available.

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