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Correlation between cerebral perfusion and depressive symptom scores from morning to evening

I am writing to point out an error in our paper on cerebral perfusion correlates of depressed mood (Ebmeier *et al*, 1997). Although the description of methods in the paper is accurate, the interpretation of the interaction between condition (time of day) and depression scores (Befindlichkeitsscale (BFS)) is not accurate. This interaction does not represent the "within-subjects correlation with BFS change", but the change in correlation between cerebral perfusion and symptom scores from morning to evening.

Consequently, "correlations with BFS" in the text ought to read "diurnal changes in correlations". The reported "positive correlation between severity of depression and anterior limbic perfusion" is, in fact, a significantly stronger correlation between symptom scores and cerebral perfusion in the morning *v.* evening. In other words, there is a relatively greater (positive) slope of the regression line between perfusion and symptoms in the morning, whereas the slope in the evening is significantly less positive. The correlations reported with factor scores were interpreted accurately and, for example, support the claim for a positive correlation between severity of depression/weakness/fatigue and anterior limbic perfusion.

Although this may seem an arcane point, the additional change in the 'tightness' of the mood–brain perfusion association from morning to evening implied by these results is actually rather exciting. It could reflect the difference between a direct and a compensatory relationship between brain activity and behaviour at different times of the day and should provide a motive for follow-up experiments.

Ebmeier, K. P., Cavanagh, J. T., Moffoot, A. P. R., *et al* (1997) Cerebral perfusion correlates of depressed mood. *British Journal of Psychiatry*, **170**, 77–81.

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Lithium-induced hypothyroidism

I would like to congratulate Johnston & Eagles (1999) on the scale of their study and for providing a clearer idea regarding the prevalence of hypothyroidism related to lithium and the potential risk factors. I would like to comment on several important issues, including the presence of pre-existing thyroid disease prior to initiation of lithium, the presence of antibodies and the possibility of diagnosis as a risk factor.

With regard to the presence of pre-existing hypothyroidism (as suggested by patients receiving replacement thyroxine) the study excluded a total of 18 cases, which, given the total number of cases on thyroxine, is a substantial proportion of the sample. This would suggest that patients who have hypothyroidism are more likely to suffer from conditions that require treatment with lithium.

It is unfortunate that thyroid antibodies were not measured more frequently. The finding that 13 out of 15 patients with hypothyroidism were positive for antibodies would suggest that the prevalence of antibodies would have been high and would have clarified the role played by autoimmunity in contributing to hypothyroidism. Thyroid autoimmunity mediating the hypothyroid effect of lithium has been studied extensively and there is considerable evidence to support this. As early as 1973, Crowe *et al* (1973) suggested that two different types of hypothyroidism occur with lithium, one with evidence of underlying autoimmune hypothyroidism and one without, based on a review of cases reported. Studies by Lazarus *et al* (1981) and Leroy *et al* (1988) suggest a high prevalence for antithyroid antibodies in patients who are hypothyroid on lithium, thus supporting the role of autoimmmunity mediating this effect. Indirect evidence that autoimmune factors may mediate the actions of lithium on the thyroid comes from cases of hyperthyroidism, a well-documented side-effect of lithium, that cannot be explained on the basis of a direct pharmacological effect of lithium on the thyroid.

The issue of a particular diagnosis being a potential risk factor for lithium-induced hypothyroidism has not been highlighted in the literature although it has been studied, albeit indirectly. It is reasonable to conclude from the literature that thyroid autoimmunity is increased in conditions in which lithium is likely to be prescribed (i.e. bipolar affective disorder and depressive disorders). A study by Lazarus *et al* (1986), in which thyroid antibodies were investigated prior to the prescription of lithium, reported a prevalence of 43%. Importantly, the entire group had a diagnosis of bipolar affective disorder. This compares with only 8.6% in a study of unipolar depression (Joffe, 1987). This would indicate that there is a case for studying the relationship between the psychiatric diagnosis, thyroid autoimmunity and the hypothyroid effect of lithium. This could answer the question raised by the authors as to why hypothyroid patients on lithium are selected to remain on both treatments. It is possible that lithium is more likely to be continued when the diagnosis is that of bipolar affective disorder than depression alone.

I hope that further studies in this area will help to dissect out the factors that play a role in lithium-induced hypothyroidism.

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