Reviewer's report

**Title:** Study of the serotonin transporter (SLC6A4) and BDNF genes in French patients with non syndromic mental deficiency

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**Reviewer:** JA Sved

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I regret not being able to give this paper a higher recommendation. It is a straightforward study, written up in an acceptable way. Had the results been positive the paper would clearly be of importance. Negative results are sometimes of equal interest, but in this case the negative results are not particularly revealing, especially in an era where genome-wide association studies are possible rather than association studies with just two loci, one of which has only a single polymorphism.

The validity of this study depends critically on the choice of the two loci. I am not an insider in this field, but it is not clear to me that a sufficient case has been made here. Doubtless from the work on mice they are important loci. But this is a long way from showing that variation in serotonin is an important factor in a trait so generic as 'non syndromic mental deficiency'. Some studies are cited, but as far as I can see nothing that is decisive.

Even for loci where there is a strong effect, association with linked polymorphisms is not guaranteed. The relatively low level of success of genome-wide association studies for traits known to have a high heritability would indicate that there is a low probability of finding associations with candidate loci.

One slightly promising positive result is reported on P5: "However, linkage disequilibrium (LD) patterns of the four polymorphisms in SLC6A4 were different in the two studied populations (Figure 2)". I am not certain how one would interpret such a result in the absence of direct associations with the condition. However looking at the numbers in Figure 2, I think that it is unlikely that the authors could demonstrate that the patterns of LD in the two populations are really significantly different.