Reviewer's report

Title: Different associations of white matter lesions with depression and cognition

Version: 1 Date: 1 August 2012

Reviewer: Ben Seltzer

Reviewer's report:

This is a very good paper.

The Background section is a little confusing because they begin by focusing on WMLs in general but then shift the emphasis on to the frontal lobe without any transition.

I suggest a sentence (placed before the last sentence of paragraph 2) that introduces the idea that the frontal lobe is a region of especial interest because of its possible relationship to both mood and cognition. Here they can put many references.

In the third paragraph, the sentence beginning "If WML are associated..." isn't clear. Possibilities of what? I suggest rewording the later sentences to say, in effect, "WMLs could be related to depression, cognitive impairment, or both, either directly or via cortical volume."

In the second sentence of the second paragraph, I would say "presumptive" cerebrovascular pathology.

I cannot comment on the appropriateness of the statistics, but I have one methodological concern. The exclusion of 'severe depressed patients' could, as they recognize, affect the results. What was their rationale for this exclusion? Was there a cut-off score for the Depressive score or just a categorical decision used to make this determination? Twenty-five subjects did have "major depressive disorder" which implies non-trivial symptoms. How can we be sure that this degree of depression cannot in itself cause frontal lobe changes?

Under Discussion, third paragraph, first sentence, say "because WML and frontal cortex atrophy both are related."

In Conclusions, why does the frontal lobe "primary neocortical synaptic degeneration" necessarily have to be related to WMLs? Couldn't some other process, e.g. aging, also play a role?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

Declaration of competing interests:

I declare that I have no competing interests.