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Letter to the Editor

Location and progression of white-matter lesions, lacunar infarcts and atrophy associated with motivational and mood symptoms in patients with symptomatic atherosclerotic disease: things to ponder

The recently published article 'Location and progression of cerebral small-vessel disease and atrophy, and depressive symptom profiles: The Second Manifestations of ARTerial disease (SMART)-Medea study' (Grool *et al*. 2011) generates much interest. The authors have done justice to the topic. We take the opportunity to highlight a few scientific facts related to the study. The main aim of the authors was to study the correlation between white-matter lesions (WMLs), lacunar infarcts and atrophy with motivational and mood symptoms in patients with symptomatic atherosclerotic disease. We think that the baseline blood investigations did not include full blood count, renal profile and thyroid function test, which would help identify and exclude metabolic causes such as anaemia, uraemia and hypothyroidism or hyperthyroidism. These metabolic causes could be the reasons for features such as anhedonia, energy loss, concentration problems, depressed mood and appetite disturbance. The exclusion criteria in this study seemed to be rather loose.

We feel that the reference used to categorize and define the different types of brain infarcts was not mentioned properly. The sentence 'We defined lacunar infarcts as infarcts of 3–15 mm in diameter and located in the frontal, parietal, temporal …' suggests that the definition of brain infarcts was arbitrary. The most important question asked is whether the 15 mm size for the lacunar infarct was still considered as a cut-off mark. It is pertinent to mention that an earlier study debated the acceptance of 15 mm size as a criterion for lacunar infarct (Cho *et al*. 2007).

The Patient Health Questionnaire-9 is a subjective tool of assessment. The ill-defined points of the scale (i.e. 'on several days', 'on more than half the days' or 'nearly every day') may confuse the patients and lead to inaccurate information. We feel that a preferable method should objectively state the number of days per week for example (0 days, 1–2 days/week, 3–5 days/week, 6–7 days/week). We also wonder how the Patient Health Questionnaire-9 was filled out. In a cohort of patients with concentration problems and anhedonia, the information gathered from the patients themselves is questionable.

Overall, the paper by Grool *et al*. (2011) is an interesting article and we applaud the meticulous work of the authors and especially the editor for publishing such an informative paper.

Declaration of Interest

None.

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A reply to Sakthiswary & Das (2011)

We read the response of colleagues Sakthiswary & Das (2011) to our article 'Location and progression of cerebral small-vessel disease and atrophy, and

depressive symptom profiles: the Second Manifestations of ARTerial disease (SMART)-Medea study' (Grool *et al*. 2011*b*) with great interest. We regret if Sakthiswary & Das (2011) found the discussion of our methodological section incomplete, and would hereby like to react to their comments.

First, in our study we adjusted our analyses of brain changes with depressive symptoms for the most common potential confounders, including age, sex, education, Mini-Mental State Examination (MMSE) score, life-style and vascular risk factors, physical functioning and antidepressant use. In the SMART-Medea study, blood investigations included renal and thyroid function tests, whereas full blood count was only available for part of the study population. Since the effect estimates and significance levels did not change after we additionally adjusted for renal and thyroid function tests, we do not expect that uraemia, hypothyroidism or hyperthyroidism accounted for the observed relations between brain changes and depressive symptoms in our study.

Second, subcortical infarcts on magnetic resonance imaging (MRI) were divided into lacunar infarcts (3–15 mm) and large subcortical infarcts (>15 mm). Although a grey area of uncertainty around the cut-off size of 15 mm for lacunar infarcts exists (Lodder, 2007), it is frequently used in the literature. Also, it has been recently argued that counting cavities >15 mm as lacunes should be done with caution, since many acute lacunar lesions will decrease in size over time (Potter *et al*. 2011).

Third, the Patient Health Questionnaire-9 (PHQ-9) is a brief and commonly used measure for assessing the severity of depressive symptoms, and has been well-validated in the general population (Kroenke *et al*. 2001) and in patients with coronary heart disease (Thombs *et al*. 2008). We therefore do not share the opinion that a method asking the respondent about the number of days that symptoms are present would necessarily be preferable. Further, our population had, on average, normal age-adjusted cognitive performance and few subjects in our sample scored below the normal range of global cognitive function; also, crude scores for immediate and delayed recall, mental flexibility, attention, processing speed and intelligence were previously shown to be comparable with age- and education-adjusted scores in another study that included independently living men (Muller *et al*. 2007; Grool *et al*. 2011*a*). We therefore do not expect that the use of a self-report measure such as the PHQ-9 to assess subjective symptoms of anhedonia and concentration problems in this population will have led to unreliable information.

Declaration of Interest

None.

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