Psychological Medicine (2011), **41**, 446–447.

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Psychological Medicine, **41** (2011).
doi:10.1017/S0033291710001522
First published online 24 August 2010

Letter to the Editor

A rejoinder to Grool *et al.* (2010)

We read with great interest the response from Grool and colleagues (Grool *et al*. 2010) on our article 'Localization of white-matter lesions and effect of vascular risk factors in late-onset major depression' in the Journal (Dalby *et al*. 2010). We agree overall with their methodological considerations about manual labelling and slice thickness in magnetic resonance imaging (MRI). However, we have some important comments to their critique. Limitations to manuscript length may sometimes compromise a thorough discussion of all important aspects in an article and we regret if Grool *et al*. (2010) found our discussion of the methodological issues incomplete.

First, we used a 3-T MRI scanner in our study. In the SMART-MR study (Geerlings *et al*. 2010) that Grool and colleagues refer to in their letter, they used a 1.5-T MRI scanner. The use of 3-T MRI improves the detection of more subtle white-matter changes than 1.5-T MRI due to better spatial resolution and increased signal-to-noise ratio. This has been shown for white-matter changes in both normal adults (Neema *et al*. 2009), multiple sclerosis (Di *et al*. 2009), and epilepsy (Phal *et al*. 2008). Therefore, we expected to detect more lesions and thus a higher lesion volume than most previous studies using 1.5-T MRI.

Second, we appreciate the effort of Grool *et al*. to calculate medians of our deep white-matter lesion (DWML) volume. However, we would have preferred to provide the original data for this purpose. The true median values of DWML volume in our sample is 0.18 ml for patients and 0.26 ml for controls, and not 0.4 ml and 0.5 ml, respectively, as Grool *et al*. propose. When excluding the proposed outliers in Fig. 1, the median DWML volume is 0.33 ml for patients and 0.25 for controls. Lesion volume was modelled with a log-Gaussian regression model and showed no statistically significant difference in lesion volume between groups ($t = -0.46$, $p = 0.65$). Neither did the non-parametric Mann–Whitney rank sum test ($z = 1.20$, $p = 0.23$), even after excluding three possible outliers in the control group in Fig. 1 with high lesion volumes ($z = 0.47$, $p = 0.64$) and additionally three possible outliers in the patient group with small lesion volumes ($z = -0.22$, $p = 0.83$).

Finally, we recognize Grool *et al*.'s comment about possible selection bias. Generally, recruitment to most clinical studies introduces the risk of selection bias. Because this study involved depressed patients admitted to a psychiatric hospital or treated in outpatient facilities, our patients may be presumed to be more severely ill and presenting with more comorbidity than patients seen in general practice. Selection towards more severely ill patients may cause an overestimation of the effect measures, which may not be demonstrated in large population-based studies. Our control group was recruited from advertisement in a local paper, and responders were carefully screened by telephone prior to the formal, structured diagnostic interview, partly to exclude controls wanting to participate because of suspected symptoms of depression and dementia. Another type of potential selection bias is the recruitment of 'super-normals', i.e. not being representative of 'average' controls. In the present study, the distribution of socio-demographic variables and vascular risk factors, except for social class and smoking, was very similar in patients and controls. Adjusting for social class did not alter the result of no significant difference in DWML volume between groups ($t = -1.19$, $p = 0.24$); these results were not shown in the original article. We have no reason to believe that our control group is not representative of the background population.

Declaration of Interest

None.

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https://doi.org/10.1017/S0033291710001522 Published online by Cambridge University Press