Response to: 'Neuropsychiatric lupus or not? Cerebral hypoperfusion by perfusion-weighted MRI in normal-appearing white matter in primary neuropsychiatric lupus erythematosus' by Papadaki *et al*' by Wallace

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We thank Dr Wallace[1] for his interest in our paper entitled 'Neuropsychiatric lupus or not? Cerebral hypoperfusion by perfusion-weighted MRI in normal appearing white matter in primary neuropsychiatric lupus erythematosus' by Papadaki *et al*[2] and for giving us the opportunity to clarify aspects of our work. Our response to the points raised, follow next:

1. *American College of Rheumatology (ACR) nomenclature*. We do agree that this nomenclature, although useful, is indeed outdated and may need refinement and updating. In our study, the attribution of primary NPSLE was done by physician judgement and according to the European League Against Rheumatism (EULAR) recommendations[3] after taking into consideration the ACR nomenclature and Italian Study Group attribution model.[4]
2. *Lumbar puncture for the diagnosis of primary neuropsychiatric lupus*. The modest sensitivity and specificity of cerebrospinal fluid (CSF) studies for diagnosis of Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) led to the EULAR recommendation statement that its value is predominantly to exclude other non-lupus related causes of neuropsychiatric disease, such as infections or demyelinating disease. This recommendation was supported by data from the Italian Study Group, where abnormal CSF is not considered as a favouring factor for attribution to lupus in most neuropsychiatric manifestations.
3. *Hypoperfusion in systemic lupus erythematosus (SLE)*. We never claimed that our study is the first to evaluate the presence of hypoperfusion in neuroimaging in NPSLE. Notwithstanding, our study is the first Dynamic Susceptibility Contrast-MRI perfusion study in SLE that included patients with secondary NPSLE as a separate clinical group. In this study, we differentiate between patients with primary NPSLE and those with neuropsyhiatric symptoms not attributed to the disease by adopting a normalised left semioval centre cerebral blood flow (CBF) cut-off value of 0.77.
4. *Hypoperfusion in the watershed areas of the brain in SLE and vasospasm/autonomic dysfunction*. Our results of widespread hypoperfusion in *normal-appearing white matter* of patients with NPSLE, which is more pronounced in the semioval centre, are in agreement with hypoperfusion in the watershed regions of the frontal lobes in 81% of lupus patients with neuropsychiatric symptoms found by Driver *et al*.[5] These changes are likely consistent with the diffuse chronic ischaemia and neuronal loss due to widespread vasculopathy in these patients. Although a role of cerebral vasospastic phenomena in the development of some neuropsychiatric syndromes (including cognitive dysfunction) in patients with SLE and Raynaud's phenomenon has been proposed,[6] autonomic nervous system involvement in patients with SLE varies widely among studies, is often asymptomatic and its prevalence does not correlate with clinical neuropsychiatric manifestations.[7]

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