Minocycline Impedes the Evolution of Gd-enhancing Lesions into Black Holes in Patients with Multiple Sclerosis

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Introduction
New lesions in multiple sclerosis (MS) are commonly initiated with perivascular inflammation, followed by focal blood brain barrier (BBB) damage. Such pathological changes can be reflected as enhancement on post-contrast T1-weighted (T1w) MRI, accompanied by hyperintensity on T2-weighted (T2w) MRI. At this stage, the lesions appear either hypointense or isointense on the corresponding pre-contrast T1w MRI. It has been shown that 38% of the new MS lesions evolve into persistent hypointense lesions (‘black holes’) after five months.1 Black holes represent severe and irreversible axon and myelin loss.2 Strong correlations have been found between pre-contrast T1w MRI. It has been shown that 38% of the new MS lesions evolve into persistent hypointense lesions ('black holes ') by hyperintensity on T2-weighted (T2w) MRI. At this stage, the lesions appear either hypointense or isointense on the corresponding (BBB) damage. Such pathological changes can be reflected as enhancement on post-contrast T1-weighted (T1w) MRI, accompanied

Results
As previously reported,4 5/10 patients had active scans pretreatment. All patients completed months 6 study, but only eight completed months 36 scan. In total, 12 Gd-enhancing lesions were identified: 8 at baseline and 4 at month one after commencement of treatment. None of the identified lesions had reoccurrence of enhancement during follow up period. 6/12 lesions were T1-hypointense, and 6/12 were T1-isointense at the time of their appearance (Table). 3/12 lesions were assessed as new in this sample. None of them became black holes. There were 4 old T1-hypointense lesions, none of these lesions evolved into black holes. Of the 5 old T1-hypointense Gd-enhancing lesions, two changed to NAWM on the T1w MRI at months 6 and 36 respectively (Figure). Overall, by month 6 there were fewer black holes than at baseline (p < 0.05). Also, by month 36 there were fewer black holes than at month 6 (p < 0.05).

Discussion and Conclusions
This small study shows that, in addition to suppressing Gd-enhancement, minocycline treatment impedes the evolution of Gd-enhancing lesions into black holes. This may be due to the rapid effect of minocycline down-regulating inflammation by inhibiting the secretion and activity of matrix metalloproteinase.5 However, the recovery of Gd-enhancing hypointense T1 lesions to NAWM suggests that minocycline may also aid white matter repair. This is consistent with a previous study showing that minocycline is neuroprotective in a murine model of spinal cord injury.6 Nonetheless, minocycline reduced significantly the formation of destructive black holes. Larger definitive trials are underway to confirm the therapeutic effect of minocycline in MS, its impact on other MRI-derived parameters, and their correlation with clinical indicators of disease status.

References