LETTER TO THE EDITOR

Reply: Beneficial effects of exogenous CDP-choline (citicoline) in EAE

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Sir,

We read with great interest the comment of Dr Grieb that two independent groups previously investigated the effects of CDP-choline (citicoline) on the course of EAE in Lewis rats and found beneficial effects of the substance. The results were presented at scientific meetings by Clayton et al. (1999) and Grieb et al. (2004). However, the results were not published as research papers and thus full experimental details are not available. We are thus thankful for the additional information provided by Dr Grieb, as the data confirm the beneficial effects of CDP-choline on the course of EAE in our experiments by independent investigators and thus strengthen the case.

However, in EAE, mechanisms and extent of demyelination as well as oligodendrocyte damage depend on the rodent strain and peptide/antigen used in the immunization regimen. While many models using SJL/J mice and Lewis rats provide good paradigms to investigate acute T cell-mediated disease with varying degree of demyelination, few models are well characterized with regard to neurodegeneration and repair, especially with respect to oligodendroglial repopulation and remyelination (Gold et al., 2006). Further, in all EAE models, CNS inflammation predominates and investigation of pure remyelination is difficult to delineate (Linker et al., 2002). The aim of our experiments was to investigate potential beneficial effects of CDP-choline on de- and especially remyelination and used, therefore, a second model where the peripheral immune system plays no or only a minor role. The toxic cuprizone model of de- and remyelination is widely accepted to study remyelination processes in the CNS (Kipp et al., 2009; Skripuletz et al., 2011). Thus our focus extended to the more inflammatory model of EAE.

We have clearly shown that CDP-choline exerted beneficial effects on remyelination, in particular in the cuprizone model (Skripuletz et al., 2015). The effects on remyelination arose from an increase in the numbers of oligodendrocyte precursor cells and thus oligodendrocytes. We agree with Dr Grieb that the mechanisms of action are not completely understood. However, the fact that CDP-choline was effective in two such fundamentally different models of demyelination (both of which reflect only aspects of the human disease multiple sclerosis) strengthens the matter and gives us hope and confidence that CDP-choline may also promote remyelination in multiple sclerosis. Due to the known excellent safety profile of CDP-choline (Adibhatla and Hatcher, 2005; Grieb, 2014), we suggest that CDP-choline may become a promising substance for
patients with multiple sclerosis that is worth further investigation.

References


