Rheumatology

The dispersion during lesion.

We consider

We believe the different morphometry did not therefore argue against the newly proposed "opening of NMDA channels" of PD, but may be related to: 1) the pharmacokinetic profile of the drug; 2) a rather weak influence of pharmacokinetic profile...lesion binding site of the NMDA receptor compared with the channel blockers on NMDA receptor function or 3) a pathologically altered NMDA receptor binding in PD. These points have to be examined in future studies.

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Montastruc et al reply: We acknowledge Drs Kornhuber and Riederer's comments concerning our trial on ifenprodil in Parkinson's disease (PD). We are well aware that the adaminantamines amantadine and memantine have anti-NMDA properties but amantadine is also known to release dopamine from striatal neurons, to inhibit the reuptake of dopamine and to have anticholinergic effects. Despite some experimental data, the respective role of these different pharmacological mechanisms remains unknown to explain the clinical anti-Parkinsonian properties of these drugs. Amantadine has only weak and transient clinical anti-Parkinsonian efficacy which may be compatible with a weak dopamine effect. There are mainly speculative links between the anti-NMDA and the anti-Parkinsonian effects of amantadine. In our opinion, it is therefore still premature to support Kornhuber and Riederer, because of the amantadine and memantine data only, that "NMDA antagonists are used successfully for many years in the treatment of PD". This is why we were interested in investigating the clinical effects of another drug, such as, ifenprodil, which does not have dopamine effects. It is perfectly clear, as we had already stated in our first letter, that "our work does not exclude a definite role for NMDA antagonists in PD" because of the negative ifenprodil data. We had also already written that other NMDA antagonists with better pharmacodynamic or pharmacokinetic profile may be effective. Since our results have been published, we know that there is another NMDA antagonist which is available in clinical practice. A recent open study has suggested that dextromethorphan, an antitussive drug that is also a non competitive antagonist of the NMDA receptor, might have efficacy in PD.
N-methyl-D-aspartate (NMDA) antagonists in Parkinson's disease.

J Kornhuber and P Riederer

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