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### *Reply:*

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# REPLY:

We thank Drs Scheel and Finke for their insightful comments and for sharing their opinions on our article, "Brain MR Imaging Characteristics of Patients with Anti-N-Methyl-D-Aspartate Receptor Encephalitis and Their Associations with 2-Year Clinical Outcome." We agree with Drs Scheel and Finke's important comments that it is crucial to differentiate isolated anti-N-methyl-D-aspartate (NMDA) receptor encephalitis from herpes simplex encephalitis (HSE) followed by anti-NMDA receptor encephalitis.

In this publication, we tried to investigate the brain MR imaging characteristics of patients with anti-NMDA receptor encephalitis. We classified the brain MR imaging manifestations into 4 types: type 1, normal MR imaging findings; type 2, only hippocampal lesions; type 3, lesions not involving the hippocampus; and type 4, lesions in both the hippocampus and other brain areas. Type 4 (11 patients) was relatively common in our study; we presented in this article the brain MRIs of the remaining 10 patients presenting with type 4 lesions (not including the sample figure in our article) (Figure).

In our study, the patients were diagnosed as having as anti-NMDA receptor encephalitis by 2 experienced neurologists (one with >20 years of experience and one with 5 years of experience in neurology) on the basis of the clinical symptoms, physical examinations, laboratory tests, and treatment responses. The neurologists were careful to exclude the herpes simplex virus followed by

anti-NMDA receptor encephalitis, and they reached a consensus that all the patients had isolated anti-NMDA receptor encephalitis. Furthermore, the virus antibody tests such as those for herpes simplex virus and cytomegalovirus antibodies in the CSF were regularly performed in our hospital when encephalitis was suspected, and the results of virus antibody tests were negative in all the patients in our group. Despite the above effort, it is still very difficult to fully exclude HSE followed by anti-NMDA receptor encephalitis from isolated anti-NMDA receptor encephalitis in the routine clinical setting. Thus, our results about the type 4 lesions of patients with anti-NMDA receptor encephalitis should be interpreted carefully and need to be further validated. Further studies are warranted to investigate the association between isolated anti-NMDA receptor encephalitis and HSE followed by anti-NMDA receptor encephalitis, and to develop a differential diagnosis strategy.

We thank Drs Michael Scheel and Carsten Finke again for their constructive comments on our article, as well as sharing their experience for a deeper understanding of this disease entity.

**T. Zhang**

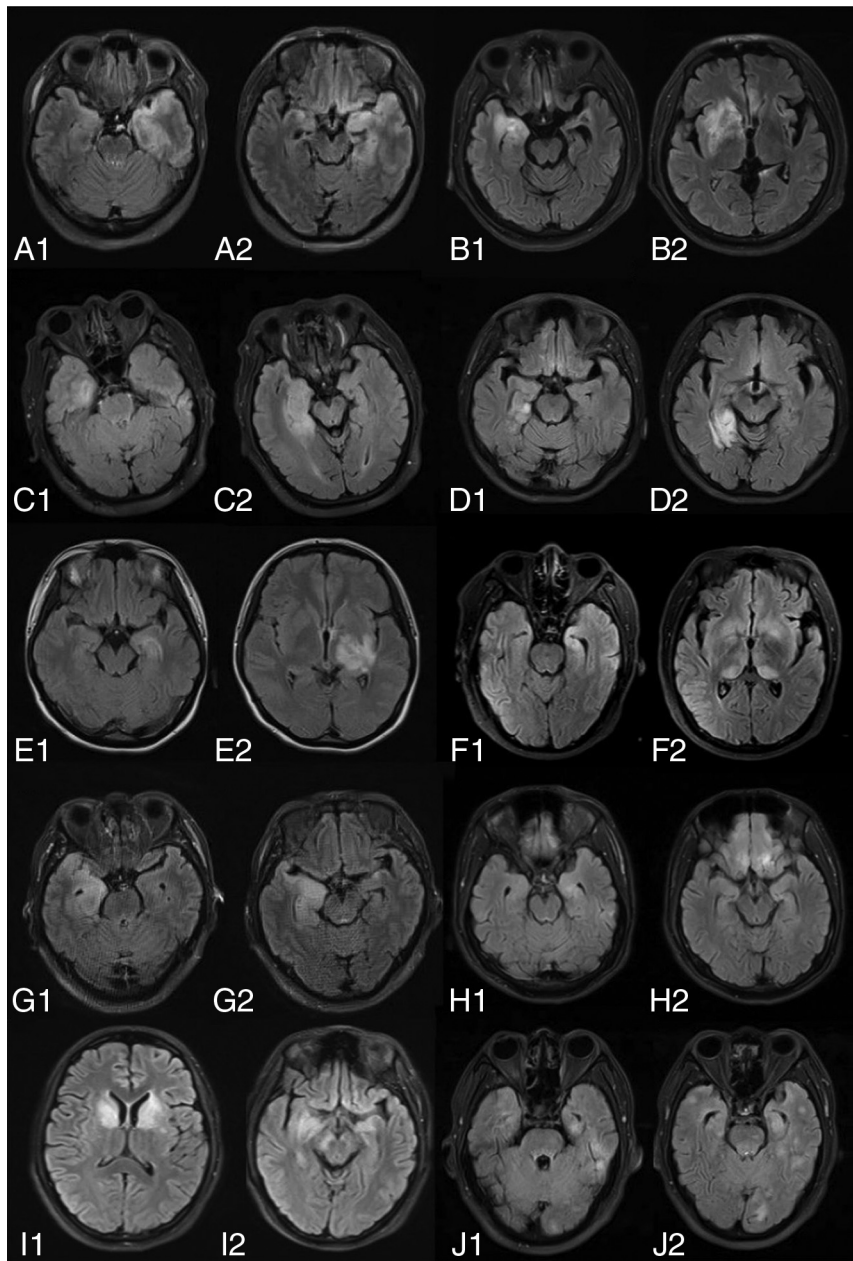
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**FIGURE.** Axial FLAIR images of the 10 patients from A to J with anti-NMDA with type 4 lesions.