

O622

2-hour Oral Session

Infections of the brain and meningitis

N-methyl-D-aspartate receptor autoimmunity affects cognitive performance in herpes simplex encephalitis

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Background: Herpes simplex encephalitis (HSE) is a devastating brain infection, mainly affecting immunocompetent patients. Antiviral treatment has decreased both mortality and morbidity. However, the majority of survivors are left with moderate or severe neurological sequelae. The virus elicits cytolysis as well as a vigorous intrathecal immune response. It has previously been suggested that autoimmune reactions involving the N-methyl-D-aspartate receptor (NMDAR) could complicate recovery after HSE, and specific anti-NMDAR autoantibodies have been found in cases of clinical relapse.

Material/methods: In this prospective study of 49 HSE patients, we investigate the prevalence and temporal development of anti-NMDAR IgG, CSF cell count, brain MRI and repeated evaluation of the neurocognitive recovery during 2 years after infection. Detection of NMDAR autoantibodies in CSF and serum was performed using biochip slides constructed with HEK293 cells transfected with plasmids encoding the NMDA NR1 type glutamate receptor.

Results: In total, 12 of 49 study subjects (24.5 %) developed anti-NMDAR IgG during the course of the study. At onset of disease, no CSF (0 of 31) or serum (0 of 35) samples were anti-NMDAR positive. At the end of the 14-21 day iv aciclovir treatment period, when follow-up was started, 2 of 43 CSF samples but no (0 of 44) serum samples were positive. After 3 months of follow-up, 11 of 44 CSF samples and 2 of 43 serum samples were positive. Antibody positive subjects presented with significantly less improvement from baseline in Mattis Dementia Rating Scale (MDRS) total score (Figure 1) and conceptualization score, compared to negative subjects. Interestingly, CSF cell count was lower in the anti-NMDAR positive group. There were no differences regarding seizures, adjuvant therapy, MRI abnormalities or time from first clinical sign to initiation of aciclovir (ACV) therapy.

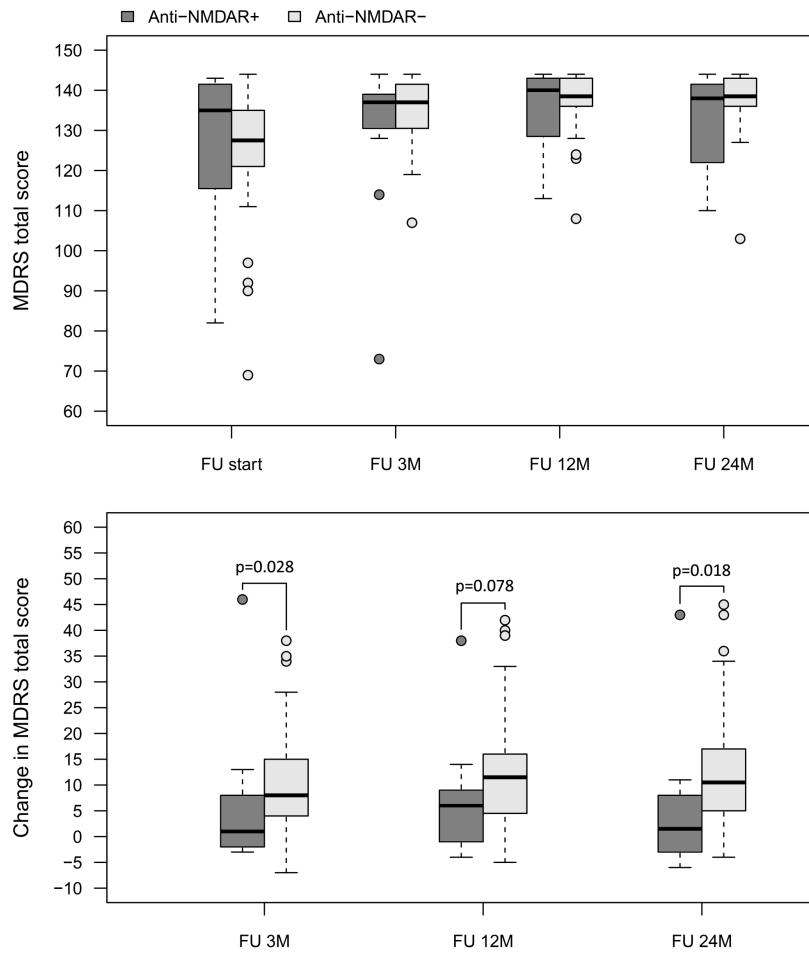


Figure 1. Mattis Dementia Rating Scale (MDRS) total score and rate of recovery in relation to anti-NMDAR IgG. Top: No significant differences in MDRS total score between anti-NMDAR IgG positive and negative subjects, but numerically higher scores in the antibody positive group at start of follow-up (FU start). Bottom: Significantly lower increase of MDRS total score in anti-NMDAR IgG positive subjects at 3 and 24 month follow-up (FU 3M, FU 24M) and a similar trend at 12 months (FU 12M).

Conclusions: To our best knowledge, this is the first study to prospectively show the temporal development of anti-NMDAR IgG and the clinical impact of this autoimmune mechanism in HSE. The association between NMDAR antibodies and impaired neurocognitive recovery could have therapeutical implications, as CNS autoimmunity is potentially responsive to immune therapy.