CSF Free Light Chain profile in Autoimmune Encephalitis

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Introduction

Autoimmune encephalitis constitutes an expanding spectrum of CNS autoimmune diseases with antibodies targeting various receptors. Although cerebrospinal fluid (CSF) oligoclonal bands are sensitive to general CNS inflammation, it may not tease out the subtleties between the possible pathologies. Here, we investigated the levels of kappa and lambda free light chains (FLC) in the two main forms of autoimmune encephalitis and assess whether there is a differential pattern between the two syndromes.

Method

Two new sensitive sandwich ELISAs, specific to either kappa or lambda free light chains, have been developed to precisely measure their concentrations in the CSF. CSF from five VGKC-complex and six NMDAR antibody related encephalitis patients were tested and compared with nine healthy controls.

Results

Pairwise t-tests showed that anti-NMDAR encephalitis patients' CSF had more kappa (Mean = 1.56 mg/L) compared to normal population (0.06 mg/L) and to VGKC-related encephalitis (0.22 mg/L) ($p \leq 0.05$) (Figs 1 and 2). However, the VGKC encephalitis did not have statistically significant difference in kappa levels compared to normal controls. Interestingly, lambda levels showed a significant differences between all three, using pair-wise comparisons (Fig 3). The kappa-lambda ratio was also an useful discriminator in patients with NMDAR antibodies (Fig 4). Furthermore, multiple sclerosis presents with a different lambda level to normal controls and to the NMDAR/VGKC-complex related encephalitides.

We then went ahead and analysed patients whose samples were send for antibody testing for limbic encephalitis but were "seronegative" for the autoimmune encephalitis screen (n=75), and found that the range was variable in this cohort (Figs 5 and 6). Two further NMDAR encephalitis patients were tested during this analysis and the mean levels were comparable to the original study. Further detailed clinical analysis is currently underway to check how many of these had clinically definite autoimmune encephalitis and whether the patients with higher than normal values of kappa or lambda light chains behave differently from a clinical point of view. If so, this assay may help in identifying patients who are likely to respond to immunomodulatory therapy, but without easily detectable serum/CSF antibodies in the commercial assays.

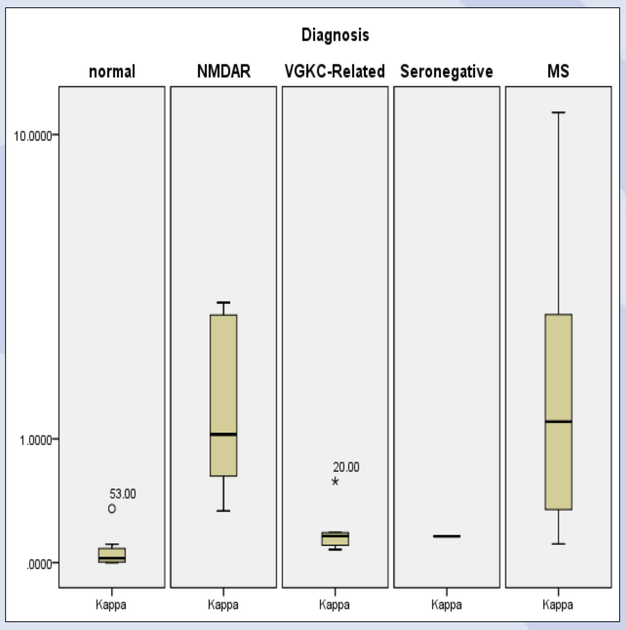


Figure 1

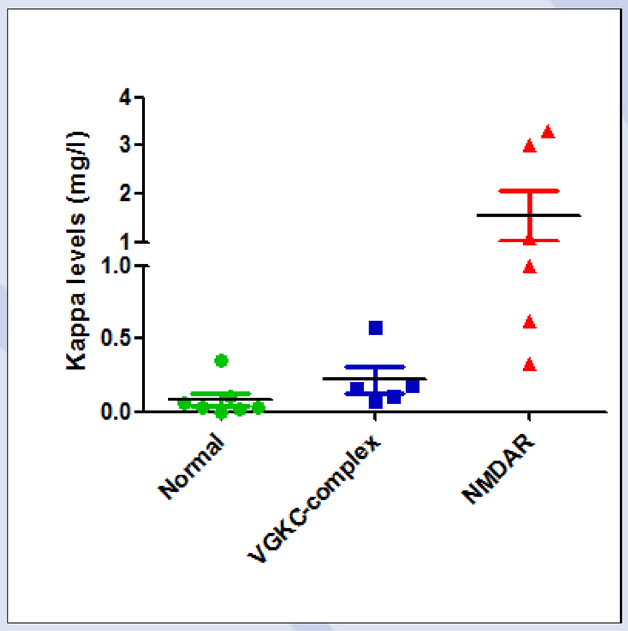


Figure 2

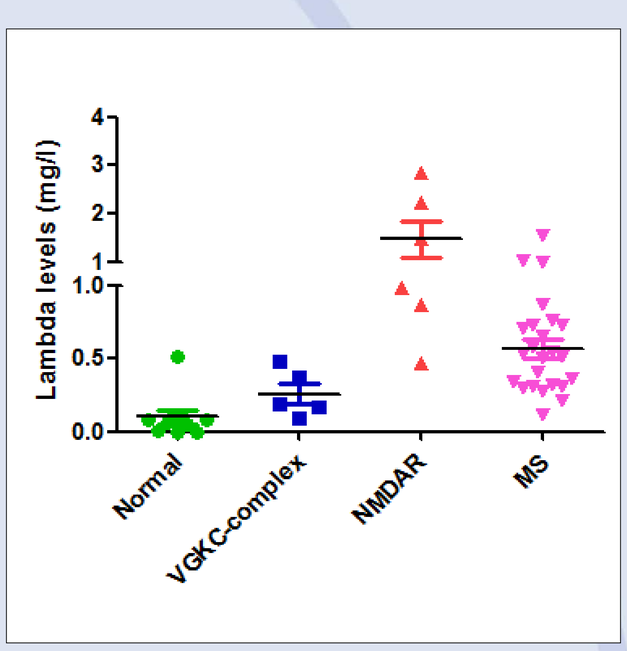


Figure 3

Figure 5

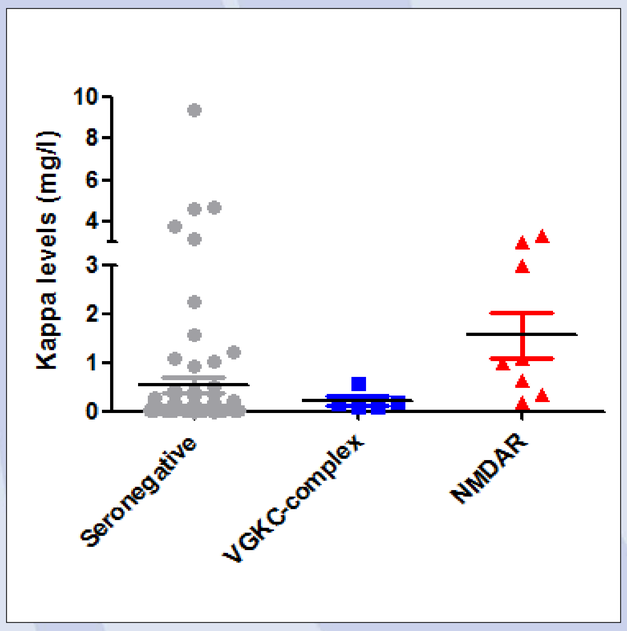
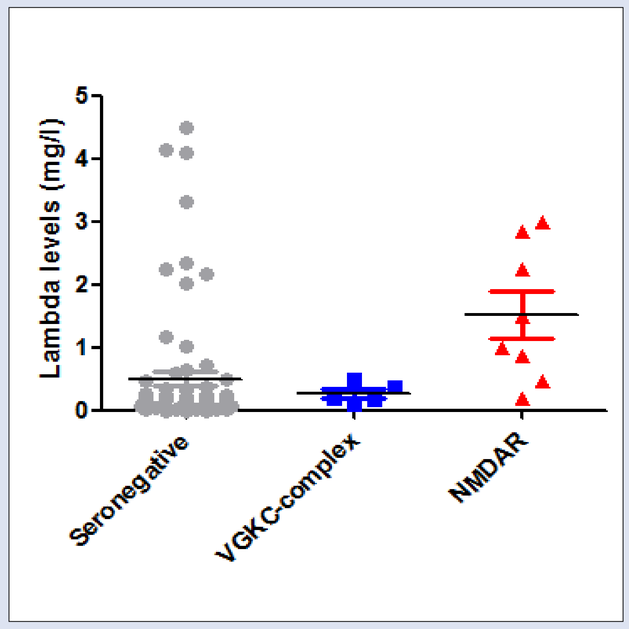


Figure 6



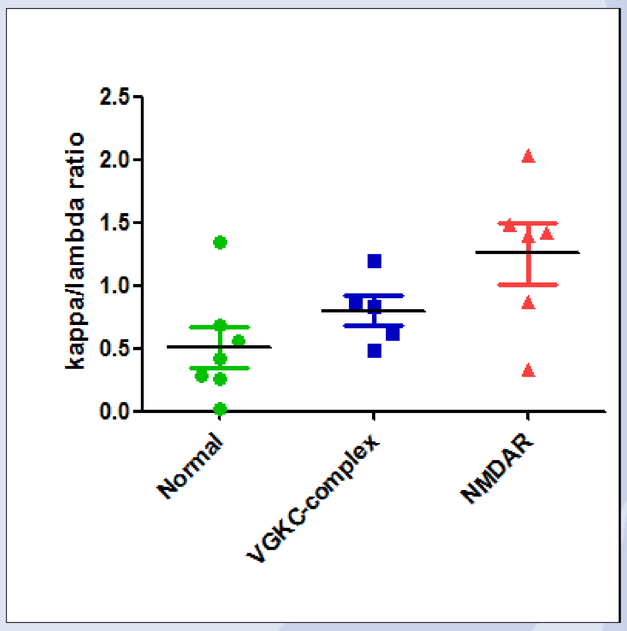


Figure 4

Conclusion

Free light chains are small molecules (22kD) which can accumulate in the CSF either as a result of a break in blood brain barrier or intrathecal inflammation. It is likely that the more severe the inflammation, the CSF FLC levels are higher.

Although sample sizes are small, these results promisingly suggest that free light chain CSF concentrations may help make specific diagnoses using only one single ELISA. NMDAR encephalitis patients have usually a more severe presentation than the VGKC-complex group and it would be interesting to see whether the CSF light chain assays would help in predicting patients with a more severe course and hence guiding more aggressive and early immunotherapy.