Absence of IgLON5 antibodies in a cohort of neurodegenerative diseases patients

MP Giannoccaro[1,2], R Liguori[1,3], P Waters[2], S Capellari[1,3], A Vincent[2]

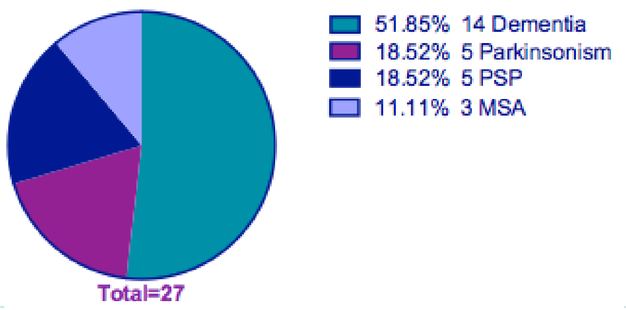
1 Department of Biomedical and Neuromotor Sciences, University of Bologna;
2 Nuffield Department of Clinical Neurosciences, Oxford University, Oxford, UK;
3 IRCCS – Institute of Neurological Sciences of Bologna, Bellaria Hospital, Bologna;

Introduction and objective

Recently, a novel syndrome characterized by a peculiar sleep disorder, associating sleep movement disorders and sleep breathing disorders, and variable symptoms of brainstem involvement, movement disorders and dementia was described in association with IgG4 antibodies against a neural surface antigen (NSAb) named IgLON5 [1,2]. However, in contrast to other NSAb associated syndromes, the nine patients described so far have had a chronic course, with no response to immunotherapy, and with tau deposition found at neuropathology. Thus the symptoms and slow progression are more representative of a neurodegenerative disease than an autoimmune encephalopathy. Our aim was to look for IgLON5 antibodies in patients diagnosed with a variety of neurodegenerative diseases.

Material and methods

Serum samples were collected from 27 patients (18M, 9F) with neurodegenerative diseases and sleep disorders. Primary diagnoses were: dementia (14), parkinsonism (5), progressive supranucelar palsy (5), multiple system atrophy (3). 27 epileptic patient sera were used as disease controls.



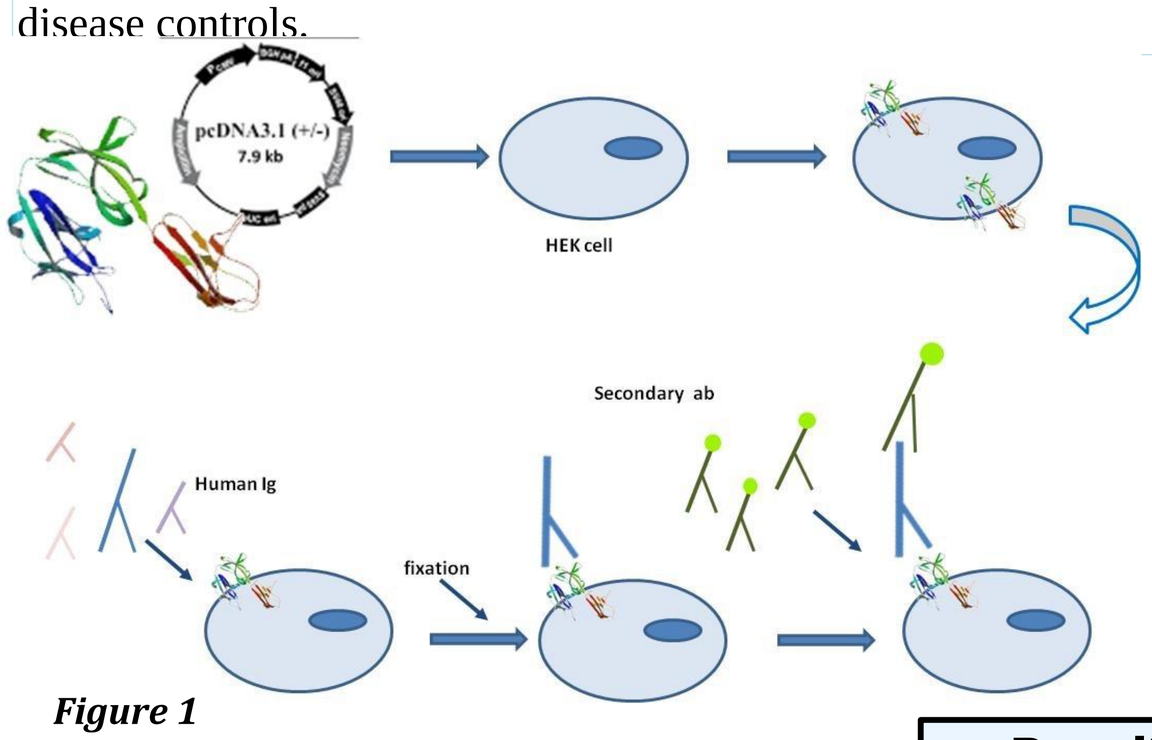


Figure 1

HEK293 T cells were transiently co-transfected with IgLON5 and EGFP constructs. 48 hours post-transfection, the live cells were incubated with patients' serum for 1 h at 1:20 dilution. Cells were than fixed in 4% paraformaldehyde for 10 minutes, and incubated with Alexa Fluor® 568 secondary anti-human IgG (H + L) at 1:750 dilution (Figure 1). In a subset of experiments, antibodies against human IgG4 were used as secondary with a third anti-mouse Alexa Fluor® 568 secondary . The bound fluorescence was visualized and scored semi-quantitatively from 0 (no binding) to 4 (strong binding). Samples scoring >1 were considered positive. A known positive serum (courtesy Euroimmun AG) was used as a positive control.

Results

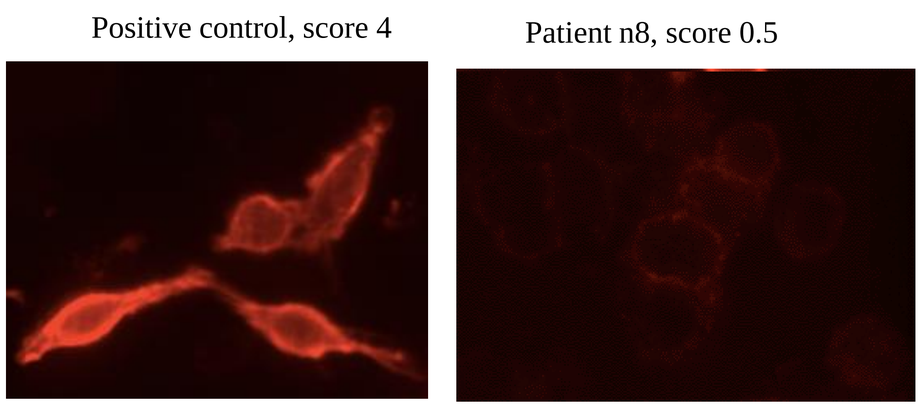


Figure 2

Figure 3

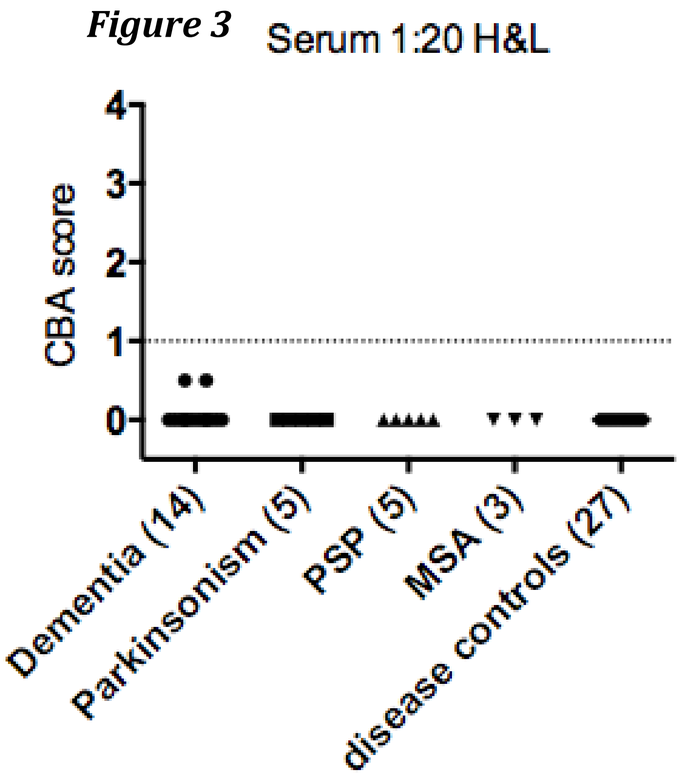
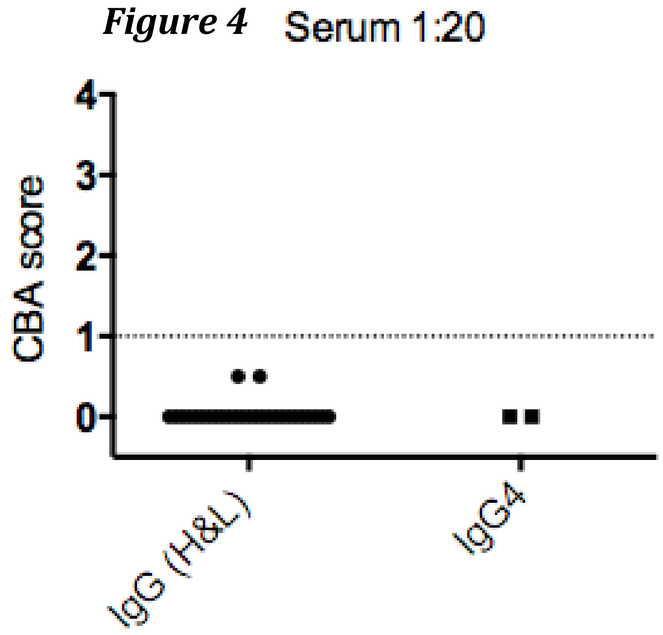


Figure 4



No serum scored >1 on the cell based assay (CBA) Figures 2,3). Two sera from patients with a diagnosis of dementia, scored <1 (Figures 2,3). These two sera were repeated using anti human IgG4 as secondary , but the results were negative (Figure 4).

Discussion

We could not find any positive patient for IgLON5 antibodies in an unselected cohort of neurodegenerative patients with associated sleep disorders. However, due to the chronic course of symptoms such as chorea, dementia, dysarthria, ataxia, dysautonomia, and vertical gaze paresis, which also occur in neurodegenerative diseases, the IgLON5 encephalopathy could easily be misdiagnosed.

Conclusions

IgLON5 antibodies are not common in an unselected cohort of patients with neurodegenerative diseases and related sleep disorders.

References

1. Sabater L, Gaig C, Gelpi E, Bataller L, Lewerenz J, Torres-Vega E, Contreras A, Giometto B, Compta Y, Embid C, Vilaseca I, Iranzo A, Santamaría J, Dalmau J, Graus F. A novel non-rapid-eye movement and rapid-eye-movement parasomnia with sleep breathing disorder associated with antibodies to IgLON5: a case series, characterisation of the antigen, and post-mortem study. Lancet Neurol. 2014Jun;13(6):575-86.
2. Simabukuro MM, Sabater L, Adoni T, Cury RG, Haddad MS, Moreira CH, Oliveira L, Boaventura M, Alves RC, Azevedo Soster L, Nitrini R, Gaig C, Santamaria J, Dalmau J, Graus F. Sleep disorder, chorea, and dementia associated with IgLON5 antibodies. Neurol Neuroimmunol Neuroinflamm. 2015;2:e136.