PRESENTATION TIME:

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Neurodegeneration in Mesial Temporal Lobe Epilepsy (MTLE): Absence of Alpha-Synuclein and TDP-43 Pathology

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Purpose

The growing body of evidence concerning the presence of pathological aggregates of hyperphosphorylated tau protein and beta-amyloid in resection specimens from patients with pharmacoresistant mesial temporal lobe epilepsy (MTLE) is well-documented. Recent studies have also suggested alterations in serum levels of alpha-synuclein in this population[1,2]. Another protein associated with neurodegeneration, TAR DNA-binding protein 43 (TDP-43), has not yet been extensively studied in epilepsy patients. Given this background, the present study aims to investigate the presence of alpha-synuclein and TDP-43 pathological aggregates in tissue samples from patients with MTLE sourced from two comprehensive tertiary epilepsy centers.

Methods

The study included 279 patients diagnosed with MTLE and hippocampal sclerosis (HS), recruited from the Brno Epilepsy Center at St. Anne's University Hospital and Motol University Hospital, Prague, Czech Republic. For each participant, a pair of representative brain samples—comprising hippocampal and temporal cortical tissue—was analyzed immunohistochemically to detect the presence of alpha-synuclein and TDP-43 aggregates. A control cohort of 120 post-mortem brain samples, obtained from both adult and pediatric cases without a history of epilepsy or other neurological conditions, was processed similarly. These samples were provided by the First Pathology Department and Forensic Medicine Department at St. Anne's University Hospital. Each run of the immunohistochemical analysis included positive and negative controls (see Figures 1 and 2). All analyses were performed by the two experienced neuropathologists, who reached a consensus on their findings.

Gender	M 113, F 166
Age at surgery	median 31 yrs (min 5 – max 67 yrs)
Age of epilepsy onset	median 9 yrs (min 1 month – max 46 yrs)
Epilepsy duration	median 38.5 yrs (min 2 – max 61 yrs)

Table 1. Clinical characteristics of the studied MTLE cohort.

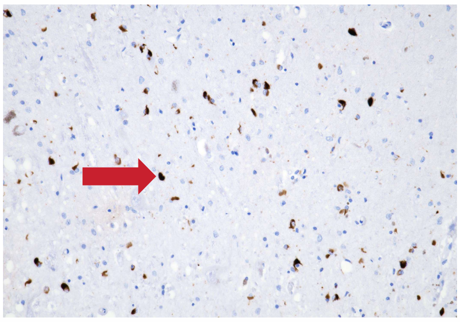

Figure 1. Immunohistochemistry evaluation: positive control, Alpha-synuclein aggregate (200x), antibody Alpha-Synuclein, clone 5G4.

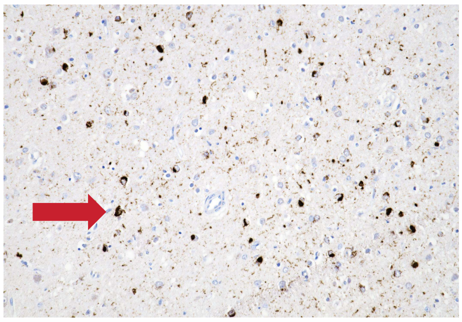

Figure 2. Immunohistochemistry evaluation: positive control, TDP-43 aggregate (200x), antibody Phospho-TDP-43 (pS409/410), clone 11-9.

Results

No evidence of pathological alpha-synuclein or TDP-43 aggregates was observed in either the MTLE cohort or the control group.

Conclusion

In contrast to the established associations with tau protein and beta-amyloid pathology, neither alpha-synuclein nor TDP-43 appears to play a significant role in the neurodegenerative processes associated with pharmacoresistant MTLE with HS. Previously reported elevated serum levels of alpha-synuclein could be attributed to the neural tissue damage. These findings suggest that future research may benefit from a continued focus on tau-related and beta-amyloid pathways in this context.

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