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Science
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Developing a model of autoimmune epilepsy using a mouse model of systemic lupus erythematosus

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Background

- Epilepsy affects approximately **50 million people** worldwide
- Epilepsy is a disease characterized by seizures
- A newly discovered feature of epilepsy is the presence of antinuclear autoimmunity
- Autoantibodies attack intracellular and extracellular targets
- There is no mouse model for antinuclear autoimmune epilepsy
Problem/Purpose

- Antinuclear autoimmunity in epilepsy is a new area of study
- The mechanisms of this epilepsy are not fully understood
- Antinuclear autoimmune epilepsy may have features in common with systemic lupus erythematosus (SLE)
- Therefore, using SLE as a model for autoimmune epilepsy may aid in future characterization and diagnoses of this disease
Hypothesis

- SLE-like mice share neuroimmunological features found in the epileptic brain
Methodology

- NZBWF1 (SLE) and C57BL/6 (control) mice were obtained
- Mouse brains were harvested and stored in PBS
- Brain hemispheres were sectioned and mounted on slides
- Slides underwent IHC for IgG, neutrophils and B-cells or were stained by Cresyl violet
- The brains were observed, photographed, and compared
Data

C57BL/6 controls and NZBWF1 brains’ morphologies are compared
Data

Cells with nuclei are compared under DAPI fluorescence

C57BL/6 24wk Female  NZBWF1 24wk Female
Data

IgG in the brain is compared to find possible leakage

C57BL/6 24wk Female

NZBWF1 24wk Female
Data

IgG accumulation in neurons

NZBWF1 24wk Female
C57BL/6 24wk Female: both images are the same tissue and location.

DAPI and IgG staining overlapped on a suspected neutrophil

Neutrophil fluorescence does not confirm suspicion

Data
Data

NZBWF1 4wk Female: a suspected neutrophil next to IgG leakage is examined

No neutrophil presence was confirmed
Results

- Abnormalities were detected in NZBWF1 or C57BL/6 mice
- Brain micro-hemorrhages may or may not be due to SLE
- DAPI nuclear staining revealed no obvious difference in size or shape between NZBWF1 and C57BL/6 mice
- Accumulation of IgG brain was detected in NZBWF1 but not in non-SLE mice
Results

• Leakage of IgG into the brain was uncommon
• There were 3 instances of IgG accumulation in neurons
• No neutrophils were detected in NZBWF1 brain
• B-cells were only detected in NZBWF1 brain
Conclusions

- Additional experiments are needed to establish NZBWF1 as a suitable model for antinuclear autoimmune epilepsy.
- Our data shows potential for SLE sharing neuroimmunological characteristics with antinuclear autoimmune epilepsy:
  - IgG extravasation into brain parenchyma
  - IgG uptake by neurons
Recommendations

- Perfusing mice before extracting brains (improved quality)
- More mice should be examined with an emphasis on females
- Induce seizures into NZBWF1 mice before examination
- Increase cryostat temperature to prevent rolling of tissue
- Section brains as soon as possible after sacrifice
References

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