

Evaluation of Reproductive Function in a Rat Model of Genetic Epilepsy Absence Seizures

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Context: Genetic Epilepsy Absence Seizures (GEAS) are more commonly found in women. However, the mechanisms implicated in sex differences and its negative impact in female reproductive function is poorly understood. Epilepsy animal models have been fundamental for the understanding of physiopathology of epilepsy and may be an important tool to investigate interferences and correlations among epileptic crisis, hormonal cycles and reproductive abnormalities.

Objective: characterize estrous cycles and to describe morphologic and molecular aspects of reproductive tract in a GEAS rat model.

Methods: Female GEAS (N=12) and controls Wistar (N=12) rats were used. Mean weight was 249 ± 19 g (5 months of age). Vaginal smears were collected during 15 days for determination of estrous cycles. Subsequently, rats were anesthetized and their weight and nasoanal distance were collected for body mass index (BMI) evaluation and Lee Index. Anogenital distance was measured for the characterization of female external genitalia. Animals were then euthanized and had their ovaries dissected, weighted. RNA was extracted, cDNA synthesized and LH receptor (Lhr), citocromal P450c17 (Cyp17) enzyme and citocromal P450c19/aromatase (Cyp19) enzyme genes expression were evaluated by Real Time PCR.

Animals: Female Wistar Rats and GEAS Rats.

Interventions: None.

Outcome Measures: estrous cycle, morphological measurements of reproductive tract and expression of steroidogenesis related genes in the ovaries.

Results: GEAS rats presented lower ovaries weight (34.97 ± 6.86 mg) than controls (49.50 ± 5.14 mg) ($p = 0.004$). GEAS rats had increased anogenital distance (1.56 ± 0.15 cm) compared to controls (1.41 ± 0.08 cm) ($p = 0.03$). There were no differences in body weight, BMI and Lee Index. Regarding estrous cycles, GEAS rats presented longer proportion of estrous phase time (35.8 ± 6.8 %) compared to controls (26.7 ± 6.0 %) ($p = 0.02$). There was a tendency towards a decrease in the expression of Cyp19 gene in GEAS rats compared to controls (Relative expression: 0.43 ± 0.53 vs 1.00 ± 1.00 , respectively) ($p = 0.07$).

Conclusions: GEAS rats presented morphological differences in the ovaries and in the reproductive tract similar to the ones found in androgenized female rats. These animals also presented alterations in estrous cycles. These findings suggest that GEAS have intrinsic reproductive dysfunctions and may be an animal model to study the reproductive dysfunctions in epilepsy

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