CALIFORNIA STATE SCIENCE FAIR
2007 PROJECT SUMMARY

Name(s)

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Project Number

S1508

Project Title

Alloprenanolone: Neurogenic Property and Therapeutic Potential in AD Treatment

Abstract

Objectives/Goals

Objectives: We investigated whether APa promotes generation of new neurons in vivo by peripheral administration in transgenic 3xTgAD and non-Tg mouse AD models; and whether GABAA receptor complex (GBRC) is involved in the neurogenic activity of APa in hNPCs.

Methods/Materials

Methods: The newly-formed cells were labeled by BrdU and the samples were evaluated by stereological analyses in the subgranular zone (SGZ) of dentate gyrus. Neurogenic abilities of APa and its analogs in hNPCS are determined by BrdU incorporation. Expression of GBRC subunits in hNPCs were determined by RT-PCR and immunocytochemistry.

Results

Results: Stereological analyses demonstrated that the basal level of BrdU labeled cells in the dentate gyrus of 3xTgAD mouse was lower than that of non-Tg mice. APa induced a significant increase of newly-formed cells in SGZ of both non-Tg and 3xTgAD mouse. APa restored SGZ proliferation to that of control non-Tg mice. Immunochemical labeling demonstrated the expression of GABAergic system in hNPCs and RT-PCR detection demonstrated the expression of alpha 1/5, beta 2 and delta subunits. Steroid specificity assay demonstrated the involvement of GBRC and structural specificity.

Conclusions/Discussion

Conclusions: In vivo, APa rescues the neurogenic impairment of 3xTgAD mouse and enhances the proliferative capacity of both the non-Tg and transgenic phenotypes. Results suggest that APa may be an effective neurogenic therapeutic to promote neurogenesis prior to the onset of AD pathology.

Summary Statement

The effects of neurosteroid Allopregnanolone has positive results with cell proliferation in brain.

Help Received

Mentor: Lifei Liu, PI: Dr. Roberta Diaz Brinton, USC School of Pharmacy