

Beneficial effects of *trans* ϵ -viniferin, a natural polyphenol, in a murine Alzheimer disease model

FREYSSIN Aline¹, SERRIERE Sophie², PAGE Guylène¹, TAUBER Clovis², CHASSAING Damien¹, VERCOULLIE Johnny², PERRIN Flavie³, GODET Julie⁴, BODARD Sylvie², GUILLARD Jérôme³, FAUCONNEAU Bernard¹, CHALON Sylvie², RIOUX BILAN Agnès¹

¹ University of Poitiers, EA3808 Neurovascular Unit and Cognitive Disorders, France, ² University of Tours, INSERM U1253 Imagery and brain, France, ³ University of Poitiers, UMR CNRS 7285 Institute of chemistry of Poitiers: Materials and Natural Resources, France, ⁴ Poitiers University Hospital, Department of Pathology, France



BACKGROUND

Alzheimer's disease (AD) is a major and progressive neurodegenerative disorder leading to cognitive impairment and dementia. This disease is notably characterized by the presence of senile plaques and neurofibrillary tangles, inducing extensive neuronal loss. The senile plaques are constituted by accumulation of aggregated β -amyloid peptide. The neurotoxicity of A β peptide induces severe damages to synaptic plasticity, especially in hippocampus, resulting in impaired memory and learning [1]. Moreover, β -amyloid peptide induces activation of microglia and astrocytes, and enhance the production of proinflammatory cytokines [2].

Previous studies in the laboratory showed that resveratrol and one of its derivatives, *trans* ϵ -viniferin (a dehydromer of resveratrol), reduced the aggregation of amyloid peptide and induced its disaggregation. Furthermore, it inhibited the inflammatory response in primary cellular model of AD [3, 4]. Recently, *trans* ϵ -viniferin was shown to have a preventive role in AD [5]. Indeed, when administrated in Alzheimer mice between 3 and 6 months of age, it reduced size and density of amyloid deposits and decreased astrogliosis and microglial activation. These promising results demonstrating preventive role of viniferin had to be completed by evaluation of curative effects of this natural polyphenol.

AIMS

The purpose of this study was to compare curative effects of *trans* ϵ -viniferin and resveratrol in a murine model of AD, APPswe/PS1dE9 mice, after a weekly intraperitoneal injection at 20 mg/kg from 7 to 11 months.

MATERIALS AND METHODS

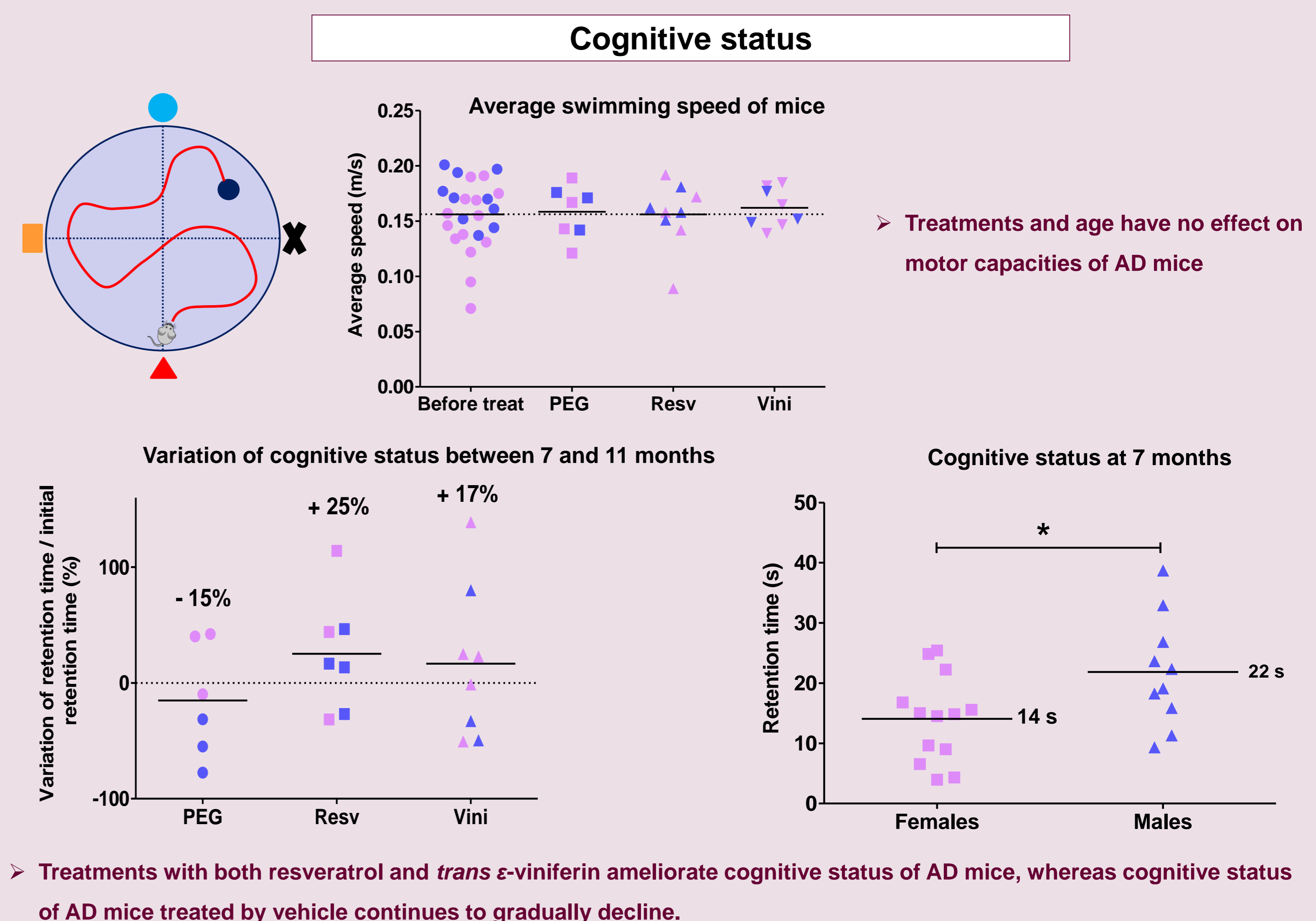
Alzheimer APPswe/PS1dE9 mice were treated with resveratrol (Resv), *trans* ϵ -viniferin (Vini) or PEG 200 (PEG), their vehicle, by weekly intraperitoneal injections (20 mg/kg) from 7 to 11 months. Before the first injection and after the last one, cognitive status was evaluated using water-maze. At 11 months, amyloid deposits and neuroinflammation were visualized *ex-vivo* after euthanasia, by immunolabelling of amyloid peptide, astrocytes and microglia. Expressions of GFAP and Iba1 were evaluated by western-blot.

Results were expressed as means \pm SEM. Data for multiple variable comparisons were analyzed by Kruskal Wallis' test followed by Dunn's test as a post hoc test using the statistical program GraphPad Prism. Comparison between 2 groups was analyzed by Mann Whitney's test.

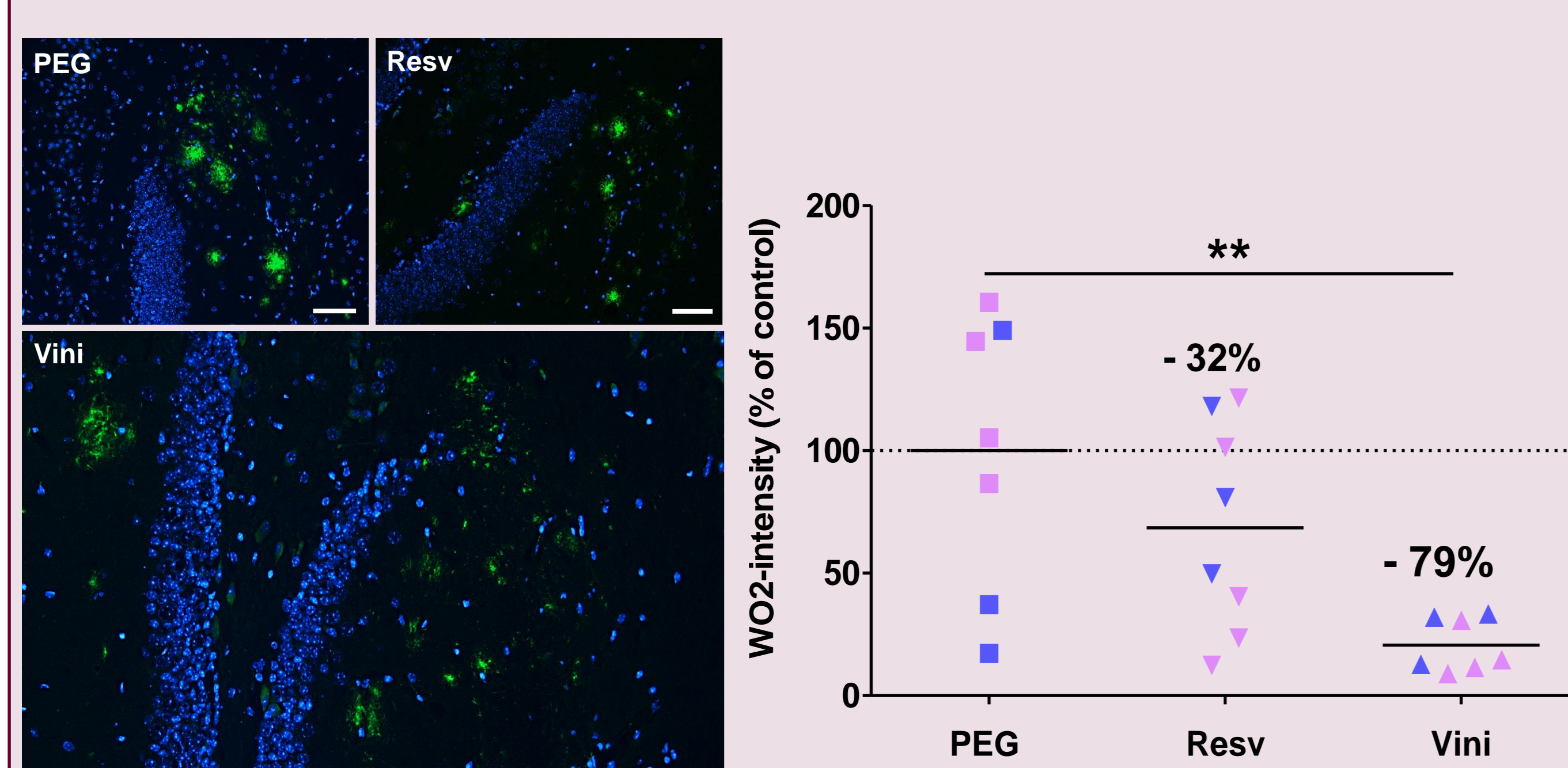


RESULTS

- Resveratrol and *trans* ϵ -viniferin improve the cognitive status of Alzheimer mice.
- *Trans* ϵ -viniferin decreases amyloid deposits and neuroinflammation in the hippocampus.

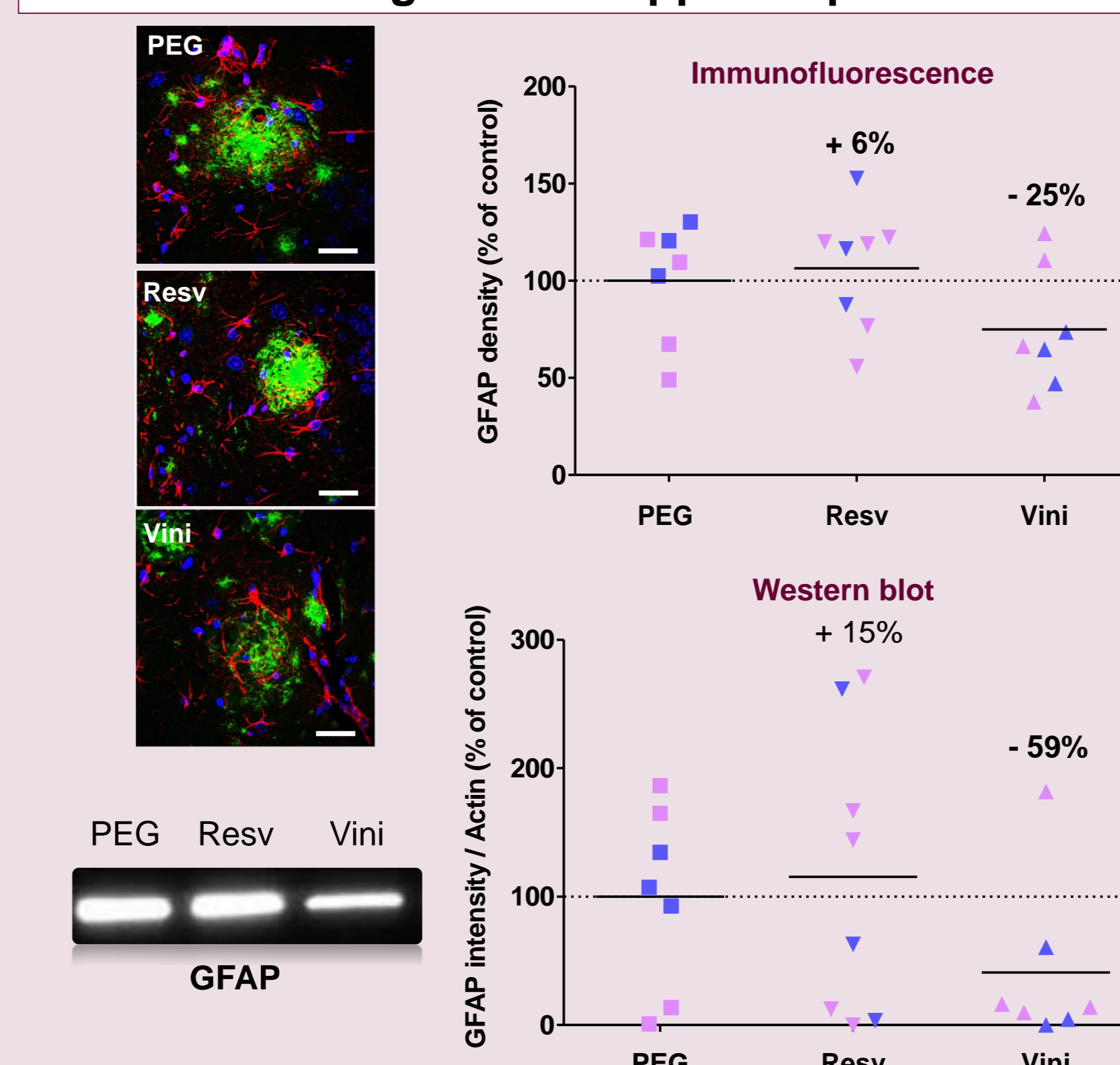


Amyloid deposits in hippocampus



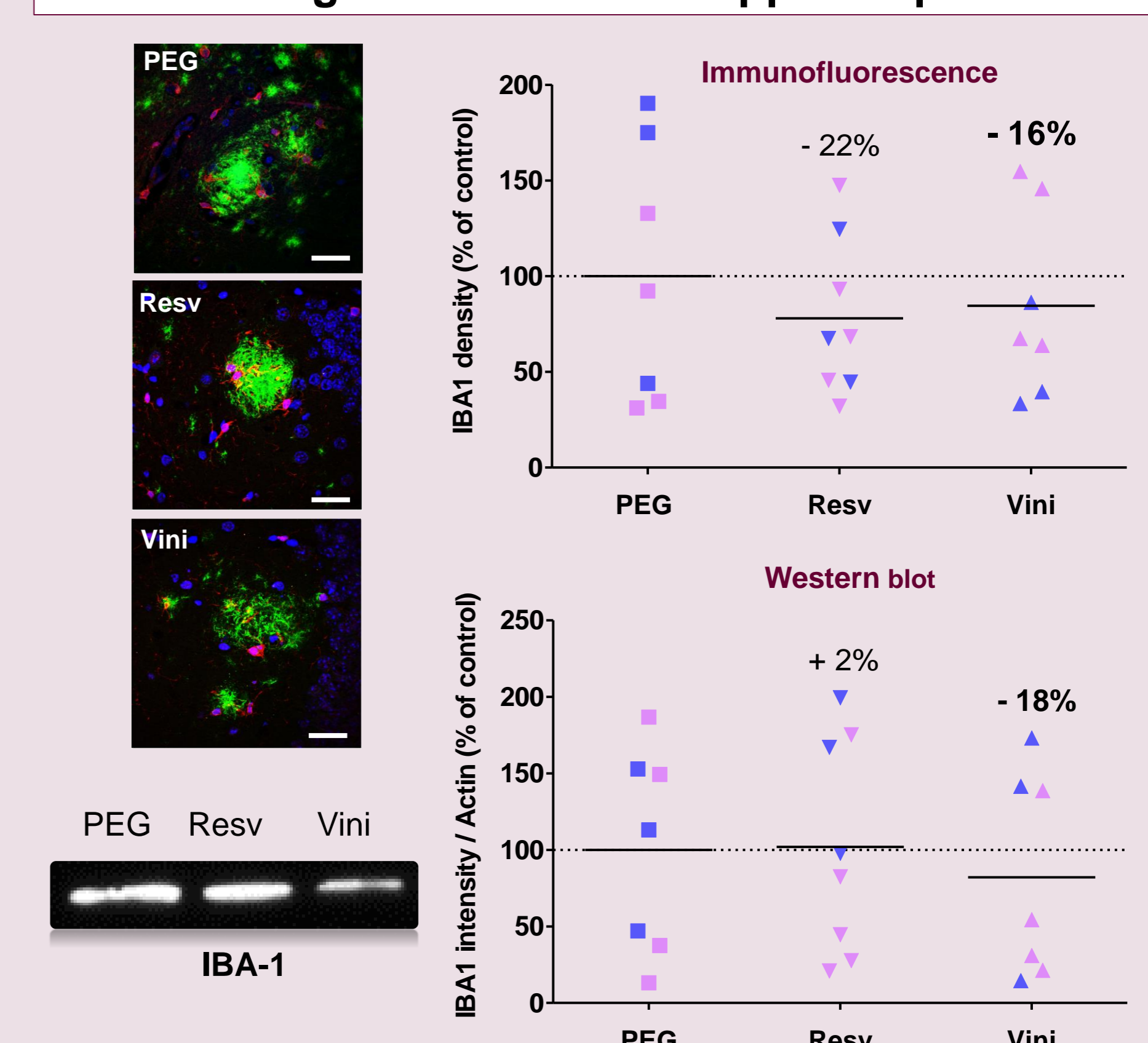
- *Trans* ϵ -viniferin induces a significant decrease of amyloid deposits ($p < 0,01$)
- Resveratrol induces a downward trend of amyloid deposits

Astrogliosis in hippocampus



- *Trans* ϵ -viniferin induces a downward trend of both astrogliosis microglial activation

Microglial activation in hippocampus



CONCLUSION

We demonstrated that *trans* ϵ -viniferin had higher preventive effects than resveratrol to reduce amyloid deposits and neuroinflammation in this murine model of Alzheimer disease. Moreover, this natural polyphenol seems to improve cognitive status of these mice.

Consequently, it could be a relevant therapeutic candidate for this disease.

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