D-serine is involved in the $\beta$-amyloid-related pathophysiology in Alzheimer’s disease

E Ploux, L. Gorisse, I Radzishevsky, H Wolosker, T Freret, J-M Billard

To cite this version:

E Ploux, L. Gorisse, I Radzishevsky, H Wolosker, T Freret, et al.. D-serine is involved in the $\beta$-amyloid-related pathophysiology in Alzheimer’s disease. 14eme Colloque de la Société des Neurosciences, May 2019, Marseille, France. hal-02331616

HAL Id: hal-02331616
https://normandie-univ.hal.science/hal-02331616
Submitted on 24 Oct 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
D-SERINE IS INVOLVED IN THE β-AMYLOID-RELATED PATHOPHYSIOLOGY IN ALZHEIMER’S DISEASE

Ploux E., Gorisse-Hussonnois L., Radzishovsky I., Wolosker H., Freret T., Billard J-M.
Normandie Univ, UNICAEN, INSERM, COMETE, GIP CYCERON, 14000 Caen, France

Activation of N-methyl-D-aspartate subtype of glutamate receptors (NMDAR), key regulators of functional brain plasticity and memory process, requires the binding of the co-agonist D-serine. The homeostasis of these receptors are affected by soluble oligomers of the beta-amyloid peptide (Aβ0) in Alzheimer’s disease (AD). Aβ0 toxic effects possibly pass through mechanisms involving D-serine since Aβ0 stimulates in vitro the production of the co-agonist. However, the actual in vivo contribution of D-serine in the functional NMDAR-related deregulations mediated by Aβ0 is still unknown.

In this study, we wonder if D-serine contributes in vivo to NMDAR deregulations mediated by Aβ0. Behavioral analysis combined to extracellular electrophysiological recordings at hippocampal synapses is conducted in the SxFAD transgenic mice model of amyloidogenesis displaying marked increase in Aβ0 rates. They are compared to SxFAD animals in which the homozygous gene of the serine racemase (SR) that synthesizes D-serine, has been jointly invalidated.

Our results show that deletion of serine racemase prevents, at least partially, memory-related behavioral deficits observed in mice with prominent features of amyloidogenesis. Besides, impairment of NMDAR-dependent functional plasticity, indicated a significant contribution of D-serine in NMDAR-dependent β-amyloid related pathophysiology of AD.