THE PARTIALLY STEREOSPECIFIC INTERACTION OF AMYLOID BETA PEPTIDE 1-40 AND OF CEREBROSTEROL

Z. Kristofikova, V. Kopecky, K. Hofbauerova, Z. Kriz, D. Ripova

Prague Psychiatric Centre, Institute of Physics, Charles University in Prague, Prague, National Centre for Biomolecular Research, Brno, Czech Republic

Introduction: Amyloid beta peptides and oxysterols (especially 24S-hydroxycholesterol known as cerebrosterol) appear to play a very important role in the pathogenesis of Alzheimer disease. Our previous experiments demonstrated that nonaggregated as well as aggregated amyloid beta fragments 1-40/1-42 interacted with racemic 24-hydroxycholesterol. However, it is not clear if the binding occurs exclusively between natural L-isomers of amyloid beta peptides and natural 24S-hydroxycholesterol (i.e., the interaction could be fully stereospecific) or if it is rather nonspecific (i.e., the interactions between synthetic reverse L-isomers/synthetic D-isomers of peptides and synthetic 24R-hydroxycholesterol could also occur).

Aims: To evaluate stereospecificity in the interactions of soluble amyloid beta peptide 1-40 and cerebrosterol.

Methods: We have applied in vitro test using rat hippocampal hemicholinium-3 sensitive carriers from cholesterol-depleted synaptosomes displaying an increased vulnerability to the effects of amyloid beta peptides, Raman spectroscopy and computational simulations.

Results: Our experiments indicate that the binding is nor fully stereospecific nor nonspecific (i.e., there are the bindings between natural 24S-hydroxycholesterol and natural L-fragment 1-40/synthetic D-fragment 1-40 but not between cerebrosterol and synthetic reverse L-fragment 40-1, on the other hand, synthetic 24R-hydroxycholesterol does not interact with L-fragment 1-40/reverse L-fragment 40-1 but it can probably bind to D-fragment 1-40).

Conclusions: We suggest that the partially stereospecific binding of soluble amyloid beta peptide 1-40 and of cerebrosterol could reflect physiological relevance of the interaction and that the binding of aggregated peptides could be involved in the pathogenesis of Alzheimer disease. Supported by GACR (305/09/0457) project.