THE ROLE OF C-ABL IN THE SYNAPTOTOXICITY CAUSED BY Aβ OLIGOMERS; INVOLVEMENT OF THE EPHRINE RECEPTOR

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Introduction: Alterations in synaptic function and structure are one of the early events in Alzheimer disease. Specifically, it has been showed that Aβ oligomers induced a decreased in dendritic spines, synaptic loss, plasticity alterations and cognitive damage. However, the molecular mechanisms activated by Aβ oligomers leading to synaptic dysfunction and loss have not been completely explained. In our laboratory we described that Aβ fibers induce c-Abl activation and this kinase is present in both pre and post synaptic structures. Has been described that the tyrosine kinase receptor ephrine A4 (EphA4) is able to interact with c-Abl and this interaction allows the reciprocal tyrosine phosphorylation.

Then, we propose that c-Abl is involved in the synaptotoxicity induced by Aβ oligomers through the EphA4 receptor.

Materials and methods: We treated wild type and EphA4⁻/⁻ hippocampal neurons (15 DIV) and synaptoneurosomes preparations with synthetic Aβ₄₂ oligomers and evaluated c-Abl and EphA4 signaling.

Results: Our results show that Aβ oligomers induce the c-Abl activation when we treated hippocampal neurons and synaptoneurosomes. Phospho c-Abl colocalized with oligomers Aβ-FITC and PSD-95 in dendritic spines. Interestingly we observed that Aβ₄₂ oligomers increase the phospho tyrosine levels in EphA4 receptor. Also, we observed that Aβ oligomers increase the interaction between c-Abl and EphA4. This interaction is dependent of c-Abl and EphA4 kinase activity.

Discussion: Our data suggest that synaptotoxicity produced by Aβ oligomers induce the c-Abl kinase activation through the EphA4 receptor.

Financing by FONDECYT 1080221