Synaptic plasticity in the hippocampus during post weaning development and aging: influence of basal phosphorylation levels of synaptic proteins

Place of work: Epilepsy and Aging Lab, BioISI – GER- Gene expression and Regulation

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Abstract / MSc thesis project proposal:

Synaptic remodelling is believed to contribute to altered cognition and synaptic plasticity during postnatal development and upon ageing. Recently, we have shown that hippocampal LTP, a cellular synaptic plasticity event crucial for learning and memory, undergoes postweaning developmental maturation and distinct modulation by the GABAergic-associated neuropeptide vasoactive intestinal peptide (VIP)[1–3]. LTP also changes with ageing[4]. Hippocampal CA1 LTP depends on rapid events like phosphorylation of AMPA receptors, the autophosphorylation of CaMKII and other protein kinases like PKM (or PKCzeta). The basal phosphorylation status of these proteins may be a strong conditioning for LTP expression It has not been determined how the basal levels and phosphorylation status of these proteins change during postweaning development or during aging.

Developmental and ageing-associated changes in synaptic plasticity markers, VIP and VIP receptors and hippocampal monoaminergic inputs will be performed by western blot in:

a) During postweaning development (from 3-week-old to 12-week-old rats).
b) Along aging in rats (from early adulthood – 4 months - to old age -21 months).

Western blot analysis will be performed in total hippocampal membranes and/or Percoll-purified hippocampal synaptosomes[1,5] to evaluate phosphorylation levels of AMPA receptor subunit GluA1 (associated with enhanced LTP), CaMKII and PKM. In addition, membrane levels of NMDA receptor subunits GRIN1, GRIN2 and AMPA GluA2 subunit (associated with pathological synaptic mechanisms) will also be evaluated. The expression of VIP and VIP $VPAC_1$ and $VPAC_2$ receptors and GABAergic markers may also be evaluated.

For targets showing enhanced membrane levels, PCR will be performed in total hippocampal membranes to determine changes in gene expression (as opposed to membrane recruitment from intracellular stores).

Bibliography:

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