Oligomeric amyloid-β peptide disrupts olfactory information output by impairment of local inhibitory circuits in rat olfactory bulb

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Abstract: Objective Although early olfactory dysfunction has been found in patients with Alzheimer’s disease (AD), the underlying mechanisms remain unclear. Oligomeric amyloid-β peptide (Aβ) has been implicated to be a primary pathological factor in olfactory dysfunction of AD. However, the local mechanisms related to Aβ-associated pathophysiology in involved olfactory regions remain largely unknown. The present study is to explore whether and how Aβ affects the responses of mitral cells (MCs), the principal output neurons in the olfactory bulb (OB). Methods In this study, using patch-clamp electrophysiological recordings in rat OB slices, we investigate whether and how Aβ oligomers affect the spontaneous and evoked firing rates, spontaneous inhibitory postsynaptic currents (sIPSCs) and miniature IPSCs (mIPSCs), as well as recurrent and lateral inhibition of MCs. Results (1) Oligomeric Aβ 1-42 induces MC hyperactivity by impairment of GABAnergic transmission in the OB. (2) Oligomeric Aβ 1-42 impairs GABAergic transmission through both presynaptic and postsynaptic mechanisms. (3) Oligomeric Aβ 1-42 disrupts recurrent inhibition and lateral inhibition of MCs. Conclusion Aβ impairs local inhibitory circuits and thereby leads to perturbations of olfactory information output in the OB.

Keywords: Alzheimer’s disease; Amyloid-β peptide; gamma-Aminobutyric acid; Inhibitory neuronal circuit; Mitral cell; Olfactory bulb