Alzheimer's Disease (AD) Related Pathological Processes in the Olfactory System

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Early olfactory dysfunction is a common symptom associated with neurodegenerative diseases including Alzheimer's disease (AD). Interestingly, some clinical studies have suggested that AD patients suffering from smell dysfunction displayed difficulties to detect only some of the presented odors. This intriguing symptom of AD has not been yet experimentally fully characterized. To examine the characteristics of the AD smell dysfunction, we performed an odor detection test on 3-month 5xFAD mice, and subsequently, synaptic activity of the olfactory glomeruli was measured using calcium imaging to account for and quantify the functional activity patterns of the olfactory system. We found partial deficits in smelling capability as well as neural activity that is considered as input signals of olfactory sensory neurons (OSN). To confirm the association between the diminished activities of the olfactory neurons and smell dysfunction in the AD, we also investigated at the peripheral olfactory synapses, distribution of oligomerized β-amyloid (Aβ) deposits known to have synaptic toxicity by immunohistological quantification. Our results showed that the Aβ oligomers were accumulated asymmetrically, and its pattern is highly correlated with the activity decline in the olfactory system. We also demonstrated by immunohistochemical quantification of the markers of synaptic function in the olfactory glomeruli; expressions of both TH and synaptophysin were decreased. We also examined the turnover rate of the OSN reconstitution based on the well-balanced feature of the peripheral olfactory system. Our results confirmed that the Aβ asymmetry scale was consistent with the direct damage pattern of the peripheral olfactory system through the impairment of the turnover rate in the peripheral olfactory system. In summary, asymmetric destruction of the olfactory and peripheral olfactory system could provide clues to AD-specific olfactory dysfunction interpretation. This region-specific damage in the olfactory system early in the progression of AD may be closely related to the AD related pathological abnormality and partial olfactory dysfunction found in patients in their early stage of AD.

Key words: olfactory, Alzheimer's disease, tyrosine hydroxylase, BACE1, β-amyloid

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