

**Tanaka C, McGeer PL, Ihara Y, editors. *Neuroscientific Basis of Dementia*. Basel: Birkhäuser; 2001. 298 pages; ISBN 3-7643-6205-7; price: US\$124.00**

**Field of medicine:** Neuroscience.

**Format:** Hardcover book.

**Audience:** Scientists and graduate students in medical, pharmacological, and biological research; physicians and researchers in the biotechnological and pharmaceutical industries.

**Purpose:** To give a comprehensive and detailed overview of the current knowledge about dementia disorders, particularly Alzheimer's disease (AD).

**Content:** The book opens with two articles dealing with the phenomena of membrane lipid signaling, neuroinflammation, and neuronal degeneration in AD. The next section deals with memory and its impairment and contains chapters on long-term memory, amygdala damage in AD, memory in the hippocampus, and hippocampal long-term potentiation. The following eight chapters discuss the pathogenesis of dementing disorders, such as the tau protein whose aggregation causes neuronal degeneration in AD, and other disorders where neurofibrillary tangles and other tau deposits occur. One of those chapters describes transgenic mice overexpressing the human tau; such mice develop a progressive tauopathy similar to frontotemporal dementia with Parkinsonism linked to chromosome 17. Two chapters are on tau mutations; one chapter suggests that the amyotrophic lateral sclerosis/parkinsonism-dementia complex of the Kii peninsula is a new form of familial tauopathy; the next chapter brings a new disease entity: senile dementia of the neurofibrillary tangle type; and three chapters cover the cellular pathology of tau. The following section contains three chapters on dementia related to alpha-synuclein, a common mediator of many neurodegenerative diseases called synucleinopathies (Parkinson's disease, dementia with Lewy bodies, Lewy body variant of AD, multiple system atrophy), as well as on alpha-synuclein fibrillogenesis as a target for drug development. The role of the presenilins (PS) in amyloid precursor protein (APP) processing and beta-amyloid (A-beta) production in AD are elaborated in the following thirteen chapters. These chapters give evidence that the accumulation of A-beta peptide deposits (the presumed prime-mover in AD) in the cortex requires cleavage within the transmembrane domain of APP. Gamma-secretase has been postulated as the agent responsible for this cleavage, but has not been isolated and identified yet. Four reports published in 1999 appear to be closing in on this long-sought goal. Three of them show that PS-1 is necessary for the cleavage of Notch, which mediates cell-cell interactions in deter-

mining cell fate specification during development. To carry out its signaling function, Notch requires cleavage in its transmembrane domain in a manner reminiscent of A-beta production. The fourth chapter brings report on mutations in PS-1 that completely abolish APP cleavage and suggests that PS-1 itself is gamma secretase. Finally, there are five chapters on the diagnosis and therapy of dementia. They comprise phenotype/genotype correlation in familial AD, risk factors and longitudinal studies of at-risk individuals from families with AD pedigrees, biological markers for differential diagnosis, cognitive deficits, and functional neuroimaging techniques. One of these articles focuses on the intake balance of polyunsaturated fatty acids called omega-3 and omega-6, which are not synthesized in mammals, and gives convincing evidence that genetic risk of AD might be lowered by the increased omega-6/omega-3 ratio (together with increased vitamin C, carotene and antioxidant levels). The last chapter gives a review of the recent progress in possible future therapeutic strategies, with anti-tau phosphorylation (the propyl isomerase Pin-1 can restore the ability of phosphorylated tau to bind microtubules and promote microtubule assembly) and vaccine therapy (after immunization, young monkeys produced high titres of serum A-beta antibody, which almost completely prevented development of A-beta deposition, dystrophic neurites, astrocytosis, and microgliosis, while immunized older animals also markedly reduced the extent and progression of the AD-like brain lesions) as the most promising.

**Highlights:** The book is cohesive and highly readable. It fully covers a vast and scattered literature on latest progress in dementia research.

**Limitations:** As in any multiauthored text, there is some degree of redundancy. However, overlapping chapters on presenilins and A-beta are quite consistent with each other.

**Related reading:** Two well-established books in the field are *Alzheimer's disease and related disorders: Etiology, pathogenesis and therapeutics* (Iqbal, Swaab, Winblad, Wisniewski, editors. Wiley, 1999) and *Alzheimer's disease* (Terry, Katzman, Bick, editors. Lippincott Williams & Wilkins, 1999). Since new editions of these books are expected not sooner than 2003, *Neuroscientific basis of dementia* neatly fits the gap and provides an integrative current view of one of the major medical problems of our time.

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