

# Sex differences in Alzheimer’s disease

Yi Xing

Department of Neurology, Xuan Wu Hospital, Capital Medical University, Beijing 100050, China.



Dr. Yi Xing, Department of Neurology, Xuan Wu Hospital, Capital Medical University, Beijing 100050, China. Research interest: the effects of hormones and metabolism on the pathogenesis of neurodegenerative disorders, especially Alzheimer’s disease. Publications: eight SCI articles as the first author, including progress in Neurobiology, *Journal of Alzheimer’s Disease*, et al.

Recently, Koran *et al.*<sup>[1]</sup> published an article, named “Sex differences in the association between Alzheimer’s disease (AD) biomarkers and cognitive decline” in *Brain Imaging and Behavior*. The result proved that there were sex-specific associations between biomarkers of AD. This article added evidence to the theory of sex differences in AD.

Sex difference is a common phenomenon in AD and manifests in many ways. Females are disproportionately affected by AD. It is well known that females have higher prevalence of AD than males. In China, for urban population, the AD prevalence in male is 1.27%, while in female, it is 3.54%; for rural population, this difference is even more dramatic: 1.95% in men vs. 6.30% in women.<sup>[2]</sup> However, sex differences in the incidence of AD are still inconsistent. Studies tend to show that there are no sex differences in incidence of AD until very late of age when females have the higher incidence.<sup>[3]</sup> However, females seem to have higher

risk of progression from mild cognitive impairment (MCI) to AD. A meta-analysis showed that the risk of progression from MCI to AD is 1.33 fold higher in women than in men.<sup>[4]</sup>

The pathological changes of AD are characterized by the deposition of extracellular amyloid- $\beta$  (A $\beta$ ) and the presence of neurofibrillary tangles. Pathological studies showed that females had more global AD pathology than males, especially for neurofibrillary tangles. More interestingly, females were more susceptible for AD pathological changes. It was reported that 1 additional unit of AD pathology was associated with a nearly 3-fold increase in the risk of clinical AD in men; while for women, this odd increased to 20-fold.<sup>[5]</sup>

Nowadays, researchers seek to observe brain pathological changes *in vivo*, using magnetic resonance imaging (MRI), positron emission tomography or cerebrospinal fluid (CSF). More and more studies on biomarkers of AD are underway. MRI is a common and convenient method to help

**Corresponding Author:** Dr. Yi Xing, Department of Neurology, Xuan Wu Hospital, Capital Medical University, Beijing 100050, China. Email: xingyi\_211@163.com

Access this article online	
Quick Response Code:	Website: <a href="http://www.nnjournal.net">http://www.nnjournal.net</a>
	DOI: 10.20517/2347-8659.2016.27

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** [service@oaepublish.com](mailto:service@oaepublish.com)

**How to cite this article:** Xing Y. Sex differences in Alzheimer’s disease. *Neuroimmunol Neuroinflammation* 2016;3:165-6.  
**Received:** 02-06-2016; **Accepted:** 02-06-2016.

us observe brain atrophy. After 1,368 MRI scans, a study demonstrated that brain atrophic rates were about 1-1.5% faster in females than males.<sup>[6]</sup> The levels of  $A\beta_{42}$  and tau protein in CSF are promising biomarkers of AD. Although by now, there is no remarkable evidence suggesting sex differences in  $A\beta_{42}$  and tau levels in CSF, Koran's study showed that associations between  $A\beta_{42}$  and tau levels in CSF and brain atrophy in MRI were sex-specific. A total of 348 normal control, 565 patients with MCI and 185 patients with AD from Alzheimer's disease neuroimaging initiative were included in this study. Participants were followed for an average of 2.5 years. A significant interaction between sex and CSF  $A\beta_{42}$  levels was found on longitudinal hippocampal atrophy and longitudinal decline in memory and executive function. A similar interaction between sex and CSF tau levels was also observed. With the decrease of CSF  $A\beta_{42}$  levels or increase of tau levels, females showed faster hippocampal atrophy and cognitive decline compared with males. This result was not modified by different diagnosis.

The authors pointed out in discussion that the result could be explained by age-related changes in estrogen levels. Actually, the decline of estrogen levels after menopause is only one of the reasons that are related to sex differences in AD. The interaction between genes, hormones and social

environments may be the key to unraveling broad sex differences in AD.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Koran ME, Wagener M, Hohman TJ. Sex differences in the association between AD biomarkers and cognitive decline. *Brain Imaging Behav* 2016; Doi: 10.1007/s11682-016-9523-8.
2. Jia J, Wang F, Wei C, Zhou A, Jia X, Li F, Tang M, Chu L, Zhou Y, Zhou C, Cui Y, Wang Q, Wang W, Yin P, Hu N, Zuo X, Song H, Qin W, Wu L, Li D, Jia L, Song J, Han Y, Xing Y, Yang P, Li Y, Qiao Y, Tang Y, Lv J, Dong X. The prevalence of dementia in urban and rural areas of China. *Alzheimers Dement* 2014;10:1-9.
3. Mielke MM, Vemuri P, Rocca WA. Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Clin Epidemiol* 2014;6:37-48.
4. Li JQ, Tan L, Wang HF, Tan MS, Tan L, Xu W, Zhao QF, Wang J, Jiang T, Yu JT. Risk factors for predicting progression from mild cognitive impairment to Alzheimer's disease: a systematic review and meta-analysis of cohort studies. *J Neurol Neurosurg Psychiatry* 2016;87:476-84.
5. Barnes LL, Wilson RS, Bienias JL, Schneider JA, Evans DA, Bennett DA. Sex differences in the clinical manifestations of Alzheimer disease pathology. *Arch Gen Psychiatry* 2005; 62:685-691.
6. Hua X, Hibar D P, Lee S, Toga AW, Jack CR Jr, Weiner MW, Thompson PM. Sex and age differences in atrophic rates: an ADNI study with  $n = 1368$  MRI scans. *Neurobiol Aging* 2010;31:1463-80.