INTRODUCTION

Neurological diseases are characterized by high frequency of disability and mortality with pathogenesis largely unknown. Genetic, refractory, and rare diseases account for a large proportion of neurological diseases; sympathetically, limited curable treatments are available. Hundreds of millions of people worldwide are affected by neurological disorders. The diagnosis and treatment of neurological disorders have made significant progress in recent years, especially in the past two decades with the rapid development of technology. For example, regarding acute ischemic stroke, the disability, mortality, and recurrence rate were notably decreasing with the improvement of intravenous and intra-artery treatment and with the emphasis on secondary prevention in recent years worldwide. More surprisingly, gene therapy is emerging as a powerful approach to help patients suffering from gene defects with the potential to treat and even cure the genetic disorders. Almost at the same time, remarkable changes have been made in terms of diagnosis, treatment, and prevention of neurological diseases in China. Even more importantly, China is a country having very large geographical areas with disequilibrium of economic development and having enormous population covering diversified cultures and customs. Therefore, risk factors and spectrum for some of the neurological disease are different from Western countries. Hereby in this paragraph, we reviewed the progression of neurological diseases in the recent two decades and further compared the differences between China and Western countries. The comparison will help medical practitioners and researchers to better understand the gap, to make better medical decisions for patients, and to encourage progress in research field.

STROKE AND CEREBROVASCULAR DISEASE

Stroke is the second most common cause of death worldwide, and a major global cause of disability.[1] There are significant geographical differences in stroke burden by regions and country income levels. In the past two decades, within Western countries, there has been a great reduction in stroke incidence, mortality, mortality-to-incidence ratios, and disability-adjusted life years (DALYs) lost, which could be explained by the good health services and strategies for stroke prevention and medical care in these countries. Conversely, in China, stroke incidence has increased, and mortality-to-incidence ratios and DALYs lost are much higher than those in high-income countries. Although reductions in stroke mortality have taken place globally, compared to the high-income countries, a two-fold higher stroke mortality rate was observed in the low-income and middle-income countries.

In 2017, the up-to-date stroke epidemiology survey in China was published in Circulation.[2] The age-standardized stroke prevalence, incidence, and mortality rates were 1114.8/100,000 people, 246.8/100,000, and 114.8/100,000 person-years, respectively. Stroke burden in China has increased over the past three decades and remains
particularly high in rural areas. This might be explained by the westernized lifestyle and sociodemographic changes in China which may have had an impact on the prevalence of common stroke risk factors. Geographical gradients (North to South) of stroke burden within China were observed as well. The highest incidence and mortality of stroke were in the Northeast region, while Central China ranked second, and the regions with lowest incidence and mortality rates were in South China.

Compared with populations of European and US origin, Chinese populations have a higher proportion of strokes attributable to intracerebral hemorrhage (ICH). It has been reported that there is a twice higher rate of ICH incidence in Asian people compared with that in other ethnic populations.\[^{[1]}\] Chinese also have an apparently different distribution of ischemic stroke subtypes, in comparison with Caucasian populations. There are higher overall proportions of small vessel disease (lacunar) and large artery atherosclerotic ischemic stroke in Chinese and a lower proportion of cardioembolic stroke.\[^{[2]}\] The frequency of ischemic stroke due to intracranial atherosclerotic stenosis seems to be higher in Asian people (30–50%) than in Caucasian populations (5–10%).\[^{[3]}\]

Previous studies investigating the epidemiology of asymptomatic small vessel disease (CSVD) in the general population were mainly carried out in Western countries, including the Framingham study, the Rotterdam scan study, and the Cardiovascular Health study. The prospective community-based Shunyi Study, which was conducted in 2013 in the rural area nearby Beijing, supplemented the epidemiological data of CSVD in Chinese population. When comparing participants in the same age group from Western world region, a higher burden of lacunas but a relatively lower prevalence of cerebral microbleeds was observed, which might be attributable to the very low awareness, treatment, and control rate of vascular risk factors (data from our team, not published).

Intravenous thrombolysis (IVT) for acute ischemic stroke represents one of the most important and recent breakthroughs in medicine. Recombinant tissue-type plasminogen activator (alteplase, rtPA) was first approved by the Food and Drug Administration in the United States in 1996.\[^{[4]}\] The safety and efficacy of rtPA when administered within the hyperacute time frame after ischemic stroke onset are solidly supported by combined data from multiple randomized controlled trials ever since then. It is strongly recommended in Chinese guidelines, and its efficiency has been confirmed by extensive clinical experiences in China. Endovascular thrombectomy with stent retrievers for acute ischemic stroke has evolved substantially after 2015, which could significantly reduce disability for patients with large vessel ischemic stroke.\[^{[5]}\] Based on the best evidence currently available in the Chinese guideline for the early management of patients with acute ischemic stroke, mechanical thrombectomy, in addition to IVT, is recommended for treatment of acute stroke in patients with large artery occlusions in the anterior circulation up to 6 h after symptom onset. Intensive efforts have been made by Chinese health systems and neurologists to minimize delays of hyperacute phase management and thus to maximally improve the efficacy and safety of stroke reperfusion therapies. According to the official government report, increase of both IVT and thrombectomy rates, as well as a reduction of door-to-needle time has been observed year by year in the experienced stroke centers of China.

China is also making great progress in the aspect of stroke secondary prevention. The government has supported the organization and publication of several national stroke prevention guidelines to improve standards of care. The cluster-randomized, guideline-based, structured care program, known as the Standard Medical Management in Secondary Prevention of Ischemic Stroke in China (SMART) study, demonstrated that using a program of guideline-based structured care and patient education in China is feasible, which could increase the patient adherence to the medical therapy and further reduce the recurrent stroke risk and improve patient health status.\[^{[6]}\] Furthermore, the subgroup analysis of SMART study showed that implementation of the structured program can improve the 6-month functional outcome in low-educated patients\[^{[7]}\] and also demonstrated that elevated fasting blood glucose was found to be predictive of poor functional outcome in nondiabetic stroke patients.\[^{[8]}\] Analysis for prescription of traditional Chinese medicine (TCM) for the acute stroke patients found that nearly one-third of the hospitalized patients were prescribed TCM at discharge.\[^{[9]}\] Findings from Clopidogrel in High‑Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) trial, which was conducted in China, showed that, among patients with high-risk transient ischemic attack or acute minor ischemic stroke, treatment with a combination of clopidogrel with aspirin for 21 days, followed by clopidogrel alone for a total of 90 days, is superior to aspirin alone in reducing the risk of subsequent stroke events.\[^{[10]}\] The CHANCE study has made a great international impact and updated the current guidelines for the management of acute ischemic stroke published by both Chinese Medical Association and American Heart Association/American Stroke Association.

**Dementia**

Dementia is one of the leading causes of disability in the elderly population across the world. Given the huge social burdens put by this devastating disease, efforts to elucidate the mechanisms and find optimal treatments have been made for decades; however, challenges still exist.

In recent years, the prevalence of dementia in China has been reported to be similar to that in Western countries.\[^{[11]}\] Moreover, with the aging of the population in China, the prevalence of dementia increased slightly based on recent population-based study compared to that of 20 years ago.\[^{[12,13]}\] Jia et al. reported the prevalence of dementia, Alzheimer’s disease (AD) and vascular dementia (VaD)
Age-dependent prevalence of PD is found in worldwide populations, ranging between 41/100,000 inhabitants between 40 and 49 years and 1903/100,000 inhabitants older than 80. A study from Beijing, Xi’an, and Shanghai of China, published in 2005, showed that the prevalence of PD was 1.7%, suggesting that the prevalence of PD in China was similar to that in developed countries. Another meta-analysis revealed that the prevalence of PD in China was about 1.99 million in 2005, and it is estimated to reach 4.94 million in 2030, with an increased proportion of the patients in selected countries arising from 48% to 57%. Since PD predominantly affects older adults, as populations’ age, PD is expected to impose an increasing social and economic burden on societies, especially in economically developing countries. There is increasingly need to develop strategies to meet the health-care needs of patients with PD.

In contrast to the high prevalence, much lower incidence of motor complications in Chinese populations was identified than that in Western countries. Many of the PD patients in China were treated with low-dose levodopa and combination of low-dose antiparkinsonian agents, which might be influenced by Chinese cultures. Further investigation is also warranted to identify the possible mechanism and optimal treatment for PD.

Recently, there is also progress in genetic movement disorders. Chinese neurologists and researchers identified some new causative genes for single gene disorder. For instance, PRRT2 was identified by Chinese neurologists as the causative gene of paroxysmal kinesigenic dyskinesias (PKD) as well as other paroxysmal dyskinesias. While genetic etiology may not show great differences in movement disorders of Chinese from other ethnic groups, abundance of patient resources would facilitate the identification of novel pathogenic genes. With collaboration, other potential causative candidates for PRRT2-negative PKD patients had recently been spotted by Chinese researchers such as KCNMA1, SLC9A1, and SCN8A. Today, the gene therapy has become the potentially promising strategies for treatment of neurological diseases; further work is inevitably needed for treatment of genetic movement disorders.

**Amyotrophic Lateral Sclerosis**

Amyotrophic lateral sclerosis (ALS), as a progressive neurological disease that causes disability and death, is catching great attention recently. The aim of the establishment of the ALS International Executive Committee is to promote the clinical and research work on the diagnosis of ALS. Epidemiologic data from Europe, America, and Japan showed that the peak age of ALS onset is between 60 and 70 years. Unfortunately, there are no epidemiologic data about ALS in the mainland of China so far. However, our ALS national collaboration team collected data from ten ALS centers in seven cities of China. The results indicated that the mean age of onset was 52.4 ± 12.1 years. The peak age at onset was 55–59 years for men and 45–49 years for women. Genetic backgrounds and environmental factors may account for the differences.
The genetic features of ALS in the mainland of China are distinct from that in Caucasian populations. In Europe, the most common mutations were the C9orf72 repeat expansions, for both familial and sporadic ALS patients, followed by SOD1, TARDBP, and FUS mutations. Since ALS patients carrying C9orf72 mutation often present with frontotemporal dementia concomitantly, this might be the reason that the incidence of dementia in ALS patients in Europe and America is much higher than that in China and other Asian countries. In contrast, SOD1 is the gene with highest mutant frequency in Chinese ALS patients, followed by FUS and TARDBP, while the repeat expansion in C9orf72 is very rare.

**Inflammatory Demyelinating Diseases of the Central Nervous System**

Inflammatory demyelinating diseases (IDDs) of the central nervous system, for example, multiple sclerosis (MS) which predominantly affects young adults, are characterized by disease relapses and progressive disability. The significant difference of IDD between China and Western countries is the incidence and prevalence of MS and neuromyelitis optica spectrum disorder (NMOSD). For MS, the incidence and prevalence vary geographically, higher latitude correlating with increased prevalence, incidence, and mortalities. The high-frequency areas of the world include all of Europe (including Russia), Southern Canada, the Northern United States, New Zealand, and southeast Austria. In these areas, the prevalence ranges from 60 to 300/100,000. China, Japan, and Korea belong to the low-frequency areas. A population-based survey suggested that the prevalence of MS in Shanghai, the South part of China, is 1.39/100,000. For the past 20 years, many studies investigated the pathophysiology and mechanism of actions of the disease-modifying drugs (DMDs) for treatment of MS, to reduce the frequency of episodes, disability accrual, and severity of irreversible nerve damage. Although availability of DMD increase, there is still the need to personalized DMD since only some of the patients respond satisfactorily to a given treatment based on evidence from clinical trials and daily clinical practice.

Contrast to MS, the incidence and prevalence of NMOSD in China is much higher than that in Western countries. Prevalence rates (1/100,000) of NMO/NMOSD were reported to be 3.9 in the United States, 4.4 in Denmark, 2.0 in South East Wales, and 0.7 in North West England. Until now, there was no epidemiological study about NMOSD in China. However, data from the MSNMO database, collected from an observational and prospective cohort organized by Peking Union Medical College Hospital (PUMCH), showed that the ratio of MS: NMOSD is about 1.2–3. A study from North East Tuscany showed that this ratio is 42.7:1.

**Syphilis and Neurological Syphilis**

Epidemiology and disease spectrum of syphilis have changed greatly in recent decades. Based on the data from Chinese Center for Disease Control and Prevention, the incidence of syphilis has been increasing significantly since the 1980s, especially during 1995–2000s. Latent syphilis increased by more than 50%, while the rate of primary and secondary syphilis had declined in recent years, which was different from that of the 1950s. The data of neurological syphilis from PUMCH showed that notable increasing trend was present since 1980s. In detail for stages and clinical types of syphilis, compared to that of the 2001–2010, the prevalence of third-stage neurological syphilis including tabes dorsalis (syphilitic myelopathy) and general paresis increased significantly after 2011 (28% vs. 69%). Contrastly, meningovascular syphilis decreased from 36% to 0% (data from our team, not published). These changes make clinical challenges to physicians for the diagnosis and prompt treatment of syphilis.

Syphilis still remains a major popular public health issue in China and national measures according to the epidemiological features are urgently warranted to control the disease.

In conclusion, with dramatic growth of the economics and significant transformation of lifestyle for the past two decades, the epidemiology and spectrum of neurological disorders are potentially changing and imposing great challenges for neurologic practice in China. Numerous clinical researches and population-based studies are emerging for understanding the risk factors, disease progression, management, and prognosis of certain neurological diseases, and the spontaneous development in neuroscience advance the understanding of pathogenesis of neurological disorders. Chinese neurologists would need to balance the domestic and international challenges and opportunities and to be part of the world force for imminent discoveries and development of neurologic practices.

**References**

1. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: Findings from the Global Burden of Disease Study 2010. Lancet 2014;383:2155-67. doi: 10.1016/S0140-6736(13)61290-3.
2. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, et al. Prevalence, incidence, and mortality of stroke in China: Results from a nationwide population-based survey of 480,687 adults. Circulation 2017;135:759-71. doi: 10.1161/CIRCULATIONAHA.116.025250.
3. van Asch CJ, Luifjes MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ, et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: A systematic review and meta-analysis. Lancet Neurol 2010;9:167-76. doi: 10.1016/S1474-4422(09)70340-0.
4. Tsai CF, Thomas B, Sudlow CL. Epidemiology of stroke and its subtypes in Chinese vs. white populations: A systematic review. Neurology 2013;81:264-72. doi: 10.1212/WNL.0b013e31829bdfe3.
5. Holmstedt CA, Tanur TN, Chimowitz MI. Atherosclerotic intracranial arterial stenosis: Risk factors, diagnosis, and treatment. Lancet Neurol 2013;12:1106-14. doi: 10.1016/S1474-4422(13)70195-9.
6. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581-7. doi: 10.1056/NEJM199512143332401.
7. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel
ischaemic stroke: A meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723‑31. doi: 10.1016/S0140‑6736(16)00163‑X.

8. Peng B, Ni J, Anderson CS, Zhu Y, Wang Y, Pu C, et al. Implementation of a structured guideline‑based program for the secondary prevention of ischemic stroke in China. Stroke 2014;45:515‑9. doi: 10.1161/STROKEAHA.113.001424.

9. Ni J, Yao M, Zhou L, Zhu Y, Peng B, Cui L, et al. A guideline‑based program may improve the outcome of stroke among illiterate patients. Int J Stroke 2016;11:332‑7. doi: 10.1177/1747493016625161.

10. Yao M, Ni J, Zhou L, Peng B, Zhu Y, Cui L, et al. Elevated fasting blood glucose is predictive of poor outcome in non‑diabetic stroke patients: A Sub‑group analysis of SMART. PLoS One 2016;11:e0160674. doi: 10.1371/journal.pone.0160674.

11. Yuan J, Zhu Y, Yao M, Ni J, Zhou L, Peng B, et al. Traditional Chinese medicine prescribed for acute stroke patients: A cross‑sectional survey (in Chinese). Chin J Neurol 2015;48:284‑7. doi: 10.3760/cma.j.issn.1006‑7876.2015.04.006.

12. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, et al. Clonidine with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med 2013;369:11‑9. doi: 10.1056/NEJMoa1215340.

13. Jia J, Wang F, Wei C, Zhou A, Jia X, Li F, et al. The prevalence of dementia in urban and rural areas of China. Alzheimers Dement 2014;10:1‑9. doi: 10.1016/j.jalz.2013.01.012.

14. Zhang ZX, Zahner GE, Román GC, Liu J, Hong Z, Qu QM, et al. Dementia subtypes in China: Prevalence in Beijing, Xian, Shanghai, and Chengdu. Arch Neurol 2005;62:447‑53. doi: 10.1001/archneur.62.3.447.

15. Dong MJ, Peng B, Lin XT, Zhou A, Zhou YR, Wang RH, et al. The prevalence of dementia in the people’s republic of China: A systematic analysis of 1980‑2004 studies. Age Ageing 2007;36:619‑24. doi: 10.1093/ageing/afm128.

16. Yuan J, Zhang Z, Wen H, Hong X, Hong Z, Qu Q, et al. Incidence of dementia and subtypes: A cohort study in four regions in China. Alzheimers Dement 2016;12:262‑71. doi: 10.1016/j.jalz.2015.02.011.

17. Satizabal CL, Beiser AS, Chouraki V, Chêne G, Dufouil C, Seshadri S, et al. Incidence of dementia over three decades in the Framingham Heart Study. N Engl J Med 2016;374:523‑32. doi: 10.1056/NEJMoai1504327.

18. Derby CA, Katz MJ, Lipton RB, Hall CB. Trends in dementia incidence in a birth cohort analysis of the Einstein aging study. JAMA Neurol 2017;74:1345‑51. doi: 10.1001/jamanetworkneurol.2017.1964.

19. World Alzheimer Report. Alzheimer’s Disease International; 2015. Available from: http://www.worldalzreport2015.org/. [Last accessed on 2018 Feb 20].

20. Jia J, Wei C, Chen S, Li F, Tang Y, Qin W, et al. The cost of Alzheimer’s disease in China and re‑estimation of costs worldwide. Alzheimers Dement 2018 [Epub ahead of print]. doi: 10.1016/j.jalz.2017.12.006.

21. Jia J. Chinese Guidelines for Diagnosis and Management of Cognitive Impairment and Dementia. Beijing: People’s Medical Publishing House Co., Ltd., 2015.

22. Jia J, Zuo X, Jia XF, Chu C, Wu L, Zhou A, et al. Diagnosis and treatment of dementia in neurology outpatient departments of general hospitals in China. Alzheimers Dement 2016;12:446‑53. doi: 10.1016/j.jalz.2015.06.1892.

23. Fu L, Liu L, Zhang J, Xu B, Fan Y, Tian J, et al. Comparison of dual‑bimarker PIB‑PET and dual‑tracer PET in AD diagnosis. Eur Radiol 2014;24:2800‑9. doi: 10.1007/s00330‑014‑3311‑x.

24. Octohydroxamoacidraine Sucinate Tablet for Mild‑to‑Moderate Alzheimer’s Disease. Available from: https://www.clinicaltrials.gov/ ct2/show/NC1T03283059?cond=Alzheimer’sDisease&cnttry=CN&ranck=6. [Last accessed on 2018 Feb 20].

25. Ji J, Wei C, Liang J, Zhou A, Zuo X, Song H, et al. The effects of DL‑3‑n‑butylphthalaldehyde in patients with vascular cognitive impairment without dementia caused by subcortical ischemic small vessel disease: A multicentre, randomized, double‑blind, placebo‑controlled trial. Alzheimers Dement 2016;12:89‑99. doi: 10.1016/j.jalz.2015.04.010.

26. Pringsheim T, Jette N, Frohlich A, Steeves TD. The prevalence of Parkinson’s disease: A systematic review and meta‑analysis. Mov Disord 2014;29:1583‑90. doi: 10.1002/mds.25945.
Campbell JD, et al. Multiple sclerosis prevalence in the United States commercially insured population. Neurology 2016;86:1014-21. doi: 10.1212/WNL.0000000000002469.
47. Bentzen J, Flachs EM, Stenager E, Bronnum-Hansen H, Koch-Henriksen N. Prevalence of multiple sclerosis in Denmark 1950–2005. Mult Scler 2010;16:520-5. doi: 10.1177/1352458510364197.
48. Cheng Q, Miao L, Zhang J, Ding SJ, Liu ZG, Wang X, et al. A population-based survey of multiple sclerosis in Shanghai, China. Neurology 2007;68:1495-500. doi: 10.1212/01.wnl.0000260695.72980.b7.
49. Comi G, Radaelli M, Soelberg Sørensen P. Evolving concepts in the treatment of relapsing multiple sclerosis. Lancet 2017;389:1347-56. doi: 10.1016/S0140-6736(16)32388-1.
50. Chong HT, Tan CT. A review of multiple sclerosis with Asian perspective. Med J Malaysia 2008;63:356-61.
51. Flanagan EP, Cabre P, Weimshenker BG, St. Sauver J, Jacobson DJ, Majed M, et al. Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. Ann Neurol 2016 [Epub ahead of print], doi: 10.1002/ana.24617.
52. Asgari N, Lillevang ST, Skejoe HP, Falah M, Stenager E, Kyvik KO, et al. A population-based study of neuromyelitis optica in Caucasians. Neurology 2011;76:1589-95. doi: 10.1212/WNL.0b013e3182190f74.
53. Cosburn M, Tackley G, Baker K, Ingram G, Burtonwood M, Malik G, et al. The prevalence of neuromyelitis optica in South East Wales. Eur J Neurol 2012;19:655-9. doi: 10.1111/j.1468-1331.2011.03529.x.
54. Jacob A, Panicker J, Lythgoe D, Elsone L, Mutch K, Wilson M, et al. The epidemiology of neuromyelitis optica amongst adults in the Merseyside county of United Kingdom. J Neurol 2013;260:2134-7. doi: 10.1007/s00415-013-6926-y.
55. Fan S, Xu Y, Ren H, Guan H, Feng F, Gao X, et al. Comparison of myelin oligodendrocyte glycoprotein (MOG)-antibody disease and AQP4-IgG-positive neuromyelitis optica spectrum disorder (NMOSD) when they co-exist with anti-NMDA (N-methyl-D-aspartate) receptor encephalitis. Mult Scler Relat Disord 2018;20:144-52. doi: 10.1016/j.msard.2018.01.007.
56. Bizzoco E, Lolli F, Repice AM, Hakiki B, Falcini M, Barilaro A, et al. Prevalence of neuromyelitis optica spectrum disorder and phenotype distribution. J Neurol 2009;256:1891-8. doi: 10.1007/s00415-009-5171-x.
57. Gong X, Yue X, Teng F, Jiang N, Meng P. Syphilis in China from 2000 to 2013: Epidemiological trends and characteristics (in Chinese). Chin J Dermatol 2014;47:310-5. doi: 10.3760/cma.j.issn.0412-4030.2014.05.002.