Utility of Chinese Versions of Addenbrooke's Cognitive Examination

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Addenbrooke's cognitive examination (ACE) is a cognitive screening tool that has developed through three stages: ACE, ACE-Revised (ACE-R), and ACE-Ⅲ. In addition, mini-Addenbrooke's Cognitive Examination (M-ACE) and ACE mobile are the additional versions that is derived from ACE-III. ACE and its related versions show better performance than Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) in detecting mild cognitive impairment in different neurological disorders. It has been translated into numerous languages, including Chinese.

Keywords: Addenbrooke's cognitive examination ; Chinese ; mild cognitive impairment

1. Introduction

Dementia is a major challenge for global public health [1]. Currently, more than 46 million people worldwide suffer from dementia, and it is estimated that this number will increase to 131.5 million by 2050 [2]. As the most populous country in the world, the number of dementia patients in China accounts for approximately 25% of the total number of dementia cases in the world [3]. In China, the prevalence of dementia in people aged over 60 is 4.30–6.30% [4]. Despite the high prevalence of dementia, many people with cognitive impairment are still not correctly diagnosed in a timely manner. It is reported that about 75% of dementia patients worldwide have not been diagnosed, equivalent to 41 million people [5]. Failure to identify dementia earlier poses a great challenge to application of clinical treatment and healthcare. Therefore, the detection method of dementia is particularly important. One of the major methods to detect cognitive impairment is the use of cognitive examination tests. A good cognitive screening tool can help researchers and clinicians identify cognitive impairment early and accurately. So far, apart from Addenbrooke's Cognitive Examination (ACE), there are many cognitive screening tools, such as the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Blessed Dementia Rating Scale (BDRS), and Hasegawa's Dementia Scale (HDS).

2. Utility of Chinese Versions of ACE in the Detection of Cognitive Impairment

2.1. ACE-R

The Chinese version of ACE-R, the same as the original version, consists of five cognitive domains: attention/orientation, memory, fluency, language, and visuospatial. It takes about 12 to 20 min to complete the test, and the total score is 100. There are a few modifications based on the underlying principle during the translation process. For example, the name and address in the memory, recall, and recognition section are replaced by Chinese name and address; the letter 'P', which generated as many words as possible, is replaced with Chinese character 'che, 车' in the verbal fluency section; English words and sentences are replaced by Chinese characters or poems with difficulties to produce in the repetition section [6].

The Chinese version of ACE-R is a reliable examination test for detecting cognitive impairment, with its satisfactory sensitivity (0.920, 0.867), specificity (0.857, 0.706), and area under curve (AUC) (0.945, 0.836) to detect mild AD and MCI, respectively [6]. The Chinese-Cantonese version of ACE-R is also an excellent cognitive screening tool for MCI and dementia, with acceptable sensitivity (0.74, 0.93), specificity (0.84, 0.95), and AUC (0.84, 0.98) [7]. In the Cantonese speaking Chinese population, ACE-R Cantonese version is recommended, although the majority of Cantonese speaking Chinese can speak Mandarin nowadays. The Chinese version of ACE-R is widely used in the detection of cognitive impairment in amyotrophic lateral sclerosis, multiple system atrophy, PD, primary blepharospasm, and related disorders [8][9][10][11][12][13][14][15]. Three domains (attention, memory, and language) are declined in amyotrophic lateral sclerosis [9]. With the exception of attention, four domains can be affected in patients with multiple system atrophy (MSA), while four

domains (except memory) are impaired in PD [12][13]. In addition, all five domains are impaired in primary blepharospasm [14].

2.2. ACE-III

More clinicians and medical researchers are using Chinese ACE-III in cognitive assessment, as ACE is gradually modified and improved. Thus, there are more studies using the Chinese version of ACE-III than ACE-R [16][17][18][19]. ACE-III is also scored out of 100 and consists of five domains. Based on specific cultures and usage experiences of ACE-R, the Chinese version of ACE-III has been translated and modified from the original version. For example, the first and third pictures have neem replaced by 'pencil' and 'panda' in the language domain. The second question in the language domain has been revised to 'Which animal lives in Sichuan China?', while Sichuan is a province in China where pandas live. Wang et al. verified ACE-III with satisfactory sensitivity (0.911), specificity (0.831), and AUC (0.952) for detecting dementia [16]. Li et al. and Wang et al. suggested that the Chinese version of ACE-III was a reliable and valid tool for detecting MCI [17][19]. In comparison to studies on the Chinese version of ACE-R, ACE-III shows better performance. In addition, the Chinese version of ACE-III is slightly more accurate in participants with ≥12 years of education (AUC = 0.97) than those with <12 years of education (AUC = 0.93) while screening mild dementia [19]. In summary, the Chinese version of ACE-III is a reliable screening tool to detect dementia as well as MCI with different cutoffs [16][17][19]. In Pan et al.'s study, participants were classified as having a low education (1–9 years), a middle education (10–15 years), or a high education (≥16 years). The AUC for ACE-III reached a higher level in the high education subgroup (0.949) than those in the middle education subgroup (0.905) and the low education subgroup (0.894), indicating that the Chinese version of ACE-III performs better for highly educated people [18]. Apart from years of education, age at examination is another factor affecting ACE-III performance [19][20]. However, age at examination is not a strong influencer of ACE-III performance compared to education [18], similar to the findings in the study using ACE-R [21]. In addition to the simplified Chinese version, the traditional Chinese version of ACE-III is also a promising screening tool for detecting dementia in Taiwanese people (AUC = 0.895) [22]. The language spoken at home may influence ACE-III performance, as this phenomenon has been observed for different Indian language versions of ACE-III [23]. Unfortunately, apart from Mandarin and traditional Chinese versions of ACE-III, there are no other Chinese language versions available, such as Tibetan, Mongolian, Cantonese, or Uyghur. Although Mandarin is the official language in China, it may underestimate the cognitive performance for the people of non-Mandarin speaking homes [7]. In addition, premorbid IQ may also influence ACE-III performance [24], which has not been verified in the Chinese version yet.

Similar to ACE-R, aside from detecting early stages of AD, ACE-III has been used for tracking performances of cognitive domains in various neurological disorders [25][26][27][28][29][30][31][32][33][34]. Memory, rather than other cognitive domains, is more impaired in AD [25], while fluency and language are more impaired in behavioral variant frontotemporal dementia (bvFTD) and primary progressive aphasia (PPA), respectively [25]. Three domains (attention, memory, and fluency) decline in alcohol-related brain damage, and memory and visuospatial are impaired in rheumatoid arthritis [27][31]. The Hungarian ACE-III is able to delineate cognitive decline in PD with all five domains affected [30]. Memory and fluency domains are impaired in Polish patients with multiple sclerosis (MS), and attention, fluency, language, and visuospatial domains can be affected if there are focal cerebellar lesions [29][33]. Attention, memory, and fluency are impaired in schizophrenia detected by the Thai ACE-III, while memory and visuospatial function are impaired in brain glioma detected by the Malayalam ACE-III [28][34]. Aphasia and other dysfunction induced by stroke are also important factors affecting the accuracy of cognitive tests, which means participants need assistance to complete tests or are unable to complete tests. A modified cutoff can improve diagnostic accuracy, sensitivity, and specificity in stroke patients [32]. So far, the Chinese ACE-III has only been used in AD for cognitive domain analysis, not in other neurological disorders [7].

3. Comparison of Chinese Versions of ACE with Other Screening Techniques

3.1. ACE-R

Compared with the MMSE, the Chinese version of ACE-R has a higher sensitivity and AUC to screen for MCI [6], which is consistent with other studies using different linguistic ACE-R versions [35][36]. However, the AUC value of the Chinese ACE-R for detecting mild AD is not as good as the MMSE [6], which is consistent with a study using the German ACE-R [35]. This is in contrast to the majority of other studies showing that ACE-R is superior to the MMSE in detecting dementia [35][37][38]. This may be due to the small sample size or fewer years of education of the study cohorts [6]. The study of the Chinese–Cantonese version of ACE-R shows that it is a sensitive and specific cognitive screening test, and it is similar to the MMSE in identifying MCI (0.84 for sensitivity, 0.85 for specificity) and dementia (0.98 for sensitivity, 0.98 for specificity) [7]. Thus, in the Cantonese speaking Chinese population, the ACE-R Cantonese version is recommended, despite the fact

that the majority of Cantonese speaking Chinese can speak Mandarin nowadays. A meta-analysis was conducted by Huo et al. to evaluate the diagnostic accuracy of the Chinese versions of dementia screening tools in the Chinese population [39]. One hundred and thirty-four studies including 81 screening tools in Chinese were applied in this meta-analysis. According to a study, the MMSE was the most commonly used cognitive screening scale, while the Chinese version of the ACE-R showed the best performance with the highest sensitivity (0.96) and specificity (0.96) [39].

3.2. ACE-III

Unlike the MMSE, which is unidimensional and provides a global deterioration of intellect, ACE-III is multidimensional and can be scored independently according to its five components: attention/orientation, memory, language, verbal fluency (executive functions), and visuospatial skills to generate a cognitive profile.

The verbal fluency of ACE-III provides good evaluation value for assessing frontal lobe function. ACE-III shows fewer ceiling effects and better performance in detecting MCI than the MMSE [17][19], similar to the studies using other linguistic versions of ACE-III [40][41][42]. Consistent with studies using other linguistic versions of ACE-III or ACE-R [23][43], participants with longer years of education (≥12 years) have a better performance on Chinese version ACE-III compared to the MMSE (AUC 0.97 vs. 0.90), whereas Chinese version ACE-III does not perform better than MMSE in detecting dementia in lower-educated participants (<12 years) (AUC 0.93 vs. 0.98) [19]. ACE-III is designed with more comprehensive domains and more challenging tasks compared with MMSE, while MMSE has a very strong impact on orientation and languages. Thus, for memory, the most affected cognitive domain of amnestic MCI, it accounts for a reasonable proportion in ACE-III. The Chinese version of ACE-III is either equivalent to or significant superior to MoCA in detecting MCI in different studies [17][18][19]. Other studies using different linguistic versions of ACE-III demonstrated a higher diagnostic accuracy of ACE-III for distinguishing MCI than MoCA [40][44][45].

3.3. M-ACE

The Chinese version of M-ACE appears to have a better performance in detecting MCI and mild dementia than the MMSE with higher sensitivity, specificity, and accuracy [46][47]. The results are consistent with other studies using different linguistic versions of M-ACE [40][48][49][50][51]. The M-ACE is also proven to be more sensitive and have less ceiling effect than MMSE. Studies from Japan and Greece showed that their linguistic versions of M-ACE were superior to MoCA in detecting MCI and dementia [40][52], but studies using the English or Chinese versions of M-ACE did not reach the same conclusion [47][53]. In addition, the Chinese version of M-ACE also shows comparable accuracy to the Chinese version of ACE-III (AUC 0.892 vs. 0.901) [47].

3.3. M-ACE

Due to the wide range of cognitive domains assessed and patients' cooperation, it usually takes 12 to 20 min to complete the ACE-III test, so the usage of ACE-III may be limited by time constraints in some specific conditions. Thus, M-ACE, a shorter version of ACE-III, was created for this situation in 2015. M-ACE consists of 5 items with a maximum score of 30. The Chinese version of M-ACE is a reliable and quick examination test to detect MCI and mild dementia with its fair sensitivity (0.88, 0.96), specificity (0.72, 0.87), and AUC (0.86, 0.96) [46]. Pan et al. used Chinese version of M-ACE with a total score of 38 to reduce false positive odds and improve the classification accuracy. The Chinese version of M-ACE provides a sensitivity of 0.83, a specificity of 0.80, and an AUC of 0.89. In addition, age and years of education have a significant impact on scores of the Chinese version of M-ACE [46][47], and a better performance (AUC = 0.958) is observed in aged people with low education [47].

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