World Journal of Psychiatry and Mental Health Research

Research Article
Published: 18 Mar, 2019

A Meta-Analysis of Gender Difference in Cognitive Impairment as Indicated by the P300 ERP Component in Normal Chinese Subjects

Jianshe Pan, Gungdong Chen, Ziyao Cai, Xiaodong Lin, Zifan Chen, Chuanjun Zhuo, Deguo Jiang* and Peiwei Shan**

Wenzhou Seventh People's Hospital, Wenzhou, China

Abstract

Background: To systematically assess gender differences in the P300 cognitive event-related potential in normal Chinese subjects using meta-analysis.

Methods: We searched Chinese and English databases to collect studies comparing differences in P300 latency and amplitude between normal Chinese males and females. The quality of included studies was assessed according to age-matching. Standardized Mean Differences (SMDs) were calculated for differences in P300 latency and amplitude between males and females.

Results: Nine studies (417 males and 467 females) were included in the meta-analysis. Of these, five studies were assessed as high quality. The meta-analysis results revealed no statistically significant gender differences in P300 latency and amplitude. However, subgroup analysis of higher quality studies indicated that males exhibited significantly longer P300 latencies and lower amplitudes compared with females (SMD: 0.24, 95% CI: 0.08, 0.40, P=0.026; SMD: -0.32, 95% CI: -0.48, -0.15, P<0.001, respectively).

Conclusion: The results suggest the existence of significant gender differences in P300 latency and amplitude in normal Chinese subjects.

Keywords: Normal Chinese subjects; P300; Gender; Meta-analysis

OPEN ACCESS

Correspondence:
Chuanjun Zhuo, Suilin Jiang, Peiwei Shan, Wenzhou Seventh People's Hospital, Wenzhou, Zhejiang, 325000, China,
E-mail: chuanjunzhuotjmh@163.com and cjzhuocambridge@vip.163.com

Received Date: *15 Feb 2019*
Accepted Date: *14 Mar 2019*
Published Date: *18 Mar 2019*

Citation:
Pan J, Chen G, Cai Z, Lin X, Chen Z, Zhuo C, et al. A Meta-Analysis of Gender Difference in Cognitive Impairment as Indicated by the P300 ERP Component in Normal Chinese Subjects. World J Psychiatry Ment Health Res. 2019; 3(1): 1016.

Background

Previous studies have reported gender differences in the size of various brain regions, the density of neurons in the cerebral cortex and the symmetry of the cerebral hemispheres, as well as gender differences in human cognitive function [1]. Internationally, studies in normal populations have suggested that males exhibit superior performance in some visuospatial tasks, while females exhibit superior performance in certain speech tasks, episodic memory tasks, and face recognition tasks [2-4]. Researchers in China have reported similar results, but gender differences in cognitive functions in normal Chinese subjects remain controversial. Zhao et al. [6] and Wang et al. [7] reported significant gender differences in the Tower of Hanoi task, but no differences in the Trail Making Test performance or Wisconsin Card Sorting Test between males and females [5-7]. Yao et al. [5] reported no gender difference in the Tower of Hanoi task, but a gender difference was found in the Trail Making Test.

The P300 event-related potential is a neurophysiological indicator of cognitive function, and is considered to be an endogenous cognitive component associated with higher mental processes, including attention, memory, feeling, learning and reasoning. The P300 is relatively stable, and P300 latency and amplitude are considered to reflect various levels of cognitive function [8]. Traditional neuropsychological tests can describe and quantify certain aspects of cognitive function. However, because these measures are commonly based on verbal responses or the external behavior of individual subjects, the assessment of individual cognitive functions using traditional neuropsychological tests involves limitations [9]. The P300 is used as an indicator for comprehensive assessment of cognitive function. In the present study, we performed a meta-analysis to quantitatively combine the results of studies investigating gender differences in the P300 in normal Chinese subjects, to determine whether gender differences in cognitive functions exist in normal Chinese subjects (Figure 1).

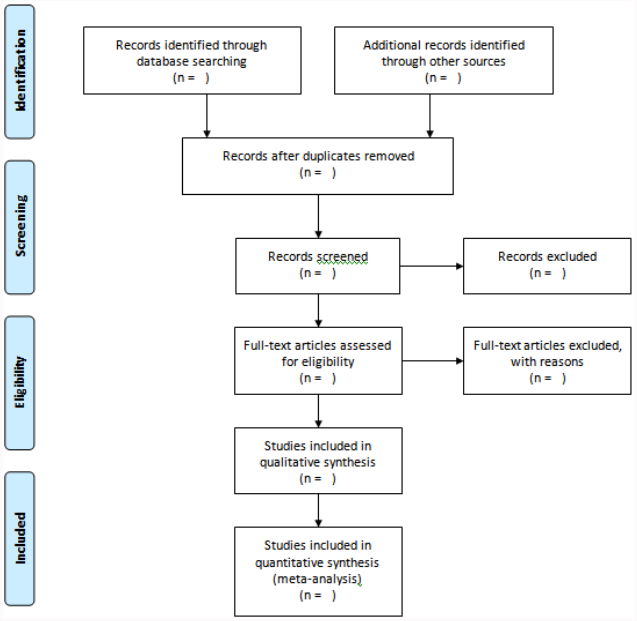

Figure 1: Flow of information through the different phases of a systematic review.

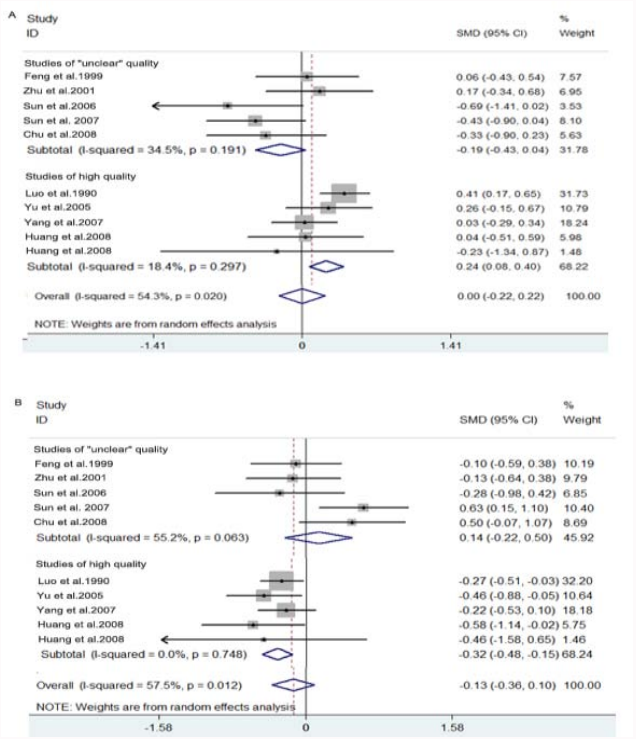

Figure 2: Forest plots of studies in the meta-analysis of gender differences in P300 latency and amplitude in normal Chinese subjects. A: P300 latency. B: P300 amplitude.

Subjects and Methods

Search method: We searched PubMed, EMBASE, Web of Knowledge, Cochrane Library, PsycINFO, CNKI, Wanfang, VIP and CMBdisc databases for publications up to June 23, 2017. We used the following search terms: "Chinese", "China", "general population", "residents", "healthy controls", "P300", "ERP", "gender/sex difference", the references listed in the resulting articles were also manually searched to increase the recall rate.

We conducted initial screening based on titles and abstracts. The potential studies initially identified were imported into reference management software (NoteExpress), and duplicates were identified and removed by reading the titles, abstracts and full text.

A total of 38 studies on gender differences in the P300 in normal Chinese subjects were initially identified. Of these, 19 reviews and studies that were not related to the P300 cognitive potential and 10 studies that did not examine gender differences in P300 were excluded. Finally, nine studies were included in the meta-analysis [10-18] (Figure 2).

Selection criteria: The inclusion criteria were as follows: (1) Studies focused on gender differences in the P300 in normal Chinese subjects, and subjects in the studies were healthy, with no physical or mental disorders. If the subjects were patients, such as individuals with schizophrenia, but healthy subjects were selected as a control group, and the P300 results of healthy controls of different genders were provided, these studies were also included; (2) Studies examined differences in P300 latency and amplitude between male and female subjects. The exclusion criteria were as follows: (1) Subjects were not Chinese; (2) Articles were reviews and case reports rather than experimental studies; (3) Articles were duplicate publications.

Quality assessment and data extraction: There is currently no recommended standard for assessing the quality of observational studies [19]. In the meta-analysis, all included studies compared differences in P300 cognitive potential between normal Chinese males and females, and study designs were case-control studies. It is essential to match males and females for baseline characteristics, such as age. In accord with a previously reported method [20] for assessing the quality of case-control studies and age, which is the most common factor influencing the P300 cognitive potential, we assessed the quality of the studies included in the meta-analysis in terms of whether male and female subjects were matched for age? If males and females were closely matched for age, the studies were assessed as high quality. If not, the studies were assessed as low quality.

The following information was extracted from the included study: the first author's name, publication year, the experimental apparatus used to evoke potentials, subject source, stimulation paradigm, target stimulus probability, number of male and female subjects, P300 latency (ms) and amplitude (μV).

Two authors independently selected and screened the articles, extracted the data, and evaluated the quality of each included study. Any discrepancies were resolved by discussion between the two authors.

Statistical analysis: All statistical analyses were performed using STATA 12.0 software with a meta-analysis module. Standardized mean differences (SMDs) and 95% Confidence Intervals (CIs) were calculated. Heterogeneity was assessed using the I^2 statistic: when P>0.1 and I2<50%, the fixed-effects model was used to pool data. Otherwise, the random-effects model was used. If there was statistical heterogeneity, meta-regression was used to explore the sources of heterogeneity. Forest plots were used to display each individual study effect and the overall combined effect. Publication bias was evaluated using funnel plots and Egger's test. Statistical significance was defined as a two-sided $P \leq 0.05$.

Table 1: Study characteristics.

Author (Publication year)	Experimental apparatus used to evoke potentials	Subject source	Stimulation paradigm	Target probabilities	Number of male	Number of female	Age matching
Luo et al. [10]	Dantic 2000C	Students, medical staff, cadres, workers, peasants	Auditory oddball paradigm	15%	138	138	Yes
Feng et al. [11]	NDI-200, China	Hospital workers and their dependents	Auditory oddball paradigm	20%	27	40	Not reported
Zhu et al. [12]	Neuropack MEB5504K, Japan	Normal subjects who underwent examination in internal medicine, and otological, audiological, neurological, mental examinations	Auditory oddball paradigm	20%	33	27	Not reported
Yu et al. [13]*	Not reported	Normal controls	Auditory oddball paradigm	15.40%	36	65	Yes
Sun et al. [14]*	Nicolet Bravo system, USA	Healthy subjects with no physical or mental disorders	Auditory oddball paradigm	25%	16	16	Yes
Yang et al. [15]*	Wond2000B EP/EMG System (China)	Normal subjects	Auditory oddball paradigm	20%	73	83	Yes
Sun et al. [16]*	Nicolet Bravo system, USA	Volunteers at Hospital and community	Auditory oddball paradigm	20%	33	38	Not reported
Chu et al. [17]*	Neuropack MEB-5508, Japan	Healthy subjects who had physical examinations	Auditory oddball paradigm	20%	31	20	Not reported
Huang et al. [18]#	Neuropack MEB7102K, Japan	University staff and students	Auditory oddball paradigm	25%	26	25	Yes

*Five studies compared gender differences in P300 between schizophrenia patients and normal controls. We only included the P300 results of normal control subjects of different genders.

#This study reported gender differences in the P300 in normal Chinese subjects in two different age groups. We included the P300 results of the two groups.

Results

Description of included studies: Nine articles involving 884 normal Chinese subjects (417 males and 467 females) were included in the meta-analysis. The auditory oddball paradigm was used in all studies, with target stimulus probabilities ranging from 15% to 25%. Five studies were rated as high quality, as males and females were age-matched. The other four studies did not report whether males and females were matched for age, and were rated as "unclear". The characteristics of the included studies are shown in Table 1.

Heterogeneity and publication bias: Heterogeneity testing revealed significant heterogeneity in the effect sizes of the reported gender differences in P300 latency (I2 = 54.3%, P = 0.020) and amplitude (I^2=57.5%, P=0.012) in normal Chinese subjects (Figures 3A and B). Thus, the random-effect model was used to pool the results.

Funnel plots were used to detect publication bias in the included studies. For the combined effect of P300 latency, the funnel plot showed an asymmetric distribution on both sides of the vertical line. Egger's test demonstrated evidence of significant publication bias (t=2.871, P=0.021). However, for the combined effect of P300 amplitude, the plot showed a symmetrical distribution on both sides of the vertical line (Figure 3A and B), indicating no evidence of publication bias using Egger's test (t=0.54, P=0.602).

Gender differences in P300 latency and amplitude in normal Chinese subjects: The meta-analysis results revealed no statistically significant differences in P300 latency or amplitude between genders (SMD=0.00, 95% CI: −0.22–0.22, P=0.978; SMD= −0.13, 95% CI: -0.36, -0.10, P=0.26, respectively) (Figure 3A and B).

However, subgroup analysis of higher quality studies revealed significant differences in P300 latency and amplitude between normal Chinese males and females (SMD=0.24, 95% CI: 0.08, 0.40, P=0.026; SMD= -0.32, 95% CI: -0.48, -0.15, P<0.001, respectively) (Figure 3A and B).

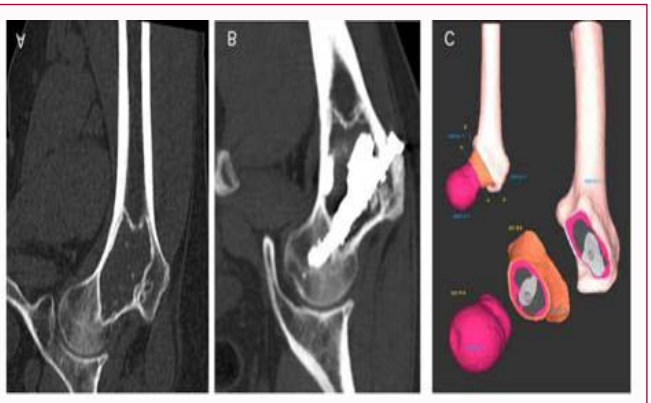

Figure 3: Funnel plot for the meta-analysis of gender differences in P300 latency and amplitude in normal Chinese subjects. A: P300 latency. B: P300 amplitude.

Source of effect size heterogeneity in the meta-analysis of gender differences in P300 latency and amplitude in normal Chinese subjects: Meta-regression analysis with restricted maximum likelihood estimation was conducted to investigate the sources of heterogeneity, using the effect sizes of gender differences in P300 latency as the dependent variable, the study quality (high *vs.* unclear) and the target probabilities (20% to 25% *vs.* 15% to 15.4%) as covariates. The results revealed that the study quality (P=0.282) and the target probabilities (P=0.076) were not sources of heterogeneity. Similarly, the study quality (P=0.079) and the target probabilities (P=0.964) were also not sources of heterogeneity in the results regarding gender differences in P300 amplitude.

Discussion

The P300 latency reflects the speed of stimulus classification, encoding, identification, and processing in the human brain, whereas P300 amplitude reflects the degree of effective resource mobilization during information processing and the subject's level of attention towards the target stimulus [21]. In the present study, a meta-analysis was conducted to examine gender differences in P300 in normal Chinese subjects. Although meta-analysis of all nine studies revealed no significant gender differences in the latency or amplitude of the P300, subgroup analysis of high quality studies revealed significant differences in P300 latency and amplitude between males and females. The high quality studies included in the meta-analysis had a lower risk of bias. The results revealed that P300 latency was significantly longer and P300 amplitudes were significantly lower in males than in females, indicating that normal Chinese males were more likely to have poor cognitive function than normal Chinese females.

A previous study focusing on gender differences in auditory and visual evoked potentials reported that, compared with males, females exhibited shorter P300 latencies and higher amplitudes [22]. The current results were consistent with these previous findings. Gender differences may be related to the neuroprotective effects of estrogen in females [23-25]. Estrogen can promote nerve growth, neuroplasticity, neurotransmitter synthesis, neuronal survival, and axonal regeneration. Gao et al. [26] also found that estrogen therapy can shorten P300 latency and increase P300 amplitude in female patients with schizophrenia.

The current study involves several limitations that should be considered. First, the meta-analysis only included 884 normal Chinese subjects. Thus, the sample might not be representative. Second, the source of the effect size heterogeneity in the meta-analysis of gender differences in P300 latency and amplitude was not identified. Finally, age-matching was used to assess the quality of the included studies. However, because of incomplete reporting in the original papers, other factors that may affect P300 gender differences were not included in quality assessment. Thus, other confounding factors may have influenced the results. Despite these limitations, the meta-analysis revealed significant gender differences in P300 latency and amplitude in normal Chinese subjects. Gender differences have many implications for neurodevelopment and regeneration, differentiation of brain function and the action of hormones. The gender differences in the P300 indicated by the current meta-analysis may be valuable for future research in biological psychiatry.

Acknowledgements

This work was supported by grants from the Tianjin Health Bureau Foundation (2014KR02 to C.Z.), the Key Projects of Natural Science Foundation of Tianjin, China (17JCZDJC35700 to C.Z.).

References

1. Ruigrok AN, Salimi-Khorshidi G, Lai MC, Baron-Cohen S, Lombardo MV, Tait RJ, et al. A meta-analysis of sex differences in human brain structure. Neurosci Biobehav Rev. 2014;39:34-50.
2. Levine SC, Foley A, Lourenco S, Ehrlich S, Ratliff K. Sex differences in spatial cognition: advancing the conversation. Wiley Interdiscip Rev Cogn Sci. 2016;7(2):127-55.
3. Handa RJ, McGivern RF. Steroid hormones, receptors, and perceptual and cognitive sex differences in the visual system. Curr Eye Res. 2015;40(2):110-27.
4. Weiss EM, Kemmler G, Deisenhammer EA, Fleischhacker WW, Delazer M. Sex differences in cognitive functions. Personality and Individual Differences. 2003;35(4): 863-75.
5. Yao J, Sun XL, Wang HM. Relationships Between Cognitive Functions and Gender, Age, Education among the Normal Adults. Zhongguo Linchuang Xinlixue Zazhi. 2004;12(4):414-6.
6. Zhao LS, Wang YC, Wei JX, Yang X, Ni PY, Gu XC, et al. Association of gender, age, education and polymorphism of DRD4 gene with cognitive functions in adults . Zhonghua Yixue Yichuanxue Zazhi. 2015;32 (3) :391-4.
7. Wang HM, Sun XL. Sex and age differences of cognitive functions in healthy adult. Sichuan Jingsheng Weisheng. 2002;15(4) :203-5.
8. Dejanović M, Ivetić V, Nestorović V, Milanović Z, Erić M. The value of P300 event related potentials in the assessment of cognitive function in subclinical hypothyroidism. Minerva Endocrinol. 2017;42(1):15-23.
9. Xie N, Deng JZ, Qi JX. Neuropsychological test and P300 in evaluation of patients with subcortical ischemic cerebravascular disease and cognitive impairment. Zhongguo Shiyong Shenjingjibing Zazhi. 2015, 18(1): 69-70.
10. Luo YJ, Wu ZY. Study on component of P300 auditory event related potential in 175 normal subjects. Zhongguo Shenjingjingshen Jibing Zazhi. 1990, 16(5): 272-5.
11. Feng X, Wang Y, Zhou W, Wang MQ. Detection of event-related potential P300 in 67 normal subjects. Sichuan Yixue. 1999;20(1):44-5.
12. Zhu L, Cheng XP, Zhu Yan. Correlation between P300 of auditory and age, sex in healthy people. Anhui Yike Daxue Xuebao. 2001;36(2):124-5.
13. Yu YW, Chen TJ, Chen MC, Tsai SJ, Lee TW. Effect of age and global function score on schizophrenic p300 characteristics. Neuropsychobiology. 2005;51(1):45-52.
14. Sun H. Study on auditory brainstem response, P50 and P300 in patients with first-episode schizophrenia. Taiyuan: Shanxi medical university. 2006.
15. Yang SC, Wang YX, Li XH, Lv XH. The study on the VEP, AEP and event related potential p300 in schizophrenia with different gender. Shenjing Jibing yu Jingsheng Weisheng. 2007;7(2):129-31.
16. Sun Y, Yang H. A follow-ups study of P300 in schizophrenic patients between differenct sex. Shanxi Yike Daxue Xuebao. 2007;38(8):711-4.
17. Chu J, Huang WS. P300 analysis of 51 cases with chronic schizophrenia in. Linchuang Shenjing Dianshengli Zazhi. 2008;17(5):317-8.
18. Huang JB. Establishing the Database of P300/CNV of Healthy Subjects by Independently Developed Stimulator Combined with Evoked Potential Measuring Systems. Shiyanshi Yaniu yu Tansuo. 2008;27(2): 11-5.
19. Zhong B, Xiang Y, Cao X, Li Y, Zhu J, Chiu HF. Prevalence of antisocial personality disorder among Chinese individuals receiving treatment for heroin dependence: a meta-analysis. Shanghai Arch Psychiatry. 2014;26(5):259-71.
20. Xu YM, Zhong BL, Cao XL, Li B, Deng F, Liu XB, et al. Effects of smoking on number of hospital admissions and hospital stay among Chinese patients with schizophrenia: A Meta-analysis. Zhongguo Yaowuyilaixing Zazhi. 2014;23(3):179-85.
21. Tsolaki AC, Kosmidou V, Kompatsiaris IY, Papadaniil C, Hadjileontiadis L, Adam A, et al. Brain source localization of MMN and P300 ERPs in mild cognitive impairment and Alzheimer's disease: a high-density EEG approach. Neurobiol Aging. 2017;55:190-201.
22. Zhang MD, Chen XS. Evoked brain potentials. Shanghai: Shanghai Science, Technology and Education Press. 1996.
23. Brinton RD. Estrogen-induced plasticity from cells to circuits: predictions for cognitive function. Trends Pharmacol Sci. 2009;30(4):212-22.

24. Sherwin BB. Estrogen and cognitive functioning in women. Endocr Rev. 200;24(2):133-51.

25. Liu X, Yu LH. Research progress on neuroprotective effect and its mechanisms of estrogen. Xiandai Yiyao Weisheng. 2016;32 (11) :1679-82.

26. Gao CY, Gan JL, Zhang WD, Duan HF. The effects of estrogen supplementation in female chronic schizophrenics on the event related potential P300. Zhonghua Shenjingke Zazhi. 2007;40(3):165-8.