Original Article

# Effects of Risperidone and Paliperidone on Brain-Derived Neurotrophic Factor and N400 in First-Episode Schizophrenia

**Rong-Qin Wu[1], Chong-Guang Lin[2], Wei Zhang[2], Xiao-Dong Lin[2], Xing-Shi Chen[3], Ce Chen[2], Li-Jun Zhang[2], Zi-Ye Huang[2], Guang-Dong Chen[2], Da-Li Xu[2], Zhi-Guang Lin[3], Ming-Dao Zhang[3]**

[1]Department of Psychiatry, Shanghai Jingan Mental Health Center, Shanghai 200436, China
[2]Department of Psychiatry, Wenzhou Seventh People's Hospital, Wenzhou, Zhejiang 325005, China
[3]Department of Electrophysiology, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China

Rong-Qin Wu and Chong-Guang Lin contributed equally to this study.

## Abstract

**Background:** Risperidone and paliperidone have been the mainstay treatment for schizophrenia and their potential role in neuroprotection could be associated with brain-derived neurotrophic factor (BDNF) and N400 (an event-related brain potential component). So far, different effects on both BDNF and N400 were reported in relation to various antipsychotic treatments. However, few studies have been conducted on the mechanism of risperidone and paliperidone on BDNF and N400. This study aimed to compare the effects of risperidone and paliperidone on BDNF and the N400 component of the event-related brain potential in patients with first-episode schizophrenia.

**Methods:** Ninety-eight patients with first-episode schizophrenia were randomly divided into the risperidone and paliperidone groups and treated with risperidone and paliperidone, respectively, for 12 weeks. Serum BDNF level, the latency, and amplitude of the N400 event-related potential before and after the treatment and Positive and Negative Syndrome Scale (PANSS) scores were compared between the two groups.

**Results:** A total of 94 patients were included in the final analysis (47 patients in each group). After the treatment, the serum BDNF levels in both groups increased (all $P < 0.01$), while no significant difference in serum BDNF level was found between the groups before and after the treatment (all $P > 0.05$). After the treatment, N400 amplitudes were increased (from $4.73 \pm 2.86$ μv and $4.51 \pm 4.63$ μv to $5.35 \pm 4.18$ μv and $5.52 \pm 3.08$ μv, respectively) under congruent condition in both risperidone and paliperidone groups (all $P < 0.01$). Under incongruent conditions, the N400 latencies were shortened in the paliperidone group (from $424.13 \pm 110.42$ ms to $4.7.41 \pm 154.59$ ms, $P < 0.05$), and the N400 amplitudes were increased in the risperidone group (from $5.80 \pm 3.50$ μv to $7.17 \pm 5.51$ μv, $P < 0.01$). After treatment, the total PANSS score in both groups decreased significantly (all $P < 0.01$), but the difference between the groups was not significant ($P > 0.05$). A negative correlation between the reduction rate of the PANSS score and the increase in serum BDNF level after the treatment was found in the paliperidone group but not in the risperidone group.

**Conclusions:** Both risperidone and paliperidone could increase the serum BDNF levels in patients with first-episode schizophrenia and improve their cognitive function (N400 latency and amplitude), but their antipsychotic mechanisms might differ.

**Key words:** Brain-Derived Neurotrophic Factor; Cognitive Function; Event-Related Potentials; N400; Schizophrenia

## Introduction

The hypothesis considered that brain-derived neurotrophic factor (BDNF) might be associated with abnormal neuronal development in the clinical symptom of schizophrenic patients. BDNF plays a critical role in neural growth, differentiation, and repair.[1] Previous studies indicated that the abnormal BDNF concentration in schizophrenic patients was associated with their mental symptoms and cognitive impairment.[2,3] However, antipsychotic drugs could increase

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.241802

**Address for correspondence:** Dr. Xing-Shi Chen, Department of Electrophysiology, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China
E-Mail: chenxingshi2008@163.com



**Received:** 03-04-2018 **Edited by:** Xin Chen
**How to cite this article:** Wu RQ, Lin CG, Zhang W, Lin XD, Chen XS, Chen C, Zhang LJ, Huang ZY, Chen GD, Xu DL, Lin ZG, Zhang MD. Effects of Risperidone and Paliperidone on Brain-Derived Neurotrophic Factor and N400 in First-Episode Schizophrenia. Chin Med J 2018;131:2297-301.

the BDNF level to a certain extent. Risperidone and its main metabolite, paliperidone, are atypical antipsychotic drugs which are widely used in clinical settings. Both drugs can improve clinical symptoms such as negative symptom, positive symptom, and cognitive function through combination with the 5-hydroxytryptamine2 and dopamine2 receptors in the central nervous system (CNS). Some studies showed that both drugs could influence the BDNF level and cognitive function.[4,5] However, studies that compare the efficacy of both drugs are limited. Hence, this study aimed to compare the effects of risperidone and paliperidone on BDNF and the N400 (an event-related brain potential component) component of the event-related brain potential in patients with first-episode schizophrenia.

## Methods

### Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committees of Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, and Shanghai Jingan Mental Health Center. Informed consent was obtained from all the participants and their guardians.

### Participants

All the patients with first-episode schizophrenia who were hospitalized in the Shanghai Mental Health Center and Shanghai Jingan Mental Health Center between March 2015 and July 2017 were recruited for this study. The patients were diagnosed as first-episode schizophrenia according to the Chinese Classification of Mental Disorders 3, Revised Third Edition (CCMD-3-R), without any history of antipsychotic drug treatment. Patients who met the following criteria were excluded from the study: with severe dementia and organic disease, intolerance to the serious side effects of the drug, and not receiving transcranial magnetic stimulation treatment. Originally, 98 patients were enrolled in the study and were randomly divided into the paliperidone and risperidone groups according to the random table number (49 patients in each group).

All the participants received two assessments for BDNF level, N400, and Positive and Negative Syndrome Scale (PANSS) score on the 1st day after enrollment and after the 12-week therapy.

### Measurement of serum brain-derived neurotrophic factor level

At 7:00 am, 10 ml of fasting venous blood was drawn from the elbow of all the participants. The blood samples were centrifuged at 3000 r/min for 20 min, and the serum was collected and stored at −20°C for measurement. The BDNF level was detected using enzyme-linked immunosorbent assay (ELISA; Shanghai Kexin Biotechnology Co., Ltd, China), with a minimum sensitivity value of 0.1 μg/L. Kits from the same batch were used for BDNF detection.

### Measurement of N400

WJ-1-type ERP instruments provided by Runjie Co., Ltd., China, were used to record N400. All the participants took a supine position and relaxed. A screen with a black background was placed 80 cm in front of them. They must stay awake and alert. Recording electrodes were attached to the front (FZ), central (CZ), and parietal (PZ) areas according to the international 10/20 system. The electrodes on the two lobes were used as reference electrodes, and that on the front parietal areas (Fpz) location was used as the grounding electrode. Electroencephalographic (EEG) data were collected offline. During the EEG data collection, the filter band was 0.05–70.00 Hz, the alternating current sampling frequency was 500.00 Hz, and the impedance between the electrode and the scalp was <5-K Omega.

The stimulus material consisted of 76 Chinese idioms (four characters),[4] chosen from the *Dictionary of Idioms for Pupils in New Curriculum Standard* (published by the Commercial Press International Limited Company, China). The fourth character of each idiom in the stimulus sequence was served as a target word. Hence, the idioms could be divided into two groups. Thirty-eight idioms with a congruent fourth word, for example, "ai bu shi shou," were the correct group. However, in the other group, the fourth character was completely different with the correct idiom, including no similarity in pronunciation, shape, and meaning with the correct word and therefore incongruent, for example, "chu mu jing tai(xin)." The idioms were presented in a random sequence with a rule, and any group of idioms could not be presented more than 3 consecutive times. The participants were asked to press the "1" key if the idiom was incongruent and "0" if it was congruent.

The stimuli were provided by E-Prime. In the experiment, first, 500 ms "+" was displayed on the screen; then, a 500-ms presentation of the target idiom appeared, and then, 3 s "+" was presented, which was the reaction time of the patient. The experiment proceeded to the next procedure automatically after the participants press the key. Before the formal experiment, all the participants practiced 10 times to familiarize themselves with the experimental procedure and respond to the press reaction easily.

### Clinical assessment

PANSS was adopted to assess the clinical symptoms of all patients. The PANSS is composed of four subscales, including a positive scale (P score, 7 items), negative scale (N score, 7 items), general psychopathology scale (G score, 16 items), and additional symptoms (3 items). Each item was rated from 1 to 7 in the PANSS, ranging from no symptoms to extremely serious symptoms. The higher the score, the more serious were the patient's mental symptoms. The reduction in PANSS score was used to evaluate the treatment efficiency. The calculation formula of the reduction rate is as follows: the reduction rate of the PANSS score = (Tb − Ta)/Ta × 100%, where Tb is the total PANSS score after the treatment and Ta is the total PANSS score before the treatment.

The relative scales were evaluated by two attending psychiatrists who were given consistency training before the research to ensure that the kappa value was >0.75. The PANSS score was used in the assessment before and at 12 weeks after the treatment.

### Statistical analysis

All data were analyzed using the SPSS version 13.0 software (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± standard deviation (SD). Data with normal distribution were compared using an independent sample *t*-test, and the nonnormal metrological data were compared using Mann-Whitney *U*-test. The Pearson correlation analysis was used in the comparison of the BDNF levels and PANSS scores and latency and amplitude of N400 at a test level of $a = 0.05$. A $P < 0.05$ was considered as statistically significant.

## Results

Four patients (two in each group) quit in the mid-term experiment because they could not tolerate the side effects of the drugs. Finally, 94 patients completed the experiment (47 patients in each group). In the risperidone group, there were 35 males and 12 females; the ages of the patients ranged from 19 years to 45 years, with a mean age of 29.7 ± 4.6 years; the mean period of education was 11.9 ± 2.8 years; and the median duration of illness was 1.4 years (range: 0.5–2.2 years). Meanwhile, in the paliperidone group, there were 34 males and 13 females; the patients' ages ranged from 18 years to 44 years, with a mean age of 28.2 ± 5.1 years; the mean period of education was 12.8 ± 3.2 years; and the median duration of illness was 1.5 years (range: 0.6–2.7 years). No significant differences in gender, age, educational background, and illness duration were found between the two groups (all $P > 0.05$).

### Comparison of serum brain-derived neurotrophic factor levels and Positive and Negative Syndrome Scale scores

After 12 weeks of treatment, the serum BDNF levels were significantly increased in both groups, compared with before treatment (all $P < 0.01$); however, no significant difference was found between the two groups either before or after the treatment (all $P > 0.05$). Meanwhile, the total PANSS scores were significantly decreased after treatment in both groups (all $P < 0.01$), but the differences between the groups were not significant either before or after the treatment [all $P > 0.05$; Table 1].

### Comparison of N400 indices between before and after treatment in the two groups

Under the congruent conditions, the N400 latencies were significantly reduced (from 420.13 ± 115.06 ms and 412.13 ± 119.48 ms to 405.15 ± 128.09 ms and 388.2 ± 132.51 ms, respectively) and the N400 amplitudes were significantly increased (from 4.73 ± 2.86 μv and 4.51 ± 4.63 μv to 5.35 ± 4.18 μv and 5.52 ± 3.08 μv, respectively) after 12 weeks of treatment in risperidone and paliperidone groups, compared with before treatment (all $P < 0.01$). However, under the incongruent conditions, the N400 latency was significantly shortened only in the paliperidone group (from 424.13 ± 110.42 ms to 4.7.41 ± 154.59 ms) and the N400 amplitude was significantly increased only in the risperidone group (from 5.80 ± 3.50 μv to 7.17 ± 5.51 μv; $P < 0.01$; Table 2).

### Correlation analysis between N400 and serum brain-derived neurotrophic factor concentration, Positive and Negative Syndrome Scale score

Both before or 12 weeks after treatment, no significant correlation were found between N400 and the serum BDNF concentrations, PANSS scores. Further Pearson correlation analysis found that a negative correlation was

**Table 1: Comparison of serum BDNF levels and PANSS scores between before and after treatments in risperidone and paliperidone groups**

| Items | Risperidone group ($n = 47$) | | | | Paliperidone group ($n = 47$) | | | |
|---|---|---|---|---|---|---|---|---|
| | Before treatment | After treatment | *t* | *P* | Before treatment | After treatment | *t* | *P* |
| BDNF (ng/ml) | 8.74 ± 4.62 | 11.70 ± 5.51 | 21.937 | 0.000 | 8.92 ± 4.17 | 12.54 ± 6.16 | 11.830 | 0.000 |
| PANSS | 81.02 ± 19.43 | 51.19 ± 26.49 | 27.353 | 0.000 | 79.45 ± 22.08 | 48.30 ± 29.14 | 28.555 | 0.000 |

BDNF: Brain-derived neurotrophic factor; PANSS: Positive and Negative Syndrome Scale.

**Table 2: Comparison of N400 latency and amplitude between before and after treatments in risperidone and paliperidone group**

| Items | Risperidone group ($n = 47$) | | | | Paliperidone group ($n = 47$) | | | |
|---|---|---|---|---|---|---|---|---|
| | Before treatment | After treatment | *t* | *P* | Before treatment | After treatment | *t* | *P* |
| Congruent | | | | | | | | |
| Latency (ms) | 420.13 ± 115.06 | 405.15 ± 128.09 | 2.78 | 0.006 | 412.13 ± 119.48 | 388.2 ± 132.51 | 2.81 | 0.005 |
| Amplitude (μv) | 4.73 ± 2.86 | 5.35 ± 4.18 | 2.67 | 0.002 | 4.51 ± 4.63 | 5.52 ± 3.08 | 2.73 | 0.002 |
| Incongruent | | | | | | | | |
| Latency (ms) | 417.70 ± 113.29 | 415.30 ± 147.08 | 1.03 | 0.116 | 424.13 ± 110.42 | 407.41 ± 154.59 | 2.69 | 0.002 |
| Amplitude (μv) | 5.80 ± 3.50 | 7.17 ± 5.51 | 2.54 | 0.009 | 5.90 ± 3.97 | 6.33 ± 5.51 | 0.94 | 0.120 |

observed between the reduction rate of PANSS score and the increase in the serum BDNF level after the treatment in the paliperidone group, but no correlation was observed in the risperidone group.

## Discussion

Schizophrenia is a serious and complicated mental disease accompanied with cognitive deterioration, delusion, hallucination, provocation, hostility, and noncooperation. Some researchers proposed the BDNF hypothesis on schizophrenia, which assumed that brain function in schizophrenia is associated with BDNF level and/or the abnormal expression of its receptor. In this hypothesis, the low BDNF expression level in the CNS plays a vital role in the cognitive deterioration, pathogenesis, and treatment efficacy in schizophrenia treated with antipsychotic drugs.[6] The neuroimaging and neurophysiological studies demonstrated that the occurrence of schizophrenia was related to an abnormal neurodevelopmental origin.[3]

In recent years, several overseas and domestic studies indicated that BDNF level correlated with the clinical symptoms of schizophrenia.[3] A study confirmed that the serum BDNF concentration in patients with schizophrenia was lower than that in healthy controls, which was related to the severity of the mental disorder. Chen *et al*.[7] evaluated 156 patients with schizophrenia who met the DSM-IV diagnosis criteria and 168 age- and sex-matched healthy volunteers and found that the serum BDNF concentration in the patients with schizophrenia was lower. A negative correlation was found between the BDNF concentration and the severity of negative symptoms and illness duration. In other words, the more serious of negative symptoms and the longer of illness duration, the lower of patient's BDNF concentration. To accumulate data, our present research used ELISA to evaluate BDNF concentration and the PANSS to assess the clinical symptoms of schizophrenia. The results showed that the serum BDNF level of the patients with schizophrenia was lower than that of the healthy controls reported previously.[2,3,7-9]

In this study, we found that serum BDNF levels were significantly increased after 12 weeks of treatment with the antipsychotic drugs (risperidone or paliperidone). BDNF is widely distributed in the CNS, including the cerebral cortex, hippocampus, basal forebrain, striatum, hypothalamus, and cerebellum, and is especially abundant in the cerebral cortex and hippocampus.[10] In the cerebrum, BDNF can combine with a specific transmembrane receptor, known as arginine protein kinase B (Trkb), which can participate in neuronal development, differentiation, and repair through its effects on neuronal cells, glial cells, and immune cells. The abnormal nervous system in schizophrenia might be related to the low BDNF expression level. This study confirmed that the clinical symptoms improved (with decreased PANSS scores) and the BDNF levels were increased in both groups after 12 weeks of drug treatment. In the further correlation analysis, a negative correlation between the reduction rate of the PANSS score and the increase in serum BDNF level after the treatment was found in the paliperidone group but not found in the risperidone group. The phenomenon may explain that paliperidone is the downstream metabolite. Further study is needed to confirm whether mechanisms other than that of the BDNF exist.

Recently, an increasing number of studies have investigated the cognitive impairment in schizophrenia. One study considered that the cognitive symptom was not only the core symptom but also one of the cognitive disorder endophenotypes of schizophrenia, which was relatively stable and closely related to prognosis.[11] Patients with schizophrenia often show serious loosening of association ability and splitting, indicating that their linguistic cognitive function is obviously abnormal. N400 is an event-related brain potential component which is widely involved in the cognitive process and relative psychological activities.[12] Since the 1990s, it was first reported that N400 amplitude decreased in schizophrenia, abundant evidence have shown that N400 amplitude was decreased, and N400 latency was delayed in patients with schizophrenia.[13,14]

Phonetic word, especially English, is used as a stimulus paradigm to study N400 in schizophrenia in abroad. However, it is not fit for study because of the cognitive impairment in schizophrenia who are Chinese and they are limited understanding in English.[15] To discuss N400 elicited by Chinese idioms ending with congruent or incongruent Chinese characters, this study used an event-related brain potential instrument and related technology produced by Guangzhou Runjie Medical Instruments. Chinese idioms are characterized by a set of four words, semantic integrity, and word fixity which strictly confined the idiom-ending words and highly compacted the context. The feature of the clear and compact semantics of the explicit idiom context strictly defined the ending word, which encourages the cognitive coding of the word to be processed in advance and allows the expectation value to be large and the cognitive priming efficiency to be more prominent. In a previous study,[16] researchers found that N400 was suitable for application in patients with schizophrenia. In this study, we found improvements in the N400 latency and amplitude under congruent conditions after paliperidone treatment. The N400 latency was reduced, and the N400 amplitude was increased. In the risperidone group, the N400 latency and amplitude were improved under congruent conditions. Nonetheless, only the N400 amplitude was improved under incongruent conditions. Two reasons for this are as follows: different mechanisms caused by different drugs and some problems in the research design, such as limited samples. In a future study, we will investigate the different mechanisms of the improvement of the cognitive function in schizophrenia between two antipsychotic drugs.

This study did not find any correlation between BDNF levels and N400, which will be further confirmed in future research. The reasons might be as follows: cognitive impairment symptoms and cognitive improvement in schizophrenia are

not mediated by BDNF and the effects of drugs on BDNF and cognitive symptoms might have different mechanisms. Further study is required to understand the mechanisms of the drug.

In addition, whether serum BDNF level can reflect CNS BDNF level is a hot topic. Some studies indicated that serum BDNF level could cross the blood-brain barrier in rats, showing a positive correlation with CNS BDNF level. Karege *et al*.[17] demonstrated that BDNF could cross the blood-brain barrier and was parallel to CNS BDNF level. Ahmed *et al*.[18] suggested a positive association of peripheral BDNF level with neurocognition in patients with schizophrenia. Further studies are need to investigate the exact relationship and clinical significance among serum BDNF level, cognitive function, and N400.

There were several limitations of this study. The sample size of this study was small, which could not allow a comprehensive elaboration of the mechanism of risperidone and paliperidone treatments on BDNF and N400 in schizophrenia. In a future study, a large sample size study will be conducted to investigate the mechanisms of these treatments.

In summary, this study found that both risperidone and paliperidone could increase the serum BDNF levels in patients with first-episode schizophrenia and improve their cognitive function (N400 latency and amplitude). The difference in mechanism between the two antipsychotics lies in the inconformity correlation between BDNF level and the improvement of clinical symptoms (PANSS reduction). Clinicians could choose different drugs depending on the treatment target.


## Financial support and sponsorship

This study was supported by grants from the National Natural Science Foundation of China (No. 81471357) and Shanghai Natural Science Foundation (No. 13ZR1439300).


## Conflicts of interest

There are no conflicts of interest.

## References


1. Pillai A, Schooler NR, Peter D, Looney SW, Goff DC, Kopelowicz A, *et al.* Predicting relapse in schizophrenia: Is BDNF a plausible biological marker? Schizophr Res 2018;193:263-8. doi: 10.1016/j.schres.2017.06.059.
2. Klein AB, Williamson R, Santini MA, Clemmensen C, Ettrup A, Rios M, *et al.* Blood BDNF concentrations reflect brain-tissue BDNF levels across species. Int J Neuropsychopharmacol 2011;14:347-53. doi: 10.1017/S1461145710000738.
3. Shen YD. Psychiatry. 4th ed. Beijing: Peple's Medical Publishing House; 2002. p. 158-85.
4. Bo G, Yanrong W. Effects of antipsychotics on the level of brain-derived neurotrophic factor and cognitive function in patients with schizophrenia. J Clin Med Pract 2013;17:100-1. doi: 10.7619/}emp.201317036.
5. Dachun C, Yanli L, Meihong X. Effect of risperidone treatment on serum levels of BDNF and the correlation of between serum BDNF levels. Chin J Nerv Ment Dis 2010;36:529-32. doi: 10.1080/08039488.
6. Nuernberg GL, Aguiar B, Bristot G, Fleck MP, Rocha NS. Brain-derived neurotrophic factor increase during treatment in severe mental illness inpatients. Transl Psychiatry 2016;6:e985. doi: 10.1038/tp.2016.227.
7. Chen D, Xiu H, Li Y, Wang N, Wang K, Tan Y, *et al*. Relationship between brain derived neurotrophic factors and clinical characteristics in schizophrenia. J Clin Psychiatry 2010;20:79-81. doi: 1005-3220(2010)02-0079-03.
8. Pino O, Guilera G, Gómez-Benito J, Najas-García A, Rufián S, Rojo E, *et al*. Neurodevelopment or neurodegeneration: Review of theories of schizophrenia. Actas Esp Psiquiatr 2014;42:185-95.
9. Heitz U, Papmeyer M, Studerus E, Egloff L, Ittig S, Andreou C, *et al.* Plasma and serum brain-derived neurotrophic factor levels and their association with neurocognition in at-risk mental state, first episode psychosis and chronic schizophrenia patients. World J Biol Psychiatry 2018;21:1814-412. doi: 10.1080/15622975.2018.1462532.
10. Shoval G, Weizman A. The possible role of neurotrophins in the pathogenesis and therapy of schizophrenia. Eur Neuropsychopharmacol 2005;15:319-29. doi: 10.1016/j.euroneuro.2005.12.005.
11. Liu MS, Chen XS. Modern Practical EEG Studies. 1st ed. Beijing: China Scientific and Technical Publishers; 2013. p. 37-41.
12. Boyd JE, Patriciu I, McKinnon MC, Kiang M. Test-retest reliability of N400 event-related brain potential measures in a word-pair semantic priming paradigm in patients with schizophrenia. Schizophr Res 2014;158:195-203. doi: 10.1016/j.schres.2014.06.018.
13. Metzler S, Theodoridou A, Aleksandrowicz A, Müller M, Obermann C, Kawohl W, *et al.* Evaluation of trait adjectives and ego pathology in schizophrenia: An N400 study. Psychiatry Res 2014;215:533-9. doi: 10.1016/j.psychres.2013.12.025.
14. Besche-Richard C, Iakimova G, Hardy-Baylé MC, Passerieux C. Behavioral and brain measures (N400) of semantic priming in patients with schizophrenia: Test-retest effect in a longitudinal study. Psychiatry Clin Neurosci 2014;68:365-73. doi: 10.1111/pcn.12137.
15. Laurent JP, Kostova M, Passerieux C. N400 and P300 modulation as functions of processing level in schizophrenia patientas exhibiting formal thought disorder. Int J Psychophysiol 2010;5:177-82. doi: 10.1016/j.ijpsycho.2009.10.001.
16. Jiang W, Zhang W, Zhao X, Sun D, Chen X, Song L, *et al.* Three-year follow up of event-related potentials PPI, P50 and color map of N400 during the rehabilitation of first episode schizophrenia patients (in Chinese). Natl Med J China 2015;95:3813-7. doi: 10.3760/cma.j.issn.0376-2491.
17. Karege F, Schwald M, Cisse M. Postnatal developmental profile of brain-derived neurotrophic factor in rat brain and platelets. Neurosci Lett 2002;328:261-4.
18. Ahmed AO, Mantini AM, Fridberg DJ, Buckley PF. Brain-derived neurotrophic factor (BDNF) and neurocognitive deficits in people with schizophrenia: A meta-analysis. Psychiatry Res 2015;226:1-13. doi: 10.1016/j.psychres.

# 新型抗精神病药对首发精神分裂症患者脑源性神经营养因子及N400的影响研究


## 摘要

**背景：**抗精神病药可能通过影响脑源性神经营养因子（BDNF）浓度，对精神分裂症产生治疗作用。然而，对利培酮及其代谢产物帕利哌酮这方面的研究甚少。本文研究比较这两种新型抗精神病药对首发精神分裂症患者血清BDNF以及事件相关脑电位成分（N400）的影响，进一步探讨药物治疗精神分裂症的机制。

**方法：**98例首发精神分裂症患者随机分为帕利哌酮组与利培酮组（49例/组），采用帕利哌酮及利培酮治疗12周，比较两组治疗前后血清BDNF浓度及N400潜伏期和波幅，同时通过阳性与阴性症状（PANSS）量表对其治疗疗效进行评估。

**结果：**最终有94例患者纳入统计（每组47例）。抗精神病药治疗后，两组患者血清BDNF浓度均有明显上升（$P$<0.01），但组间比较未见统计学差异（$P$>0.05）。治疗后，匹配条件下利培酮和帕利哌酮组患者的N400波幅明显上升（治疗前4.73±2.86 μv, 4.51±4.63 μv, 治疗后 5.35±4.18 μv, 5.52±3.08 μv），具有统计学意义（$P$<0.01）；在非匹配条件下，帕利哌酮组N400潜伏期缩短（424.13±110.42 ms vs. 407.41±154.59 ms, $P$<0.05），而利培酮组N400波幅明显增高（5.80±3.50 μv, vs. 7.17±5.51 μv，$P$<0.01）。治疗后，两组患者PANSS总分均明显下降（$P$<0.01），而组间比较无显著性差异（$P$>0.05）。进一步分析发现，帕利哌酮组PANSS减分率与血清BDNF升高值存在正相关，而利培酮组未发现二者间存在相关。

**结论：**新型抗精神病药物可在不同程度改善首发精神分裂症患者血清BDNF浓度、改善患者认知功能，提高临床治疗疗效，具体机制值得进一步研究。