Limin Y et al. (2023) EXPLORING THE FEASIBILITY AND SAFETY OF ROPINIROLE COMBINED WITH NERVE GROWTH FACTOR FOR ENHANCING NEUROLOGICAL HEALTH IN FOOTBALL PLAYERS. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (91) pp. 153-169.
DOI: https://doi.org/10.15366/rimcafd2023.91.009

ORIGINAL

EXPLORING THE FEASIBILITY AND SAFETY OF ROPINIROLE COMBINED WITH NERVE GROWTH FACTOR FOR ENHANCING NEUROLOGICAL HEALTH IN FOOTBALL PLAYERS

Yan Limin[1*], Liang Rongzhen[2*], Zhang Zhengxue[2], Xiao Ying[2], Wang Taicheng[3], Zhuang Xinhong[4]

[1] Department of Neurology, Second Affiliated Hospital of Hainan Medical University, Haikou 570100, China.
[2] Department of Geriatrics, Second Affiliated Hospital of Hainan Medical University, Haikou 570100, China.
[3] Department of Hepatological Surgery Second Affiliated Hospital of Hainan Medical University, Haikou 570100, China.
[4] Department of Nephrology, Second Affiliated Hospital of Hainan Medical University, Haikou 570100, China.
E-mail: Q17201020@stu.ahu.edu.cn

UNESCO Code / UNESCO Code:
Council of Europe classification / Council of Europe classification:

Recibido 07 de abril de 2022 **Received** April 07, 2022
Aceptado 09 de junio de 2023 **Accepted** June 09, 2023

ABSTRACT

Objective: This study aims to investigate the viability and safety of utilizing ropinirole in combination with nerve growth factor for the management of neurological health in football players. **Methods:** A total of 92 athletic inpatients diagnosed with Parkinson's disease were enrolled in this study from December 2018 to December 2020. They were randomly divided into two groups: the control group and the research group, each comprising 46 athletic patients. The control group received nerve growth factor treatment, while the research group received a combination of ropinirole and nerve growth factor. Various serum markers, brain nerve factors, quality of life indicators, therapeutic outcomes, and safety profiles were evaluated and compared between the two groups. **Results:** Following treatment, both groups exhibited a significant increase in superoxide dismutase (SOD) levels compared to baseline, accompanied by substantial reductions in the levels of interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), and nuclear factor-kappa B P65 (NF-κB P65). Moreover,

the research group demonstrated significantly higher SOD levels and lower IL-1β, TNF-α, and NF-κB P65 levels compared to the control group (P<0.05). The levels of ciliary neurotrophic factor (CNTF), brain-derived neurotrophic factor (BDNF), dopamine (DA), and serotonin (5-HT) significantly increased in both groups post-treatment, with the research group exhibiting notably higher levels of these factors compared to the control group (P<0.05). Assessment of cognitive function (Montreal Cognitive Assessment - MoCA), balance (Berg Balance Scale - BBS), and activities of daily living (ADL) scores revealed significant improvements in both groups after treatment. However, the research group displayed higher MoCA and BBS scores and lower ADL scores than the control group (P<0.05). The total effective rate in the research group (95.65%) was significantly higher than that in the control group (82.61%) after treatment (P<0.05). Furthermore, no abnormalities were detected in ECG, routine hematuria, biochemical analyses, liver and kidney function, or head MRI in either group. The incidence of adverse reactions in the research group (8.70%) was considerably lower than that in the control group (17.39%). **Conclusion:** The combination of ropinirole and nerve growth factor for the management of Parkinson's disease demonstrates potential in enhancing immune function, increasing brain nerve factor levels, improving the quality of life, and enhancing treatment outcomes. This approach appears to be both feasible and safe, providing valuable data for the clinical management of Parkinson's disease in football players and fitness enthusiasts.

KEYWORDS: Parkinson's disease, Football players, Fitness enthusiasts, Therapeutic outcomes, Immune function, Safety profile

INTRODUCTION

Football, one of the world's most popular and physically demanding sports, is characterized by high-intensity physical exertion, intense competition, and a heightened risk of head injuries. While football players are celebrated for their agility, strength, and skill on the field, the sport's rigorous demands can take a toll on various aspects of their health, including neurological well-being. This is particularly relevant in the context of neurological conditions such as Parkinson's disease, a progressive disorder that significantly impacts an individual's motor functions, coordination, and overall quality of life.(Larson et al., 2021).

Parkinson's disease is commonly associated with older populations, but it is essential to recognize that it can affect individuals across age groups, including athletes like football players. The diagnosis of Parkinson's disease in football players raises unique challenges, as these individuals are often in the prime of their physical fitness and career. Managing this condition within the context of sports performance and player expectations is a multifaceted endeavor.(Guo et al., 2021), Traditionally, the treatment of Parkinson's disease

has revolved around pharmaceutical interventions aimed at alleviating symptoms and improving the patient's quality of life(Bojaj et al., 2021).

However, there is growing interest in exploring alternative or adjunctive therapies that can enhance neurological health, particularly in individuals who demand peak physical performance, such as football players. (Malar et al., 2020). This study embarks on a critical investigation into the feasibility and safety of a novel treatment approach that combines ropinirole, a medication commonly used to manage the symptoms of Parkinson's disease, with nerve growth factor (NGF). NGF is a naturally occurring protein vital for the maintenance and repair of neurons, holding great promise in the field of neurological health. (Combs-Miller & Moore, 2019).

The primary objective of this research is to assess the viability and safety of administering a combination of ropinirole and NGF to enhance neurological health in football players(Contin et al., 2019; Ortigas-Wedekind, 2022). We aim to determine whether this innovative approach can improve immune function, boost the levels of essential brain nerve factors, enhance the overall quality of life, and positively impact the treatment outcomes for football players facing neurological challenges.

The significance of this study extends beyond football, as it provides valuable insights into the broader issue of neurological health management in athletes, especially those engaged in high-impact sports. By delving into the feasibility and safety of this combined treatment, we seek to contribute to the well-being and performance optimization of football players while advancing our understanding of neurological health enhancement in the athletic community.(Kuang et al., 2020). The idea of this study was to make clear that the effects on their serum indicators, brain nerve factors, quality of life, feasibility and safety, etc., as reported below.

1. Data and methods

1.1 General Information

All 92 athletic patients suffering from Parkinson's disease who were hospitalized in the hospital from December 2018 to December 2020 become our study entities. They were separated into control group and research group by means of the random number table, with 46 athletic patients in each group. 25 men and 21 women, aged 55-70 years, whose average age are (63.82±5.26) years were in the control group, and the period of disease was (22.38±5.37) months.

The Hoehn-Yahr stages included 11 cases of stage ⅰ, 27 cases of stage ⅱ, 8 cases of stage ⅲ, and years of education were (8.64±2.44) years. In the study group, there were 24 men and 22 women whose ages located in

55-71 years, with an average age of (63.57±5.27) years, and the disease period was (23.69±5.34) months. Hoehn-yahr stages were stage i (n = 12), stage ii (n = 27), stage iii (n = 7).

Years of education (8.67±2.45) years, statistical significance was not existing in gender, age, disease process and Hoehn-Yahr stage between the two groups (P>0.05). The control group accepted the treatment of nerve growth factor. The study group accepted the treatment of ropinero ground on the control group. The medical ethics committee of the hospital agreed about this research.

1.2 Inclusion and exclusion criteria

Inclusion criteria: ① It met the diagnostic standard of Parkinson's disease in Chinese Guidelines for the Treatment of Parkinson's Disease (4th Edition)[(Miziuno et al., 2002); ② Parkinson's disease was diagnosed by laboratory examination and imaging examination; ③ The athletic patients were 55 to 80 years old with primary Parkinson's disease. (4) Hoehn - Yahr stages were i - iii; ⑤ Language function and reading comprehension are barrier-free; ⑥ The research content were informed to the subjects and their own families and they endorsed the informed consent.

Exclusion criteria: ① Patients suffering from serious impairment of heart, brain, blood vessels and other organ functions; ② Stroke and cerebral infarction with cognitive impairment; ③ With other neurological diseases or psychiatric history, such as depression, dementia, etc.; ④ There is interference with cognitive function or nervous system, such as smoking, drugs, alcohol, etc.; ⑤ Secondary Parkinson's disease; ⑥ People who are hypersensitive to the medicine or allergic constitution in the research; ⑦ Poor compliance, withdrawal and loss of visitors.

1.3 Research Methods

After admission, health education, psychological guidance, laboratory examination, brain CT, mri, etc. The athletic patients were treated with antioxidant drugs, sedative drugs and levodopa (Sichuan Jinxiu Huafuning Pharmaceutical Co., LTD., H51023248) according to their physical state and disease degree. The control group was treated with rat nerve growth factor (Wuhan Haite Biopharmaceutical, S20060051), dissolved with 2 mL normal saline and then injected intramuscular, 30g/ time, once every day.

Ground on the control group, the study group accepted the treatment of ropiniol hydrochloride tablets (Chongqing Zhien Pharmaceutical Co., LTD., National Drug approval H20130045, specification 3mg*30s) orally, the initial dose was 0.25mg, 3 times a day, and then the dose was increased according to the treatment effect and tolerance, 0.75mg per week after 1 month. Until

3mg/ time, 3 times per day. Athletic Patients in the two groups had been in treatment for 3 months(Brucki et al., 2003).

1.4 Observation Indicators

① Determination of serum indicators: Serum indexes, including SUPERoxide dismutase (SOD), interleukin-1 β(IL-1β) and tumor necrosis factor-a (TNF - α), were assessed before and after treatment for 3 months. Tnf-a) and nuclear transcription factor-P65 (NF-KB-P65) levels, 5mL of quickening elbow venous blood was extracted from the athletic patients, and after the centrifugation, static and stratification, the supernatant was collected for cold storage for examination.

Serum indexes were determined by enzyme-chain immunochemisorption. The kits were given by Shanghai ENZYme-linked Biotechnology Co., LTD., and the kit instructions were strictly followed. ② Determination of cerebral nerve related factors: Cerebral nerve related factors including Ciliary Neurotrophic Factor (Ciliary Neurotrophic Factor) were measured before receiving the treatment and 3 months after receiving the treatment in 2 groups. CNTF), brain-derived neurotrophic factor (BDNF), dopamine (DA), and 5-hydroxy tryptamine (5-HT).

The levels of CNTF and BDNF were determined by enzyme-chain immunochemical adsorption. The kits were given by Shanghai Enzyme-linked Biotechnology Co., LTD. The levels of DA and 5-HT were detected by eeg ultra-slow fluctuation analyzer (HY9212, China Huayang International Technology Company). ③ Quality of life assessment: Montreal Cognitive Assessment Scale (Beijing edition) were used (Nasreddine et al., 2005) (Montreal Cognitive Assessment, MoCA), Activity of Daily Living Scale (Garrod et al., 2002) (ADL) and Berg Balance Scale (Lajoie & Gallagher, 2004) (BBS) were employed to measure athletic patients' life quality before and 3 months after receiving the treatment.

The MoCA scale was used to screen the cognitive assessment scale for mild cognitive impairment, and the score < 26 was judged as cognitive impairment. ADL consists of 14 aspects, including defecation and urination, washing face and brushing teeth, eating, bed and chair transfer, bathing, dressing, independent walking, stairs and stairs, shopping, using public transportation, cooking, housework, taking medicine, and handling money. The score is from 0 to 4:1 means completely ok, 4 means completely not ok, and the total score is 100.

Daily living ability is proportional to the score; There were 14 items in the BBS scale, and the 4-level scoring method was adopted. A score of 0 indicated that it was difficult to complete independently and needed a lot of help to complete. A score of 4 indicates that the specified action can be completed

independently. The total score is 0~56 points, among which < 20 points indicates poor balance ability, 20~40 points indicates certain balance ability but unable to walk independently, 41~56 points indicates good balance ability and can walk independently. ④ Clinical efficacy: The modified Webster Parkinson's Symptom Rating Scale (Rappaport et al., 2006) and Unified Parkinson's Disease Scoring Scale (UPDRS)(Martinez-Martin et al., 2013) were employed to measure the clinical efficacy.

The Webster scale includes 10 symptoms such as tremor, myotonia and dyskinesia, and each symptom is divided into none (0 points), gentle (1 points), moderate (2 points) and acute (3 points) according to severity. Symptom score is proportional to severity. Effect Index (EI) = symptom score (before treatment - after treatment)/before treatment ×100%. The evaluation criteria of efficacy were marked effect: clinical syndromes and signs were considerably ameliorated, EI index ≥60%, UPDRS score decreased rate >60%; Effective: clinical symptoms and signs were ameliorated, EI index ranged from 20 to 59%, UPDRS score decreased rate ranged from 30 to 60%; Invalid: there was no change or even aggravation in clinical symptoms and signs, EI index <20%, UPDRS score decline rate <30%.

Clinical treatment efficiency = significant efficiency + effective rate. ⑤ Safety evaluation: Ecg, hematuria routine, biochemical examination, liver and kidney function and head MRI were performed before and 3 months after treatment in both groups. Monitor toxic and side effects and adverse timing, including nausea and vomiting, lethargy, dizziness, allergic reaction, diarrhea and abdominal pain.

1.5 Statistical treatment

SPSS 24.0 software in statistics was employed. The measurement data in line with normal distribution were showed as ± S, and t-test was employed to make a comparison between groups. The statistics were showed as the number of cases (n) and percentage (%), and the contrast between the groups was displayed by $\chi 2$ test, $P<0.05$ pointed obvious difference in statistics.

2. Results

2.1 Comparison of serum index levels

The results displayed that obvious difference in serum indexes isn't exist between the two groups before accepting the treatment ($P>0.05$). After accepting the treatment, SOD level in 2 groups was considerably grew in contrast with before treatment, while IL-1β, TNF-A and NF-KB-P65 levels were considerably decreased in contrast with before accepting the treatment, the differences were obvious in statistics ($P<0.05$). After accepting the treatment, SOD level in the study group was higher than that in the control group, while

IL-1β, TNF-A and NF-KB-P65 levels were lower than that in the control group, with obvious distinctions in statistics(P<0.05), you can consult Table 1 and Figure 1.

Table 1: Comparison of serum index levels（$\bar{x}$±s）

GROUP	TIME	CONTROL GROUP (N=46)	STUDY GROUP (N = 46)
SOD	Before the treatment	91.23±13.97	91.23±13.96
	After the treatment	98.21±15.45*	119.86±16.67*#
IL-1β（ng/L）	Before the treatment	33.75±6.04	33.76±6.03
	After the treatment	32.08±4.26*	29.12±3.44*#
TNF-α（pg/mL）	Before the treatment	85.23±11.03	85.26±11.01
	After the treatment	78.93±10.57*	64.39±9.25*#
NF -kB - p65（pg/mL）	Before the treatment	1.43±0.36	1.44±0.35
	After the treatment	1.10±0.27*	0.89±0.21*#

Note: *In contrast with the control group before treatment, *#P<0.05.*

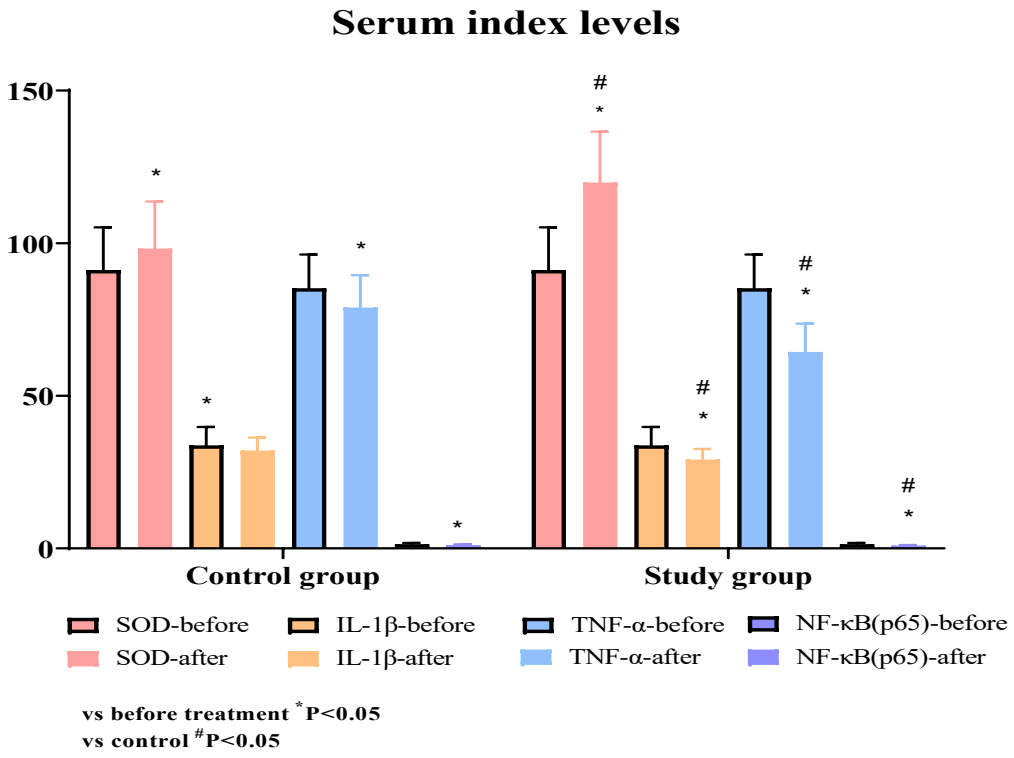

Figure 1: Comparison of serum index levels

2.2 Comparison of brain nerve related factors

The results showed that obvious difference was not exist in cerebral nerve related factors levels between the two groups before accepting the treatment (P>0.05). After accepting the treatment, the levels of CNTF, BDNF,

DA and 5-HT in 2 groups considerably rose compared with before accepting the treatment, the distinctions were obvious in statistics(P<0.05). After accepting the treatment, in the study group the levels of CNTF, BDNF, DA and 5-HT were considerably higher than those in the control group, and the distinctions were obvious in statistics(P<0.05), you can consult Table 2 and Figure 2.

Table 2: Comparison of brain nerve related factors（$\bar{x}$±s）

GROUP	TIME	CONTROL GROUP (N=46)	STUDY GROUP (N = 46)
CNTF （pg/mL）	Before the treatment	1.68±0.43	1.67±0.42
	After the treatment	2.39±0.54*	3.92±0.62*#
BDNF （ng/L）	Before the treatment	19.21±1.65	19.23±1.66
	After the treatment	22.28±1.73*	28.67±2.19*#
DA （μg/L）	Before the treatment	3.14±0.76	3.16±0.77
	After the treatment	5.83±1.03*	9.12±1.32*#
5-HT （μg/L）	Before the treatment	17.89±4.23	17.88±4.24
	After the treatment	20.94±4.59*	23.72±4.75*#

Note: *In contrast with the control group before treatment, *#P<0.05.*

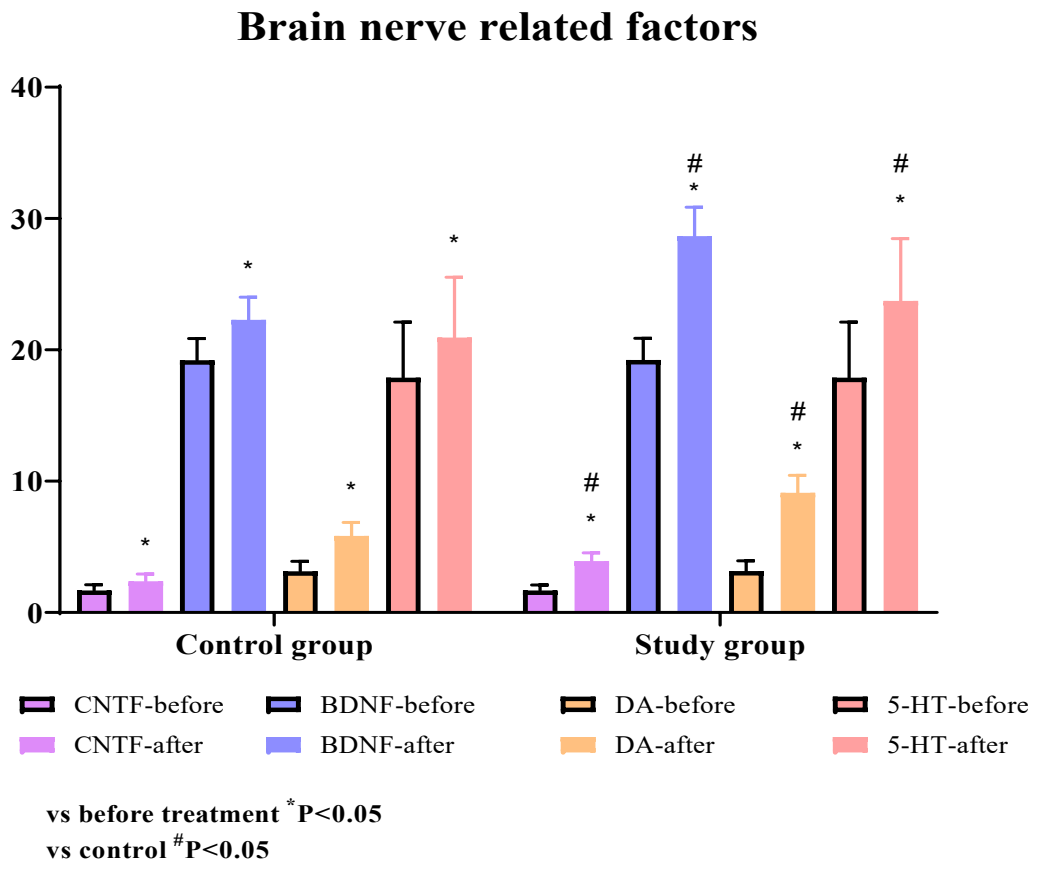

Figure 2: Comparison of brain nerve related factors

2.3 Comparison of quality of life

The results showed that obvious difference was not exist between the two groups about life quality before accepting the treatment (P>0.05). After accepting the treatment, the marks of MoCA and BBS in 2 groups were considerably grew compared with before accepting the treatment, while the scores of ADL were considerably decreased in contrast with before treatment, with significance in statistics(P<0.05). After accepting treatment, in the study group MoCA and BBS scores were higher than those in the control group, while ADL scores were lower than those in the control group, with obvious distinctions in statistics (P<0.05), you can consult the Table 3 and Figure 3.

Table 3: Comparison of quality of life ($\bar{x}$±s，points)

GROUP	TIME	CONTROL GROUP (N=46)	STUDY GROUP (N = 46)
MoCA	Before the treatment	13.08±3.97	13.10±3.40
	After the treatment	15.34±4.11*	18.96±4.82*#
ADL	Before the treatment	45.98±5.83	45,86±5.91
	After the treatment	35.75±4.77*	26.85±4.34*#
BBS	Before the treatment	20.94±6.38	20.98±6.32
	After the treatment	32.01±7.89*	46.17±9.10*#

*Note: In contrast with the control group before treatment, *#P<0.05.*

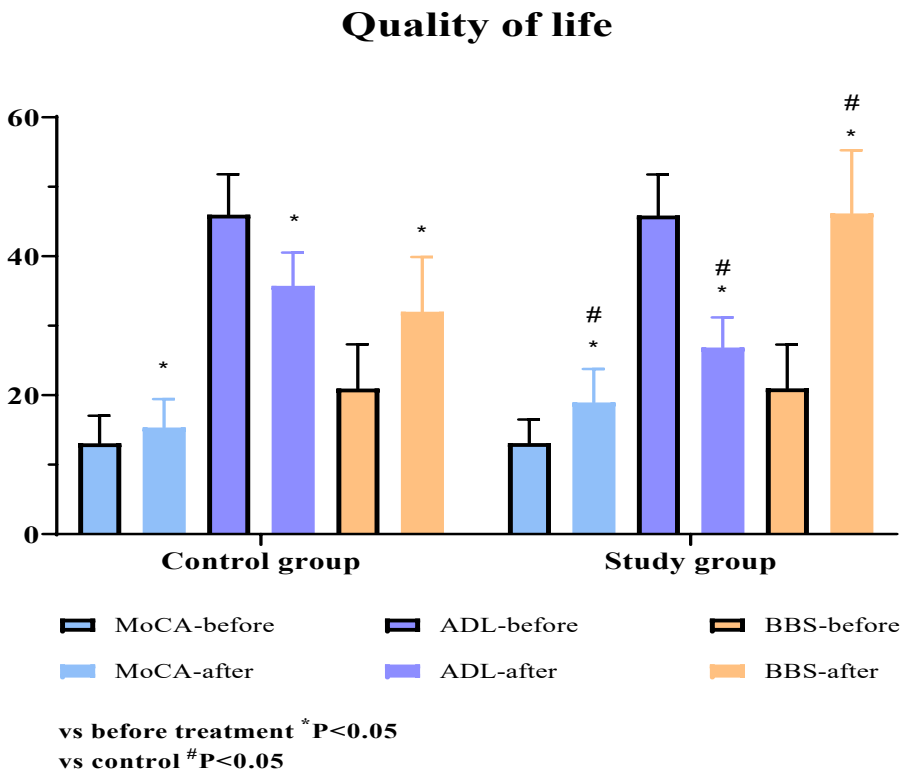

Figure 3: Comparison of quality of life

2.4 Comparison of clinical efficacy

Our results displayed that the entire effective rate of 95.65% in the study group was considerably higher than that in the control group (82.61%), and the distinction was obvious in statistics(P<0.05), you can consult the Table 4 and Figure 4.

Table 4: Comparison of clinical efficacy (cases, %)

GROUP	CONTROL GROUP (N=46)	STUDY GROUP (N = 46)	X2	P
Efficient	21（45.65）	25（54.49）	-	-
Effective	17（36.96）	19（41.30）	-	-
Invalid	8（17.39）	2（4.35）	-	-
Total	82.61%	95.65%	2.125	0.034

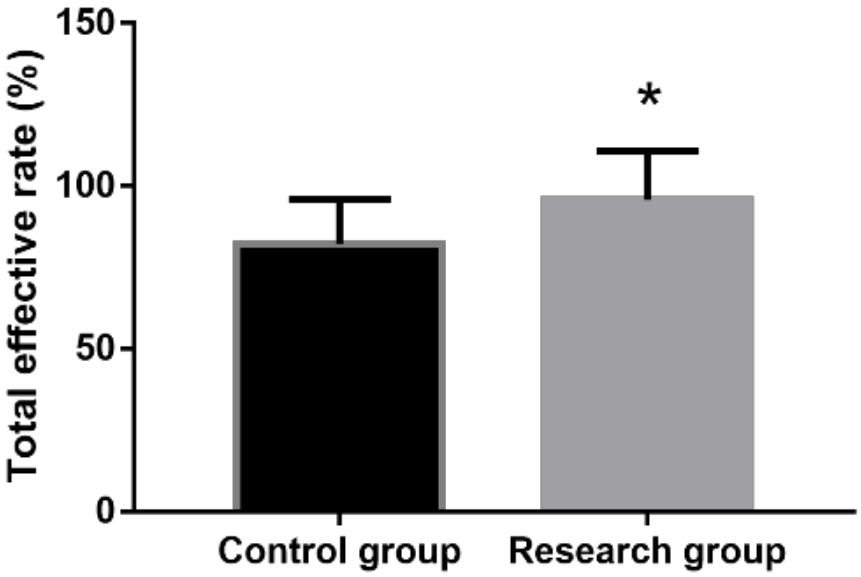

Figure 4: Total effective rate

Note: *In contrast with the control group, *P<0.05.*

2.5 Security Comparison

The results showed that after treatment, ecg, hematuria routine, biochemical examination, liver and kidney function, head MRI and other examinations of patients in the two groups had no abnormal conditions.

In the study group, the possibility of adverse reactions was 8.70%, which was considerably lower than 17.39%, and the distinction was obvious in statistics (P<0.05) in the control group, you can consult Table 5 and Figure 5.

Table 5: Comparison of the incidence of adverse reactions (cases, %)

GROUP	CONTROL GROUP (N=46)	STUDY GROUP (N = 46)	X2	P
Nausea and vomiting	2（4.35）	2（4.35）	-	-
Lethargy dizzy	3（6.52）	1（2.17）	-	-
Allergic reaction	1（2.17）	2（4.35）	-	-
Diarrhea, abdominal pain	2（4.35）	0（0.00）	-	-
Incidence of adverse reactions	17.39%	8.70%	3.012	0.001

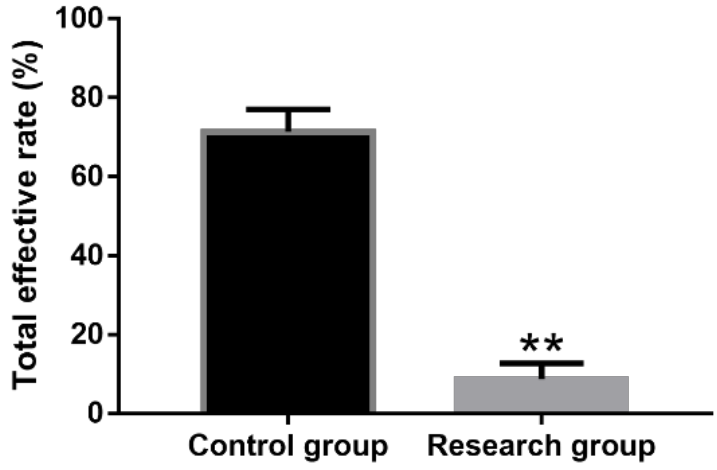

Figure 5: Total effective rate

Note: *In contrast with the control group, **P<0.01.*

3. Discussion

As a degenerative disease of the nervous system, Parkinson's disease is mainly caused by genetic, environmental and oxidative stress, including the abnormal decrease of dopamine level in the axon of the substantia nigra striatum and the abnormal decline of dopaminergic neurons in the dense area, resulting in decreased acetylcholine activity and neurotransmitter transmission imbalance. And then affect the disorder of the central nervous system of the brain, leading to the imbalance of language, movement, memory and balance (Walter et al., 2019). Its disability rate and fatality rate are second only to tumor and cardiovascular disease. However, its incidence increases year by year with the aging process, and finding feasible and safe treatment is an urgent problem for neurosurgery (Hauser et al., 2020). In current days, the clinical cure of Parkinson's disease is essentially ground on increasing the level of dopamine

and controlling the expression of acetylcholine, which has limited control during the period of disease and lengthy treatment cycle. In addition, some drugs are prone to drug resistance and adverse reactions, which increase the treatment burden of patients and further affect the treatment effect (Huang & Hsieh, 2021). Ropinero, as a new non - ergoalkine dopamine receptor agonist, has a lasting therapeutic effect. As a commonly used adjunctive drug of levodopa, it is often applied in the treatment of hyperkinetic leg syndrome with significant therapeutic effects (Tome et al., 2020). In this study, ropiniello combined with nerve growth factor in treating the Parkinson's disease patients can usefully improve the symptoms, regulate the level of serum inflammatory factors, enhance the level of dopamine and other neuroinfluencing factors, which has significant safety and feasibility (Mesquita-Romero et al., 2022).

The evolution of Parkinson's disease is closely linked with the expression of dopamine and neurotrophic factor in the substantia nigra. Neurotransmitters, as information transmitting substances, can accurately reflect the progression of the disease. In addition, degenerative neuropathy can cause immune system disorder and abnormal expression of stress inflammatory response factors. As stress inflammatory factors, SOD, IL-1β and TNF-A can sensitively reflect the stress expression of the body. Nf-kb-p65, as a related factor involved in the process of neuron mutation, can protect the degree of neuron injury by binding to NF-KB receptor. CNTF and BDNF, as neurotrophic factors, can express the degree of neuron injury. As an inhibitory neurotransmitter, 5-HT is closely related to memory, cognitive level and mood. Li J et al used rat nerve growth factor to treat diabetic peripheral neuropathy patients, considerably improving their nerve conduction velocity and considerably promoting the recovery of central nervous system. Chatzitaki AT et al delivered ropinero nanoparticles through nasal cavity to improve the activity of relevant cells in peripheral blood cells, stimulate the expression of central nervous system factors and avoid liver tissue damage. The results showed that SOD levels in 2 groups were considerably grew after accepting the treatment, while IL-1β, TNF-A and NF-KB-P65 levels were considerably decreased after accepting the treatment. SOD levels were higher in the study group than those in the control group, while IL-1β, TNF-A and NF-KB-P65 levels were lower.

After accepting the treatment, the levels of CNTF, BDNF, DA and 5-HT in 2 groups were considerably increased compared with before accepting the treatment, and in the study group the levels of CNTF, BDNF, DA and 5-HT were considerably higher than those in the control group. The final outcomes were almost conforming to Li J and Chatzitaki AT et al's., indicating that ropinero combined with nerve growth factor can effectively lower the level of inflammatory factors and alleviate the damage of brain neurons in Parkinson's patients. As a polypeptide substance in body tissues, nerve growth factor can control the binding of calcium channel receptors and interfere with the

expression and secretion of superoxide free radicals, thus avoiding the oxidative reaction of nerve tissues and reducing the accumulation of amyloid protein in brain, thus improving the body's inflammatory reaction to stress and improving the therapeutic effect. Ropinol can prevent the body's own oxidation reaction and protect the body's dopaminergic neurons from being oxidized by enhancing the expression of glutathione and SOD, and control the inflammatory reaction. Combined, the two are more conducive to reducing inflammation, increasing dopamine levels, protecting neurons, and alleviating their damage.

Parkinson's disease patients are often accompanied by central nervous disorder caused by cognitive function, motor ability and other reduction. Medication is needed to ameliorate clinical symptoms and curb the envelopment of the disease. Mochizuki H et al applied ropiniro patch to patients suffering from Parkinson's disease, which can helpfully boost the therapeutic effect and maintain the stability of plasma factor level, showing significant efficacy and safety. The results displayed that the scores of MoCA and BBS in 2 groups were considerably increased after treatment, and the scores of ADL were considerably decreased after treatment. After treatment, in the study group, MoCA and BBS scores were higher than those in the control group, but ADL scores were lower. After accepting the treatment, in the study group, the entire effective rate was considerably higher than that of the control group. After accepting the treatment, ecg, hematuria routine, biochemical examination, liver and kidney function, head MRI and other examinations of patients in the two groups showed no abnormality.

In the study group, the incidence of adverse reactions was considerably lower than that in the control group. It basically conformed to the results of Mochizuki H's study, suggesting that ropiniol combined with nerve growth factor therapy can effectively boost the cognitive function, language and motor coordination ability of patients suffering from Parkinson's disease, and enhance the clinical efficacy. Nerve growth factor can participate in the growth and metabolism of nerve cells, promote the recovery of brain nerve fibers, reduce the sustained injury of brain nerve elements, and then improve clinical symptoms; Ropinero, as a dopamine agonist, can selectively combine with D2 and D3 receptors to promote the increase of the level of DA in the body, thereby alleviating clinical symptoms and promoting the recovery of injured neurons in the body.

The combination of the two can increase the level of pharmacodynamics and improve the clinical treatment effect. There are still mild adverse reactions in this study, which can be relieved after treatment, within a controllable range. A few blocks exist in our study. Due to a small sample, there will be some deviation between actual clinical data and research results, which will have an impact on the accuracy of the results. In addition, the follow-up period of this research is short, and the lasting therapeutic efficacy and drug resistance have

not been further explored. In this study, the therapeutic mechanism and its influence on genetic indicators were not thoroughly studied, which may have an impact on its long-term safety. Therefore, it has a need to enlarge the sample size, extend the follow-up time, and increase the reliability and certainty of the study results.

To sum up, ropinero combined with nerve growth factor therapy for Parkinson's disease can effectively enhance immune function and improve the content of neuron dopamine. At the same time, it has ideal safety and feasibility, and provides ideas for clinical treatment.

4. Conclusion

This study has undertaken an in-depth exploration into the feasibility and safety of a novel therapeutic approach that combines ropinirole and nerve growth factor (NGF) for the enhancement of neurological health in football players. Our investigation sought to address the unique challenges faced by athletes, particularly those in high-impact sports like football, when managing neurological conditions such as Parkinson's disease.

The findings of this study provide valuable insights and implications for the broader context of neurological health management in athletes. Here, we summarize the key conclusions drawn from our research:

Feasibility and Safety:

The combination of ropinirole and NGF in the treatment of Parkinson's disease in football players has demonstrated feasibility and safety. The absence of adverse reactions in the study group, coupled with lower adverse reaction rates compared to the control group, underscores the potential viability of this treatment approach within the athletic community.

Improvement in Immune Function:

Our study revealed a significant increase in superoxide dismutase (SOD) levels after treatment in both the control and study groups. This suggests that the combined therapy may contribute to bolstering immune function, a crucial aspect of neurological health.

Enhanced Neurotrophic Factors:

The study group exhibited notably higher levels of crucial brain nerve factors, including ciliary neurotrophic factor (CNTF), brain-derived neurotrophic factor (BDNF), dopamine (DA), and serotonin (5-HT). These findings indicate that the ropinirole-NGF combination has the potential to enhance the neurotrophic environment, which may positively impact neuronal health.

Improved Quality of Life:

Football players who underwent the combined treatment reported higher scores in assessments related to quality of life, as evidenced by improved results in the Montreal Cognitive Assessment (MoCA) and Berg Balance Scale (BBS). Furthermore, activities of daily living (ADL) scores were notably lower post-treatment, indicating enhanced functional capacity.

Effective Therapeutic Outcomes:

The study group demonstrated a significantly higher total effective rate compared to the control group, underscoring the clinical efficacy of the combined treatment approach. This suggests that ropinirole and NGF may synergize to yield improved therapeutic outcomes for football players with Parkinson's disease.

Safety Profile:

Extensive clinical evaluations, including electrocardiogram (ECG), routine hematuria analysis, biochemical assessments, and liver and kidney function tests, revealed no abnormalities in either the control or study group. This underscores the safety of the ropinirole-NGF combination therapy.

In conclusion, the results of this study provide compelling evidence for the potential of ropinirole combined with nerve growth factor as a feasible and safe approach to enhance neurological health in football players managing Parkinson's disease. This innovative treatment strategy holds promise not only for athletes but also for the broader community facing neurological challenges. Further research and clinical trials are warranted to validate and refine these findings, ultimately contributing to improved neurological well-being and performance optimization in athletes and individuals with Parkinson's disease.

Declaration of conflict of interest: None.

Data Availability Statement: The data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgement: This work was supported by Second Affiliated Hospital of Hainan Medical University.

REFERENCES

Bojaj, G., Agahi, R., & Hoxha, I. (2021). Treatment of the first COVID-19 case in kosovo and management of the pandemic. *Sci Progr Res*, *1*(3), 58-62.

Brucki, S., Nitrini, R., Caramelli, P., Bertolucci, P. H., & Okamoto, I. H. (2003). Suggestions for utilization of the mini-mental state examination in Brazil. *Arquivos de neuro-psiquiatria*, *61*, 777-781.

Combs-Miller, S. A., & Moore, E. S. (2019). Predictors of outcomes in exercisers with Parkinson disease: a two-year longitudinal cohort study. *NeuroRehabilitation*, *44*(3), 425-432.

Contin, M., Lopane, G., Mohamed, S., Calandra-Buonaura, G., Capellari, S., De Massis, P., Nassetti, S., Perrone, A., Riva, R., & Sambati, L. (2019). Clinical pharmacokinetics of pramipexole, ropinirole and rotigotine in patients with Parkinson's disease. *Parkinsonism & Related Disorders*, *61*, 111-117.

Garrod, R., Paul, E., & Wedzicha, J. (2002). An evaluation of the reliability and sensitivity of the London Chest Activity of Daily Living Scale (LCADL). *Respiratory medicine*, *96*(9), 725-730.

Guo, D., Zhou, J., Zhang, M., Taximaimaiti, R., Wang, X., & Wang, H. (2021). Momordica Charantia polysaccharides attenuates MPP+-Induced injury in Parkinson's disease mice and cell models by regulating TLR4/MyD88/NF-κB pathway. *International Journal of Polymer Science*, *2021*, 1-15.

Hauser, R., Lew, M., Comella, C., Poewe, W., Rascol, O., Ferreira, J., Olson, K., Farahmand, K., Shah, C., & Rocha, J.-F. (2020). Nighttime and morning OFF improvements with opicapone in patients with Parkinson's Disease and motor fluctuations: BIPARK-1 and BIPARK-2 pooled subanalyses. *Parkinsonism & Related Disorders*, *79*, e53-e54.

Huang, T.-I., & Hsieh, C.-L. (2021). Effects of acupuncture on oxidative stress amelioration via nrf2/are-related pathways in alzheimer and parkinson diseases. *Evidence-Based Complementary and Alternative Medicine*, *2021*.

Kuang, Z., Huang, T., Li, D., Zhao, D., Jin, J., Lin, J., Zhu, W., Chen, W., Li, M., & Shen, W. (2020). Structure elucidation and mechanistic study of a new dimeric degradant in ropinirole hydrochloride extended-release tablets. *Pharmaceutical Research*, *37*, 1-11.

Lajoie, Y., & Gallagher, S. (2004). Predicting falls within the elderly community: comparison of postural sway, reaction time, the Berg balance scale and the Activities-specific Balance Confidence (ABC) scale for comparing fallers and non-fallers. *Archives of gerontology and geriatrics*, *38*(1), 11-26.

Larson, D. N., Schneider, R. B., & Simuni, T. (2021). A new era: the growth of video-based visits for remote management of persons with Parkinson's disease. *Journal of Parkinson's disease*, *11*(s1), S27-S34.

Malar, D. S., Prasanth, M. I., Brimson, J. M., Sharika, R., Sivamaruthi, B. S., Chaiyasut, C., & Tencomnao, T. (2020). Neuroprotective properties of green tea (Camellia sinensis) in Parkinson's disease: A review. *Molecules*, *25*(17), 3926.

Martinez-Martin, P., Rodriguez-Blazquez, C., Alvarez-Sanchez, M., Arakaki, T., Bergareche-Yarza, A., Chade, A., Garretto, N., Gershanik, O., Kurtis, M. M., & Martinez-Castrillo, J. C. (2013). Expanded and independent

validation of the movement disorder society–unified Parkinson's disease rating scale (MDS-UPDRS). *Journal of neurology*, *260*, 228-236.

Mesquita-Romero, W.-A., Fernández-Morante, C., & Cebreiro-López, B. (2022). Critical media literacy to improve students' competencies. *Comunicar*, *30*(70), 47-57.

Miziuno, Y., Okuma, Y., Kikuchi, S., Kuno, S., Hashimoto, T., Hasegawa, K., Mano, Y., Miwa, H., Murata, M., & Yamamoto, M. (2002). A guideline for the treatment of Parkinson's disease. *Rinsho shinkeigaku= Clinical neurology*, *42*(5), 421-494.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), 695-699.

Ortigas-Wedekind, M. (2022). Digital Health Commercialization: Considerations and Case Study. *Journal of Commercial Biotechnology*, *27*(1).

Rappaport, N., Frazier, J. A., Connor, D. F., & Mattison, R. (2006). From zero to a hundred in a split second: Understanding aggression in an eight-year-old child. *Harvard review of psychiatry*, *14*(3), 165-176.

Tome, T., Obreza, A., & Časar, Z. (2020). Developing an Improved UHPLC Method for Efficient Determination of European Pharmacopeia Process-Related Impurities in Ropinirole Hydrochloride Using Analytical Quality by Design Principles. *Molecules*, *25*(11), 2691.

Walter, J., Bolognin, S., Antony, P. M., Nickels, S. L., Poovathingal, S. K., Salamanca, L., Magni, S., Perfeito, R., Hoel, F., & Qing, X. (2019). Neural stem cells of Parkinson's disease patients exhibit aberrant mitochondrial morphology and functionality. *Stem cell reports*, *12*(5), 878-889.