Effects of resistance exercise on the cognitive function through modulation of AMPK, PGC-1, BDNF protein expression in PD mice

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INTROTUCTION

Degenerative brain disease is the fourth most common cause of death in Korea. Among them, the incidence of Parkinson's disease (PD) increases about 2.5 times per year, which is a serious problem in an aging society. Although the cause of PD is not clear, PD is characterized by decreased motor function and cognitive impairment due to dopamine dysfunction and reduced neurogenesis. Drugs used clinically have serious side effects, so it needs to find an effective and safe method of treatment from a pathophysiological point of view.

In degenerative brain disease, peroxisome proliferator-activated receptor gamma co-activator 1-alpha (PGC-1α) is suggested as a cause of cognitive impairment, whereas PGC-1α induces the expression of fibronectin type III domain-containing protein 5 (FNDC5) and brain-derived neurotrophic factor (BDNF). Currently, exercise therapy is drawing attention as a treatment method for PD. The benefits of exercise therapy are that it promotes body function recovery and improves cognitive function. Best of all, it is safe from side effects. However, muscle strength is required to prevent deterioration of motor function in PD patients, but studies on the effects of resistance exercise are insufficient compared to aerobic exercise studies.In this study, we investigated the effect of resistance exercise on AMP-activated protein kinase(AMPK), Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), brain-derived neurotrophic factor(BDNF) protein expression in the PD mouse.

MATERIALS AND METHODS

The experimental groups were divided into 4 groups: control group, PD-induction group, PD-induction and resistance exercise group, PD-induction and levodopa treated group.

Control	Parkinson's disease(PD)
PD – resistance exercise	PD – drug (levodopa)

The PD mouse model was induced by an intraperitoneal injection of MPTP for twice a week(10 times).

Probenecid injection | MPTP injection | Ladder exercise | Levodopa oral injection

For the resistance exercise group was performed for 5 weeks, and levodopa treated group received levodopa at dose of 20mg/kg for 5 weeks

Set	1 – 2 weeks	3 – 4 weeks	4 – 5 weeks
Warm-up		Conducted twice without weight	
1 - 2	30% of the weight of the mouse	40% of the weight of the mouse	50% of the weight of the mouse
3 - 4	37.5% of the weight of the mouse	47.5% of the weight of the mouse	57.5% of the weight of the mouse
5 - 6	45% of the weight of the mouse	55% of the weight of the mouse	65% of the weight of the mouse
7 - 8	52.5% of the weight of the mouse	62.5% of the weight of the mouse	72.5% of the weight of the mouse
9 - 10	60% of the weight of the mouse	70% of the weight of the mouse	80% of the weight of the mouse

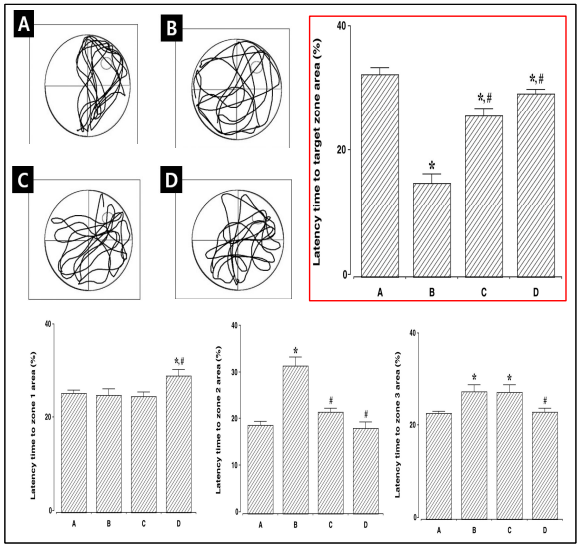
The Morris water maze test and step down avoidance test were used to evaluate cognitive function

Water maze test | Step down avoidance test | Immunohistochemistry | Western blot

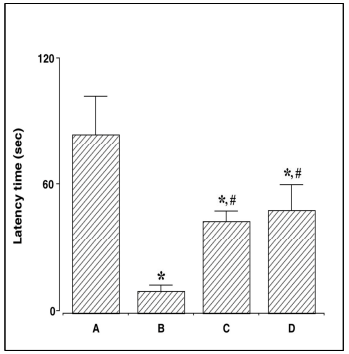
5-bromo-2'-deoxyuridine(BrdU) immunohistochemistry was used to assess neurogenesis. Western blotting was also performed to assess levels of AMPK, PGC-1α, BDNF. RESULTS: Decreased spatial memory with reduced AMPK and PGC1α, BDNF protein expressions were found in the PD mice.

RESULTS

Morris water maze test



Step down avoidance test



A : Control

B : Parkinson's disease(PD)

C : PD - resistance exercise

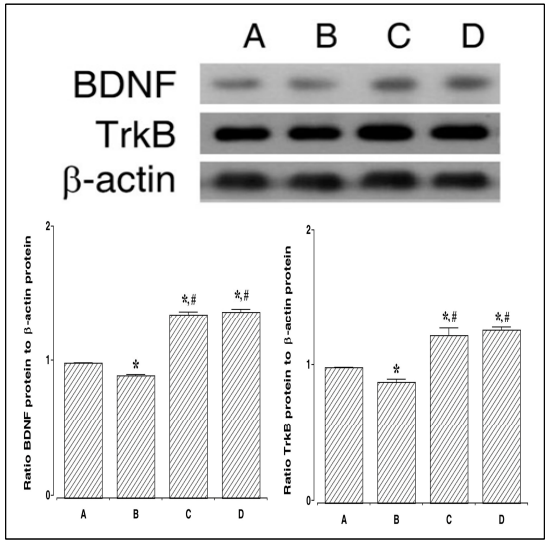
D : PD – drug (levodopa)

*represents P < 0.05 compared to control group.

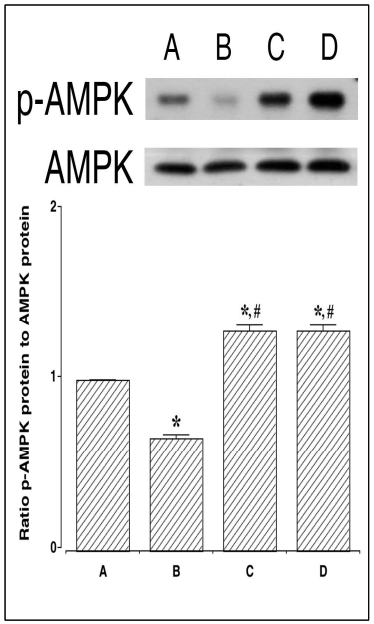
#represents P < 0.05 compared to the Parkinson's disease-induced group.

RESULTS

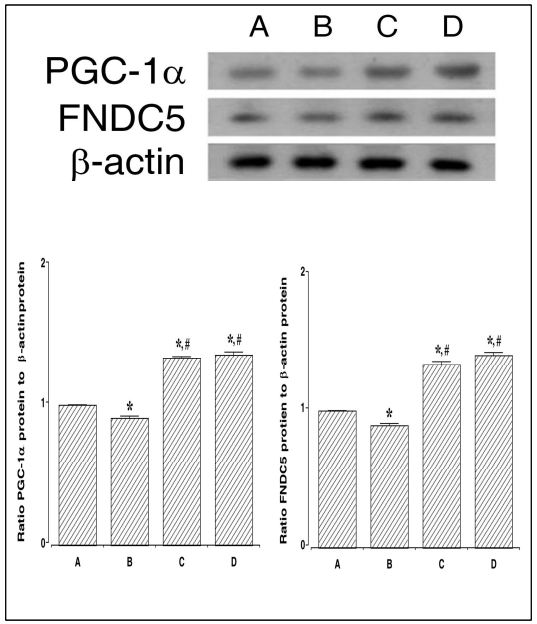
BDNF



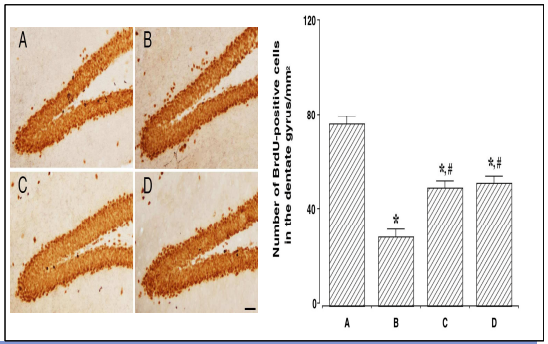
AMPK



PGC-1α, FNDC5



BrdU (neurogenesis)



CONCLUSIONS

- As a result of this study, it was found that the induction of PD reduced cognitive function and the expression of AMPK, PGC-1α, FNDC5, TrkB, and BDNF in the hippocampus was reduced due to PD, resulting in decreased neurogenesis.
- However, resistance exercise increased AMPK, PGC-1α, FNDC5, TrkB, and BDNF expression, resulting in increased neurogenesis and improved cognitive function.
- Compared to levodopa, resistance exercise showed a similar improvement of levodopa in treatment PD, and thus it was confirmed that treatment efficacy is high.
- Through this study, it was found that resistance exercise improves PD's motor and cognitive function..