

INTISARI

Latar Belakang. Cerebellum adalah bagian otak yang berperan untuk fungsi motorik. Berkurangnya kadar estrogen akibat menopause atau ovariektomi dapat mengganggu struktur dan fungsi cerebellum. Latihan fisik *endurance* kontinu menjadi terapi pada berbagai gangguan otak, tetapi belum ada data tentang bagaimana efek latihan fisik interval intensitas sedang (LFIIS) terhadap fungsi neurotropik, neuroprotektif, dan motorik cerebellum tikus pascaovarietomi.

Tujuan. Penelitian ini bertujuan untuk mengungkapkan pengaruh LFIIS terhadap cerebellum tikus pascaovarietomi dengan mengkaji fungsi neurotropik, neuroprotektif, dan motorik.

Metode. Penelitian dilakukan pada 32 ekor tikus *Sprague Dawley* betina, usia 12 minggu, dan berat 150-200 g. Subjek penelitian dibagi menjadi 4 kelompok ($n=8$ per kelompok), yaitu kelompok *sham*, ovariektomi (ovx), *sham*+LFIIS, dan ovariektomi+LFIIS (ovx+LFIIS). LFIIS dilakukan selama 7 minggu yang didahului dengan *graded exercise test*. Pada akhir periode LFIIS, dilakukan uji fungsi motorik yaitu uji *rotarod*, *footprint test*, *open field test*, dan *wire hanging test*. Pemeriksaan *real time* PCR dilakukan untuk mengetahui ekspresi mRNA PGC-1 α , BDNF, sinaptofisin, NF- κ B, BCL-2, dan BAX. Perhitungan jumlah sel Purkinje cerebellum dilakukan menggunakan metode stereologi non bias. Uji *one-way* ANOVA dan *post hoc* Bonferroni digunakan untuk menguji beda rerata seluruh variabel antar kelompok penelitian, kecuali panjang langkah kaki depan dan belakang, serta tumpang-tindih penempatan kaki pada *footprint test* yang menggunakan *Kruskal-Wallis test* dan *post hoc* Mann-Whitney test dengan koreksi Bonferroni. Analisis korelasi dan regresi linier sederhana digunakan untuk menguji korelasi antar variabel penelitian.

Hasil. Setelah LFIIS, kelompok ovx+LFIIS memiliki fungsi neurotropik dan neuroprotektif lebih tinggi dibandingkan kelompok ovx ($p<0,05$) pada parameter mRNA PGC-1 α ($2,0\pm0,8$ vs $0,7\pm0,7$), mRNA BCL-2 ($1,5\pm0,6$ vs $0,15\pm0,1$), jumlah sel Purkinje ($292.285,7\pm74.586,0$ vs $210.000,0\pm40.686,1$), dan sebaliknya dengan ekspresi mRNA BAX ($1,3\pm0,6$ vs $0,7\pm0,3$). LFIIS menyebabkan perbedaan bermakna ($p<0,05$) seluruh fungsi motorik antara kelompok *sham*, ovx, *sham*+LFIIS, dan ovx+LFIIS. Ekspresi mRNA BCL-2 dan BAX berkorelasi bermakna dengan jumlah sel Purkinje ($r=0,46$ dan $r=-0,35$). Korelasi bermakna juga terjadi antara jumlah sel Purkinje cerebellum dan ekspresi mRNA sinaptofisin dengan fungsi motorik, terutama pada kemampuan *gait* dan aktivitas lokomotor.

Kesimpulan. LFIIS meningkatkan fungsi neurotropik, neuroprotektif, dan motorik cerebellum tikus pascaovarietomi

Kata kunci: Cerebellum, ovariektomi, latihan interval, fungsi motorik, neurotropik, neuroprotektif.

ABSTRACT

Background. The cerebellum is part of the brain that plays a role in motor function. A decrease of estrogen levels due to menopause or ovariectomy can disrupt the structure and function of the cerebellum. Continuous endurance exercise has been used as a therapy in a variety of brain disorders, but there was no data on the moderate intensity intermittent exercise (MIIE) impact on neurotrophic, neuroprotective, and motor function of cerebellar ovariectomized rats.

Aims. This study aims to reveal the effects of MIIE on cerebellar ovariectomized rats by assessing neurotrophic and neuroprotective functions, as well as cerebellar motor function.

Methods. The study was conducted on 32 female Sprague Dawley rats, age 12 weeks, and weight 150-200 g. The subjects were divided into four groups ($n = 8$ per groups), ie. sham, ovariectomy, sham+MIIE, and ovariectomy+MIIE groups. MIIE performed for 7 weeks preceded by graded exercise test. At the end of the LFIIS period, motor functions were assessed using rotarod, footprint, open field, and wire hanging tests. A real-time PCR examination was performed to determine the expression of PGC-1 α , BDNF, synaptophysin, NF- κ B, BCL-2, and BAX mRNA expressions. The estimation of Purkinje cell numbers was performed using a non-biased stereological method. One-way ANOVA and post hoc Bonferroni test were used to test the mean difference of all variables between study groups, except stride length and overlapping of foot placement on footprint test using Kruskal-Wallis test followed by post hoc Mann-Whitney test with Bonferroni corrections. Correlation and regression analysis were used to test the correlation between research variables.

Results. After MIIE, the ovx+MIIE group had higher neurotrophic and neuroprotective functions than the ovx group ($p < 0.05$) in the PGC-1 α mRNA (2 ± 0.8 vs 0.7 ± 0.7), BCL-2 mRNA (1.5 ± 0.6 vs 0.15 ± 0.1), number of Purkinje cells ($292,285.7 \pm 74,586.0$ vs $210,000.0 \pm 40,686.1$) parameters, and vice versa with BAX mRNA expression (1.3 ± 0.6 vs 0.7 ± 0.3). MIIE causes a significant difference ($p < 0.05$) of all motor functions between sham, ovx, sham+MIIE, and ovx+MIIE groups. BCL-2 and BAX mRNA expressions correlated significantly with the number of Purkinje cells ($r = 0.46$ and $r = -0.35$). Significant correlations also occurred between the number of cerebellar Purkinje cells and the expression of synaptophysin mRNA with motor functions, particularly in gait ability and locomotor activity.

Conclusion. The MIIE improve neurotrophic, neuroprotective, and cerebellar motor functions on ovariectomized rats.

Keywords: Cerebellum, ovariectomy, intermittent exercise, motor function, neurotrophic, neuroprotective.