

## INTISARI

**Latar Belakang:** Demensia merupakan salah satu penyakit neurodegeneratif yang dapat dicegah dengan latihan fisik terprogram. Salah satu program latihan fisik yang dikembangkan adalah latihan fisik intermiten intensitas sedang (LFIIS) karena lebih efisien dan efektif dibandingkan latihan fisik kontinu. Penelitian ini bertujuan untuk mempelajari pengaruh LFIIS terhadap struktur dan fungsi hippocampus tikus model degenerasi saraf yang diinduksi trimethyltin (TMT).

**Metode:** Penelitian dilakukan pada 24 ekor tikus Sprague Dawley jantan berusia 12 minggu. Subjek penelitian dibagi menjadi 4 kelompok ( $n=6$  per-kelompok), yaitu kelompok tanpa induksi TMT+tanpa LFIIS (TI), induksi TMT (I), tanpa induksi TMT+LFIIS (LTI), dan induksi TMT+LFIIS (LI). LFIIS dilakukan selama 12 minggu yang didahului dengan *graded exercise test*. Pada akhir periode LFIIS, dilakukan uji memori menggunakan *Morris water maze* (MWM). Estimasi jumlah neuron pyramidale dan volume hippocampus didapatkan dengan metode stereologi non-bias. Kadar PSEN-1 dan p-tau diukur dengan ELISA. Uji *one way ANOVA* digunakan untuk menguji beda rerata seluruh variabel antar kelompok penelitian. Data hasil MWM dianalisis menggunakan *general linear model repeated measures ANOVA*. Imunohistokimia kualitatif dilakukan untuk menilai ekspresi BDNF, IL-6, TNF- $\alpha$ , dan IL-10 pada irisan blok parafin hippocampus.

**Hasil:** Persentase waktu dan panjang lintasan di kuadran target pada kelompok LI tidak berbeda bermakna dibandingkan kelompok TI dan LTI ( $p=0,25$  dan  $p=0,15$ ). Kelompok LI menunjukkan kadar p-tau dan PSEN-1 jaringan hippocampus yang paling rendah dibandingkan kelompok lainnya ( $p=0,10$  dan  $p=0,25$ ). Rerata jumlah neuron pyramidale regio CA hippocampus kelompok LI lebih tinggi dibandingkan kelompok I ( $p=0,00$  untuk regio CA1 dan CA2-3). Pada kelompok LI terlihat ekspresi sitokin inflamasi IL-6 dan TNF $\alpha$  yang lemah dan ekspresi antiinflamasi IL-10 yang lebih kuat dibandingkan kelompok kontrol. Ekspresi faktor neurotropik BDNF meningkat pada kelompok dengan induksi TMT (kelompok LI dan I).

**Simpulan:** LFIIS mencegah kerusakan struktur hippocampus dan memori spasial tikus yang diinduksi TMT, kemungkinan melalui pencegahan peningkatan kadar penanda demensia dan pencegahan inflamasi.

## ABSTRACT

**Background:** Moderate-intensity intermittent exercise (MIIE) has been proposed as an effective method for preventing Alzheimer dementia (AD). This study aimed to investigate the effects of MIIE on the spatial memory and levels of AD protein markers in the hippocampus of TMT-induced rat model of hippocampal degeneration.

**Methods:** Male Sprague Dawley rats were randomly assigned into four groups, i.e. normal control (TI), exercise control (LTI), TMT control (I), and exercise & TMT (LI). Rats of the exercise groups (LTI & LI) were forced to run on a treadmill for 30 minutes each day at maximum for 12 weeks. Intraperitoneal injection of 8 mg/kg BW TMT was administered as a single dose, 10 days before the last exercise treatment for I and LI groups. The spatial memory of rats was examined using Morris Water Maze (MWM) test after the exercise period. After euthanasia, hippocampal tissue was dissected out and the level of hippocampal PSEN-1 and p-tau protein were measured using ELISA. The total number of hippocampal pyramidal neurons was estimated using unbiased stereological analysis. The mean difference of all variables was analyzed using one way ANOVA. MWM data were analyzed using general linear model repeated measures ANOVA. Qualitative immunohistochemistry was performed to examine the expression of BDNF, IL-6, TNF- $\alpha$ , and IL-10 in the hippocampal paraffin block sections.

**Results:** TMT exposure induced memory impairment as the I group had the lowest percentage of time and percentage of path length in the target quadrant compared to other groups. MIIE prevented the memory impairment effect of TMT exposure as the ET group had no significantly different MWM performance compared to the E and N groups. The ET group had significantly lower levels of hippocampal AD markers, p-tau and PSEN-1, as well as significantly higher estimated total number of pyramidal neurons of hippocampal CA1 and CA2-3 region compared to the T group. The immunostaining of IL-6 and TNF- $\alpha$  were weak, while the expression of IL-10 was stronger in the LI group compared to the control group. The TMT-induced group exhibited stronger anti BDNF immunoreactivity.

**Conclusion:** MIIE prevents impaired spatial memory upon TMT exposure most probably via preventing elevated levels of hippocampal AD markers and neuroinflammation.