

## A Cyclopeptide (Heterophyllin B) from *Pseudostellaria heterophylla*: Implications for Cognitive Enhancement and Neuronal Regeneration

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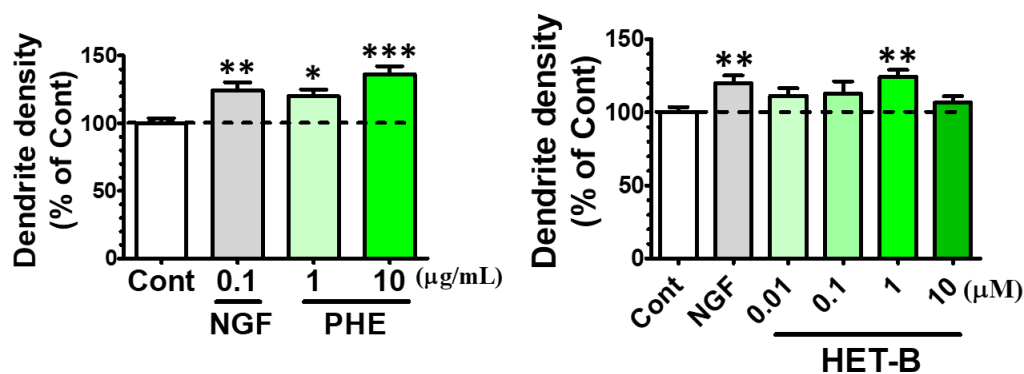
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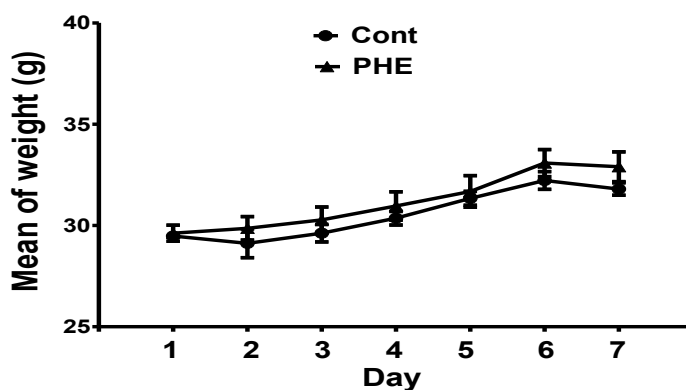
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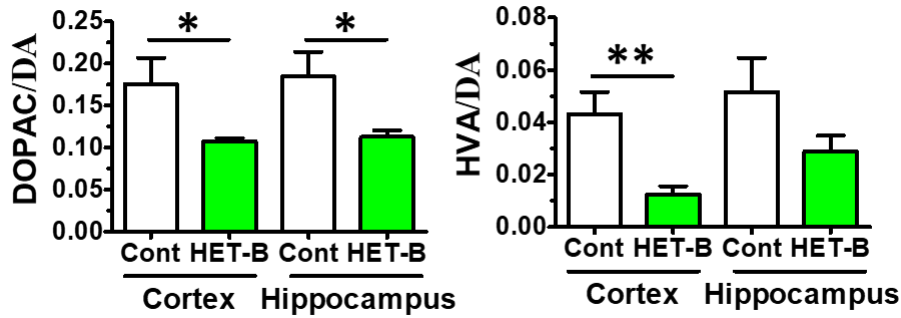
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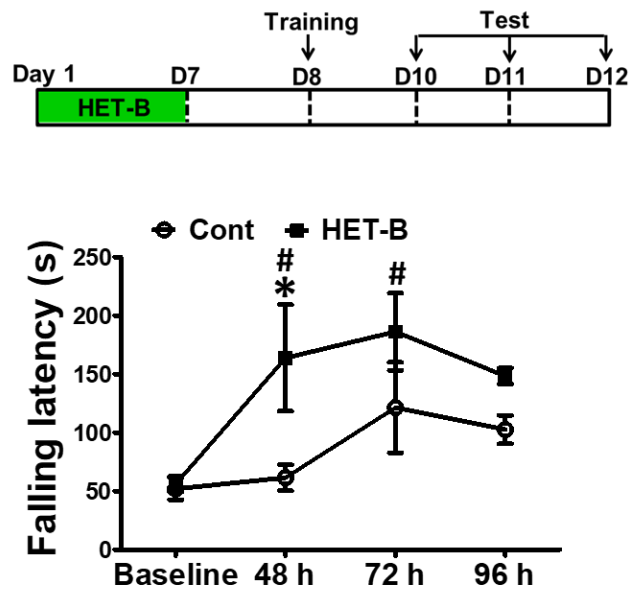
**Figure S1.** PHE and HET-B promoted dendrite outgrowth in primary cortical neurons. Primary cortical neurons were cultured for 2 days following treated with control (Cont, 0.1% DMSO), PHE (1 and 10  $\mu\text{g}/\text{mL}$ ), or HET-B (0.01–10  $\mu\text{M}$ ) for another 4 days. The neurons were fixed and immunostained for MAP2 and  $\beta$ 3-tubulin. The MAP2 positive neurites were measured. The results are shown as the mean  $\pm$  SEM of three independent experiments. \* $p < 0.05$ , \*\* $p < 0.01$  and \*\*\* $p < 0.001$  versus control (Cont), one-way analysis of variance and *post hoc* Dunnett's test.



**Figure S2.** Effects of PHE on mice body weight. The PHE extract (500 mg/kg) or vehicle solution (Cont) was orally administered for 7 days to ICR mice (male, 8-week old). The results were analyzed by repeated measures two-way ANOVA *post hoc* Bonferroni test.



**Figure S3.** HET-B regulated dopamine turnover in young mice. HET-B (10  $\mu\text{mol/kg}$ ) or vehicle solution (10% DMSO in saline) was administered (i.p.) for 7 days to ICR mice (male, 12-week old). The ratio of DOPAC and/or HVA to DA was quantified in the prefrontal cortex and hippocampus. \* $p < 0.05$  and \*\* $p < 0.01$  versus Cont, Student's unpaired  $t$ -test,  $n = 5-6$ .



**Figure S4.** HET-B promoted motor learning ability in young mice. HET-B (10  $\mu\text{mol/kg}$ ) or vehicle solution (10% DMSO in saline) was administered (i.p.) for 7 days to ICR mice (male, 12-week old). The modified rotarod test was performed by a Rotarod Treadmill (YLS-4C, Yiyan Tech., Jinan, China). Before the training session, the mice were habituated to stay on the stationary drum for 1 min. On day 8, the training session was performed at a speed of 30 rpm. On day 10 and 11, the test session was performed at a speed of 30 rpm. On day 12, the test session was performed at a speed of 40 rpm. The falling latency was recorded automatically by photo-cells and the total latencies on the rod on each day was analyzed.  $P < 0.001$ , drug  $\times$  time interaction was analyzed using repeated measures two-way ANOVA,  $F(3,10) = 1.85$ , \* $p < 0.05$  vs control, *post hoc* Bonferroni test, # $p < 0.05$  vs baseline, one-way ANOVA *post hoc* Dunnett's test,  $n = 6$ .