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RESVERATROL ATTENUATES NEUROINFLAMMATION, MAINTAINS HIPPOCAMPAL BDNF LEVELS AND ALLEVIATES DEPRESSIVE-LIKE BEHAVIOR IN AGED RATS

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PURPOSE

It is well recognized that major depressive disorder is associated with inflammation. Accumulating evidence has reported that depressive patients exhibit an increase in inflammatory cytokine levels as well as an activation of the inflammatory response. Recently, we showed peripheral inflammation and neuroinflammation as shown increased plasma and hippocampal tumor necrosis factor (TNF)-alpha levels, in addition to decreased hippocampal brain derived neurotrophic factor (BDNF) expression in aged rats [1]. We have previously reported beneficial effects of resveratrol on cognitive functions in aged rats [2]. Therefore, our objective was to assess in aged rats whether chronic resveratrol treatment alleviates depressive-like behavior and hippocampal BDNF expression and attenuates neuroinflammation.

METHODS

Groups:

Rats were divided into four equal groups: **Young control** (4 month old, 250–300 g), **resveratrol-treated control** (4 month old, 50 mg/kg/day, ip., during 12 weeks) **aged** (24 month old, 400–450 g) and **resveratrol-treated aged** (24 month old, 50 mg/kg/day, ip., during 12 weeks) male rats were used.

Forced swimming test (FST) and Sucrose consumption test (SCT):

FST and SCT were used to determine the effects chronic resveratrol treatment on depressive-like behavior in aged rats.

Immunohystochemistry:

Hippocampal brain derived neurotrophic factor (BDNF) expression were assessed by immunohistochemically.

ELISA:

Hippocampal TNF-α and IL-1 Beta levels were assessed with an ELISA kit according to the manufacturer's instructions.

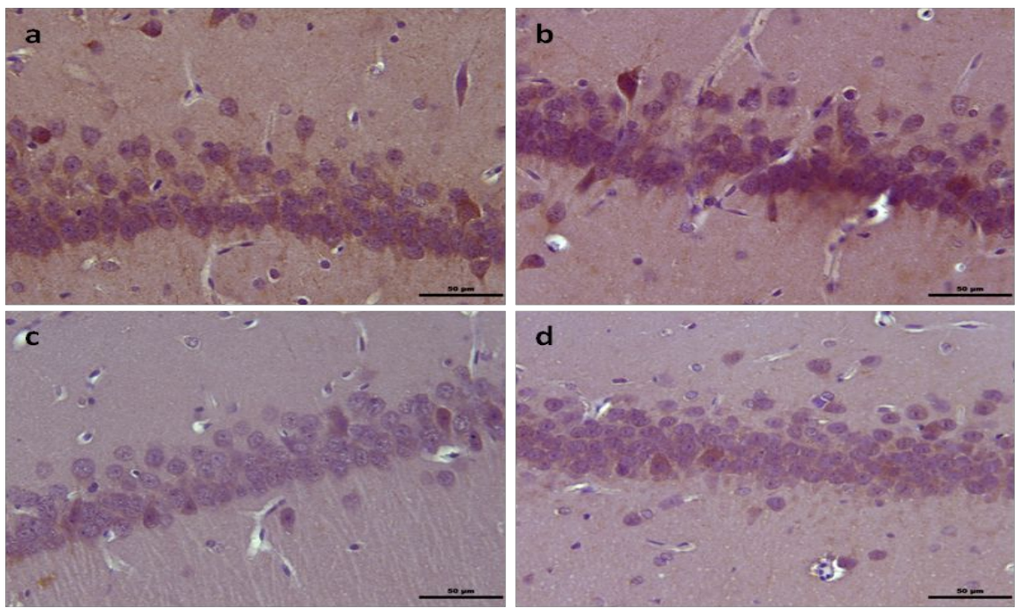
Data Analysis:

The significance was conducted by one-way ANOVA followed by a post hoc Tukey-Kramer test. The immunoreactivity scores were compared by the Kruskal–Wallis test following Dunn's multiple comparison test; $p < 0.05$ was considered significant.

RESULTS

Hippocampal BDNF Levels

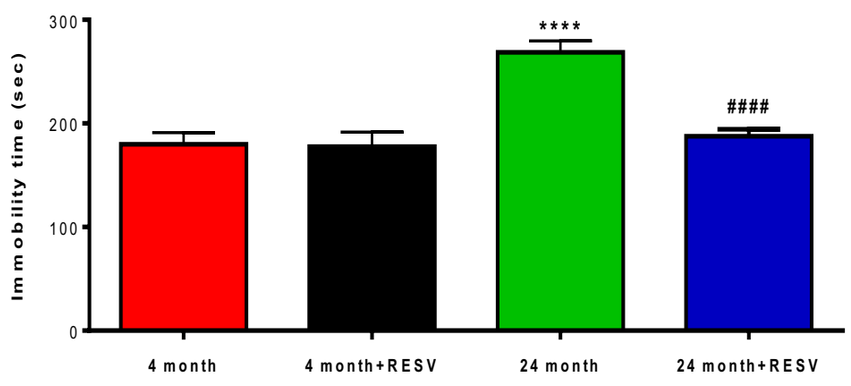
4 month **4 month+RESV**



24 month **24 month+RESV**

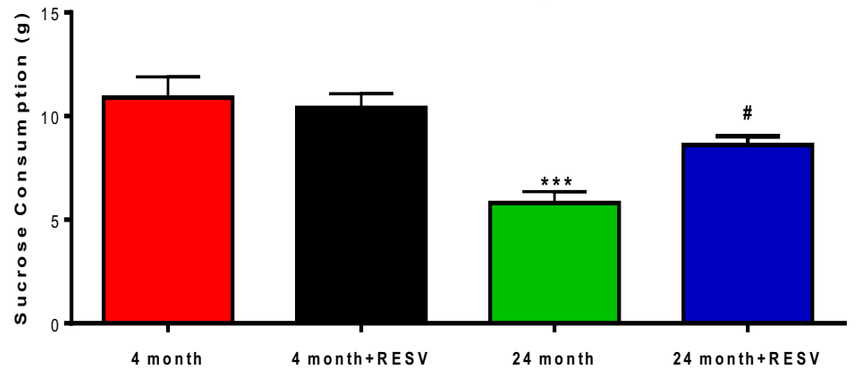
Kruskal-Wallis test showed that the hippocampal BDNF levels differed significantly between the three groups. BDNF immunoreactivity were decreased in aged rats in compared to young control group ($p<0.05$). However, there were no differences between resveratrol-treated aged group and the young control group ($p>0.05$).

Effects of aging and chronic resveratrol treatment in the forced swimming test



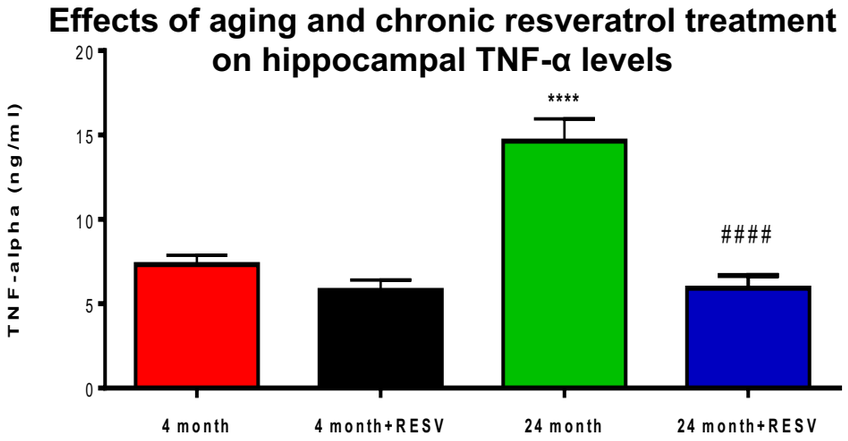
In the FST, aged rats exhibited more immobility than age-matched Wistar rats and there was no difference between resveratrol-treated aged rats and young control rats.
****A significant differences compared with the young control rats, where $p<0.0001$.

Effects of aging and chronic resveratrol treatment in the sucrose consumption test



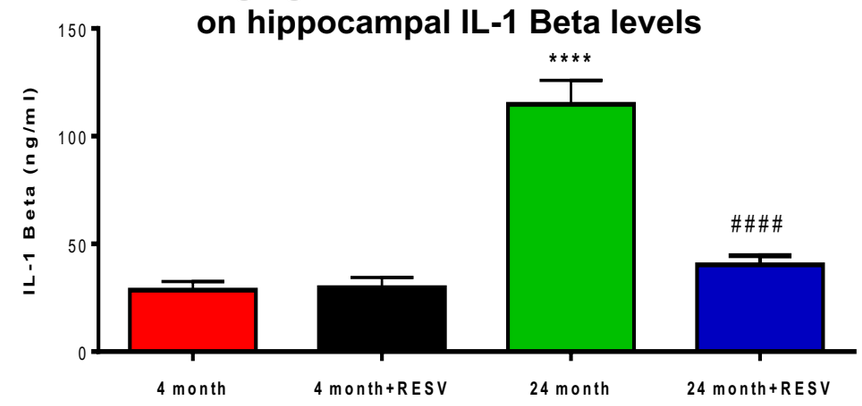
In the SCT, aged rats consumed less sucrose solution than young control rats. However, in resveratrol-treated aged rats, the sucrose consumption did not differ significantly from the young control rats.
***A significant differences compared with the young control rats, where $p<0.001$.

Effects of aging and chronic resveratrol treatment on hippocampal TNF-α levels



Hippocampal TNF-alpha levels were significantly elevated in aged rats and there was no difference between resveratrol-treated aged rats and young control rats.
****A significant differences compared with the young control rats, where $p<0.0001$.

Effects of aging and chronic resveratrol treatment on hippocampal IL-1 Beta levels



Hippocampal IL-1 Beta levels were significantly elevated in aged rats and there was no difference between resveratrol-treated aged rats and young control rats.
****A significant differences compared with the young control rats, where $p<0.0001$.

CONCLUSION

Our data demonstrated that resveratrol exhibited antidepressant-like behavior in aged rats through reduced neuroinflammation and also maintaining neurogenesis, suggesting that anti-inflammatory treatment could be a new therapeutic approach to alleviate depressive-like behavior in aging.

REFERENCES

[1] Yazir, Y., Utkan, T., Demirtas-Sahin, T., Gocmez, S.S., Gacar, G., Arkan, S., Karson, A., 2016. Etanercept improves cognitive deficits by reducing both peripheral inflammation and neuroinflammation and maintaining hippocampal BDNF levels in aging. Eur J Neuropsychopharm 26(Suppl 2), S615.

[2] Gocmez, S.S., Gacar, N., Utkan, T., Gacar, G., Scarpace P.J., Tumer, N., 2016. Protective effects of resveratrol on aging-induced cognitive impairment in rats. Neurobiol Learn Memory 131, 131-136.

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*No potential conflict of interest.