ABSTRACT

THE EFFECT OF GONADAL STEROIDS ON COGNITION IN AGED RATS

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Age-related cognitive decline along with the more sudden cognitive decline that accompanies senile dementia (SD) have become closely associated with gonadal steroid reduction. The incidence and risk of SD are greater in postmenopausal females than males of a similar age cohort. Similarly, the scale of the change seen in gonadal steroid production in ageing females is greater than that seen in ageing males. Data also suggest that postmenopausal women taking oestrogen (E_2) are less likely to suffer from SD, have delayed onset or reduced severity of the condition as compared to their age-matched counterparts. Interestingly, in contrast to postmenopausal women, the basal plasma oestradiol level in males increases moderately as they age. In this study, the relative effect of E_2 insufficiency and high E_2 levels on learning and memory in aged male rats were examined to determine whether E_2 differentially influences learning and memory in ageing male versus female rats. The effect of testosterone on the rate of acquisition and retrieval of the behavioural task was also evaluated. Eighteen 24 months old male rats were assigned to three treatment groups (n = 6 per group), *viz:* oestradiol, anastrozole (an aromatase inhibitor) and oil; and their performance compared with that of twelve non-treated aged male and twelve aged female rats

(controls) on a negative patterning discrimination behavioural task. Animals were trained in an operant system. Rats learned (and were rewarded) to press a lever when a single stimulus, light or tone (L^+/T^+) was presented and to avoid pressing when both stimuli, light and tone (LT^-), were simultaneously presented. Upon attainment of 75% correct performance rate, half of the male controls were orchidectomized (OCH) and half of the female rats were ovariectomized (OVX). Memory was then assessed in all groups following a two (2) week delay interval and subsequently, at two week intervals, until the extinction of negative patterning discrimination memory traces. Following extinction, the OCH and OVX groups were placed on oestrogen. All groups were then retrained for seven (7) days and reassessed after a 2 week delay interval. Aged male rats chronically treated with oestradiol showed a significant enhancement of learning ($p = 0.007$); those with low oestrogen (anastrozole group) showed a significant impairment in learning ($p < 0.001$). Additionally, aged control males out-performed their female counterparts ($p < 0.001$). Also, the oestradiol treated animals showed a significant ($p < 0.001$) increase in time-to-extinction of negative patterning discrimination as compared to anastrozole, oil and control groups. These findings suggest that 17β-oestradiol enhances acquisition and retention of negative patterning discrimination in aged male rats.

Keywords: Oestrogen; age-related cognitive decline; senile dementia; negative patterning discrimination; aged rats; learning and memory.