Role of paroxetine in brain cytokine changes after interferon-α treatment

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Purpose: The purpose was to explore the role of paroxetine (SSRI) in brain cytokine changes after chronic interferon-α (IFN-α) treatment in rats since it may account for depression in the patients treated for hepatitis C and certain cancers (Schaefer et al., 2002).
Method: *Rats* - Male Wistars (250-300 g) were assigned as 4 groups of 10: (1) saline control - subcutaneous injection of 0.9% Saline (0.2 ml/kg) daily for 7 weeks; (2) paroxetine control - paroxetine (10 mg/kg, oral) for 7 weeks; (3) Interferon (IFN) - saline for 14 days followed by subcutaneous injection of IFN-α (provided by Schering Plough) (50,000 IU/kg) 3 days/week for 5 weeks; (4) paroxetine + interferon (P+IFN) - paroxetine for 14 days followed by IFN-α for 5 weeks.
Biochemical procedures: At the end of the experiment, rats were euthanized and the prefrontal cortex, hypothalamus and hippocampus were dissected out on the ice. The brain tissues were stored in Protease inhibitor cocktail at -70°C. Total protein concentrations of specific brain areas were analysed in homogenate using Lowery's method. The supernatant of the homogenates after centrifugation were used for analysis of cytokines. The pro-inflammatory IL1-β, TNF-α and anti-inflammatory IL-10 cytokines were analysed using DuoSet ELISA reagents from R&D System.
Data analysis: The multiple comparisons between groups were analysed using one-way ANOVA with post-hoc Bonferroni correction. The probability of 0.05 or below was considered as significant.
Results: In prefrontal cortex area, the pro-inflammatory cytokine IL1-β showed the highest in IFN group and lowest in paroxetine group ($F=3.5$; $p=0.027$) and the anti-inflammatory cytokine IL-10 also showed highest in IFN group and lowest in paroxetine group ($F=6.4$; $p=0.002$). In hypothalamus, the pro-inflammatory cytokine IL1-β showed the highest in IFN group and lowest in paroxetine group ($F=21.4$; $p=0.000$) and the anti-inflammatory cytokine IL-10 also showed highest in IFN group and lowest in paroxetine group ($F=22.4$; $p=0.000$). In hippocampus, only the anti-inflammatory cytokine IL-10 showed significant difference and was highest in paroxetine group and lowest in IFN group ($F=5.4$; $p=0.004$).
Discussion and Conclusions: Both pro- and anti-inflammatory cytokines in prefrontal cortex and hypothalamus were highest in IFN group. In paroxetine pre-treated group, high production of those cytokines were not observed. In addition, the paroxetine alone group showed opposite effects. Therefore, paroxetine (SSRI) pre-treatment seems to prevent the development of depressive symptoms in chronic IFN-α treatment.

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