

Interferon alpha induced depression-like behaviour in the rat

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Background

One of the accepted pathophysiological mechanisms of major depressive disorder is activated inflammatory response system (IRS) which is indicated by increased production of pro-inflammatory cytokines. The interferon- α (IFN- α) is a pro-inflammatory cytokine used in the treatment of chronic hepatitis C infection and certain type of cancer that may and this treatment can induce depressive symptoms as one of the common side effects. Here, we discuss about the behavioural changes in IFN- α treated rats as a model of activated IRS.

Animals and behavioural assessment

Rats – Male Wistars (250-300gm) were assigned as 4 groups of 10: saline control - subcutaneous injection of 0.9% Saline (0.2ml/kg) daily for 7 weeks; paroxetine Control - paroxetine (10mg/kg, oral) for 7 weeks; Interferon (IFN) - saline for 14 days followed by subcutaneous injection of Interon A (IFN- α) (provided by Schering Plough) (50,000 IU/kg) 3 days/week for 5 weeks; paroxetine + Interferon (P+IFN) - paroxetine for 14 days followed by Interon A for 5 weeks.

Behavioural and Biochemical procedures – The behavioural tests were started two week after interferon. Open field test was performed in a square arena with 5 min session per day for four days. Morris water maze test was performed in a water tank (21°C) with invisible escape platform on 3 subsequent days with 8 trials a day and a probe trial after the last trial. Home Cage Emergence test was applied once a week. The latency periods to emerge from the home cage were recorded. Data recording and analyses for open field test and water maze were done using EthoVision software.

The pro-inflammatory IL1- β , TNF- α and anti-inflammatory IL-10 cytokines were analyzed in the prefrontal cortex, hypothalamus and hippocampus areas of the brain and supernatant from both unstimulated and stimulated whole blood culture.

Results

In open field, the IFN α treated rats showed anxiety behaviour compared to the rats from the other groups. There was no significant difference in home cage emergence test, Morris water maze and object recognition test. There is no significant difference in plasma corticosterone between groups. The pro-inflammatory cytokines (TNF α , IL1 β and IFN γ), were significantly higher whereas the anti-inflammatory cytokine, IL10 was lower in the stimulated whole blood culture of IFN α treated rats. In the brain, both pro-inflammatory cytokine IL1 β and anti-inflammatory cytokine IL10 were higher in hypothalamus of the IFN α treated rats; by contrast the concentration of IL10 was lowest in hippocampus region of this group compared to the other groups. The paroxetine pre-treated rats did not show these behaviour and cytokine changes following IFN α treatment.

Conclusions

The pro- and anti-inflammatory cytokines could activate the immune response and induce behavioural changes and those changes were attenuated by the pre-treatment with SSRI, paroxetine. Open-field test might be the most sensitive behavioural test in measuring immune activation-related behavioural changes.