The Effect Of Intra-striatal Injection Of The Inflammagen, Lipopolysaccharide, On Expression Of The Cannabinoid Type-2 (CB_2) Receptor In The Rat Brain

Ruth Concannon, Bright Okine, David Finn, Eilis Dowd. National University of Ireland, Galway, Galway, Ireland

It is becoming increasingly evident that neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease, are associated with neuroinflammation that may actually contribute to the neurodegenerative process (Glass *et al*., 2010). The microglial cannabinoid type-2 (CB_2) receptor is emerging as a potential anti-inflammatory target in such conditions (Gowran *et al*., 2011). Increased understanding of CB_2 receptor expression in inflammation-driven animal models of neurodegenerative disease is essential for valid preclinical assessment of the anti-Parkinsonian efficacy of drugs targeting the CB_2 receptor. Thus, the aim of this study was to determine if striatal CB_2 receptor expression is altered in the lipopolysaccharide (LPS) model of Parkinson's disease.

Adult male Sprague Dawley rats (n=28) were injected stereotactically with LPS (10 µg in 2 µl of sterile saline) unilaterally into the striatum under 2.5% isoflurane anaesthesia. Rats were sacrificed at Days 1, 4, 14 and 28 (n=7 per time-point) and expression of the CD11b (a microglial marker) and CB_2 genes was assessed by qRT-PCR on striatal samples from both injected and uninjected sides of the brain. All data are expressed as mean ± SEM and analysed by two-way ANOVA (with Side and Time as factors) with *post-hoc* Bonferroni testing where appropriate ($P<0.05$ was deemed significant).

We found that unilateral injection of LPS into the striatum induced a significant increase in levels of CD11b mRNA on the injected striatum (Side, $F_{(1,43)}=11.54$, $P<0.0001$). This effect was significantly pronounced at the Day 4 time-point (Day 1, Uninjected: 100±23%, Injected:

267±32%; Day 4, Uninjected: 100±33%, Injected: *955±434%; Day 14, Uninjected: 100±16%, Injected: 802±427%; Day 28, Uninjected: 100±16%, Injected: 237±67%; *$P<0.05$, vs. uninjected side). Unilateral LPS injection into the striatum also induced a significant increase in levels of CB_2 mRNA on the injected side (Side, $F_{(1,42)}=23.39$, $P<0.0001$). This effect was significantly pronounced at the Day 4 and Day 14 time-points (Day 1, Uninjected: 100±40%, Injected: 449±137%; Day 4, Uninjected: 100±12%, Injected: *1018±210%; Day 14, Uninjected: 100±19%, Injected: ***1540±615%; Day 28, Uninjected: 100±46%, Injected: 490±145%; *$P<0.05$, ***$P<0.001$ vs. uninjected side).

In conclusion, this study has revealed that levels of striatal CB_2 receptor mRNA are significantly increased in the inflammation-driven LPS model of Parkinson's disease. These data indicate that this model may be useful for researchers investigating the CB_2 receptor as a target for anti-inflammatory disease modification in Parkinson's disease.

Supported by: Health Research Board (RHB0817)

References

Glass CK et al, Cell 140:918, 2010.

Gowran A et al, CNS Neurosci Ther 17:637, 2011.