It is widely known that oestrogen is neuroprotective [1] through various mechanisms which suggest that sex hormone levels, thrombotic mechanisms and inflammatory processes are strongly interconnected in predicting the outcome and consequences of cerebral ischaemia [2]. Cerebral ischaemia is associated with parameters of altered blood coagulation which may lead to the occlusion of blood vessels; including increased thrombin activity, elevated fibrinogen levels, altered fibrin network ultrastructure, increased platelet counts and even resistance to fibrinolysis [3,4]. Because platelet ultrastructure is altered in conditions like thrombosis and associated with stroke [5,6], the question arises what insight ultrastructural analyses of platelet morphology may provide into the role of oestrogen during ischaemic insult.

A hyperglycaemic modification to the two-vessel occlusion model for inducing experimental cerebral ischaemia was established in Sprague Dawley rats, divided into three experimental groups (males, cyclic and acyclic females). Subsequent to termination at four intervals, neural tissue integrity levels were correlated to corresponding platelet ultrastructure so as to determine whether there is an association between cerebral ischaemia and altered platelet ultrastructure.

It is apparent in the results that under the influence of oestrogen in cyclic females, there was indeed lesser neural tissue damage and a reduced overall degree of inflammation evident in chemical analysis and platelet ultrastructure when compared to males and acyclic (ovariectomised) females. Mirroring the biochemical ischaemic cascade [2], inflammation is shown to peak early in the morphological evidence. Platelet morphology suggests that the largest shock due to cerebral apoptosis indeed takes place within the first 24 hours after insult. At this time males and acyclic females displaying necrotic ultrastructure, whereas cyclic females are rescued by oestrogen's neuroprotective and anti-inflammatory effects. At 48 hours, the largest disruption of the blood brain barrier takes place, and this is again evidenced by the extension of platelet pseudopodia.

In conclusion, physical neural injury is closely shadowed, if not preceded, by inflammatory changes in the coagulation system, particularly manifested in platelet ultrastructure. Ultrastructural platelet study may be used successfully to follow the progression of events of cerebral ischaemia and possibly assist in the assessment of treatment strategies and their effects on haemostasis [7].

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Fig. 1: Platelet morphology representation of cyclic females. A: pre-ischaemia control minimally activated, post-ischaemic reperfusion B: 2h post-reperfusion indicative of inflammation, C: 24h post-reperfusion demonstrating anti-inflammatory effects of oestrogen, D: 48h post-reperfusion inflammation around second BBB disruption. (Scale bar = 200nm)

Fig. 2: Platelet morphology representation of males. A: pre-ischaemia control minimally activated, post-ischaemic reperfusion B: 2h post-reperfusion indicative of inflammation, C: 24h post-reperfusion 70% of platelets necrotic due to low oestrogen levels, D: 48h post-reperfusion inflammation around second BBB disruption. (Scale bar = 200nm)

Fig. 3: Platelet morphology representation of acyclic females. A: pre-ischaemia control displaying thrombotic preparedness, post-ischaemic reperfusion B: 2h post-reperfusion soothed inflammation, C: 24h post-reperfusion 60% of platelets necrotic, D: 48h post-reperfusion inflammation around second BBB disruption. (Scale bar = 200nm)