THE EFFECT OF A DOPAMINERGIC ANATAGONIST ON THE INTRACEREBRAL ABILITY TO ELIMINATE NITROXIDE RADICALS IN RATS. THE APPLICATION OF *IN VIVO* BRAIN DIALYSIS TO *IN VIVO* ESR

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The acute administration of a dopaminergic antagonist, such as haloperidol (HPD), is well known to cause an increment in the turn-over of dopamine, and it has been hypothesized that the excessive turn-over causes an over-production of free radicals, which damage catecholamine neurons. To overcome the difficult technical problems of the simultaneous estimation of the production of endogenous free radicals and functions of the defense system, we utilized 700 MHz-microwave ESR and analyzed the intracerebral ability to eliminate nitroxide radicals, which was exogenously applied by *in vivo* microdialysis techniques to the striatal extracellular space of rats through a radical-introducer. The radical-introducer was stereotaxically implanted into the rat's right striatum followed by restraining carefully in the ESR spectrometer. Following 6 hrs perfusion of nitroxide, the microinfusion pump was stopped, and each rat was administered 4.5 mg/kg of HPD (0.9 ml/kg, G-HPD; n = 6) or 0.9 ml/kg of physiological saline (G-sln; n = 6) respectively, via the peritoneal route. Because of exponential decays of ESR signals, the perfusion areas were observed in both groups, and the half-life was used as a marker for the elimination of nitroxide. The half-life in G-HPD was statistically longer than that of G-sln. In this experimental protocol, decay of the ESR signal might have been mainly due to depriving nitroxide of paramagnetism. Thus, the intracerebral capacity to eliminate nitroxide in terms of the half-life reflects a reducing ability in the brain. Therefore, the significant difference in the half-life between G-HPD and G-sln suggests that the reducing ability in the brain of acutely administered HPD is decreased compared with that of the control rat. We conclude that this exhaustion of the reduction system plays an important role in HPD-induced neurotoxicity in catecholamine neurons, and speculate that this methodology may be useful in the assessment to estimate the imbalance between offense and defense from free radicals.