

Effects of Caffeine on Dopamine and Acetylcholine Release and on Short Term Memory Function: A Brain Microdialysis and Spatial Delayed Alternation Task Study

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SUMMARY

The effects of caffeine have been studied in freely moving rats implanted with concentric microdialysis probes in the nucleus accumbens (NAc) shell and core and in the medial prefrontal cortex (PFCx). Intravenous administration of caffeine (0.25, 0.5, 1.0, 2.5 and 5.0 mg/kg) dose-dependently increased dopamine (DA) and acetylcholine (ACh) dialysate concentrations in the PFCx, while failing to affect DA in the NAc shell and core.

Such effects were duplicated by intravenous administration of the selective antagonists of adenosine A1 and A2a receptors, DPCPX (0.0625-1.0 mg/kg i.v.) and SCH 58216 (0.0625 - 1.0 mg/kg i.v.), respectively. The effect of caffeine on cortical DA and ACh transmission was also studied in rats chronically administered with caffeine (25 mg/kg/twice a day/seven days). At the end of this treatment rats become tolerant to the locomotor stimulating effects of a dose of caffeine of 1 and 2.5 mg/kg i.v.; these doses increased dialysate ACh in the PFCx but failed to affect DA release in this brain region. In non-tolerant subjects caffeine stimulated DA and ACh release in the PFCx while in tolerant subjects stimulated only ACh release.

The effect of the acute systemic administration of caffeine (1.0, 2.5 and 5.0 mg/kg i.p.) was also studied in the performance of a spatial delayed alternation task to assess working memory efficiency in rats. Administration of caffeine (2.5, 5 and 10 mg/kg i.p.) failed to affect the number of correct responses/trial in rats performing at $62 \pm 3\%$ correct (baseline) in a spatial alternation task made up by ten couples of a forced run followed by a choice run. These observations indicate that the psychostimulant properties of caffeine are differentiated from the property of stimulating DA release in the nucleus accumbens shell, a property that caffeine, in contrast with most drugs of abuse, does not possess. This, in turn, is consistent with the lack of addictive properties of caffeine. The dissociation between tolerance to the locomotor effects of caffeine and stimulation of ACh release in the prefrontal cortex suggests that this effect might be correlated to the arousing effects of caffeine as distinct from its locomotor stimulant properties. Finally, the present results indicate that caffeine does not improve nor impair short-term memory.