The SH rat model of ADHD has profoundly different catecholaminergic responses to amphetamine’s enantiomers compared with Sprague-Dawleys

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INTRODUCTION

The juvenile, spontaneously hypertensive (SH) rat has been used widely as a model of attention deficit hyperactivity disorder (ADHD) because it is hyperactive, impulsive and inattentive. Moreover it has been reported that amphetamine (d-AMP) and its enantiomers, d-AMP and l-AMP, which are effective treatments for ADHD, ameliorate these behavioural and cognitive deficits in the SH rats. Although d- and l-AMP produce their therapeutic actions by increasing dopamine (DA) and noradrenaline (NA) neurotransmission in the brain, their catecholaminergic profiles have not been previously compared in the SH and Sprague-Dawley (SD) rat strains to determine if there are important differences. To achieve this objective, we have carried out a dual-probe microdialysis study in both strains to compare the effects of d- and l-AMP on NA and DA efflux in the prefrontal cortex (PFC) and striatum (STR), respectively.

MATERIALS AND METHODS

Microdialysis experiments were performed using male SH or SD rats (250-350g, Charles River, UK). Two concentric dialysis probes (2 mm tip for PFC, 4mm tip for STR) were stereotaxically implanted into the PFC (coordinates:AP: +3.2 mm; L: -2.5 mm relative to bregma; V: -4.0 mm relative to the skull surface) and STR (AP: +0.2 mm; L: +3.0 mm; V: -7.8 mm). Coordinates are according to Paxinos and Watson. All procedures are described in detail by Kulkarni et al (2006).

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CONCLUSIONS

This is the first study to have compared the catecholaminergic profiles of amphetamine’s enantiomers in the SH and SD rat strains. The data show that d-AMP and l-AMP have very different effects on NA and DA neurotransmission in SH rats compared with SDs. The SH rats are more susceptible than the SDs to the pharmacological actions of both amphetamine enantiomers. The relative efficacy of l-AMP versus d-AMP was much greater in the SH rats than would have been predicted from the SD data. These results highlight the value of defining the pharmacological actions of drugs to treat ADHD in a validated animal model of the disorder.

REFERENCES