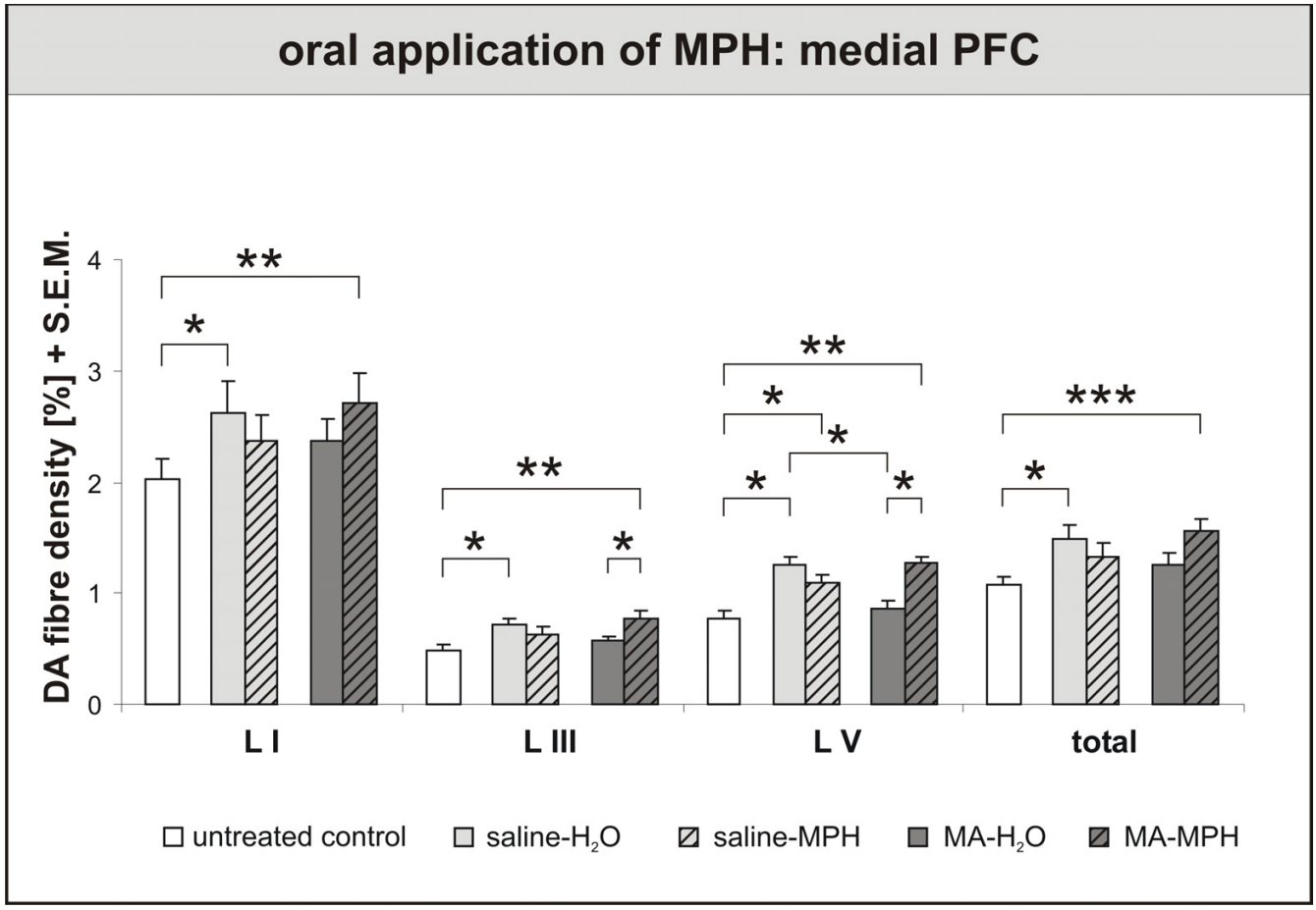

Figure 4

Oral application of Methylphenidate (MPH) – Effects on Prefrontal Cortex (PFC). Dopamine (DA) fibre density + S.E.M. is presented in lamina I, III and V of the PFC. Three effects are noteworthy. First, methamphetamine (MA) (= MA-H_2O) impaired the maturation of DA fibres in layer V, as had been shown before [78]. Second, MPH treatment for 30 days returned DA fibre densities to control values in MA-traumatised (= MA-MPH) animals. In control animals, in contrast, MPH (= saline-MPH) did not change the DA fibre densities, or even rather reduced them. Third, application of water (= saline-H_2O), i.e., pure handling, was highly effective in increasing the DA fibre densities in all layers. As isolated rearing by itself allows only for a suppressed maturation of DA fibres, this latter finding suggests that handling is a beneficial, "therapeutic" intervention (Lehmann, Grund et al., unpublished observations). For biostatistics two-way ANOVA with post-hoc contrast analysis among treated groups or pairwise comparisons with t-tests for untreated controls vs. treated groups were used for each lamina; significance values: *p < 0,05, **p < 0,01, ***p < 0,001.

very little is known about DA function of the amygdala and its modifications by MPH in these cases.

Therapeutic effects of methylphenidate

The most commonly used genetic rodent model of ADHD is the spontaneously hypertensive rat (SHR) [rev. in [68-70]]. In this model, reduced DA transmission was found in the PFC and striatum [7,71]. In the NAc, D1 receptor densities were increased, while D2 receptor densities were lowered [32,72-74] – which is in line with the current conception of ADHD in humans as outlined above. Oral MPH treatment for two weeks significantly changes these receptor densities to normal values [32,74]. Accordingly, Russell and colleagues [7] reported that MPH treatment alleviates ADHD-like symptoms in this rodent model.

In our lab, we studied the long-term plastic effects of MPH in a model of hyperkinetic behaviour that bears some resemblance to ADHD, i.e. gerbils after an early traumatic experience [33,34]. Early trauma is not a typical, but a possible factor in the aetiology of ADHD [75]. A single high dose of methamphetamine (MA), administered on postnatal day 14, causes a syndrome in young-adult gerbils that is characterised by hyperactivity, increased fearfulness and impaired PFC function in both working memory and extinction [76,77]. Neuroanatomically, this