DRD4 Exon 3 Genotype and ADHD: Randomized Pharmacodynamic Investigation of Treatment Response to Methylphenidate.

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Abstract

OBJECTIVES:
Dopamine plays an important role in modulating attention and motor behaviors, dimensions altered in attention deficit/hyperactivity disorder (ADHD). Numerous association studies have linked dopamine receptor 4 (DRD4) to increased risk of ADHD. This study investigated the effect of DRD4 exon 3 polymorphism on child behaviours in response to treatment with methylphenidate (MPH).

METHODS:
374 children diagnosed with ADHD (ages 6-12) were evaluated under three experimental conditions: baseline, placebo and MPH (0.5 mg/kg/day). This was a 2-week prospective within-subject, placebo-controlled, crossover trial. The Conners' Global Index for parents and for teachers was used to evaluate the behaviours of the children. One-way repeated measures analysis of variance was used to test the effect of the interaction between DRD4 genotype and experimental conditions.

RESULTS:
A significant interaction between DRD4 genotype and treatment was detected when the child's behaviour was evaluated by the parents (p = 0.035, effect size of 0.014), driven by a better treatment response in children homozygous for long 7-repeat allele.

CONCLUSIONS:
According to the parent assessment, children homozygous for the long 7-repeat allele were more responsive to experimental condition. This is the largest pharmacogenetic investigation of the effect of DRD4 exon 3 polymorphism in childhood ADHD.