

Shorter dinucleotide repeat length in the DRD5 gene is associated with attention deficit hyperactivity disorder

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It has been suggested that attention deficit hyperactivity disorder (ADHD) is associated with the dinucleotide repeat polymorphism of the dopamine D5 receptor (DRD5) gene and the Taq I polymorphism of the dopamine beta-hydroxylase (DBH) gene. Most of the previous family-based studies have reported preferential transmission of the DRD5 148-bp allele and the DBH Taq I A2 allele (Li *et al.*, 2006). We examined whether those polymorphisms were associated with ADHD in Korean children using both case-control and family-based analyses.

We genotyped 175 ADHD cases and 215 unaffected controls for case-control analysis. Three hundred and nineteen parents were assessed from 147 parent-child trios and 25 parent-child pairs for family-based analysis. The ADHD children and their biological parents were analyzed using the transmission disequilibrium test.

We did not find any evidence of an association between ADHD and the modal allele (the 150-bp allele: 32.5% in cases, 34.6% in controls) or the 148-bp allele (12.1% in cases, 15.4% in controls) of the DRD5 gene in either case-control or family-based analysis. Biased transmission of alleles was, however, observed. Two short alleles, the 142-bp allele ($\chi^2 = 3.86$, $P = 0.049$) and the 144-bp allele ($\chi^2 = 9.76$, $P = 0.002$), were preferentially transmitted to ADHD children, whereas a significant undertransmission was seen for two longer alleles, the 148-bp allele ($\chi^2 = 3.85$, $P = 0.049$) and the 152-bp allele ($\chi^2 = 7.11$, $P = 0.008$). No difference in the distribution of the four alleles between cases and controls was observed. In case, the 150-bp allele was the modal allele and the 146-bp allele was the antimodal (the second most common) allele. Since the distribution of alleles in the cases was bimodal, we dichotomized the alleles into short and long categories as previously described by Vanyukov *et al.* (1995).

Although the alleles with the dinucleotide repeat under or equal to 146 bp were classified as short alleles, the alleles with the repeat longer or equal to 148 bp were classified as long alleles. We found differences between cases and controls when all alleles were divided into short and long groups. Shorter alleles were more frequent in cases than in controls (odds ratio = 1.6; confidence interval at 95% = 1.2–2.1; $P = 0.002$). This finding was supported by family-based analysis, which showed preferential transmission of shorter alleles in ADHD ($\chi^2 = 8.19$, $P = 0.004$). No significant association or preferential transmission of any alleles was detected for the Taq I polymorphism of the DBH gene, although transmission disequilibrium test analysis revealed a tendency toward preferential transmission of the A1 allele ($\chi^2 = 1.95$, $P = 0.16$).

Even though our data do not support an association between the DRD5 148-bp allele and ADHD, some biased transmissions were detected in family-based analysis and shorter alleles were associated with ADHD in both case-control and family-based analyses. Interestingly, a recent family-based study reported a significant undertransmission for two longer alleles, the 150-bp allele and the 152-bp allele, in adults with ADHD (Squassina *et al.*, 2007). No evidence was found for an association of the Taq I DBH gene polymorphism with ADHD. Further studies are required to replicate our findings and to unravel the link between ADHD and the length of the dinucleotide repeat polymorphism of the DRD5 gene.

References

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