A genome-wide association study on medulloblastoma

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Medulloblastoma is a malignant embryonal tumor of the cerebellum that occurs predominantly in children. To find germline genetic variants associated with medulloblastoma risk, we conducted a genome-wide association study (GWAS) including 244 medulloblastoma cases and 247 control subjects from Sweden and Denmark.; Genotyping was performed using Illumina BeadChips, and untyped variants were imputed using IMPUTE2.; Fifty-nine variants in 11 loci were associated with increased medulloblastoma risk (p < 1 Œ 10; -5;), but none were statistically significant after adjusting for multiple testing (p < 5 Œ 10; -8;). Thirteen of these variants were genotyped, whereas 46 were imputed. Genotyped variants were further investigated in a validation study comprising 249 medulloblastoma cases and 629 control subjects. In the validation study, rs78021424 (18p11.23, PTPRM) was associated with medulloblastoma risk with OR in the same direction as in the discovery cohort (OR; T; = 1.59, p; validation; = 0.02). We also selected seven medulloblastoma predisposition genes for investigation using a candidate gene approach: APC, BRCA2, PALB2, PTCH1, SUFU, TP53, and GPR161. The strongest evidence for association was found for rs201458864 (PALB2, OR; T; = 3.76, p = 3.2 Œ 10; -4;) and rs79036813 (PTCH1, OR; A; = 0.42, p = 2.6 Œ 10; -3;).; The results of this study, including a novel potential medulloblastoma risk loci at 18p11.23, are suggestive but need further validation in independent cohorts.
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