Identification of genetic loci associated with nocturnal enuresis: a genome-wide association study

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What we know already:

- Nocturnal enuresis has high heritability of approximately 70%, based on twin studies. However, there have been inconsistent findings regarding the specific genes that are involved.

Aims of this study:

- This study aimed to identify genetic variants associated with nocturnal enuresis in a large Danish cohort.

Type of study and methods:

- This was a genome-wide association study of nocturnal enuresis cases (n=3882) and controls (n=31,073) in a Danish population-based case cohort. All significant genome-wide associations were also analysed in an independent Icelandic sample (5475 cases and 303,996 controls).

Findings:

- Six genetic variants at two loci on chromosome 6 and chromosome 13 were significantly associated with nocturnal enuresis.
- All 5 variants on chromosome 6 were replicated in the Icelandic cohort
- The common genetic variants explained 23.9–30.4% of the phenotypic variance in nocturnal enuresis

Risk genes included:

- PRDM13 – a nuclear protein involved in transcriptional regulation, with a circadian and age-dependent expression, which is thought to affect quality and depth of sleep in mice
- EDNRB – this receptor plays a role in endothelin-mediated natriuresis and diuresis, and is widely expressed in the lower urinary tract
- SIM1 – regulates the formation of arginine vasopressin-producing magnocellular neurons in the supraoptic and paraventricular nuclei; it is highly expressed in the kidney

Conclusions and clinical implications:

- This is the first report of genome-wide significant loci associated with nocturnal enuresis.
- There is a strong genetic vulnerability to nocturnal enuresis - it is nobody's fault; plausible risk genes have been identified