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Genetic analysis of obstructive sleep apnoea discovers a strong association with cardiometabolic health

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Five OSA-associated loci were found, highlighting the causal link between obesity and OSA, and providing evidence for non-BMI-dependent effects. OSA comorbidities were correlated genetically for OSA, showing these diseases may have a shared genetic basis. https://bit.ly/36Rfq1Y

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ABSTRACT There is currently limited understanding of the genetic aetiology of obstructive sleep apnoea (OSA). We aimed to identify genetic loci associated with OSA risk, and to test if OSA and its comorbidities share a common genetic background.

We conducted the first large-scale genome-wide association study of OSA using the FinnGen study (217 955 individuals) with 16 761 OSA patients identified using nationwide health registries.

We estimated 0.08 (95% CI 0.06–0.11) heritability and identified five loci associated with OSA ($p<5.0\times10^{-8}$): rs4837016 near *GAPVD1* (GTPase activating protein and VPS9 domains 1), rs10928560 near *CXCR4* (C-X-C motif chemokine receptor type 4), rs185932673 near *CAMK1D* (calcium/calmodulin-

dependent protein kinase ID) and rs9937053 near *FTO* (fat mass and obesity-associated protein; a variant previously associated with body mass index (BMI)). In a BMI-adjusted analysis, an association was observed for rs10507084 near *RMST*/*NEDD1* (rhabdomyosarcoma 2 associated transcript/NEDD1 γ-tubulin ring complex targeting factor). We found high genetic correlations between OSA and BMI (r_g=0.72 (95% CI 0.62–0.83)), and with comorbidities including hypertension, type 2 diabetes, coronary heart disease, stroke, depression, hypothyroidism, asthma and inflammatory rheumatic disease (r_g>0.30). The polygenic risk score for BMI showed 1.98-fold increased OSA risk between the highest and the lowest quintile, and Mendelian randomisation supported a causal relationship between BMI and OSA.

Our findings support the causal link between obesity and OSA, and the joint genetic basis between OSA and comorbidities.