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GENETICS OF THE ANDROGEN RECEPTOR INFLUENCES CRAVING OF MEN IN ALCOHOL WITHDRAWAL

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Introduction: The clinical observation suggests a relation between alcoholism and dysregulation of the hypothalamus-pituitary-gonadal hormone axis. Chronic alcohol abuse leads to hypogonadism and sexual dysfunction. Testosterone and the genetics of the androgen receptor [AR] are related to impulsivity as well as appetite/hunger, both associated with addiction.
Aims: This study investigated whether the length of a CAG trinucleotide repeat within the coding region of the AR is associated with alcoholism in general and whether it is linked to craving during withdrawal. Moreover, we concentrated on finding possible mediators of the observed effects.
Methods: We included 112 male inpatients who were admitted for detoxification treatment and who were compared to 50 age-matched controls. To measure the extent of craving we used the Obsessive Compulsive Drinking Scale (OCDS) on the day of hospital admission. For laboratory analysis we used whole blood (genetics) and serum (protein quantification).
Results: The group of patients (21.6±3.7 repeats) did not differ significantly from the control group (21.3±3.3 repeats, p=0.632) in terms of the number of CAG repeats. We found a significant negative correlation for the AR repeat length regarding OCDS-to (R^2=0.053, p=0.016) and OCDS-obs (R^2=0.058, p=0.011). Carrying out a path analysis of the mediating effect of leptin on the association between the number of CAG repeats of the AR and alcohol craving we found that direct effects (r=-0.144) accounted for 60% and indirect leptin-mediated effects (r=-0.096) for 40% of the total effect.
Conclusions: Today, the impact of the sexual hormone axis seems to be underestimated in alcoholism.

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