Epigenetic age in Prader-Willi Syndrome and essential obesity: a comparison with chronological and vascular ages.

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Background: Prader-Willi syndrome (PWS) is a rare genetic disorder mapping to the imprinted 15q11-13 locus, specifically at the paternally expressed snord116 region, which has been implicated in controlling epigenetic mechanisms. Some aspects of the PWSrelated clinical phenotype, such as the high mortality rate in adulthood, might be attributed to accelerated epigenetic ageing.

Objectives: the aim of the present case-control study was to evaluate epigenetic age, age acceleration, vascular age (VA), and vascular ageing in adults with PWS (n = 24; F/M = 11/13; age = 36.8 [26.6; 45.3] years; body mass index, BMI = 36.8 [33.9; 44.8] kg/m^2), compared with a sex- and age-matched group of subjects with essential obesity (EOB) (n = 36; F/M = 19/17; age = 43.4 [30.6; 49.5] years; BMI = 44.8 [41.2; 51.7] kg/m^2).

Results: in subjects with PWS, there was a younger epigenetic age and a lower age acceleration than in subjects with EOB. No differences were found between VA and vascular ageing in the two groups. Epigenetic age was associated with chronological age and VA within each group. For each group, no relevant associations of epigenetic age or age acceleration with demographic, biochemical, and clinical parameters were found. When considering individuals with PWS, there were no associations of epigenetic age with growth hormone (GH) deficiency, duration of hormone replacement therapy, and plasma levels of insulin-like growth factor 1 (IGF-1).

Conclusions: the hypothesis of accelerated epigenetic ageing in PWS should be rejected. Additionally, considering the existence of a SNORD116-dependent epigenetic dysregulation in PWS, the results of the present study might be misleading, since an epigenetics-based approach was used to measure ageing.