Rural environment as a risk factor for the age at onset of Machado-Joseph disease

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**ABSTRACT:**

**Background**: Machado-Joseph disease (SCA3/MJD) is a neurodegenerative condition caused by a dominant expansion of a CAG repeat (CAGexp). Most of the variability of the age at onset of symptoms (AO) remains unexplained, and environmental influences were scarcely studied. This study aimed to test if the AO of SCA3/MJD carriers can be associated with markers of the rural environment, such as demographic density (DeD), proportion of rural population (PRP), and consumption of untreated well water (CWW).

**Methods**: Symptomatic subjects from Rio Grande do Sul, Brazil, diagnosed between 1999 and 2017, and living in the same municipalities where they were born, were included, provided their CAGexp and AO were available, and the residual AO (RAO) could be estimated. DeD, PRP and CWW were obtained from the Brazilian Census of 2010. Participants were stratified in high versus low DeD, PRP and CWW groups, and their RAO were compared, for a p<0.05.

**Results**: 188 subjects were studied. The mean (SD) RAO of subjects from low and high DeD groups were -1.90 (6.98) and -0.11 (6.20) (p=0.046); from low and high PRP groups were -0.12 (6.20) and -1.90 (6.99) (p=0.046); and from low and high CWW groups were -0.11 (6.04) and -1.89 (7.11) (p=0.034).

**Conclusions**: AO of SCA3/MJD carriers was earlier in groups related to rural life. Our evidence suggests the presence of a risk factor in the rural environment, for earlier onset of symptoms in SCA3/MJD.