# Histamine-deficient mice have decreased occurrence of tibialis anterior electromyographic bursts during non-REM sleep.

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**Introduction**: Assumption of anti-histamine medications has been linked to increased restless legs syndrome (RLS) risk. However, the limited data available are conflicting, particularly concerning links with leg movements during sleep (LMS), which are common in RLS and involve bursts of tibialis anterior (TA) electromyogram (EMG). Here, we tested whether the occurrence of TA EMG bursts during non-REM sleep is altered in histidine decarboxylase knock-out (HDC-KO) mice with congenital histamine deficiency.

**Methods**: Six HDC-KO mice were implanted with electrodes for neck muscle EMG, bilateral TA-EMG, and electroencephalogram recordings, that were performed during the rest (light) period. Results were compared with those previously obtained with the same experimental protocol and scorer (VLM) on 9 congenic wild-type mice of the C57Bl/6J strain (Sleep Res. 2015; 24:695-701), analyzed by t-test with significance at $p < 0.05$, and shown as mean ± SE.

**Results**: HDC-KO and WT mice did not differ significantly in terms of sleep architecture. The numbers of total, "short-interval" (<10 s intervals), and -"periodic" (sequences of ≥4 bursts, 10-60 s intervals) TA-EMG bursts per hour non-REM sleep were significantly lower in HDC-KO (52 ± 12, 28 ± 8, and 6 ± 2) than in C57Bl/6J mice (110 ± 5, 68 ± 4, and 18 ± 4). The fraction of total TA-EMG bursts that were separated by short intervals was significantly lower in HDC-KO than in C57Bl/6J mice (49 ± 4% vs. 62 ± 3%).

**Conclusions**: HDC-KO mice show a markedly decreased occurrence of TA-EMG bursts, particularly of those separated by short intervals <10 s. These data are inconsistent with the hypothesis that anti-histamine medications promote RLS. Rather, the data suggest that LMS, and particularly LMS separated by short intervals, are a manifestation of arousal requiring the integrity of the histamine neurons, which are a known arousal system.