

## **The upper limit of the intermovement interval of periodic leg movements in sleep**

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While the lower limit of the periodic movements in sleep (PLMS) intermovement interval (IMI) range has been analyzed in detail, the upper limit of 90 s has never been challenged and was considered to be valid by Ferri et al. In 2006, only because a statistical difference between the IMI distributions of controls and restless legs syndrome (RLS) patients was found exactly up to this value. In order to evaluate statistically the upper limit of the PLMS IMI range, we performed a study on a large group of RLS patients in whom an approach based on the fitting of distribution functions to the observed data, within a distribution mixture analysis, was carried out.

All sleep leg movement onset-to-onset IMIs were counted, in each subject, for 2-second classes ( $0.5 < \text{IMI} \leq 2$ ,  $2 < \text{IMI} \leq 4$ ,  $4 < \text{IMI} \leq 6$ , ...,  $148 < \text{IMI} \leq 150$ ) and a grand average was obtained which was used for the following statistical analysis. A nonlinear least squares fitting (nonlinear regression) was used to find the function best fitting the main peak at approximately 20 s IMI (range 10-150 s) from a list of several functions, including the most common and known in statistics, such as normal, log-normal, gamma, chi-square, exponential, etc. The function that was found to provide the smaller loss function value was then retained; then a similar fitting was done for the observed data in the IMI range 2-10 s and the new fitted values were appended to the previous ones to recalculate the total loss function value and the new residuals. In the last step, a third function was fitted to the data observed in the IMI range 40-150 s and the corresponding values added to those obtained in the same range after the first fitting. Finally, again, the loss function value was computed and the final residuals plotted. After the last step, the loss function was reduced to a very low value (0.006); consequently, the plot of the residuals showed only very small deviations from zero. With respect to the specific purpose of this study, it was possible to note that fit 1 crossed fit 3 at IMI = 50 s (with a cumulative percentage of 98.4% of the

fitted values) and reached values very close to 0 at IMI = 60 s (with a cumulative percentage of 99.7% of the fitted values).

This analysis seems to indicate that the curve fitting best the PLMS IMI range explains the observed data only up to 60 s and that another phenomena might be at the basis of IMIs >60 s and that a more appropriate and data-driven upper limit for IMIs contributing to the PLMS count might be 60 instead of 90 s. Even if this is expected to have little influence on the final PLMS count (only 6.8% of the total number of IMIs within the 10-90 s range were above 60 s).