How significant is the difference between drug doses influencing the threshold for electroconvulsions?

Jarogniew J. Łuszczki1,*, Stanisław J. Czuczwar1,2

1 Department of Pathophysiology, Medical University of Lublin, Jaszewskiego 8, PL 20-950 Lublin, Poland
2 Department of Physiotherapeutics, Institute of Agricultural Medicine, Jaszewskiego 2, PL 20-950 Lublin, Poland

Correspondence: Jarogniew J. Łuszczki, e-mail: jarogniew.luszczki@amu.lublin.pl
* Recipient of the Fellowship for Young Researchers from the Foundation for Polish Science.

Abstract:
In this study, three computational methods (log-probit, one-way analysis of variance and linear regression analysis) were applied to statistically determine and compare a minimal dose of the antiepileptic drug – levetiracetam (LEV), which significantly increased the threshold for maximal electroconvulsions in mice. Results analyzed with log-probit method revealed that such a dose for LEV was 50 mg/kg. In contrast, one-way ANOVA indicated that the minimal dose of LEV, fulfilling the criterion of the significant increment in the threshold for electroconvulsions, was 100 mg/kg. Moreover, linear regression analysis allowed for the determination of threshold increasing doses by 20% (TID20) and 50% (TID50) for LEV, which amounted to 44 mg/kg and 150 mg/kg.

This comparative study demonstrated distinct differences between the electroconvulsive threshold-influencing doses of LEV calculated with these three methods, and only statistical evaluation of data using one-way ANOVA provided the most adequate determination of statistical significance. The application of log-probit method and linear regression analysis in the search for significant drug-dose effects should be substantially restricted to specific experimental conditions.

Key words:
electroconvulsive threshold, log-probit method, analysis of variance, linear regression analysis, dose-response relationship, levetiracetam

Introduction
The search for a pharmacologically active substance is usually performed in a series of screening tests in which the researchers and investigators attempt to provide overwhelming evidence that the examined compound is truly effective. In other words, the investigated agent is expected to produce a specific biological effect in a dose-dependent manner. On the other hand, in pharmacological studies, a special attention is paid to the evaluation of a minimal drug-dose that significantly influences the desired effects. For instance, in epilepsy research studies, a protection against experimentally induced seizures is the most important criterion for determining a minimal drug dose considerably suppressing the seizures. Noticeably, the search for the minimal dose of a drug that significantly reduces seizure activity in experimental...