Multilevel Meta-Analysis of Single-Subject Experimental Designs

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Single-case or single-subject experimental designs (SSEDs) are used when one is interested in the effect of a treatment for one specific subject, a person or another entity [1]. In these kind of designs, the subject is observed repeatedly before the treatment is introduced, and during or after the treatment (Figure 1). Because it is difficult to generalize the results from such an experiment to other subjects, the experiment can be replicated within or across studies. The results of several single-subject studies can be combined by performing a multilevel meta-analysis. In a multilevel meta-analysis, the results of each subject are first converted to an effect size, and next, these effect sizes are combined, taking into account that measurements are clustered in subjects, and subjects are effect size metrics: the effect of the treatment on the intercept and the effect of the treatment on the slope. They also proposed to standardize these regression coefficients, by dividing them by the residual within-phase standard deviation, so that these effects are comparable over subjects and studies. To combine the estimates of the effect on the intercept for multiple subjects in a meta-analysis, Equation 1 can be used:

$$b_{2jk} = \gamma_{200} + v_{20k} + u_{2jk} + r_{2jk}$$
(1)
with $v_{20k} \sim N(0, \sigma_{v_{20k}}^2), u_{2jk} \sim N(0, \sigma_{u_{2jk}}^2), r_{2jk} \sim N(0, \sigma_{r_{2jk}}^2)$

With b_{2jk} the ordinary least squares estimate (OLS) of β_{2jk} , the treatment effect on the intercept for subject *j* (*j* = 1, 2, ..., *J*_k) in study *k* (*k* = 1, 2, ..., *K*). This estimate equals an overall effect γ_{200} of the intervention on the intercept, plus a random deviation for study *k*, v_{20k} , a random deviation for subject *j* in study *k*, u_{2jk} , and a residual deviation, r_{2jk} because the treatment effect for that person is not perfectly estimated. The same equation can also be used for the effect of the treatment on the trend.

We evaluated the performance of this approach, using simulation research. The results indicate that a multilevel meta-analysis of standardized effect sizes is only suitable when the number of measurement occasions for each subject is 20 or more. On the other hand, when there are only a few measurements per subject, the estimated effects were found to be biased (Figure 2, left boxplot).



Figure 1. Graphical display of the basic single-case experimental design.



Figure 2. Distribution of the deviations of the estimated mean effect on the intercept of the treatment from its populations value, with the immediate treatment effect equal to 2, the effect on the trend equal to 0.2, the number of studies equal to 10, the number of subjects per study equal to 4, the number of measurements per subject equal to 10, the between-study and the between-subject variance equal to 2.

In a following step, we tested four ways to correct for the biased estimates of the effect. In the first approach, we used the formula of Hedges [4] to correct for small-sample bias, in the second approach, we estimated the residual within-subject standard deviation by performing a two-level analysis per study, in the third approach we estimated the residual within-subject standard deviation by performing a regression analysis per study, and in the fourth approach, we used iterative raw data bootstrapping to correct for bias [5]. Based on simulation studies, the first and the last approach seemed best suited to correct the bias (Figure 2).

References

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