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Research report

Comparing a single case to a control group – Applying linear mixed effects models to repeated measures data

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ABSTRACT

In neuropsychological research, single-cases are often compared with a small control sample. Crawford and colleagues developed inferential methods (i.e., the modified *t*-test) for such a research design. In the present article, we suggest an extension of the methods of Crawford and colleagues employing linear mixed models (LMM). We first show that a *t*-test for the significance of a dummy coded predictor variable in a linear regression is equivalent to the modified *t*-test of Crawford and colleagues. As an extension to this idea, we then generalized the modified *t*-test to repeated measures data by using LMMs to compare the performance difference in two conditions observed in a single participant to that of a small control group. The performance of LMMs regarding Type I error rates and statistical power were tested based on Monte-Carlo simulations. We found that starting with about 15–20 participants in the control sample Type I error rates were close to the nominal Type I error rate using the Satterthwaite approximation for the degrees of freedom. Moreover, statistical power was acceptable. Therefore, we conclude that LMMs can be applied successfully to statistically evaluate performance differences between a single-case and a control sample.

1. Introduction

In neuropsychological research, single-case studies represent a viable approach to investigate human cognition and its neural correlates (Caramazza, 1986; Shallice, 1979; Yin, 2009, 2011). Accordingly, single case experimental designs as well as appropriate descriptive and inferential statistical methods have regained much interest recently (see Evans, Gast,

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Perdices, & Manolov, 2014, for the introduction to a whole double issue of *Neuropsychological Rehabilitation*). Often, performance of a specifically impaired patient is compared to performance of a small control sample with $n < 20$ (Crawford & Howell, 1998). Because such designs usually do not allow for applying standard statistical procedures, Crawford and colleagues developed statistical methods particularly suited for comparing a single-case to a small control group (e.g., Crawford & Garthwaite, 2002, 2005; 2007; Crawford & Howell, 1998; Crawford, Garthwaite, & Porter, 2010; Crawford, Garthwaite, & Ryan, 2011). One of the most important methods suggested by Crawford and Howell (1998) in this context is a modified *t*-test to detect a deficit in performance, which is based on a procedure by Sokal and Rohlf (1995):

$$t = \frac{x^* - \overline{x_c}}{s_c\sqrt{(n_c + 1)/n_c}} \tag{1}$$

In this equation, x^* denotes the score of the patient, $\overline{x}_c$ the mean performance, s_c the standard deviation, and n_c the size of the control sample.

By means of Monte-Carlo simulations, Crawford, Garthwaite, Azzalini, Howell, and Laws (2006) showed that their modified *t*-test is reasonably robust in case of non-normally distributed data. Moreover, the power of the modified *t*-test was observed to be low to moderate (Crawford & Garthwaite, 2006) because of the usually only small to moderate sample sizes involved. Thus, the modified *t*-test has proven to be a convenient method to test for a (specific) deficit, when a patient's score is compared to the mean of a control group. Moreover, Crawford and Garthwaite (2005) developed the unstandardized and the revised standardized difference test for comparing the performance difference in two tasks for a single case against a small control group.

However, whilst the modified *t*-test and the revised standardized difference test are practicable tools for comparing single data points per participant, more complex study designs require different test procedures. For instance, a researcher might be interested in whether main effects or interactions in a repeated measures design differ between a single-case and a control group. In those cases, researchers have to make use of other methods. One approach, which has received increasing research interest in recent years, are linear mixed effects models (LMM; see West, Welch, & Galecki, 2006; for an introduction to linear mixed effects models). These mixed models have become more and more popular for analysing repeated measures data as well as clustered data (i.e., when data points within clusters are correlated). For instance, they are already in common use in different areas of research, for instance ecology and evolution (Bolker et al., 2009) or psycholinguistics (Baayen, Davidson, & Bates, 2008). Furthermore, LMM have also been found to be useful for analysing neuropsychological data such as neglect rehabilitation data (Goedert, Boston, & Barrett, 2013) and for the integration of results from single-case experimental designs within and across studies (Baek et al., 2014).

Against this background, we aimed at investigating whether LMM might also be applicable for comparing a single-case to a small control sample. Therefore, we were first interested in whether a *t*-test for the significance of a dummy coded predictor variable (1 for the single-case and 0 for the control sample) in a linear regression is equivalent to the modified *t*-test by Crawford and Howell (1998) (see also Corballis, 2009). As an extension to this idea, we then aimed at generalizing the modified *t*-test to repeated measures data using LMM to compare the performance difference in two experimental conditions found in a single participant against that of a small control group. We conducted Monte-Carlo simulations to investigate whether the suggested test procedures control the Type I error rates at their nominal levels and what their statistical power properties are.

2. Study 1: equivalence of the modified *t*-test and linear regression

In Study 1, we show that the modified *t*-test is identical to the *t*-test for a dummy coded predictor (1 for single-case and 0 for control sample) in a linear regression analysis. Let $\mathbf{y} = (y_1, y_2, \ldots, y_n)$ be the vector of data points collected for the single-case (y_1) and the control sample ($y_2, y_3, \ldots, y_n$) and $\mathbf{x} = (1, 0, \ldots, 0)$ the vector of the dummy coded predictor variable in the following regression equation:

$$y_i = \beta_0 + \beta_1 x_i + \varepsilon_i, \quad \textit{with } \varepsilon_i \sim N(0, \sigma^2) \ \textit{ and } \ i = 1, \ldots, n \tag{2}$$

β_0 is the parameter for the intercept and β_1 is the parameter for the dummy coded predictor. It can be shown that (the least squares estimate) $\widehat{\beta}_1$ is identical to the numerator of Equation (1), when inserting the specific dummy coded predictor variable and the general expression for the slope estimate:

$$\widehat{\beta}_1 = \frac{\sum_{i=1}^{n} y_i x_i - \frac{\sum_{i=1}^{n} y_i \sum_{i=1}^{n} x_i}{n}}{\sum_{i=1}^{n}(x_i - \overline{x})^2} = \frac{y_1 - \frac{\sum_{i=1}^{n} y_i}{n}}{\left(1 - \frac{1}{n}\right)^2 + (n-1)\left(-\frac{1}{n}\right)^2}$$
$$= \frac{\frac{ny_1 - \sum_{i=1}^{n} y_i}{n}}{\frac{n^2 - n}{n}} = \frac{(n-1)y_1 - \sum_{i=2}^{n} y_i}{n-1} = y_1 - \frac{\sum_{i=2}^{n} y_i}{n-1} \tag{3}$$

Thus, $\widehat{\beta}_1$ denotes the difference between the score of the single case (y_1) and the mean of the control sample and is, therefore, identical to the numerator $x^* - \overline{x_c}$ of the *t*-statistic in Equation (1). The intercept β_0 is estimated (least-squares estimate) by the mean of the control group:

$$\widehat{\beta}_0 = \overline{y} - \widehat{\beta}_1 X = \frac{\sum_{i=1}^{n} y_i}{n} - \frac{ny_1 - \sum_{i=1}^{n} y_i}{(n-1)} * \frac{1}{n}$$
$$= \frac{(n-1)\sum_{i=1}^{n} y_i - ny_1 + \sum_{i=1}^{n} y_i}{n(n-1)} = \frac{n\sum_{i=1}^{n} y_i - ny_1}{n(n-1)} = \frac{\sum_{i=2}^{n} y_i}{n-1} \tag{4}$$

The test statistic for a significant deviation of β_1 from zero follows a central *t*-distribution with $df = n - 2$ in case the null hypothesis holds and is given by:

$$t = \frac{\widehat{\beta}_1}{SE\left(\widehat{\beta}_1\right)} \tag{5}$$

We have already shown that the numerators of the *t*-test for the regression coefficient and the modified *t*-test are identical. Next we will demonstrate that also the denominators are identical. The standard error of $\widehat{\beta}_1$ is: