ISSN : 2350-0743

www.ijramr.com

International Journal of Recent Advances in Multidisciplinary Research

Vol. 09, Issue 10, pp.8022-8023, October, 2022

RESEARCH ARTICLE

META-ANALYSIS OF VEP VS SUBJECTIVE VISUAL ACUITY: THE CORRECT PARAMETER FOR 'EFFECT SIZE'

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ARTICLE INFO

Article History:

Received 18th July, 2022
Received in revised form
19th August, 2022
Accepted 27th September, 2022
Published online 30th October, 2022

Keywords:

Visual Acuity, Meta- Analysis, Effect Size, Heteroscedasticity, Critical Check Size, Bland-Altman Analysis, Breush Pagan test.

ABSTRACT

Regression analysis has been employed previously to express Visual Evoked Potential (VEP) VA in terms of its subjective equivalent. Bland-Altman analysis was also used in the modelling process to check for good agreement between test methods before deriving the regression equation. However, application of these methods to the full range of electrophysiological/subjective VA comparisons resulted in few making the cut for full analysis. This article considers the statistical parameters that were used in the past, and how they could be relaxed to increase inclusion in meta-analysis. The regression coefficient of VEP VA is the recommended 'effect size', and where a more sophisticated meta-analysis is possible, the degree of heteroscedasticity is proposed as a second variable.

INTRODUCTION

Visual Evoked Potentials (VEPs) have been used to assess Visual Acuity (VA) since the 1970's (Regan, 1977; Tyler, 1979), with the smallest stimulus element size eliciting a response (Tobimatsu 1995; Mackay 2003) or extrapolation of the spatial frequency-VEP amplitude function (Sokol, 1978; Norcia, 1985) defining VA. Recently ISCEV have created a protocol for ssVEPs that advocates the extrapolation method (Hamilton, 2021). The focus of this report, however, is the quantitative relationship between electrophysiological and subjective VA in a population, and steps towards its widespread clinical utility. The relationship between Step VEPs and Optotype Acuity Cards has been quantified for Ophthalmologically normal adults wearing a series of neutral density filters (Mackay, 2008). Using the smallest element size (critical check size = 'CCS') rather than extrapolation resulted in consistent agreement across the range of VA; a consistency that was extended over an even broader range of VA in a group of neurologically impaired children (Mackay, 2022). The relationships were described by equations expressing subjective VA as a function of VEP CCS, and in LogMAR units. Multiple regression modelling (MRM) of clinical and technical factors in the paediatric group resulted in two clinically applicable equations for Optotypes and Preferential Looking Cards respectively. A 'ten events per variable' minimum is advocated when choosing parameters to investigate during MRM (Introduction to Regression, 2005), ideally reinforced by a post-hoc power calculation (PASS Manual, 2022). The MRM comprises a series of univariate tests with the critical p-value set to $p<0.25$, to maximally retain possible influences on subjective VA. Regression of any proven influential parameters during this process, and their interactions with each other, is the next step. Factors can be added and removed in different combinations- with the goal of continually increasing test statistics. The statistical software can be set to include a constant term to encompass unexplained influences in the relationship and maintain homoscedasticity- this has been required in most of my analyses so far. The degree of heteroscedasticity in a relationship can be quantified statistically using a Breusch Pagan test (Breusch, 1979) which will be re-considered later. The original motive for modelling these relationships was to express electrophysiological VA in terms of 'gold standard' subjective tests, making the result meaningful to a range of healthcare professionals. The former, therefore, should be the independent variable in regression and the latter the dependent variable. Influential factors are best used to form subgroups with their own regression equation, for ease of interpretation, and to set the scene for subsequent meta-analysis. The coefficient of the VEP term in each equation is the 'effect size' for entry into the statistical software. There is a version of the meta-analysis software allowing for additional variables (Comprehensive Meta-analysis Software Manual, 2022) and so it is possible that the Breusch Pagan statistic could also be incorporated to identify what is and isn't contributing to the as yet unexplained variation (heteroscedasticity) in the relationship between tests.

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Bland-Altman Analysis (BA-A) is the method of assessing agreement between tests (Bland 1986). Mathematically, regression of BA-A data should be essentially flat, with a small 'r' value, and $p>0.05$. When used for screening in a meta-analysis, the BA-A step could be employed after MRM has identified subgroups, before expressing the final equations. However, if we want a range of independent sources in a meta-analysis, the $p>0.05$ threshold of BA-A may have to be relaxed to exclude only the most biased agreements. Numerically, this means reducing the critical p-value to 0.025. In my experience of reviewing electrophysiological and subjective VA comparisons (Mackay, 2008), the majority of studies showed divergence as VA gets poorer. Also, even a reasonably shallow regression line on BA-A can cross the x-axis giving artefactually small values for 'accuracy' therefore eliminating it from the possibilities for 'effect size' in meta-analysis. The accuracy and precision parameters of BA-A have been used extensively in a recent systematic review (Hamilton, 2021) which, using the extrapolation method of determining VEP VA, revealed mostly biased relationships between electrophysiological and subjective VA. This may have an anatomical or physiological basis, but equally could reflect the mismatch of resolution in measurement scales.

I have also found that even when data were unbiased in their agreement during BA-A, unexplained influences on subjective VA persisted, and a constant term was needed in the final regression equation to maintain homoscedasticity. As stated, the degree of heteroscedasticity can be quantified using the Breusch and Pagan test (Breusch 1979). In future, local studies might choose to include clinical and technical factors in MRM, allowing straightforward identification of 'effect sizes' for meta-analysis. However, existing data sets with just the two VA measures per subject could still be incorporated if clearly defined by clinical and technical subgrouping. Theoretically, Meta-analysis would pool all the data creating one equation for use by health professionals globally. However, the detailed comparisons between sub-groups will be enlightening in the first instance.

Acknowledgments

Thank you to my parents Alistair and Margaret Mackay.

I did not receive any funding for this work, but it was performed under an honorary contract with the University of Manchester using data collated from the literature , and collected at the Royal Hospital for Sick Children in Glasgow between 2000 and 2002.

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