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Statistical Approach to the Efficacy of Individual Cognitive Stimulation in Alzheimer's Disease: The Added Value of Meta-Regression and Subgroup Analysis

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Introduction: Alzheimer's disease (AD) is the most common form of dementia, accounting for approximately 60–70% of all cases. Its prevalence is expected to double by 2050, potentially affecting over half a million people in Portugal. Cognitive stimulation is a recommended psychosocial intervention for individuals with AD. To assess the effectiveness of such interventions, repeated-measures ANOVA or mixed linear models (MLMs) are commonly used.

Methods: Data were drawn from a multicenter randomized controlled trial with a repeated-measures experimental design (pre-intervention, post-intervention, and follow-up). Assessments were conducted at three time points: before the intervention (baseline, T0), immediately after its completion (T1), and 12 weeks later (follow-up, T2). Global cognitive functioning, memory, and executive function were assessed using standardized instruments. The 'moderate' and 'moderately severe' of the Alzheimer's Disease Severity classification were considered. The standardized mean difference (SMD), adjusted using Hedges' g method, was calculated to estimate the direction and magnitude of the effect between the experimental and control groups. Effects were presented using forest plots, and heterogeneity across outcomes was assessed using the I^2 , τ^2 , and Q-test statistics. In cases of low heterogeneity, the analysis was complemented with meta-regression models and subgroup analyses.

Results: Low heterogeneity was observed across group assessments ($I^2 = 23.1\%$; $\tau^2 = 0.035$; Q-test p-value = 0.22), leading to subgroup analysis and meta-regression to compare effects across severity levels. Subgroup analysis revealed a significant positive effect in the experimental group (0.4848, 95% CI [0.2222; 0.7474], $p < 0.001$). The meta-regression model, using severity level as an explanatory variable and SMD as the response variable, showed an intercept of 0.48 and a coefficient of -0.6891 (95% CI [-1.0911; -0.2872], $p < 0.001$).

Conclusions: This study demonstrated a significant difference between the two severity levels, suggesting that disease severity may moderate the intervention's effectiveness. The proposed statistical approach offers a viable alternative to standard models (ANOVA and MLM) in studies involving two or more experimental groups. These findings may have potential clinical relevance for evaluating the effectiveness of non-pharmacological interventions and strategies designed to promote cognitive health in older adults with dementia.

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