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META-ANALYSIS IN TRANSLATIONAL RESEARCH IS NOT A STRAIGHTFORWARD ROAD. A CASE-STUDY ON IL-6 AND DEPRESSION

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Background: In recent meta-analyses proinflammatory cytokines, such as the interleukin-6 (IL-6), have been associated with major depression in humans. We wanted to know if the prior accumulated evidence on animal experimentation could have lead and support these findings. Objectives: To perform a rapid review on the association of IL-6 and depression models in animal research, using stress based depression models differentiating between chronic and acute stress. Methods: A PubMed and OVID search was run with appropriate terms. Effect sizes (standardized mean differences, SMD) were estimated directly from the data and/or statistics reported in the included studies. We used a random effects model to pool the effect estimates and estimate prediction intervals and also a sensitivity analysis was performed. Results: Eleven trials on the alterations of IL-6 levels in acute stress based depression models were included. Overall, IL-6 increased in depression (random effects model SMD=1.72; I2=63.1% in plasma and 0.37≤SMD≤0.70; I2=0% in different parts of the brain). Sensitivity analysis showed no trial exerted a significant influence on the pooled estimate. Thirty-nine trials on the alterations of IL-6 levels in chronic stress based depression models were included. (random effects model SMD=1.29; I2=91.3% in plasma and $0.37 \le SMD \le 1.16$; $86.7\% \le I2 \le 95\%$ in different parts of the brain). Sensitivity analysis showed no trial exerted a significant influence on the pooled estimate. Conclusions: Although it seems to be an overall increase of IL-6, high heterogeneity was found between the models, the different areas studied and between trials. Similar problems could be presented in other areas of translational research, and must be deal with appropriately before jumping directly from the bench to the human.