"Statistical validation and inferences of endophenotypes"
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Endophenotypes, which involve the same biological pathways as diseases but presumably are closer to the relevant gene action than diagnostic phenotypes, have emerged as an important concept in the genetic studies of complex diseases. In this project, we propose to develop a formal statistical methodology for validating endophenotypes. The proposed method was motivated by the conditioning strategy used for surrogate endpoints commonly seen in clinical research. Indices such as proportion of heritability explained, adjusted association and relative heritability are used as operational criteria of validation. Besides, we will provide relevant confidence intervals for these indices for making statistical inferences. Using these confidence intervals, we will construct some criteria to help us search a useful endophenotype. Usefulness of the proposed methods will be demonstrated through computer simulations.

Keywords: endophenotype; genetic analysis; heritability; variance component analysis.