

## Response

## Response to Dr Bernard Carroll

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Sir

Dr Bernard Carroll is an internationally recognized scientist who has had a long and distinguished career and has made a number of significant contributions in the past to the field of Psychiatry. Unfortunately, his current Letter to the Editor seems to misinterpret the thrust of our paper published in *Neuropsychopharmacology*. This paper has three distinct and clear messages: (1) this large, multicenter international trial was unable to demonstrate a benefit for continuation augmentation treatment with risperidone when compared and contrasted with placebo, (2) the design and statistical analysis of continuation augmentation trials may require a reconceptualization in order for us to develop effective trials and (3) *post hoc* secondary analysis suggests that treatment-resistant depression is heterogeneous and that there may be a difference in terms of continuation response for people who were most unresponsive to monotherapy vs those who were partially responsive to monotherapy. The paper clearly states the primary hypothesis in Abstract, Introduction, and Methods. The paper repeatedly states in Abstract, Methods and in Discussion that continuation of risperidone augmentation therapy was not more beneficial than placebo, and hence the working hypothesis

was disproven. All secondary or *post hoc* analyses are clearly labeled as such. In addition, there are repeated disclaimers within the paper indicating that appropriate replication with double-blind, placebo-controlled studies using these preliminary data to generate appropriate hypotheses is necessary. The publication in *Neuropsychopharmacology* represents the first extensive and peer-reviewed presentation of our data. As the lead author of this publication, I apologize to Dr Carroll and any other reader who might have missed the three main points of the paper as we have emphasized above. I would like to thank the reviewers and the editors of *Neuropsychopharmacology* for having the courage to allow us to publish this negative finding.

**DISCLOSURE/CONFLICT OF INTEREST**

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