Author's response to reviews

Title: Mu opioid receptor availability in people with psychiatric disorders who died by suicide: A case control study.

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Author's response to reviews: see over
13th June 2012

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Dear Dr Patel:

Thank you for the Reviewers comments on our manuscript “Mu opioid receptor availability in people with psychiatric disorders who died by suicide.” In addressing these comments we feel that the revisions have improved the original manuscript to create a version suitable for publication. We would also like to take this opportunity to thank the reviewers for the time and energy they put into reviewing this manuscript.

Below we have addressed the comments made by each reviewer, where appropriate citing the section the amendment has been made in.

Reviewer: Maurizio Pomili.

1. The average time from discovery of the body to autopsy was 36 hours. This information has been included in the diagnostic evaluation on page 6.
2. The inter-rater reliability of the DIBS is described in the second citation given for the instrument (Hill et al., 1996). This information has also been added to the diagnostic evaluation on page 6.
3. The discussion section has now been modified to include a conclusion section (page 18).
4. Additional discussions regarding the findings in groups with disorders other than schizophrenia have been included in the discussion section (pages 15 & 16).
5. The article suggested by the reviewer has been added to the conclusion section (page 18).

Supriya Syal.

1. The helpful suggestions made by this reviewer regarding the simplification of the results section has been adopted (pages 11 - 13 and Table 2).
2. Whilst we appreciate this reviewers concern regarding the sizes of the groups, many studies in schizophrenia using postmortem CNS and neuroimaging are completed using smaller cohorts because of the difficulty in tissue collection and recruitment, respectively. However, we have analysed the data using strategies that are appropriate for the smaller sample sizes (non-parametric and the GLM where data was mixed) and used power analyses to further address the issue of small sample size (see discussion, page 18). Thus, we have made significant efforts to ensure the correct interpretation of the results we present.
This Reviewer also raised an issue with regards to our approach to data analyses. Importantly, consistent in having a complete experimental design before collecting data we made an *a priori* design to identify relationships between data using correlational analyses. Where strong relationships between data were found our *a priori* protocol was to use an ANCOVA to determine whether or not the effect of related variables impacted on our primary analyses. Thus, our analyses shows that the average age of the subjects with schizophrenia who died as a result of suicide was lower than that of the other groups and, most importantly, *that the effect of suicide was significant even when the impact of age and brain pH were taken into account*. We adopted this statistical approach upon the advice of a statistician and have used it in many previous manuscripts; changing analyses after the fact is not the best statistical practice. We note our approach was not seen as an issue by the other Reviewer.

3. The comparisons of the schizophrenia_suicide group to control but not schizophrenia_non_suicide were reported in order to keep the analyses in line with the original study in BA24. However, we recognize the value of the point made by the reviewer regarding comparisons between the groups with schizophrenia and this data has now been added to the manuscript (pages 12 & 13).

4. We agree that the long term effects of antipsychotics is a factor that cannot be discounted. The section of the discussion regarding antipsychotics as a potential confound has been expanded. However, it should be noted that one of the animal studies cited in this version had a treatment regimen that lasted for 24 weeks resulting in increased expression of mu opioid receptors.

Thank you for your attention to this matter, we look forward to hearing from you.

Sincerely,

Elizabeth Scarr
ARC Future Fellow