# FW: WKY?

From: **Patrick Lyden** | plyden@usc.edu Friday, Jun 11, 3:03 PM

To: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu
Cc: **Diniz, Marcio A** | Marcio.Diniz@cshs.org

Some information in #2 related to our paper.

> From: **I Mhairi Macrae** | Mhairi.Macrae@glasgow.ac.uk To: **Patrick Lyden** | plyden@usc.edu Thursday, Jun 10, 9:53 AM
>
> Dear Pat & EAB meeting participants,
>
> Many congratulations are due to you and your team at the co-ordinating centre and to the SPAN centres for making so much progress in the face of the COVID pandemic.
>
> It is already a huge data set to interrogate and I've really enjoyed pouring over the slides sent out for the meeting (I was on holiday till Sunday so have had more time to look over the data since the meeting).
>
> 1. Given the current issues with analysing the corner test data, I've focussed on looking at the Grid Test data where it appears more straightforward to look for potential treatment effects. Would it be possible to get one of the CC team to clarify the statistical tests used and comparisons made on graphs on pages 45 and 46 of the pdf?
>
> 1. With regard to a lack of correlation between functional deficits and lesion size, the inclusion of major white matter tracts such as the internal capsule within small lesions will give rise to significant functional deficits. (e.g. see Lecrux C., et al. Stroke (2008) 39(2):448-54 ) Another issue regarding sensorimotor functional deficits in rodents is their capacity to compensate & recover very quickly hence the difficulty in identifying the optimum timepoint for analysis of treatment effect .
>
> 1. With regard to inclusion of WKY, I agree with Marilyn and Mike but if no treatments are to be dropped at the end of Stage 1, it would add significantly to time and cost. Could this be considered for inclusion at Stage 3 and dependent on the results of Stage 2? If none of the treatments were to show efficacy in the

mouse, having this extra control, for the reasons Marilyn details below, would be extremely valuable.

With best wishes,

Mhairi

From: **Patrick Lyden** | plyden@usc.edu To: **Cipolla** Tuesday, Jun 8, 9:04 PM

Thank you Marilyn. Very helpful.

From: **Cipolla** | marilyn.cipolla@med.uvm.edu To: **Patrick Lyden** | plyden@usc.edu Tuesday, Jun 8, 11:03 AM

Hi Pat,
I think one reason to do the WKY in addition to SHR is for a species control Mike brought up. For example, if none of the treatments work in the SHR because it's the SHR that has poor collaterals and high sensitivity to ischemia, showing efficacy in the WKY could help to answer the question of the mouse model not being a good model. However, it would be a secondary control and would be expensive and time consuming. And it would be standalone since the other co-morbid models are in mice, potentially raising more questions if something worked in the WKY rat and not mice.

So I think in a perfect world with unlimited resources and time, I would definitely include the WKY. But those things do need to be considered.

Curious what the others think.

Congratulations again on a tremendous effort!

Best,
Marilyn