

# RE: [External] RE: topography

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From: **Patrick Lyden** | plyden@usc.edu

Tuesday, Jun 8, 3:19 PM

To: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Cc: **Diniz, Marcio A** | Marcio.Diniz@cshs.org, '**Andre Rogatko (Andre.Rogatko@cshs.org)**' | Andre.Rogatko@cshs.org, **Jessica Lamb** | lambj@usc.edu, **Karisma A Nagarkatti** | nagarkat@usc.edu

Ryan,

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What do you think?

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From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Tuesday, Jun 8, 3:26 PM

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Hi Ryan,

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Thursday, Jun 10, 6:18 AM

To: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

Oh boy. This is AMAZING.

I believe we have accidentally uncovered a crucial finding. From what I see, the two distributions are quite different, with very little overlap. As you may have gathered from our conversations, the “wrong way” turning (turns = 1 in our database) are just ignored in prior work. You have demonstrated a clear neuro-anatomic explanation for the opposite behavioral results in MCAo. This is going to be a paper in a good neuroscience journal.

I know you are busy, so I will offer you first author position to my last author. I think we need a few more things:

1. What structures are involved? In the old days, we would show 3 or 4 representative slices from a mouse atlas, and map the contour profiles onto those slices. I imagine you have access to a 3-D atlas that can report to us the involved structures, yes?
2. I predict that the lesion map from mice with intermediate scores will either map as very small, OR will map into BOTH the “0” and the “1” loci. From the data Marcio gave you, can you select the animals with turn frequencies between 0.4 and 0.6, that is, the scores that localize around normal?

Other thoughts?

PL

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From: **Patrick Lyden** | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu To: **Patrick Lyden** | plyden@usc.edu Tuesday, Jun 8, 3:26 PM

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From: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

Thursday, Jun 10, 12:15 PM

To: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Great to hear, and exciting! I appreciate the opportunity to work on sharing these results,

For #1, I'll start making overlays of the anatomical regions like you describe. We can also make 3D surface renderings in case they are able to show more too. For #2, I think Marcio only shared the cases with 0 & 1, but not the intermediate cases. So if the full table can be shared, then I can also look at those cases with intermediate values and do those additional tests. Maybe after that we could go over to discuss and plan any remaining pieces before writing?

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From: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Thursday, Jun 10, 6:18 AM

Oh boy. This is AMAZING.

I believe we have accidentally uncovered a crucial finding. From what I see, the two distributions are quite



different, with very little overlap. As you may have gathered from our conversations, the “wrong way” turning (turns = 1 in our database) are just ignored in prior work. You have demonstrated a clear neuro-anatomic explanation for the opposite behavioral results in MCAo. This is going to be a paper in a good neuroscience journal.

I know you are busy, so I will offer you first author position to my last author. I think we need a few more things:

1. What structures are involved? In the old days, we would show 3 or 4 representative slices from a mouse atlas, and map the contour profiles onto those slices. I imagine you have access to a 3-D atlas that can report to us the involved structures, yes?
2. I predict that the lesion map from mice with intermediate scores will either map as very small, OR will map into BOTH the “0” and the “1” loci. From the data Marcio gave you, can you select the animals with turn frequencies between 0.4 and 0.6, that is, the scores that localize around normal?

Other thoughts?

PL

From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu      To: **Patrick Lyden** | plyden@usc.edu      Wednesday, Jun 9, 8:52 PM

Hi Pat,

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Hope that makes sense and is of some help, please let me know if you’d like to look at more with this or discuss.

Cheers,

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Tuesday, Jun 8, 3:51 PM

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Tuesday, Jun 8, 3:49 PM

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Let me know if you need anything else,

Marcio

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From: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Thursday, Jun 10, 1:30  
PM

To: **Diniz, Marcio A** | [Marcio.Diniz@cshs.org](mailto:Marcio.Diniz@cshs.org), '**Andre Rogatko (Andre.Rogatko@cshs.org)**' |  
[Andre.Rogatko@cshs.org](mailto:Andre.Rogatko@cshs.org)  
Cc: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

Success!!

Ryan's fabulous results (see attached) confirm our theory: the "0" animals (all right turns) have striatal lesions and the "1" animals (all left turns) have mainly cortical and thalamic lesions. There is very little overlap in the frequency distributions. Ryan and I are going to start working on a paper, and I would like you involved too. I think it would be very interesting to next map the intermediate scores. Marcio, can you send Ryan a list of IDs for the animals who scored within a range of 0.5, say 0.4 to 0.6?

Thanks all,

P

---

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Friday, Jun 11, 1:12 PM

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From: **Ryan Cabeen** | [ryan.cabeen@loni.usc.edu](mailto:ryan.cabeen@loni.usc.edu)

Friday, Jun 11, 2:02 PM

To: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

To clarify, that plot shows the \*difference\* between the two lesion probability maps (group 1 minus group 0). The colormap codes negative values as blue and positive values as red (so they are not two separate distributions that map overlap). The darkest red and blue colors correspond to a 20% difference in lesion probability. So one important note, both groups had lesions in striatum, but group 1 had 20% less of them there (and more elsewhere). I can make two more plots that show each group separately too

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[plyden@usc.edu](mailto:plyden@usc.edu)

---

From: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Friday, Jun 11, 3:01 PM

To: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

Yes, I would like to see the plots that show each group separately as well.

Thank you.

From: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

To: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Friday, Jun 11, 2:03 PM

To clarify, that plot shows the \*difference\* between the two lesion probability maps (group 1 minus group 0). The colormap codes negative values as blue and positive values as red (so they are not two separate distributions that map overlap). The darkest red and blue colors correspond to a 20% difference in lesion probability. So one important note, both groups had lesions in striatum, but group 1 had 20% less of them there (and more elsewhere). I can make two more plots that show each group separately too

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Web: [cabeen.io](http://cabeen.io)  
[www.ini.usc.edu](http://www.ini.usc.edu)

From: **Patrick Lyden**

Friday, Jun 11, 1:12 PM

Ryan,

The two distributions look non-overlapping. That is, the red color does not involve the striatum. Is that true? Or does the mapping algorithm suppress red if there is blue mapped onto a voxel and vice versa.

From: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

To: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Wednesday, Jun 9, 8:52 PM

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Cheers,  
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From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Tuesday, Jun 8, 3:51 PM

Thanks, got it!

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Friday, Jun 11, 4:06 PM

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Friday, Jun 11, 5:11 PM

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Cc: **Rogatko, Andre** | [Andre.Rogatko@cshs.org](mailto:Andre.Rogatko@cshs.org), **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

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Sunday, Jun 13, 7:40 PM

To: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Cc: **Diniz, Marcio A** | [Marcio.Diniz@cshs.org](mailto:Marcio.Diniz@cshs.org), **Rogatko, Andre** | [Andre.Rogatko@cshs.org](mailto:Andre.Rogatko@cshs.org)

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Thursday, Jun 10, 1:31 PM

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Monday, Jun 14, 9:43 PM

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From: **Diniz, Marcio A** | [Marcio.Diniz@cshs.org](mailto:Marcio.Diniz@cshs.org)

Thursday, Jun 17, 11:03 AM

To: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

Hi Ryan,

Thank you for sharing it! I agree that such comparison is an internal validation, and I am glad that you found strong association. I am still getting familiar with all the datasets: Do I have volume tissue ipsi and contra hemispheres variables? Would them be `midline_tissue_volume_right` and `midline_tissue_volume_left`, respectively?

My only suggestion (If you are going to show these tests in a paper. Otherwise, please feel free to ignore it) is that the likelihood ratio test is more appropriate to test interaction than the Wald test (given as output from `summary(fit)`) because the Wald test is only able to check whether sites have different slopes comparing to the reference site (AG), while you want to test the presence of the interaction term (for any reference). See below:

```
fit0 <- lm(formula = late_tissue ~ early_lesion + site, data = compare.df)
fit <- lm(formula = late_tissue ~ early_lesion + site, data = compare.df)
anova(fit0, fit)
```

Then, you will get only one global p-value. The conclusions probably will not change though.

Most importantly, I am trying to transform the very cool frequency maps in a test of hypotheses. I talked to Patrick yesterday and he mentioned that you have done an additional step in order to show non-overlap regions on the videos. From my understanding, each animal was categorized either as striatum or cortex based on their lesion fractions. Is my understanding correct? If so, how did you classify them?

Let me know if a call would be easier for you to explain your rationale.

Marcio

---

From: **Ryan Cabeen** | [Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

To: **Diniz**

Monday, Jun 14, 9:44 PM

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Wednesday, Jun 23, 10:39 PM

To: **Diniz, Marcio A** | [Marcio.Diniz@cshs.org](mailto:Marcio.Diniz@cshs.org)

Hi Marcio,

I appreciate the guidance on testing the interaction — I'll indeed go with your recommendation of the likelihood ratio test! Also, that's right about the ipsi and contra tissue volume variables.

Agreed that it's important to transform those videos into statistical tests. I should clarify that the video showed the difference in lesion frequency (group 1 minus group 0). The colormap codes negative values as blue and positive values as red (so they are not two separate distributions that map overlap). The darkest red and blue colors correspond to a 20% difference in lesion probability. So one important note, both groups had lesions in striatum, but group 1 had 20% less of them there (and more elsewhere). I guess what's missing here is that the plot doesn't capture the variability within each group, which could be big enough to swamp the group difference.

So I was thinking a possible next step is to do voxel-based analysis, where we formalize this as a statistical test at each point in the lesion areas. I've done this in other MRI studies using this tool: [github.com/ANTsX/ANTsR](https://github.com/ANTsX/ANTsR) This could avoid the issues of hard categorization of each case as striatum vs cortex (it seems each case is a mixture of both, but at different proportions). So perhaps next, I can try this and we can then review the results and code

together?

Cheers,  
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From: **Marcio A** | [Marcio.Diniz@cshs.org](mailto:Marcio.Diniz@cshs.org)

Thursday, Jun 17, 11:03 AM

Hi Ryan,

Thank you for sharing it! I agree that such comparison is an internal validation, and I am glad that you found strong association. I am still getting familiar with all the datasets: Do I have volume tissue ipsi and contra hemispheres variables? Would them be `midline_tissue_volume_right` and `midline_tissue_volume_left`, respectively?

My only suggestion (If you are going to show these tests in a paper. Otherwise, please feel free to ignore it) is that the likelihood ratio test is more appropriate to test interaction than the Wald test (given as output from `summary(fit)`) because the Wald test is only able to check whether sites have different slopes comparing to the reference site (AG), while you want to test the presence of the interaction term (for any reference). See below:

```
fit0 <- lm(formula = late_tissue ~ early_lesion + site, data = compare.df)
fit <- lm(formula = late_tissue ~ early_lesion + site, data = compare.df)
anova(fit0, fit)
```

Then, you will get only one global p-value. The conclusions probably will not change though.

Most importantly, I am trying to transform the very cool frequency maps in a test of hypotheses. I talked to Patrick yesterday and he mentioned that you have done an additional step in order to show non-overlap regions on the videos. From my understanding, each animal was categorized either as striatum or cortex based on their lesion fractions. Is my understanding correct? If so, how did you classify them?

Let me know if a call would be easier for you to explain your rationale.

Marcio

From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

To: **Diniz**

Monday, Jun 14, 9:44 PM

Hi Marcio,

One more thing, I just wanted to loop you in on a few tests I did for validating the MRI pipeline. Dr Ayata suggested comparing early timepoint lesion volume and late timepoint tissue volume (atrophy). Our idea was that this would be some indication of the quality of the imaging pipeline, since they should have a strong association (seems to be the case empirically). The results are attached — thought I'd share with you in case they are useful, or if you might have some additional insights.

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From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Sunday, Jun 13, 7:40 PM

Thanks Marcio, looks good, and I'll work on making additional lesion maps with these!

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From: **Patrick Lyden** | plyden@usc.edu

Sunday, Jun 13, 3:27 PM

Thank you.

Ryan, you know what to do.

From: **Diniz** | Marcio.Diniz@cshs.org

To: **Patrick Lyden** | plyden@usc.edu

Friday, Jun 11, 4:05 PM

Hi Patrick and Ryan,

That's look exciting! Apologies for my delay, I was taking care of randomization for stage 2 with Jessica.

I created a variable `corner_index_cat` that includes the following categories 0, 0.01 – 0.2, 0.21 – 0.4, 0.41 – 0.6, 0.61 – 0.8, 0.81 – 0.99 and 1. Please see `corner_test_categorized.csv`.

I also filtered only mice with corner test between 0.4 and 0.6 as requested. Please see `corner_test_only_4_6.csv`.

Let me know if you need the data in different format, Ryan.

Marcio

From: **Patrick Lyden** | plyden@usc.edu

To: **Diniz**

Thursday, Jun 10, 1:31 PM

Success!!

Ryan's fabulous results (see attached) confirm our theory: the "0" animals (all right turns) have striatal lesions and the "1" animals (all left turns) have mainly cortical and thalamic lesions. There is very little overlap in the frequency distributions. Ryan and I are going to start working on a paper, and I would like you involved too. I think it would be very interesting to next map the intermediate scores. Marcio, can you send Ryan a list of IDs for the animals who scored within a range of 0.5, say 0.4 to 0.6?

Thanks all,

P

From: **Ryan Cabeen** |  
Ryan.Cabeen@loni.usc.edu

To: **Patrick Lyden** |  
plyden@usc.edu

Wednesday, Jun 9, 8:52  
PM

Hi Pat,

Just following up with some prelim results for this. I computed the lesion probability maps for each of the groups, defined by the "corner\_index\_d28" column (coded zero and one). The attached movies show the differences in lesion probability maps between the groups, where blue indicates that group "zero" was more likely have lesion, and red indicates that group "one" was more likely to have lesion. The coloring becomes more transparent as the difference approaches zero.

Hope that makes sense and is of some help, please let me know if you'd like to look at more with this or discuss.

Cheers,  
Ryan

From: **Ryan Cabeen** | Ryan.Cabeen@loni.usc.edu

Tuesday, Jun 8, 3:51 PM

Thanks, got it!

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From: **Marcio A** | Marcio.Diniz@cshs.org

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use enro animal id. The variable corner index d28 indicates whether it is 0 or 1.

Let me know if you need anything else,

Marcio

From: **Ryan Cabeen** |  
Ryan.Cabeen@loni.usc.edu

To: **Patrick Lyden** |  
plyden@usc.edu

Tuesday, Jun 8, 3:42  
PM

I think just two lists of the cases that make up the groups, corner test = 0 and corner test = 1. I don't think I have the behavior outcome measures on my end.

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From: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: **Ryan Cabeen** |  
[Ryan.Cabeen@loni.usc.edu](mailto:Ryan.Cabeen@loni.usc.edu)

To: **Patrick Lyden** |  
[plyden@usc.edu](mailto:plyden@usc.edu)

Tuesday, Jun 8, 3:26  
PM

Sounds like a great idea to me -- I'd be glad to implement it and make visualizations that we can review.

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From: **Patrick Lyden** | [plyden@usc.edu](mailto:plyden@usc.edu)

Tuesday, Jun 8, 3:19 PM

Ryan,

We are still struggling to understand our corner test data, using your analysis of cortical vs striatal vs thalamic lesion volumes. I would like to try to simplify the problem, and I recalled your most excellent frequency map in which you plotted in 3-d the lesions and showed a beautiful lesion frequency map. I would like to try the same thing but first, split the data into two populations: corner test = 0 and corner test = 1. These are the extreme values, and if lesion location plays a role in turning direction, this two groups should differ in their lesion locations. Then you make the frequency map again, but show the two populations in different colors. The two distributions should center in different locations.

What do you think?

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