# RE: [External] RE: topography

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,

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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821
plyden@usc.edu

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

Tuesday, Jun 8, 3:26 PM

To: Patrick Lyden | plyden@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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821
plyden@usc.edu

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 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

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io www.ini.usc.edu

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA Professor of Physiology and Neuroscience Professor of Neurology Zilkha Neurogenetic Institute Keck School of Medicine of USC

Room 245 MC2821 1501 San Pablo Street Los Angeles, CA 90089-2821 plyden@usc.edu

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

Tuesday, Jun 8, 3:42 PM

To: Patrick Lyden | plyden@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

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

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

plyden@usc.edu

Tuesday, Jun 8, 3:49 PM

To: Ryan Cabeen | Ryan.Cabeen@loni.usc.edu, Patrick Lyden | plyden@usc.edu

Cc: Rogatko, Andre | Andre.Rogatko@cshs.org, Jessica Lamb | lambj@usc.edu, Karisma A Nagarkatti | nagarkat@usc.edu

Hi Ryan,

To match with your data, please use <a href="mailto:enrolle-normal">enro\_animal\_id</a>. The variable <a href="mailto:corner\_index\_d28">corner\_index\_d28</a> 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.

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821
plyden@usc.edu

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

Tuesday, Jun 8, 3:51 PM

To: Patrick Lyden | plyden@usc.edu, Diniz, Marcio A | Marcio.Diniz@cshs.org

Cc: Rogatko, Andre | Andre.Rogatko@cshs.org, Jessica Lamb | lambj@usc.edu, Karisma A Nagarkatti | nagarkat@usc.edu

Thanks, got it!

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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: Patric

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA Professor of Physiology and Neuroscience Professor of Neurology Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821
plyden@usc.edu

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

Wednesday, Jun 9, 8:52 PM

To: Patrick Lyden | plyden@usc.edu

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA

Professor of Physiology and Neuroscience

Professor of Neurology

Zilkha Neurogenetic Institute

Keck School of Medicine of USC

Room 245

MC2821

1501 San Pablo Street

Los Angeles, CA 90089-2821

plyden@usc.edu

From: Patrick Lyden | plyden@usc.edu

Thursday, Jun 10, 6:18 AM

To: Ryan Cabeen | 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

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!

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821
plyden@usc.edu

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

Thursday, Jun 10, 12:15 PM

To: Patrick Lyden | 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?

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

From: Patrick Lyden | 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,

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!

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is

governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen

To: Patrick Lyden

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

PI

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | plyden@usc.edu

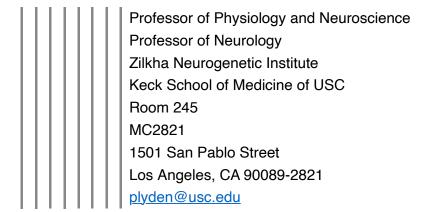
Tuesday, Jun 8, 3:19 PM

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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA



From: Patrick Lyden | plyden@usc.edu

Thursday, Jun 10, 1:30

ÞМ

To: Diniz, Marcio A | Marcio.Diniz@cshs.org, 'Andre Rogatko (Andre.Rogatko@cshs.org)' |

Andre.Rogatko@cshs.org

Cc: Ryan Cabeen | 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,

Р

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

From: Patrick Lyden | plyden@usc.edu

plyden@usc.edu

Friday, Jun 11, 1:12 PM

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

# Ryan,

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

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

From: Ryan Cabeen | ryan.cabeen@loni.usc.edu

Friday, Jun 11, 2:02 PM

To: Patrick Lyden | plyden@usc.edu

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

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.
Los Angeles, CA 90033

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

Tel: (323) 44-BRAIN

From: Patrick Lyden Friday, Jun 11, 1:12 PM

Ryan,

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

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

To: Patrick Lyden

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

PM

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA

Professor of Physiology and Neuroscience

Professor of Neurology

Zilkha Neurogenetic Institute

Keck School of Medicine of USC

Room 245

MC2821

1501 San Pablo Street

Los Angeles, CA 90089-2821

plyden@usc.edu

From: Patrick Lyden | plyden@usc.edu

Friday, Jun 11, 3:01 PM

To: Ryan Cabeen | 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

To: Patrick Lyden | 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

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.
Los Angeles, CA 90033

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

From: **Patrick Lyden** Friday, Jun 11, 1:12 PM

Ryan,

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

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,

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

Tuesday, Jun 8, 3:51 PM

Thanks, got it!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>

www.ini.usc.edu

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

To: Patrick Lyden

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

PM

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA Professor of Physiology and Neuroscience Professor of Neurology Zilkha Neurogenetic Institute Keck School of Medicine of USC Room 245 MC2821 1501 San Pablo Street Los Angeles, CA 90089-2821

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

Friday, Jun 11, 4:06 PM

To: Patrick Lyden | plyden@usc.edu, Rogatko, Andre | Andre.Rogatko@cshs.org

Cc: Ryan Cabeen | Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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

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,

Ρ

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

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

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street



From: Patrick Lyden | plyden@usc.edu

Friday, Jun 11, 5:11 PM

To: Diniz, Marcio A | Marcio.Diniz@cshs.org

Cc: Rogatko, Andre | Andre.Rogatko@cshs.org, Ryan Cabeen | Ryan.Cabeen@loni.usc.edu

Thanks Marcio.

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

Friday, Jun 11, 4:06 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.

Р

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

<corner\_test\_categorized.csv>
<corner\_test\_only\_4\_6.csv>

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

Tuesday, Jun 8, 3:51 PM

Thanks, got it!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

To: Patrick Lyden

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

From: Patrick Lyden | plyden@usc.edu

Sunday, Jun 13, 3:27 PM

To: Diniz, Marcio A | Marcio.Diniz@cshs.org, Rogatko, Andre | Andre.Rogatko@cshs.org

Cc: Ryan Cabeen | Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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.

Р

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

Tuesday, Jun 8, 3:51 PM

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

Thanks, got it!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: <u>rcabeen@loni.usc.edu</u>

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

To: Patrick Lyden |

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

DM

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology
Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

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

plyden@usc.edu

Sunday, Jun 13, 7:40 PM

To: Patrick Lyden | plyden@usc.edu

Cc: Diniz, Marcio A | Marcio.Diniz@cshs.org, Rogatko, Andre | Andre.Rogatko@cshs.org

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

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.

Hi Pat.

Р

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

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: <u>rcabeen@loni.usc.edu</u>

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> indicates whether it is 0 or 1.

Let me know if you need anything else,

Marcio

From: **Ryan Cabeen** I Ryan.Cabeen@loni.usc.edu To: Patrick Lyden

Tuesday, Jun 8, 3:42

plyden@usc.edu

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California 2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

**WARNING** 

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen |

To: Patrick Lyden |

Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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? Patrick D. Lyden, MD, FAAN, FAHA, FANA Professor of Physiology and Neuroscience Professor of Neurology Zilkha Neurogenetic Institute Keck School of Medicine of USC Room 245 MC2821 1501 San Pablo Street Los Angeles, CA 90089-2821

From: Ryan Cabeen | ryan.cabeen@loni.usc.edu

plyden@usc.edu

Monday, Jun 14, 9:43 PM

To: Diniz, Marcio A | Marcio.Diniz@cshs.org

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.

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC University of Southern California 2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN Email: rcabeen@loni.usc.edu

Web: cabeen.io www.ini.usc.edu

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

From: Patrick Lyden | plyden@usc.edu

Sunday, Jun 13, 3:27 PM

Thank you.

Ryan, you know what to do.

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.

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,

Р

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!

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.

Los Angeles, CA 90033 Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> indicates whether it is 0 or 1.

Let me know if you need anything else,

Marcio

From: Ryan Cabeen |

To: Patrick Lyden

Tuesday, Jun 8, 3:42

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

WARNING

This email is from an external source. Do not click on links or open attachments unless you know the content is safe. Protect your username and password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the

employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

|  | Ш | Ш | Patrick D. Lyden, MD, FAAN, FAHA, FANA   |
|--|---|---|--|
|  | Ш | Ш | Professor of Physiology and Neuroscience |
|  | Ш | Ш | Professor of Neurology                   |
|  | Ш | Ш | Zilkha Neurogenetic Institute            |
|  | Ш | Ш | Keck School of Medicine of USC           |
|  | Ш | Ш | Room 245                                 |
|  | Ш | Ш | MC2821                                   |
|  | Ш | Ш | 1501 San Pablo Street                    |
|  | Ш | Ш | Los Angeles, CA 90089-2821               |
|  |   | П | plyden@usc.edu                           |

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

Thursday, Jun 17, 11:03 AM

To: Ryan Cabeen | 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 <- Im(formula = late_tissue ~ early_lesion + site, data = compare.df) fit <- Im(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

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

From: **Ryan Cabeen** I 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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>

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,

Ρ

From: **Ryan Cabeen** I 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

i

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

Thanks, got it!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: http://cabeen.io http://www.ini.usc.edu

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

Tuesday, Jun 8, 3:42

plyden@usc.edu

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a></a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

This email is from an external source. Do not click on links or open

WARNING attachments unless you know the content is safe. Protect your username and

password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

From: **Ryan Cabeen** | To: **Patrick Lyden** | Tuesday, Jun 8, 3:26

Ryan.Cabeen@loni.usc.edu plyden@usc.edu PM

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

Patrick D. Lyden, MD, FAAN, FAHA, FANA
Professor of Physiology and Neuroscience
Professor of Neurology

Title Neurosciential lesibility

Zilkha Neurogenetic Institute
Keck School of Medicine of USC
Room 245
MC2821
1501 San Pablo Street
Los Angeles, CA 90089-2821

From: Ryan Cabeen | ryan.cabeen@loni.usc.edu

plyden@usc.edu

Wednesday, Jun 23, 10:39 PM

To: Diniz, Marcio A | 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 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 this a try and we can then review the results and code

together?

Cheers,

Ryan

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.
Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <u>cabeen.io</u> <u>www.ini.usc.edu</u>

From: Marcio A | 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 <- Im(formula = late_tissue ~ early_lesion + site, data = compare.df) fit <- Im(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** I 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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: http://cabeen.io

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,

Р

From: Ryan Cabeen |

To: Patrick Lyden

Wednesday, Jun 9, 8:52

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

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

Tuesday, Jun 8, 3:49 PM

Hi Ryan,

To match with your data, please use <u>enro\_animal\_id</u>. The variable <u>corner\_index\_d28</u> indicates whether it is 0 or 1.

Let me know if you need anything else,

Marcio

From: Ryan Cabeen |

To: Patrick Lyden

Tuesday, Jun 8, 3:42

Ryan.Cabeen@loni.usc.edu

plyden@usc.edu

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

This email is from an external source. Do not click on links or open

WARNING attachments unless you know the content is safe. Protect your username and

password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu

Tuesday, Jun 8, 3:38 PM

Tuesday, Jun 8, 3:26

PM

Thanks. What do you need to pull it off?

From: Ryan Cabeen | To: Patrick Lyden |

Ryan.Cabeen@loni.usc.edu plyden@usc.edu

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

review.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: http://cabeen.io

# http://www.ini.usc.edu From: Patrick Lyden | 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? Patrick D. Lyden, MD, FAAN, FAHA, FANA Professor of Physiology and Neuroscience Professor of Neurology Zilkha Neurogenetic Institute Keck School of Medicine of USC Room 245

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

MC2821

Thursday, Jun 24, 10:19 AM

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

plyden@usc.edu

1501 San Pablo Street

Los Angeles, CA 90089-2821

Cc: Patrick Lyden | plyden@usc.edu

Hi Ryan,

Thank you for the explanation! Now, I completely understand the colormaps in the videos. It was really helpful. Is your plan to produce multiple pairwise comparisons to incorporate intermediate corner test scores?

I totally agree that a voxel-based analysis would be more appropriate. Patrick and I discussed one additional analysis using the data of lesion fractions by region, but I have not been able to obtain clear results as you did. Given your much large experience with statistical analysis for imaging than mine, please feel free to take the lead on addressing this question and let me know whatever I can help you from the statistical side.

I cc'ing Patrick, so he can also contribute to this discussion.

Kind regards,

#### Marcio

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

To: **Diniz** 

Wednesday, Jun 23, 10:40 PM

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: <a href="https://github.com/ANTsX/ANTsR">https://github.com/ANTsX/ANTsR</a> 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 this a try and we can then review the results and code together?

Cheers,

Ryan

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California
2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: cabeen.io

http://www.ini.usc.edu

From: Marcio A | 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 <- Im(formula = late_tissue ~ early_lesion + site, data = compare.df) fit <- Im(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** I 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.

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a> http://www.ini.usc.edu

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!

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: http://cabeen.io

From: Patrick Lyden | plyden@usc.edu

Sunday, Jun 13, 3:27 PM

Thank you.

Ryan, you know what to do.

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.

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,

Р

From: **Ryan Cabeen** I 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!

Ryan P. Cabeen, PhD
Chan Zuckerberg Imaging Scientist
Assistant Professor of Research Neurology
Laboratory of Neuro Imaging
USC Stevens Neuroimaging and Informatics Institute
Keck School of Medicine of USC
University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: http://cabeen.io http://www.ini.usc.edu

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 |

Tuesday, Jun 8, 3:42

plyden@usc.edu

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.

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a> http://www.ini.usc.edu

This email is from an external source. Do not click on links or open

WARNING attachments unless you know the content is safe. Protect your username and

password.

IMPORTANT WARNING: This message is intended for the use of the person or entity to which it

is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is strictly prohibited. Thank you for your cooperation.

From: Patrick Lyden | plyden@usc.edu Tuesday, Jun 8, 3:38 PM

Thanks. What do you need to pull it off?

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

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

Ryan P. Cabeen, PhD

Chan Zuckerberg Imaging Scientist

Assistant Professor of Research Neurology

Laboratory of Neuro Imaging

USC Stevens Neuroimaging and Informatics Institute

Keck School of Medicine of USC

University of Southern California

2025 Zonal Ave.

Los Angeles, CA 90033

Tel: (323) 44-BRAIN

Email: rcabeen@loni.usc.edu

Web: <a href="http://cabeen.io">http://cabeen.io</a>
<a href="http://www.ini.usc.edu">http://www.ini.usc.edu</a>

From: Patrick Lyden | 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?

| Patrick D. Lyden, MD, FAAN, FAHA, FANA   |
|--|
| Professor of Physiology and Neuroscience |
| Professor of Neurology                   |
| Zilkha Neurogenetic Institute            |
| Keck School of Medicine of USC           |
| Room 245                                 |
| MC2821                                   |
| 1501 San Pablo Street                    |
| Los Angeles, CA 90089-2821               |
| plyden@usc.edu                           |