Eye tracking in opsoclonus Myoclonus Ataxia Syndrome

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Disclosures

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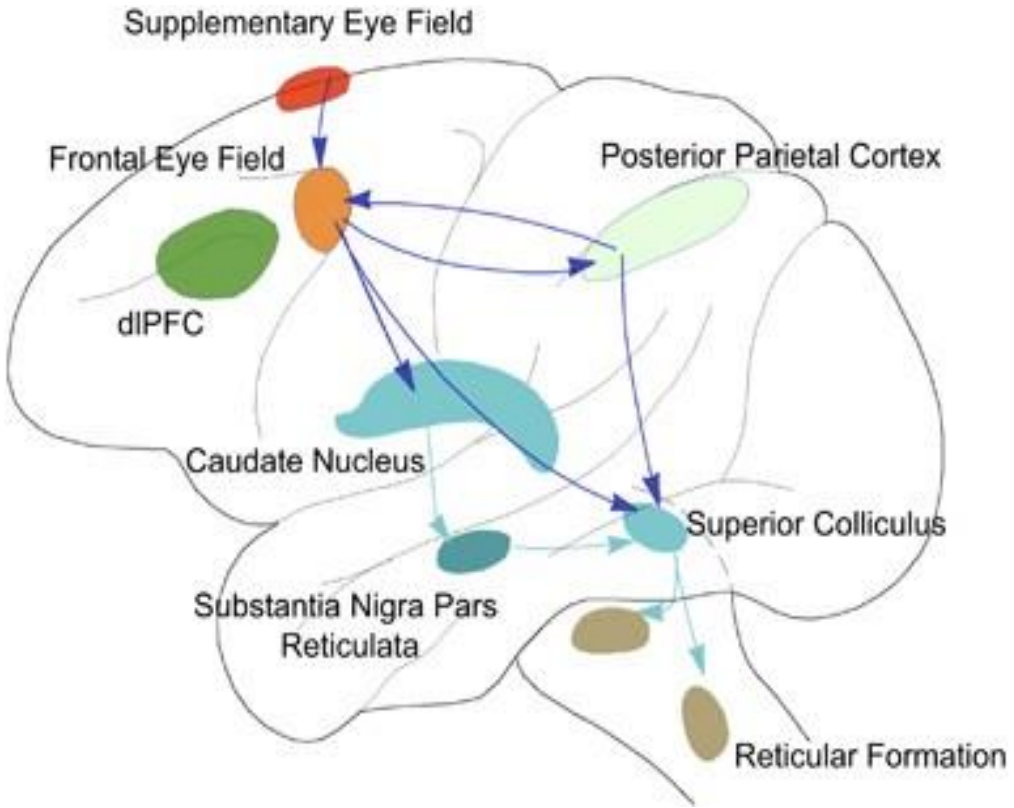
Eye movements and outcomes in OMAS



- Altered circuit dynamics in the brainstem reticular formation are known to associate with OMAS

Original Article

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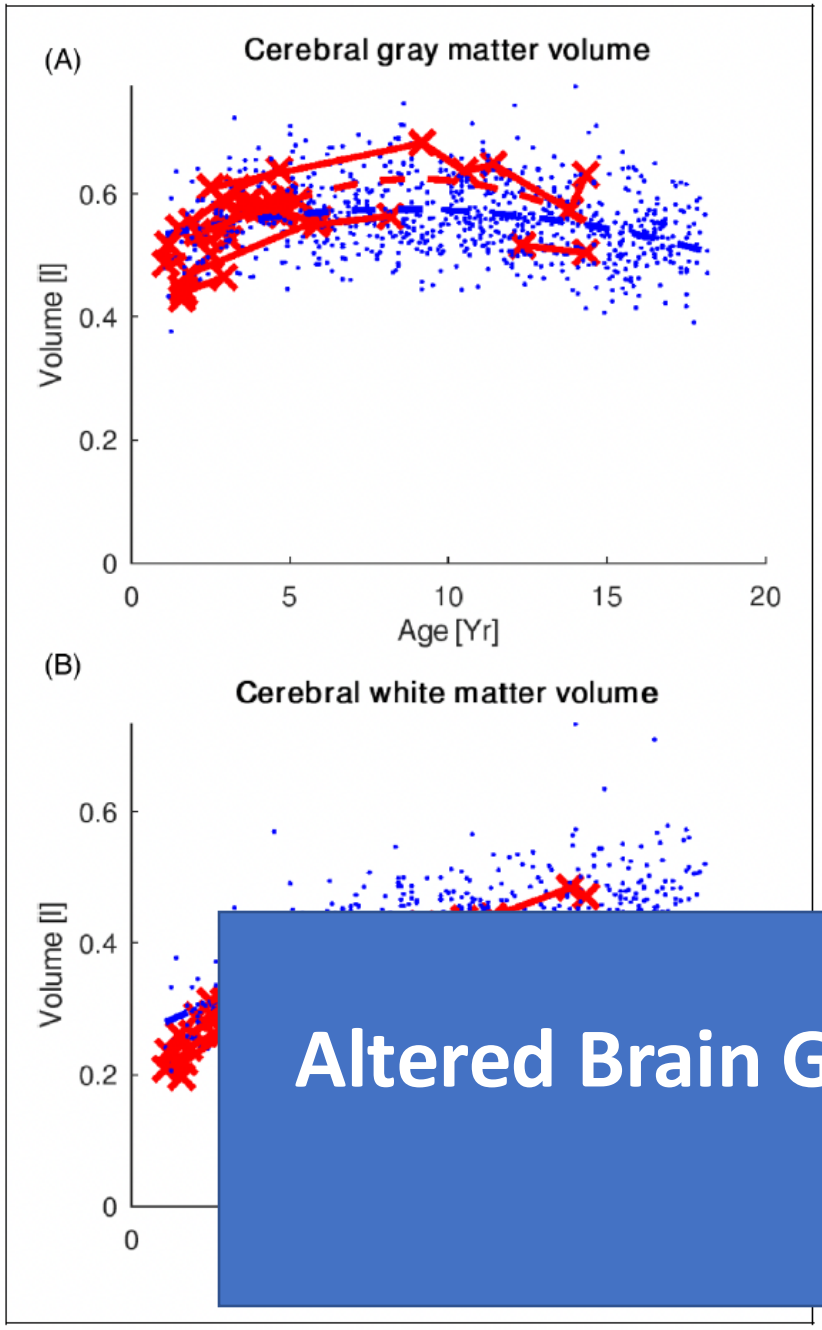
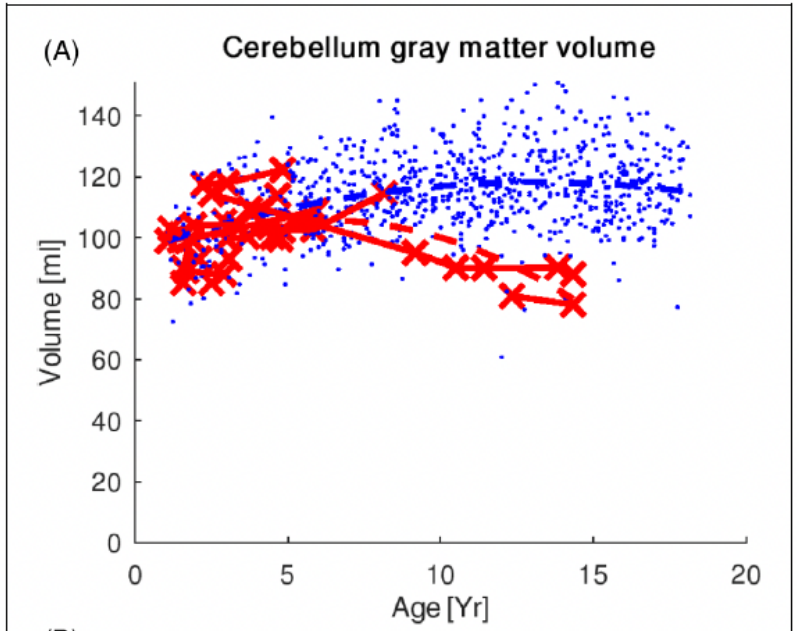
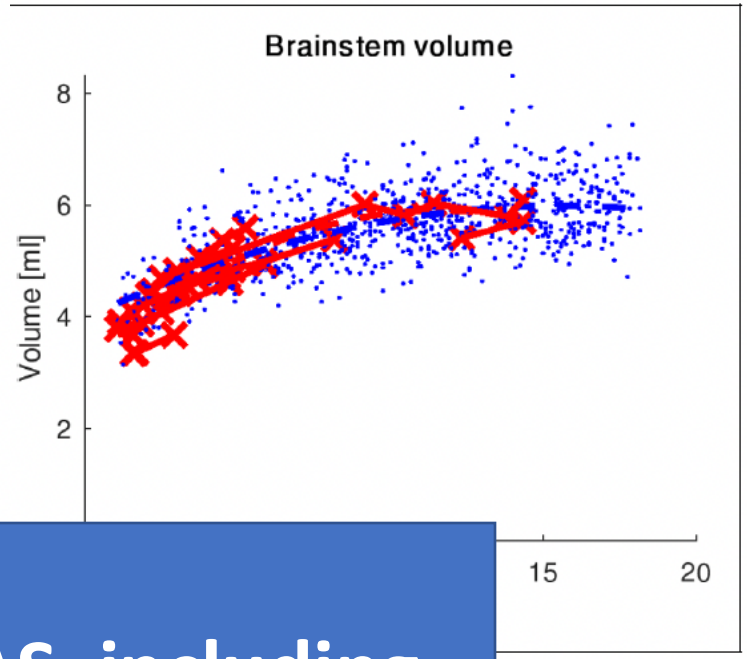
Brain Volumes in Opsoclonus-Myoclonus Ataxia Syndrome: A Longitudinal Study

Montaha Almudhry, MD[1], Matthias W. Wagner, MD[2,3], Giulia Longoni, MD[1,4], Carmen Yea, MSc[1], Logi Vidarsson, PhD[2], Birgit Ertl-Wagner, MD[1,2,5], and E. Ann Yeh, MD[1,4]







Altered Brain Growth trajectory in OMAS, including brainstem

Long term: Cognition

Tested 5 Cognitive Domains:

1. Set-Shifting
2. Inhibitory Control
3. Working Memory
4. Episodic Memory
5. Language

OMAS performed significantly worse than HC

Dimensional Change Card Sort (DCCS) Task (SET SHIFTING)

	OMAS (n=8)	**HC (n=12)**	**t df p**
Median corrected score	76.5	108.5	-3.301 18.000 **0.004**

Flanker Task (INHIBITORY CONTROL)

Median corrected score	89	103.5	-2.293. 14.000 **0.038**

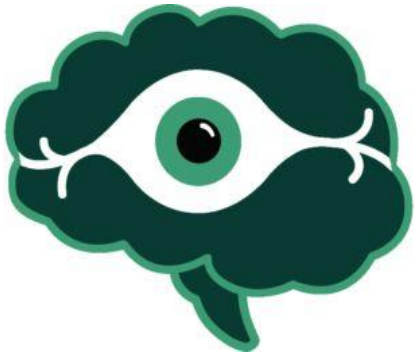
Cognitive abnormalities in OMAS: inhibitory control

Do ongoing alterations in circuit dynamics exist?

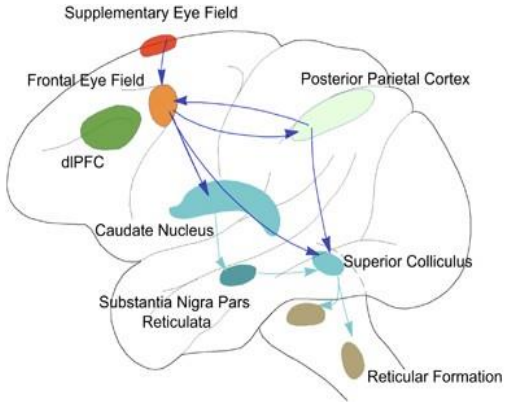
How do these abnormalities, if present, associate with functional outcomes in this population?

Is there an accessible way to ask these questions?

Eye Tracking



Eye movements + fixations are *functional outcomes* → cognitive processes[6]



Good understanding of neural circuitry that regulates eye movements[7]

Saccadic eye movements:

rapid eye movements that **shift the focus of attention** from one part of the visual field to another[8]

6 Munoz, D. P., Armstrong, I., & Coe, B. (2007). Chapter 5 - Using eye movements to probe development and dysfunction. In Eye Movements (pp. 99–124). Elsevier Ltd. https://doi.org/10.1016/B978-008044980-7/50007-0
7 Pouget, P. (2015). The cortex is in overall control of "voluntary" eye movement. Eye (London), 29(2), 241–245. https://doi.org/10.1038/eye.2014.284
8 Wong, A. M. F. (2008). Eye movement disorders. Oxford University Press.

Saccade Control Circuit

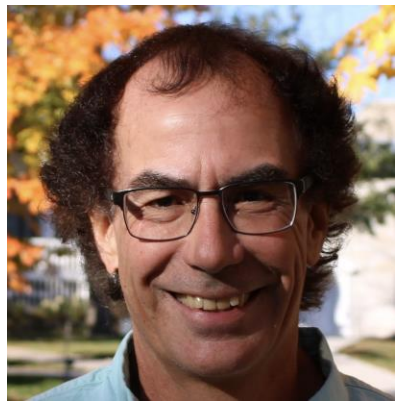
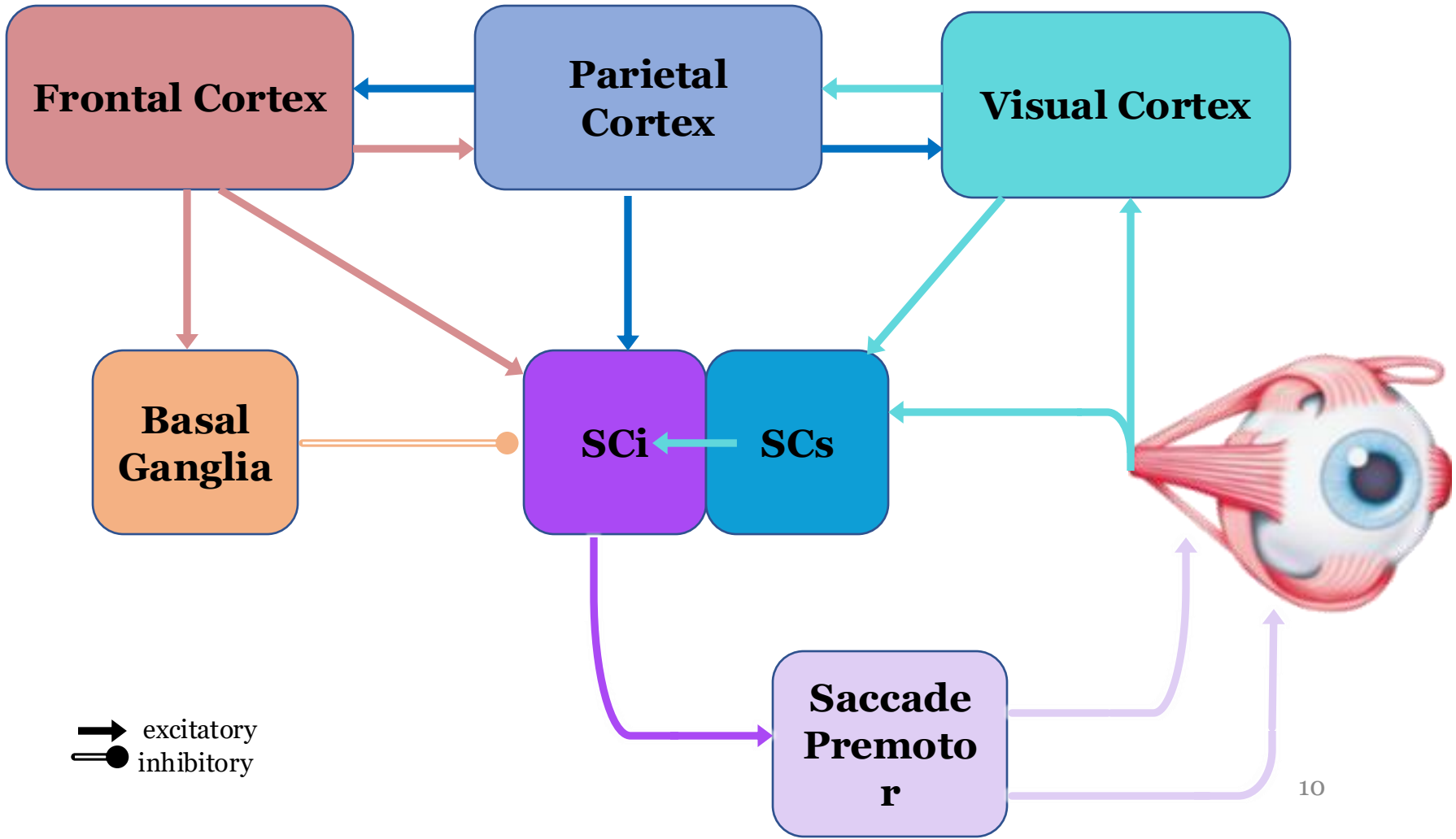


Figure adapted from Doug Munoz



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LOOK AWAY: THE ANTI-SACCADE TASK AND THE VOLUNTARY CONTROL OF EYE MOVEMENT

Douglas P. Munoz and Stefan Everling†§*

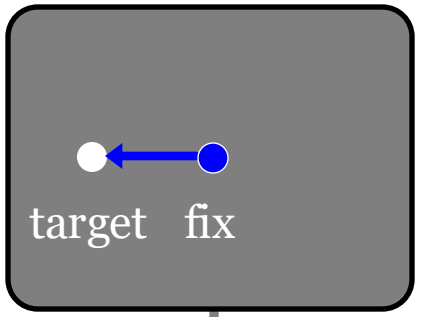
Eye Tracking can be used to evaluate executive function

12 Munoz, D. P., & Everling, S. (2004). Look away: the anti-saccade task and the voluntary control of eye movement. Nature Reviews Neuroscience, 5(3), 218-228. https://doi.org/10.1038/nrn1345

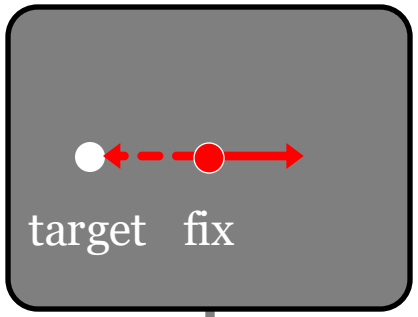
What is eye tracking?

STRUCTURED[9]

pro-saccade

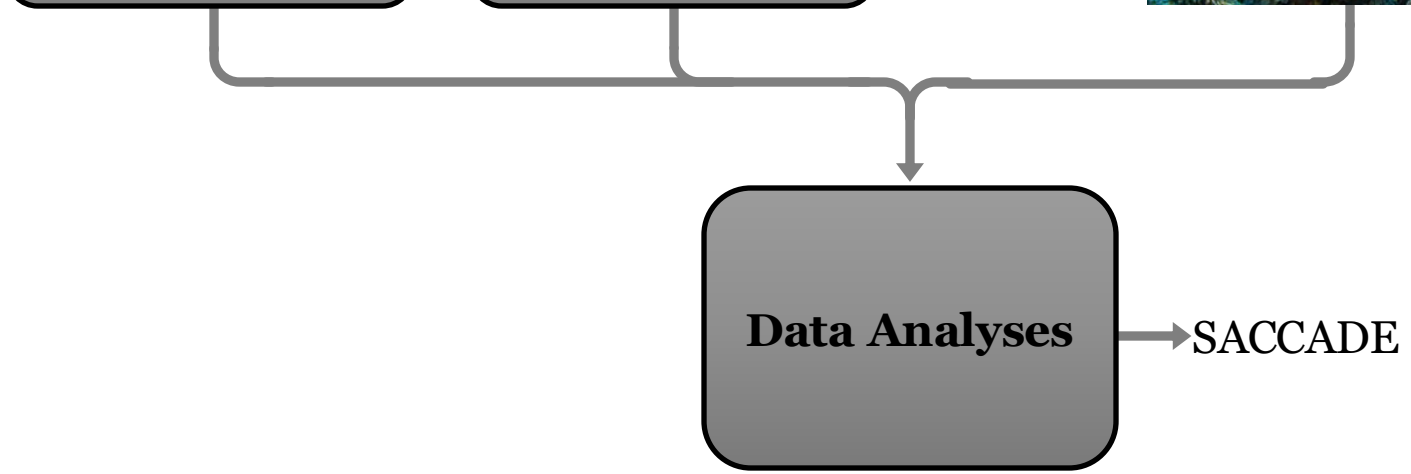


anti-saccade



UNSTRUCTURED[10]

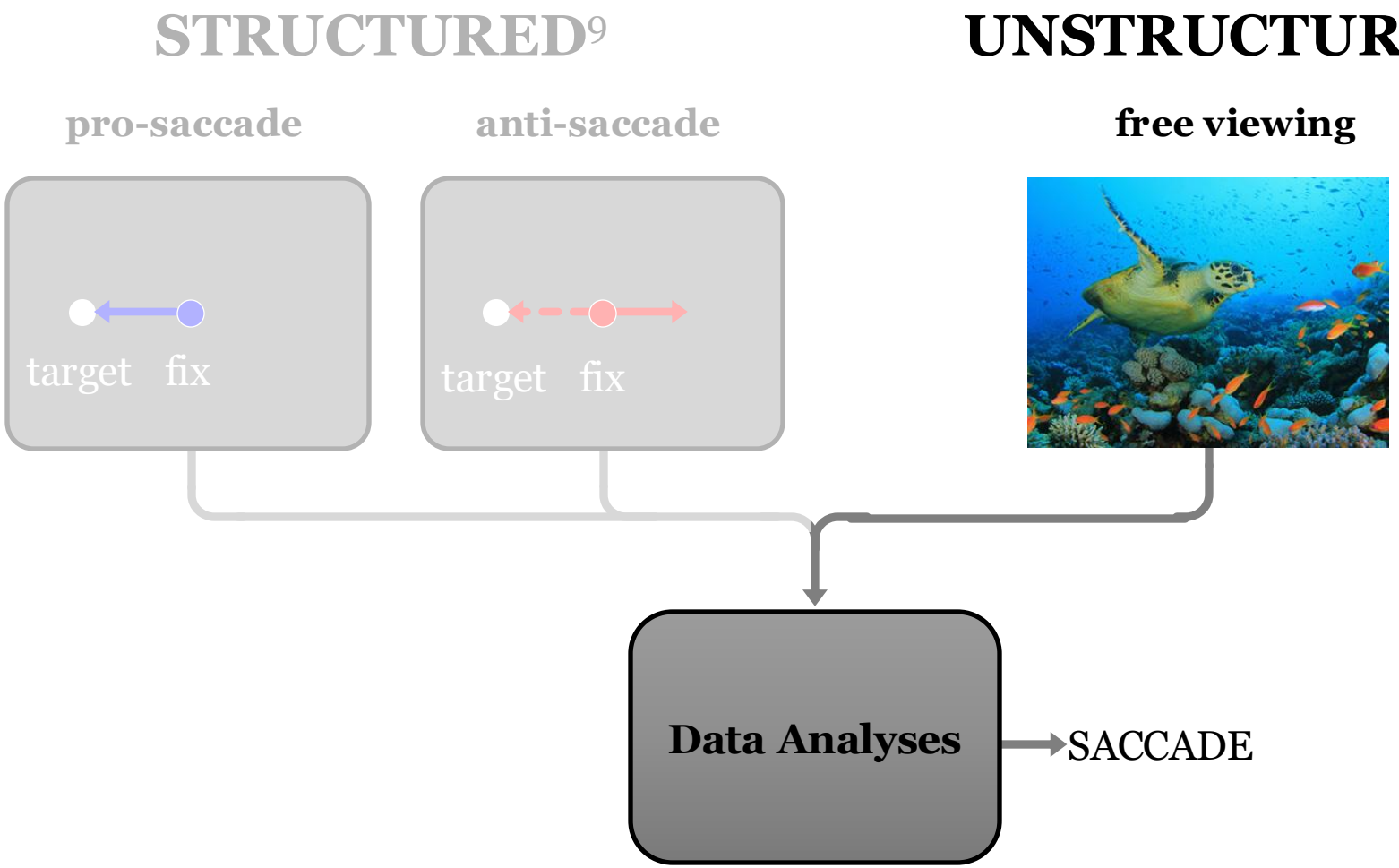
free viewing



Adapted from Doug Munoz

9 Tao, L., Wang, Q., Liu, D., Wang, J., Zhu, Z., & Feng, L. (2020). Eye tracking metrics to screen and assess cognitive impairment in patients with neurological disorders. Neurological Sciences, 41(7), 1697–1704. https://doi.org/10.1007/s10072-020-04310-y

10 Habibi, M., Oertel, W. H., White, B. J., Brien, D. C., Coe, B. C., Riek, H. C., Perkins, J., Yep, R., Itti, L., Timmermann, L., Best, C., Sittig, E., Janzen, A., & Munoz, D. P. (2022). Eye tracking identifies biomarkers in α-synucleinopathies versus progressive supranuclear palsy. Journal of Neurology, 269(9), 4920–4938. https://doi.org/10.1007/s00415-022-11136-5



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UNSTRUCTURED

free viewing

Data Analyses → SACCADE

Why Free Viewing (FV)?

1. Easy to administer – optimal for young children[9]
2. Rich assessment of saccade behaviour in a dynamic visual setting[10]
3. FV reveals saccadic parameters[10]

Adapted from Doug Munoz

9 Tao, L., Wang, Q., Liu, D., Wang, J., Zhu, Z., & Feng, L. (2020). Eye tracking metrics to screen and assess cognitive impairment in patients with neurological disorders. Neurological Sciences, 41(7), 1697–1704. https://doi.org/10.1007/s10072-020-04310-y
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Free-viewing eye tracking (EyeLink 1000 Plus)

EyeLink 1000 Plus

- Video-based monocular eye tracker – recorded eye position, pupil size, and blink rate at 500Hz

17-inch
LCD monitor

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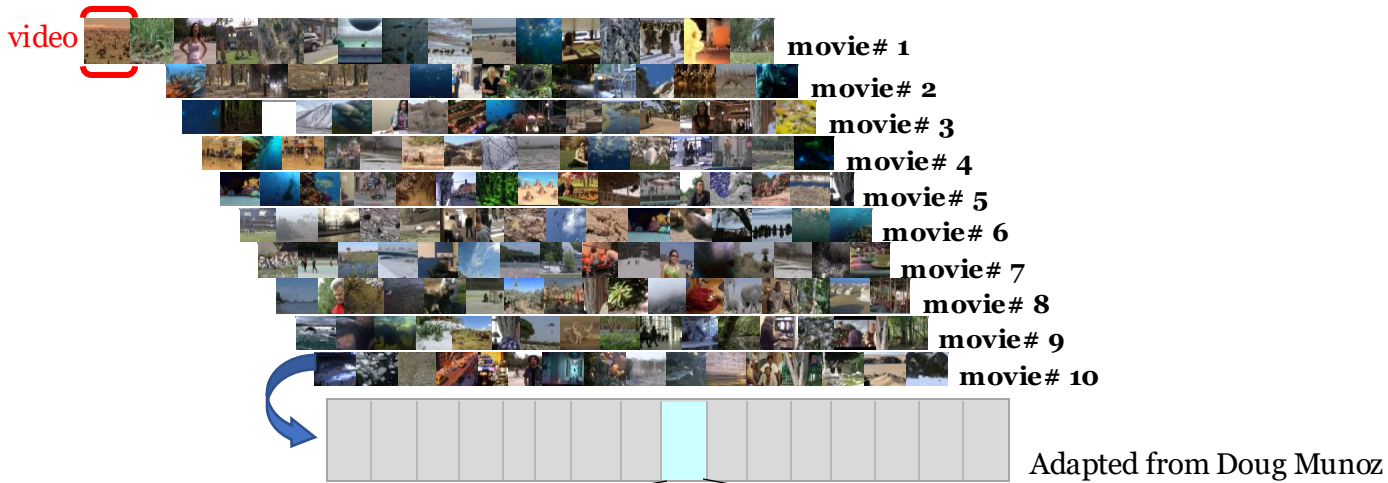
Task 1: Free-viewing eye tracking (EyeLink 1000 Plus)

video

Clip Change = large visual perturbation[12]

Adapted from Doug Munoz

12 White, B. J., Berg, D. J., Kan, J. Y., Marino, R. A., Itti, L., & Munoz, D. P. (2017). Superior colliculus neurons encode a visual saliency map during free viewing of natural dynamic video. Nature Communications, 8(1), 14263–14263. https://doi.org/10.1038/ncomms14263



Saccades, Fixations and Pupillary Behavior have been tied to cognitive outcomes

of a

13 Coe, B. C., Huang, J., Brien, D. C., White, B. J., Yep, R., & Munoz, D. P. (2022). Automated Analysis Pipeline For Extracting Saccade, Pupil, and Blink Parameters Using Video-Based Eye Tracking. *bioRxiv*, 2022.2002.2022.481518. doi:10.1101/2022.02.22.481518

Are there ongoing abnormalities

Eye tracking localizes abnormalities to the superior colliculus

Annals of the
Child Neurology Society
Open Access

RESEARCH ARTICLE

Saccade and pupil changes in children recovering from opsoclonus-myoclonus ataxia syndrome reveal midbrain alterations in oculomotor circuits

Douglas P. Munoz[1,*], Brian J. White[1], Donald C. Brien[1], Kajaal Parbhoo[2], Carmen Yea[2] & E. Ann Yeh[2]

[1]Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada
[2]Division of Neurology, The Hospital for Sick Children, Toronto, Ontario, Canada

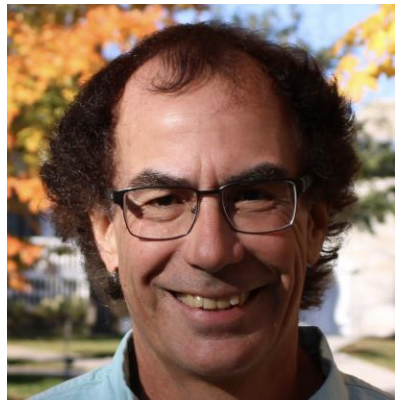
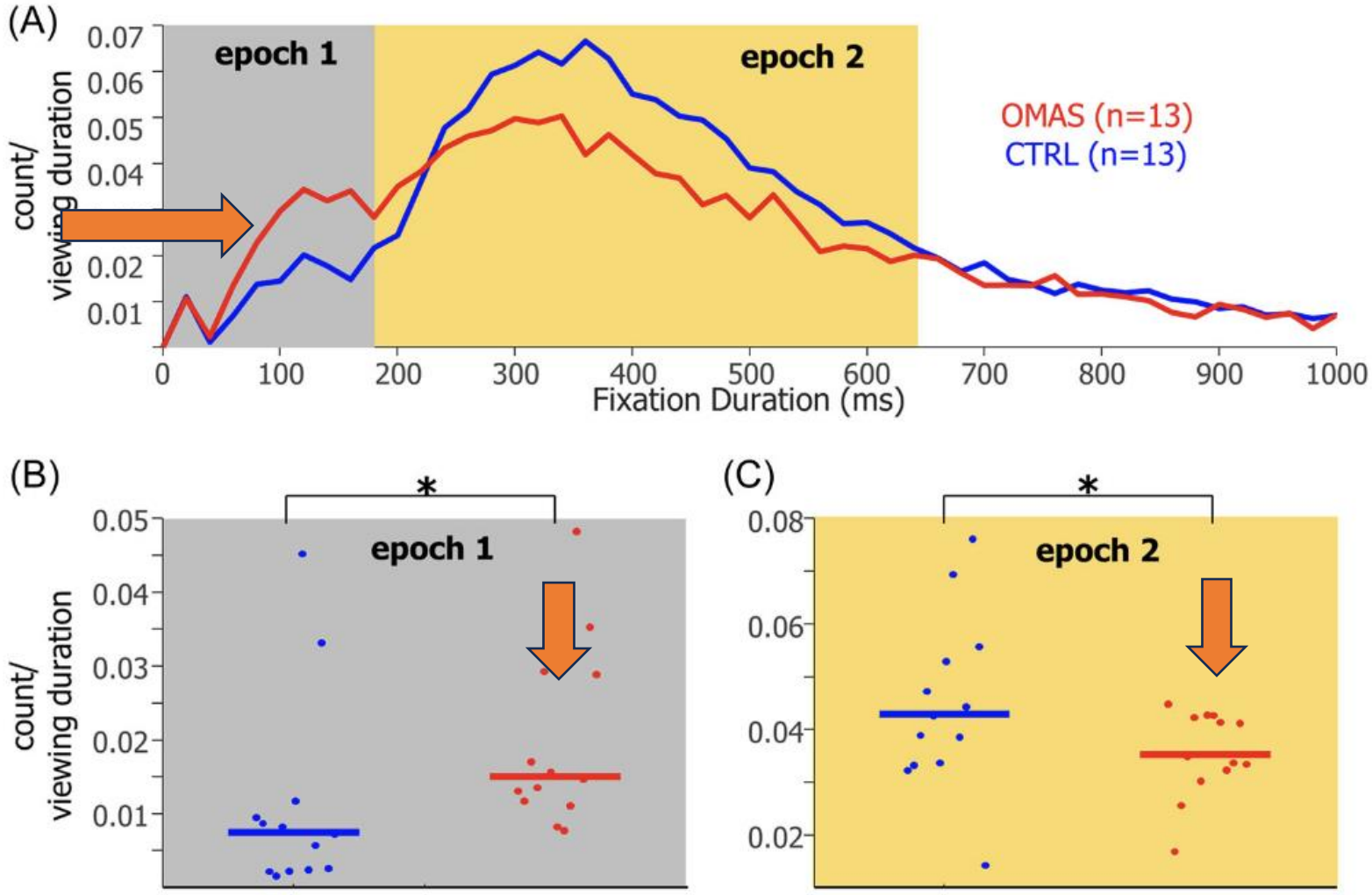
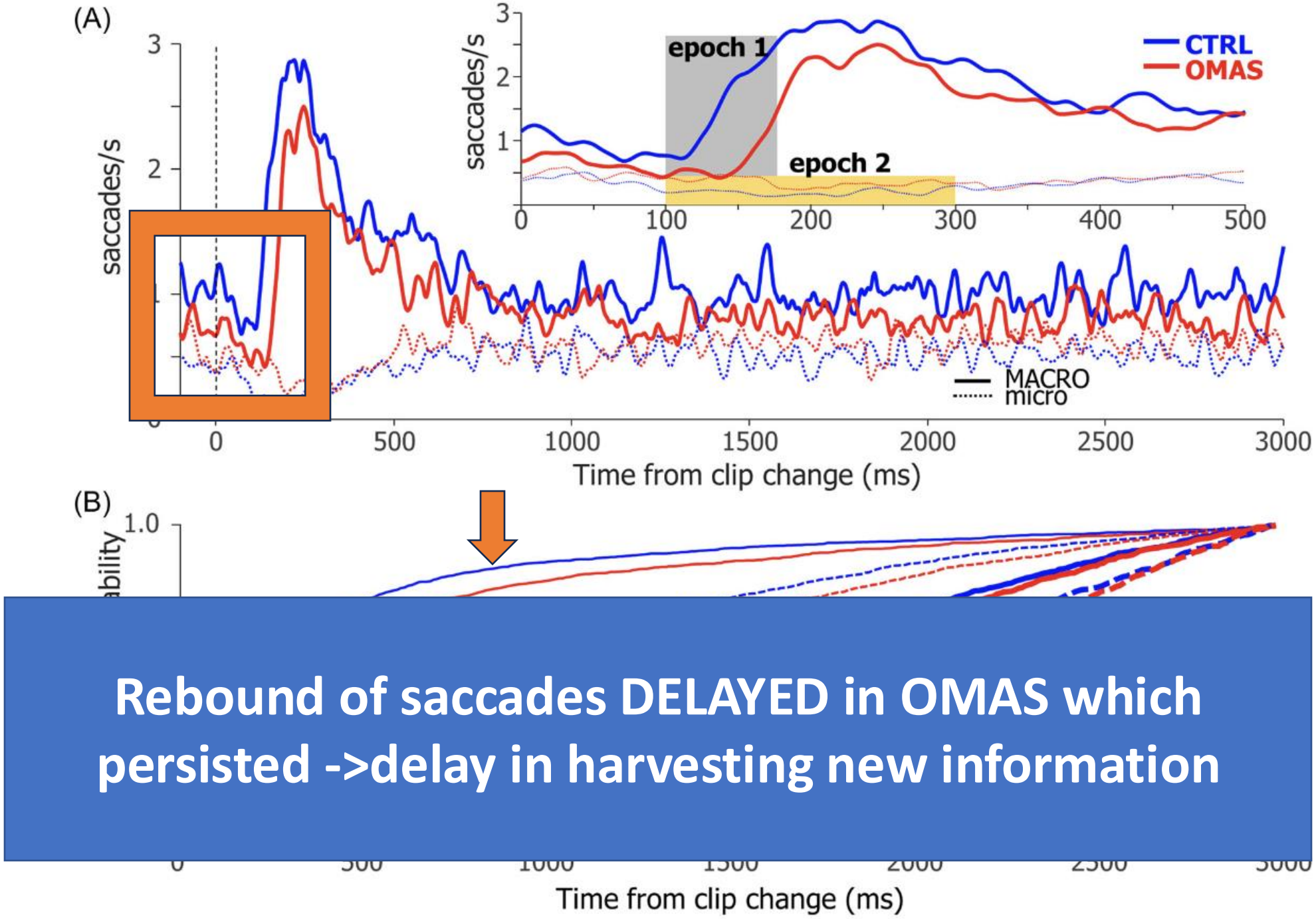


Table 1. Patient characteristics.

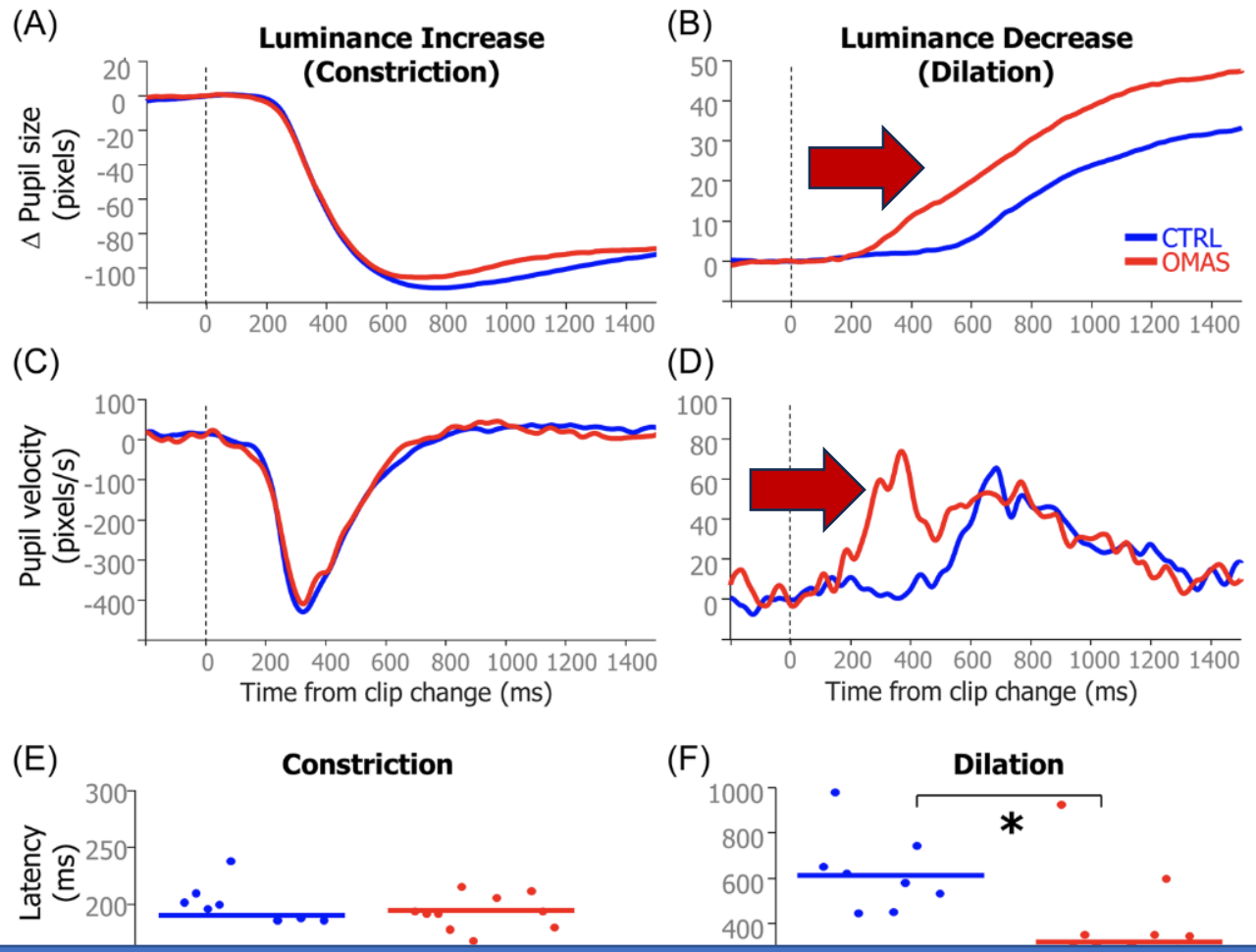
Number of patients	13 children (10 female, 3 male)
Median age of OMAS at eye-tracking	5.3 years (IQR: 2.3–5.9)
Median age at onset of OMAS	1.8 years (IQR: 1.5–2.4)
Median OMAS score at onset	8 (IQR: 5–10)
Median time from onset to first MRI	6 days (IQR: 5–17)
Structural MRI abnormalities at onset[a]	1
Median time from first MRI to first steroids	5 days (IQR: 2–13)
Median time from onset to eye tracking	2.3 years (IQR: 1.0–5.2)
Median OMAS score at eye tracking	1 (IQR: 1–2.2)
Median opsoclonus score at eye tracking	0 (no patients with ongoing opsoclonus)
Median time from onset to follow-up MRI	2.8 years (IQR: 1.4–3.9; range: 1.1–13.3)
Number of CTRL	13 children (10 female, 3 male)
Median CTRL age at eye tracking	5.0 years (IQR: 3.3–6.9)



More short duration fixations, fewer longer fixation durations



Rebound of saccades DELAYED in OMAS which persisted ->delay in harvesting new information



Reduced pupil dilatation latency, greater pupil dilatation speed

Bottom line

- More short duration fixations
- Delayed rebound in macro-saccade rate following clip change
- Reduced pupil dilatation latency, greater pupil dilatation speed

Ongoing oculomotor abnormalities persist even after clinical recovery

Can eye tracking provide a window to cognition in OMAS?

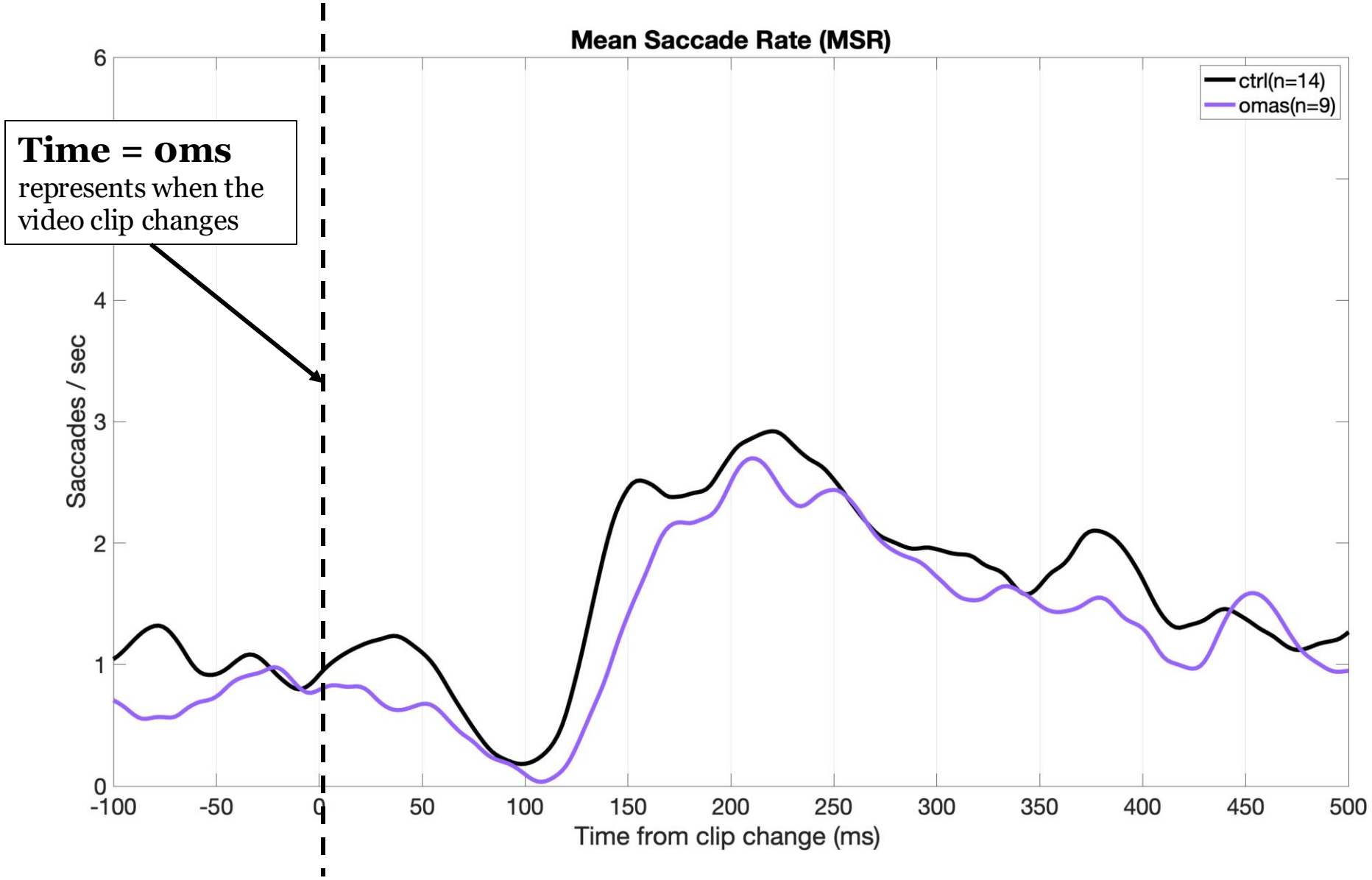
Detecting OMAS: associations of eye tracking metrics with cognitive outcomes

Susana Wu[a,b], Brian J. White[c], Donald C. Brien[c], Brian C. Coe[c], Agnes M.F. Wong[a,b], Douglas O. Cheyne[a,b], Carmen Yea[b], Douglas P. Munoz[c], E. Ann Yeh[a,b]

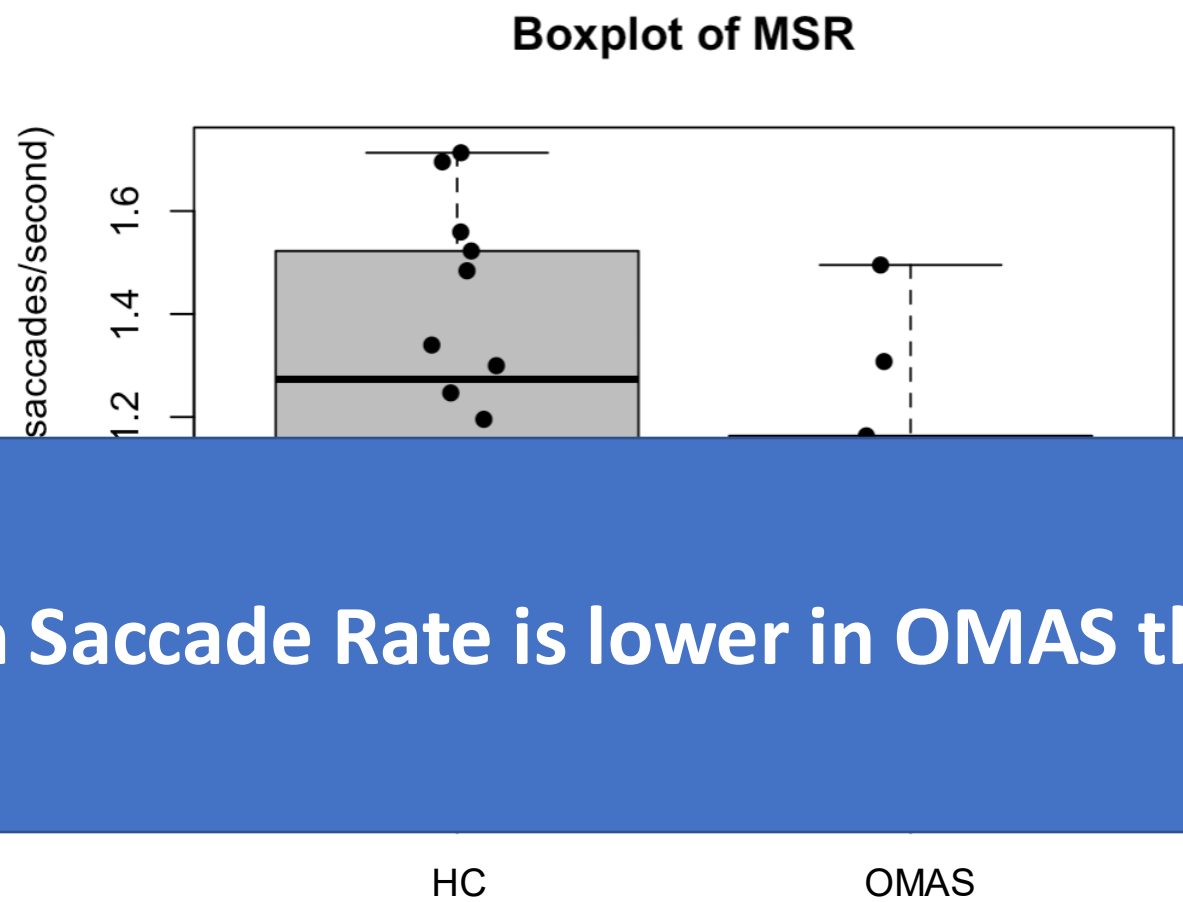
[a]University of Toronto, Toronto ON M5S 1A1, [b]The Hospital for Sick Children, Toronto ON M5G 1X8, [c]Queen's University, Kingston ON K7L 3N6

Demographics

	HC Participants (N=15)	OMAS Participants (N=11)	p-value
Female, n (%)	12 (80%)	9 (82%)	0.912
Age (months), mean (SD)	114.467 (56.342)	102.000 (50.976)	0.562
Race, n (%)			
White	6 (40%)	4 (36%)	0.858
Non-White	9 (60%)	7 (64%)	
Time from Symptom Onset to Data Collection (years), mean (SD)	---	6.2 (4.3)	---


Mean Saccade Rate (MSR)
Time = 0ms
represents when the video clip changes
ctrl(n=14)
omas(n=9)
Saccades / sec
Time from clip change (ms)
0
1
2
3
4
6
-100
-50
0
50
100
150
200
250
300
350
400
450
500

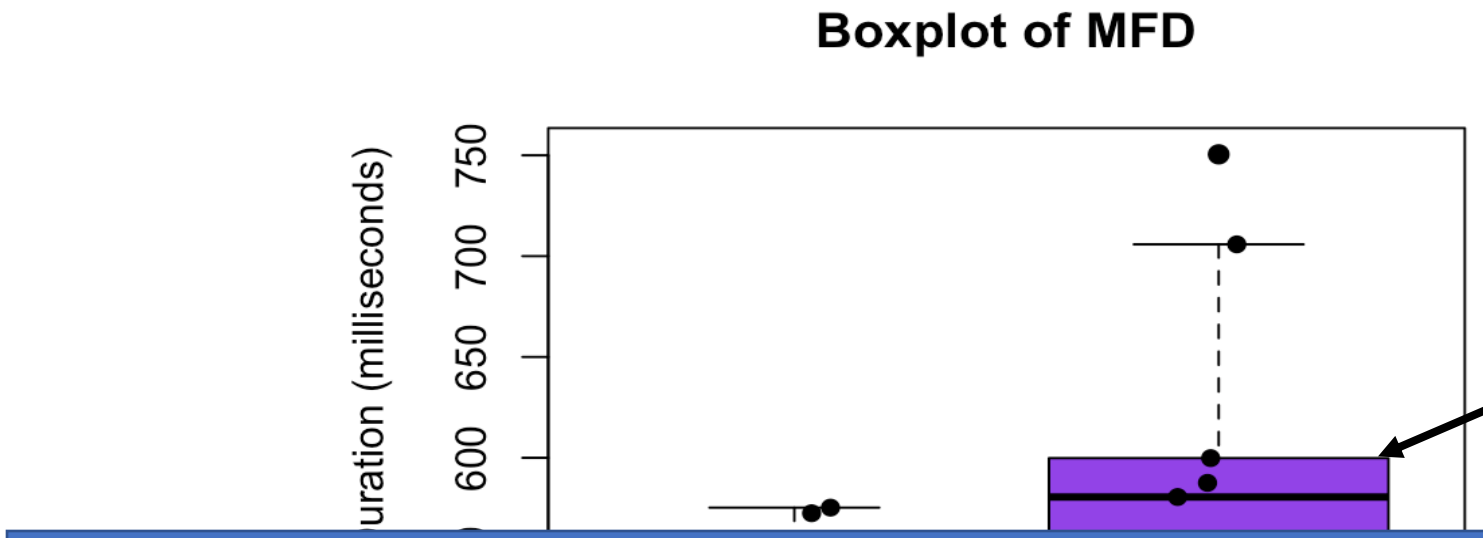
	HC (n=14)	OMAS (n=9)	p-value	effect size
Mean Saccade Rate (saccades/sec)	1.260	0.900	**0.033**	1.026



Deficits in the *initiation* and *execution* of saccades to shift attention when
v visual

Mean Saccade Rate is lower in OMAS than HC

	HC (n=13)	OMAS (n=9)	p-value	effect size
Mean Fixation Duration (milliseconds)	499.548	579.461	**0.043**	1.045

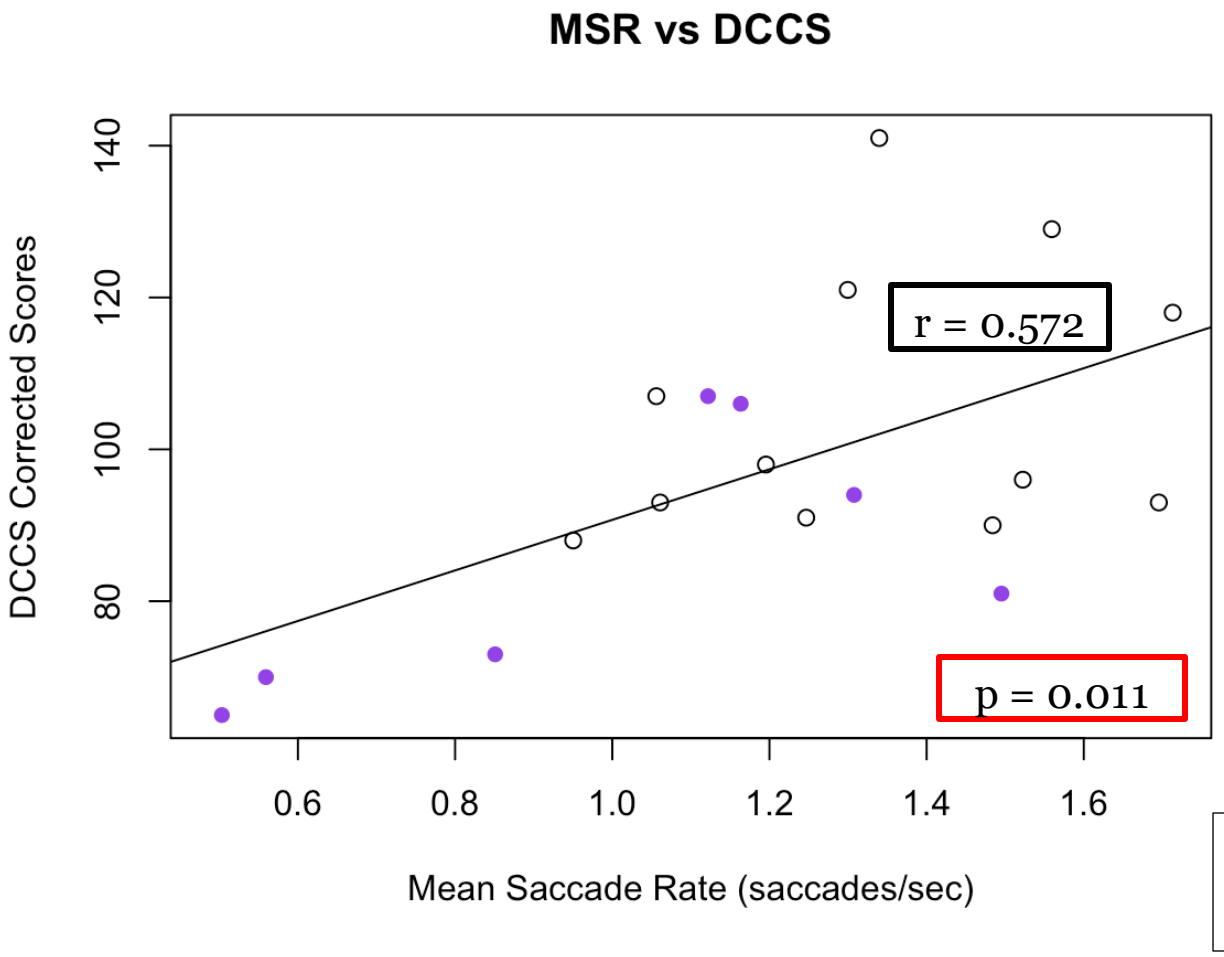


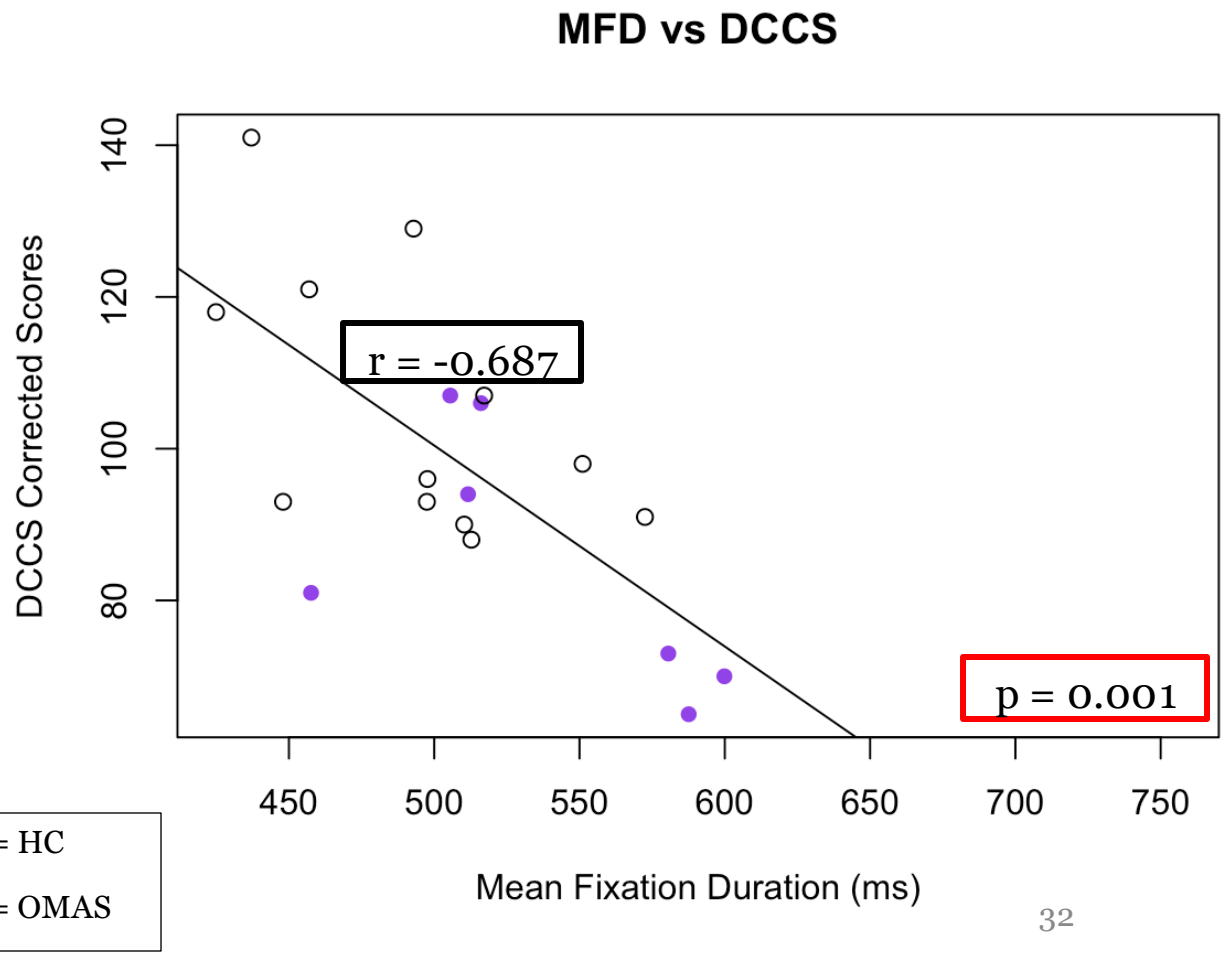
Children with OMAS are less efficient in harvesting new visual information through the generation of saccades

Mean Fixation Duration is higher in OMAS than HC

Lower MSR is correlated with lower scores on the Dimensional Change Card Sort Task (DCCS)

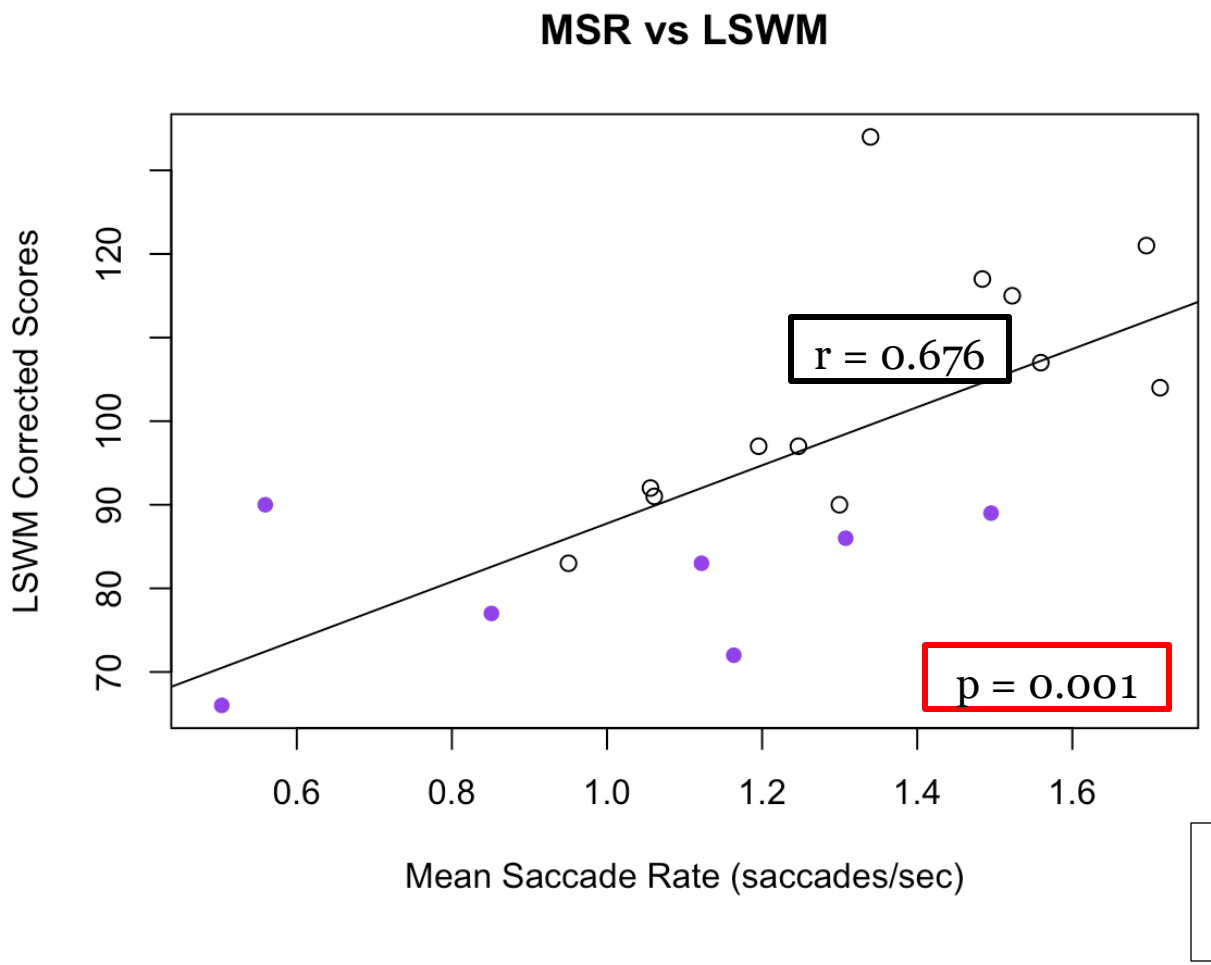
Longer MFD is correlated with lower scores on the Dimensional Change Card Sort Task (DCCS)

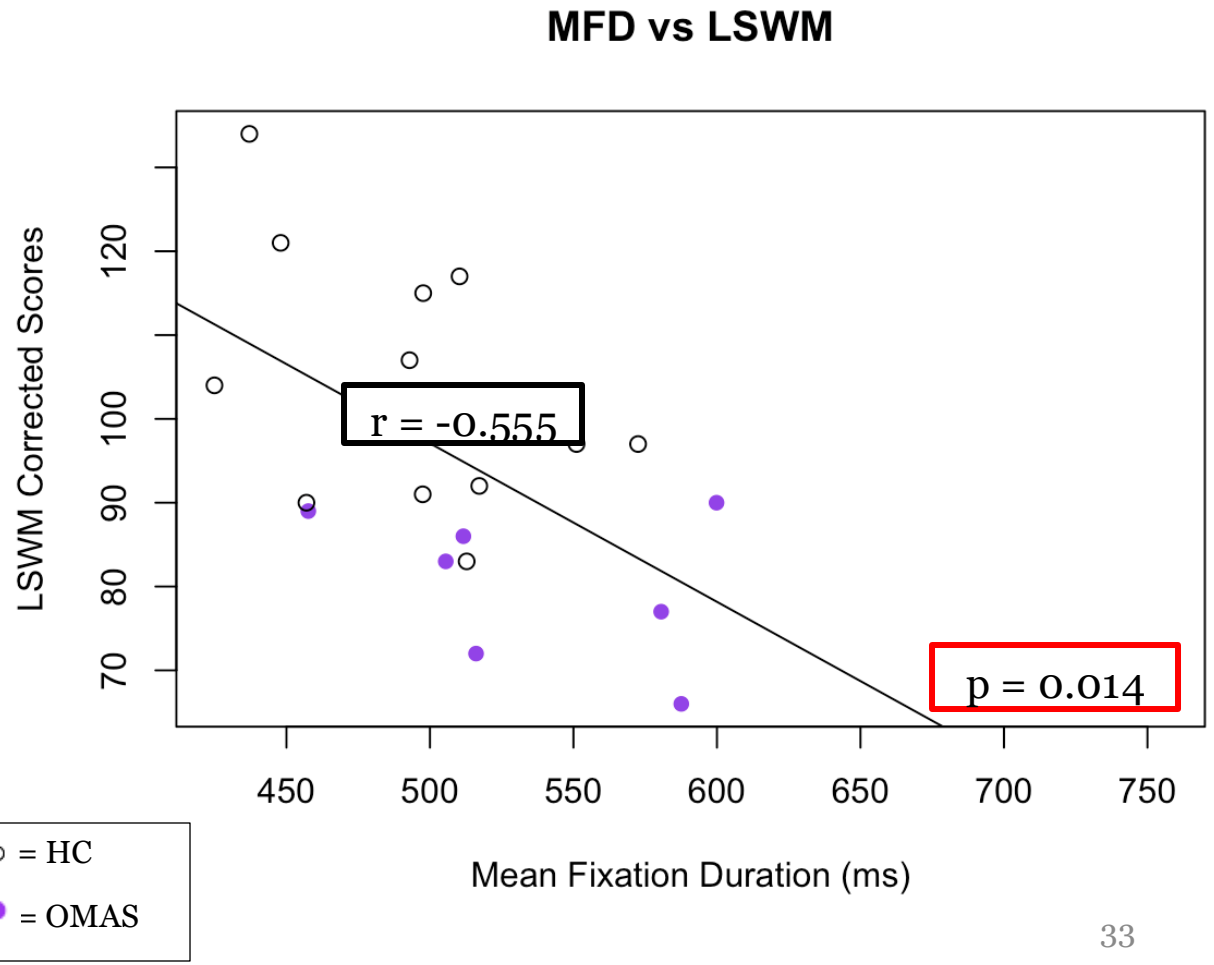




Lower MSR is correlated with lower scores on the List Sorting Working Memory (LSWM) Test

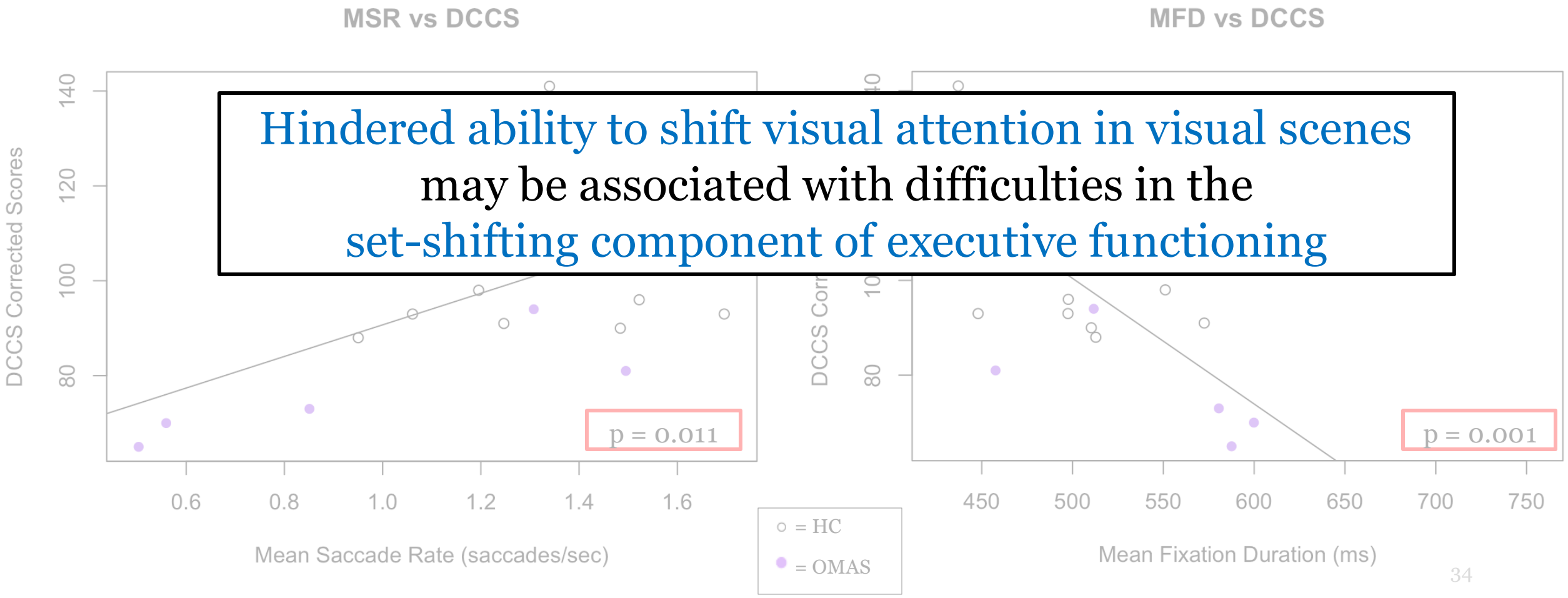
Longer MFD is correlated with lower scores on the List Sorting Working Memory (LSWM) Test





Lower MSR is correlated with lower scores on the Dimensional Change Card Sort Task (DCCS)

Longer MFD is correlated with lower scores on the Dimensional Change Card Sort Task (DCCS)



Hindered ability to shift visual attention in visual scenes may be associated with difficulties in the set-shifting component of executive functioning

- **Small cohort size!**

Larger, Multi-Site Pilot underway

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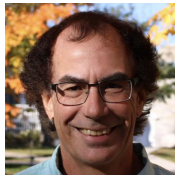
Queen's UNIVERSITY



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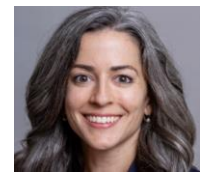
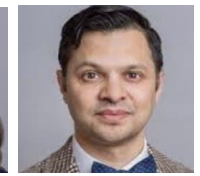
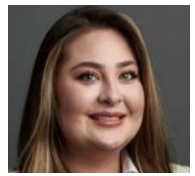
Children's Hospital LOS ANGELES

Cincinnati Children's
changing the outcome together







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Conclusions

- Eye tracking abnormalities are present even after recovery in children with OMAS
- Brain structure and cognitive function abnormalities are also seen
- Eye tracking is a window to cognitive function
- Preliminary data suggests the presence of correlations between eye tracking abnormalities and specific cognitive outcomes
- Multi-site studies are underway

Acknowlec

- SickKids/Yeh team
  - Tara Feltham
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  - Areej Mahjoub
  - Rabporn Suntornlohanakul
  - Amal Warsame
  - Carmen Yea
  - Rachel Kang
  - Sajith Rajapaksa
  - Vicky Chen
  - Curtis Hay
  - Lama Almojah
  - Ines El Najar
  - Su

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Brenda Banwell

Samantha Fernandez

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SickKids Neurosciences & Mental Health

SickKids Garry Hurvitz Centre for Brain & Mental Health

Multiple Sclerosis Society of Canada

Stem Cell Network Réseau de cellules souches

oirm Ontario Institute for Regenerative Medicine

CMSC The Consortium of Multiple Sclerosis Centers

MS National Multiple Sclerosis Society