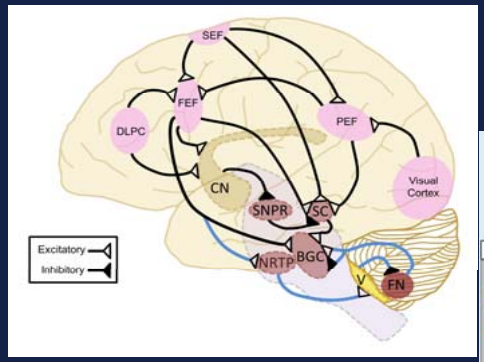
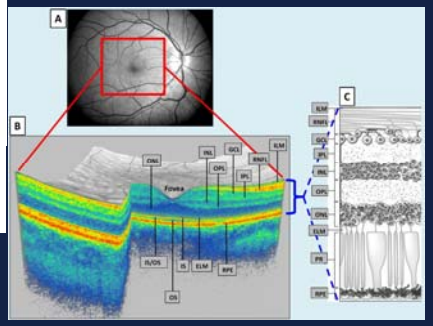
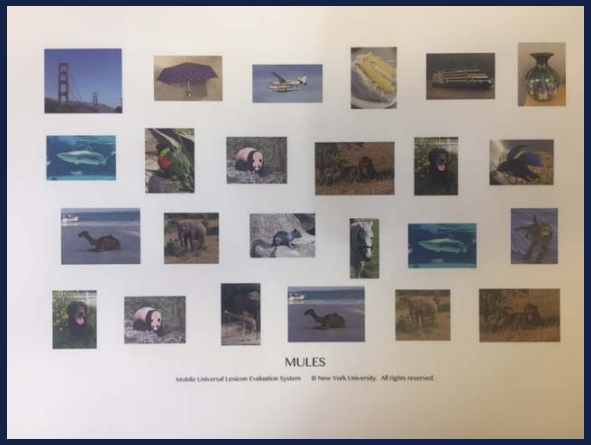
The Neuro-Ophthalmology of Traumatic Brain Injury







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Co-Director, NYU Concussion Center

The speaker and her research team have no financial interest in any of the tests or devices discussed in this presentation

Dr. Balcer has received consulting fees from Biogen for work related to multiple sclerosis visual outcome measures

We Need Vision!

Actually, the value of vision in concussion has long been recognized…

The Concussion Conundrum

- Sport concussions drawing national attention
- Learned an enormous amount in last decade
- Doubling of concussion rate may relate to increased recognition, speed and size of athletes
- Concern about short and long term effects

Concussion

- Mildest form of TBI
- Simple definition: impulsive blow to head or body + new neurological symptom
- Loss of consciousness in less than 10%
- Nearly 4 million cases yearly - may be an underestimation, kids aged 12-15 years account for more than half of cases

JAMA Pediatrics 2016

Br J Sports Med 2005;39:196

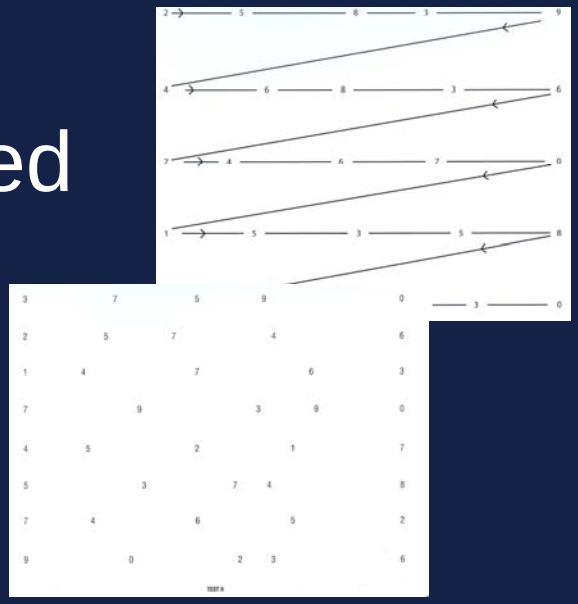
Why Do We Need a Rapid Sideline Test for Concussion?

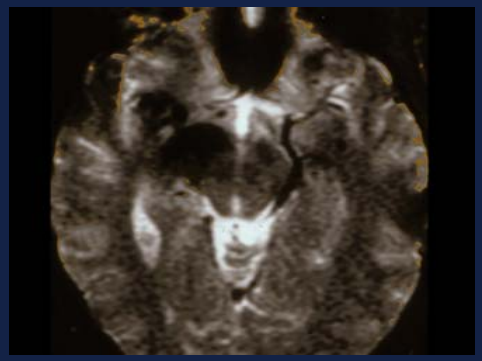
- Following a concussion, you are 3 times more likely to have another one, most risk is early
- Multiple concussions associated with prolonged recovery and multiple symptoms
- Multiple concussions linked to long term cognitive and behavioral disturbances
- 43% hid a concussion, 22% would do it again!
- Need a tool for unclear situations (undetected concussion)

Neurol Clin Pract, 2013

Concussion Tests: 2 Types

- Testing for *diagnosis*: King-Devick (K-D) test, Standardized Assessment of Concussion (SAC)
- Testing for *management*: ImPACT, other computerized testing, formal neuropsych





J Int Neuropsych 2016

Sideline Testing: What is the Evidence?

- Simple definition of concussion, but need better tools!
- SCAT3 put together by consensus, lacks a vision test (definite gap)
- New concussion consensus statements may not include vision
- This is likely not due to a lack of data!

Sideline Testing

Symptom Checklist

SYMPTOM EVALUATION

3 How do you feel?

"You should score yourself on the following symptoms, based on how you feel now".

	none		mild		moderate		severe
Headache	0	1	2	3	4	5	6
"Pressure in head"	0	1	2	3	4	5	6
Neck Pain	0	1	2	3	4	5	6
Nausea or vomiting	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Balance problems	0	1	2	3	4	5	6
Sensitivity to light	0	1	2	3	4	5	6
Sensitivity to noise	0	1	2	3	4	5	6
Feeling slowed down	0	1	2	3	4	5	6
Feeling like "in a fog"	0	1	2	3	4	5	6
"Don't feel right"	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Difficulty remembering	0	1	2	3	4	5	6
Fatigue or low energy	0	1	2	3	4	5	6
Confusion	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Trouble falling asleep	0	1	2	3	4	5	6
More emotional	0	1	2	3	4	5	6
Irritability	0	1	2	3	4	5	6
Sadness	0	1	2	3	4	5	6
Nervous or Anxious	0	1	2	3	4	5	6

Total number of symptoms (Maximum possible 22)

Symptom severity score (Maximum possible 132)

Standardized Assessment of Concussion (SAC)

COGNITIVE & PHYSICAL EVALUATION

4 Cognitive assessment

Standardized Assessment of Concussion (SAC)[4]

Orientation (1 point for each correct answer)

What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
What time is it right now? (within 1 hour)	0	1
Orientation score		of 5

Immediate memory

List	Trial 1	Trial 2	Trial 3	Alternative word list		
elbow	0 1	0 1	0 1	candle	baby	finger
apple	0 1	0 1	0 1	paper	monkey	penny
carpet	0 1	0 1	0 1	sugar	perfume	blanket
saddle	0 1	0 1	0 1	sandwich	sunset	lemon
bubble	0 1	0 1	0 1	wagon	iron	insect
Total						

Immediate memory score total of 15

Concentration: Digits Backward

List	Trial 1	Alternative digit list		
4-9-3	0 1	6-2-9	5-2-6	4-1-5
3-8-1-4	0 1	3-2-7-9	1-7-9-5	4-9-6-8
6-2-9-7-1	0 1	1-5-2-8-6	3-8-5-2-7	6-1-8-4-3
7-1-8-4-6-2	0 1	5-3-9-1-4-8	8-3-1-9-6-4	7-2-4-8-5-6
Total of 4				

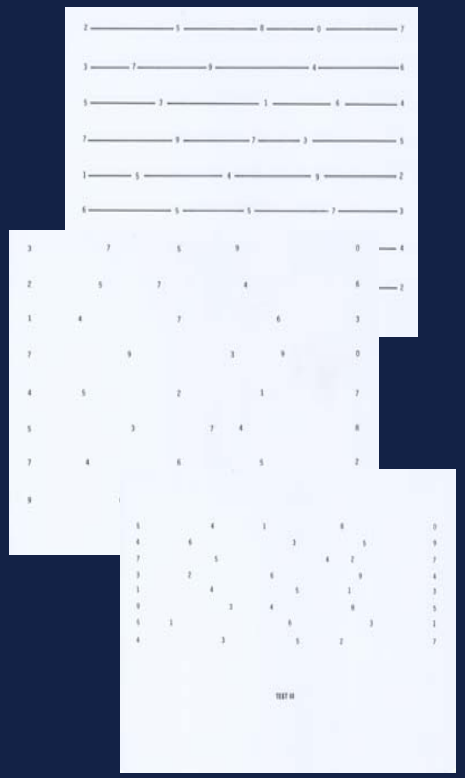
Concentration: Month in Reverse Order (1 pt. for entire sequence correct)

Dec-Nov-Oct-Sept-Aug-Jul-Jun-May-Apr-Mar-Feb-Jan	0	1
Concentration score		of 5

Sideline Testing

Balance Error Scoring System (BESS) or Timed Tandem Gait

King-Devick (K-D) Test of Rapid Number Naming or MULES (Rapid Picture Naming)

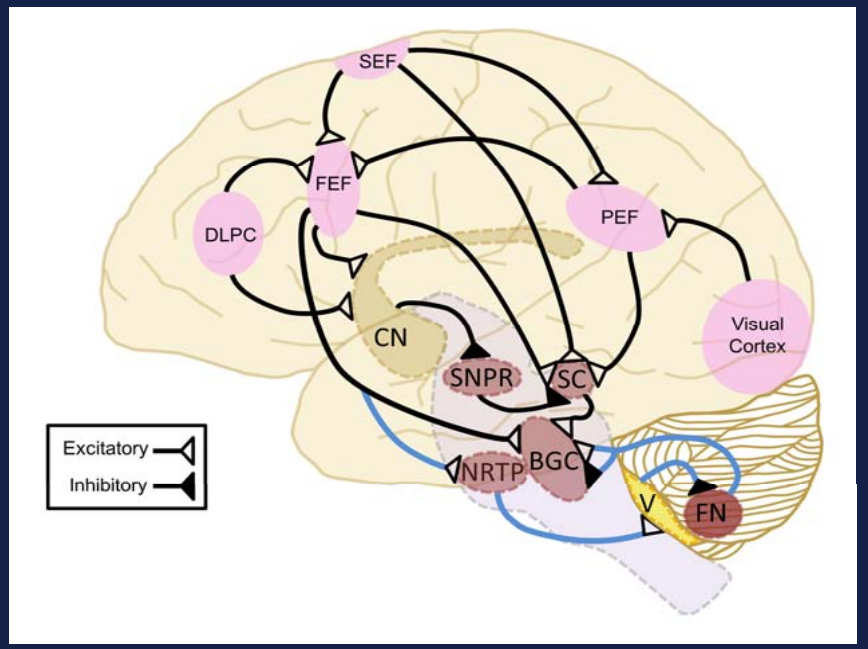


We Need Vision!

- Vision captures >50% of the brain's pathways
- Abnormal eye movements are a proven indicator of suboptimal brain function
- Can detect dysfunction not detected by cognitive tests
- Requires sensory and cognitive integration

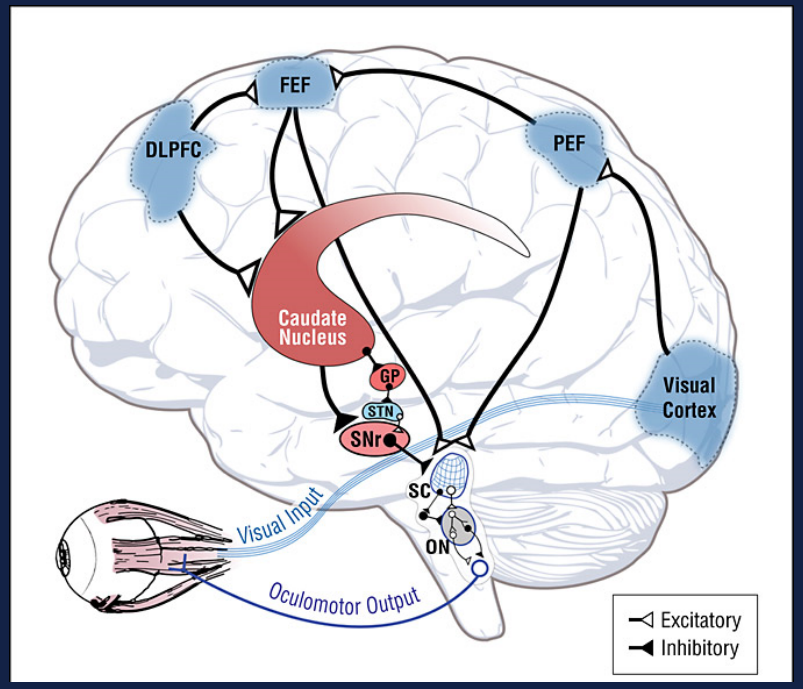

BRAIN

Impaired eye movements in post-concussion syndrome indicate suboptimal brain function beyond the influence of depression, malingering or intellectual ability



Four Major Ocular Motility Systems

- Saccadic
- Smooth Pursuit
- Vergence
- Vestibulo-ocular



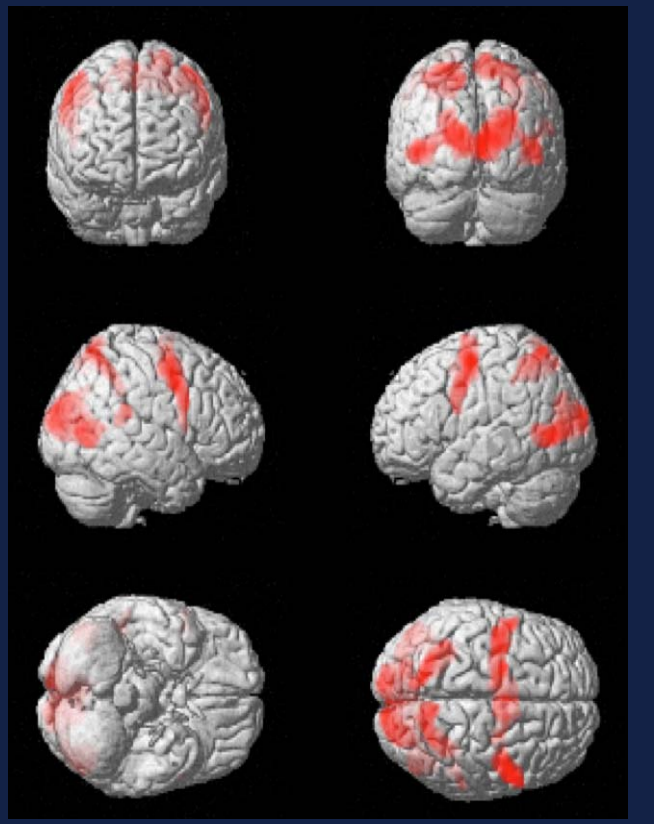
Eye Movement Abnormalities 15 to 45 Days After Mild TBI

- Saccades - 30%
- Pursuit - 60%
- Convergence - 50-60%
- Accommodation - 65%

Mil Med 2012

Many Types of Saccades

- Voluntary - FEF
- Predictive - DLPFC, FEF
- Memory - DLPFC, FEF
- Reflex - Parietal
- Antisaccade - DLPFC, FEF- direct eyes away from a target



Saccades

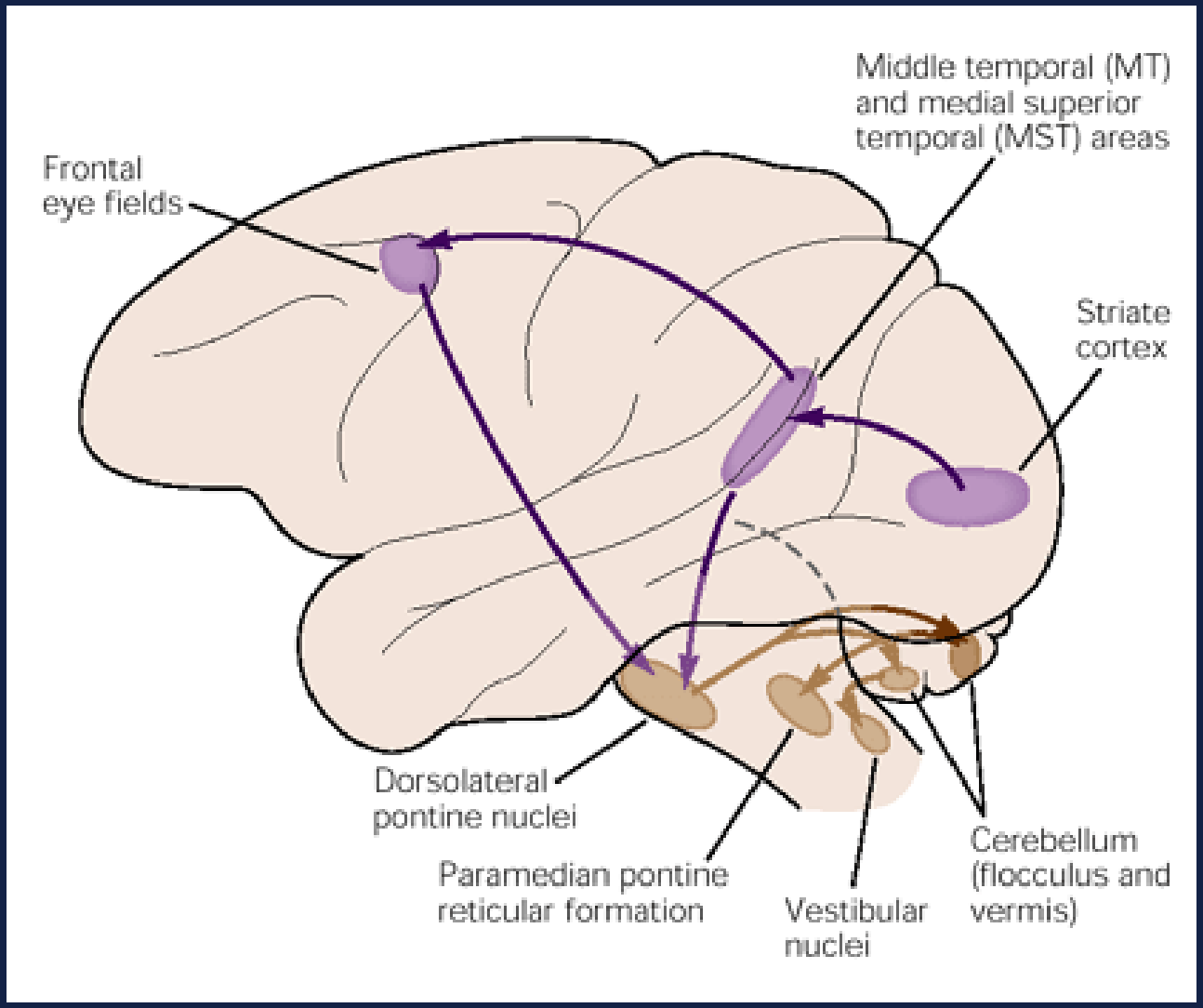
What is Abnormal on Bedside Saccade Testing?

- Most patients fall right on the target
- Some can occasionally undershoot and need one saccade
- Two saccades to a target is abnormal
- Consistently undershooting the target is abnormal
- Overshooting is abnormal

Cerebellar
(Saccade Overshoot)

Antisaccades
(Correct Responses)

Pursuit Anatomy- Cortex



Pursuit
(speed: 85 cm in 2 seconds)

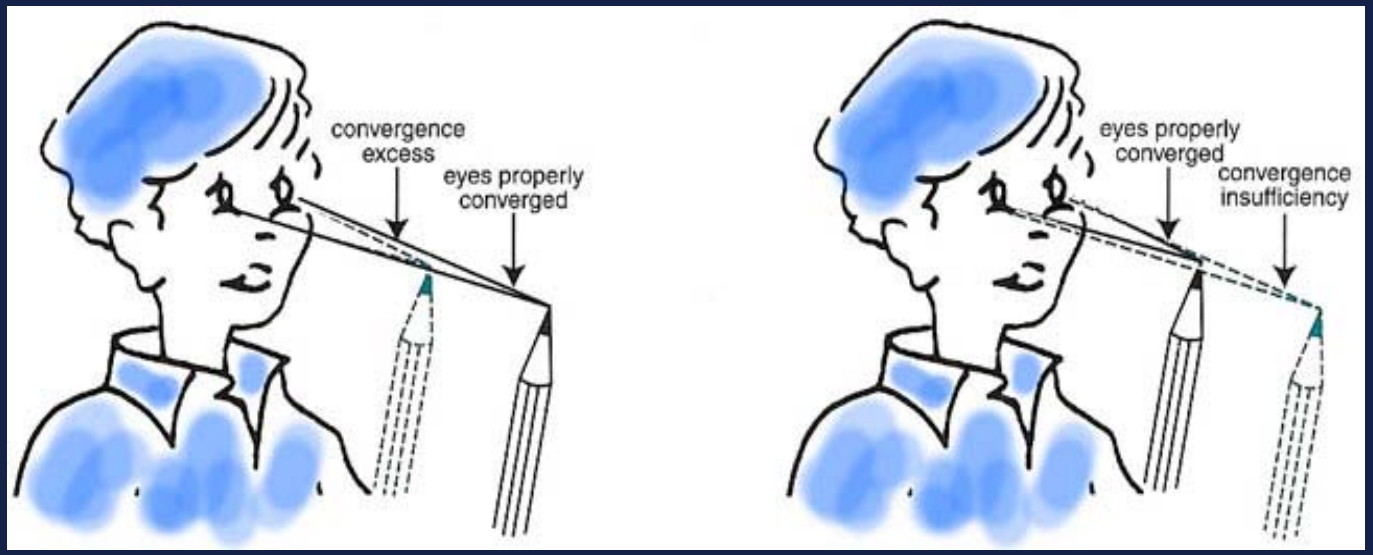
Convergence Anatomy

- Distributed Pathway
- Striate Cortex - MST, MT
- Parietal lobe
- FEF
- Projections to the supra-oculomotor area in midbrain

Testing the Convergence Response…

- Do not have patient look at your finger
- Do not have patient look at a flashlight
- Do have patient look at their own finger

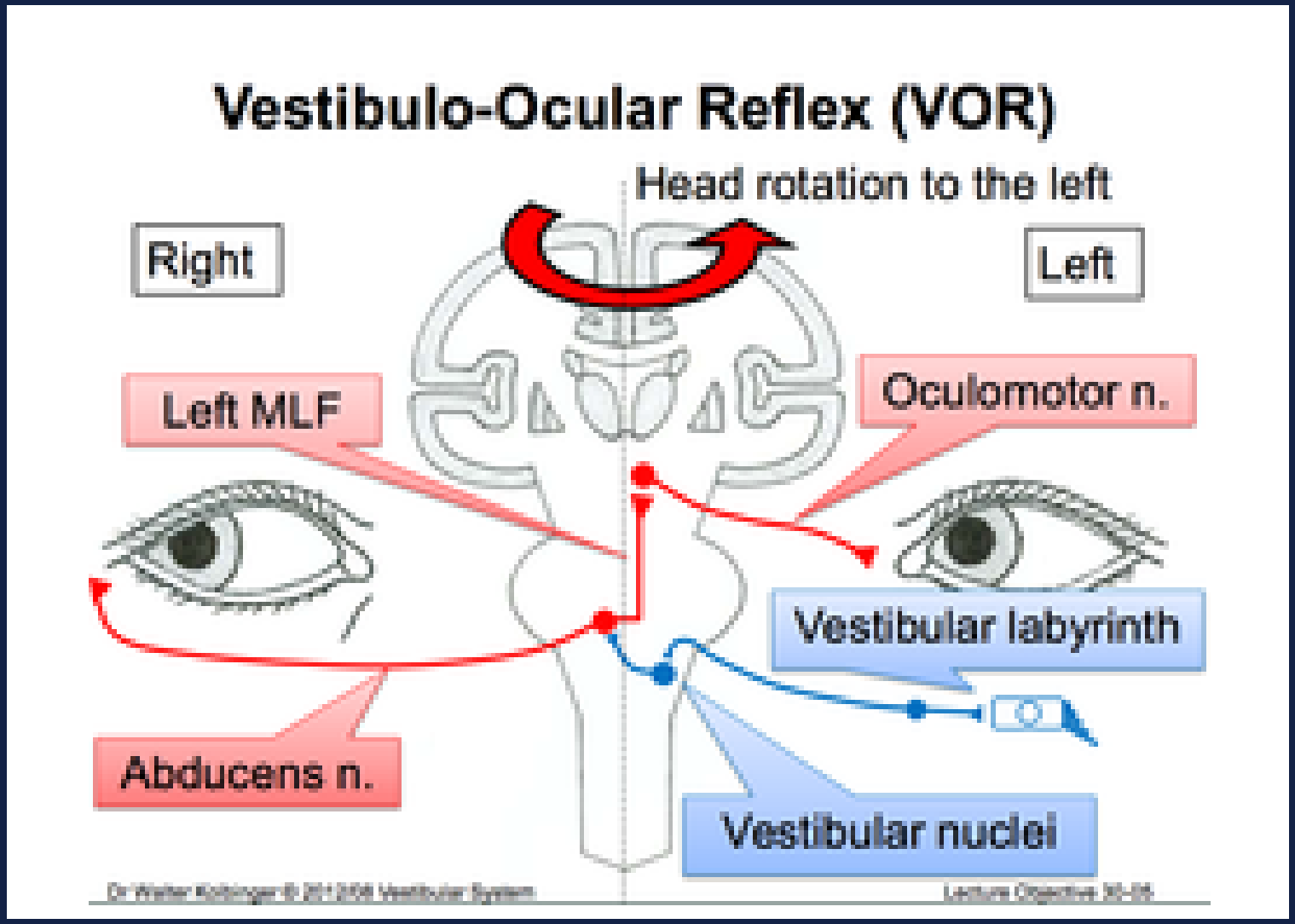
Convergence Insufficiency - Normal Range is 5 to 7 cm



Convergence Insufficiency

- Convergence amplitudes - less than 20 diopters at near
- Exophoria at near vs. distance or large exophoria of greater than 10 diopters

VOR Anatomy


Vestibulo-Ocular Reflex (VOR)
Head rotation to the left
Right
Left
Left MLF
Oculomotor n.
Vestibular labyrinth
Abducens n.
Vestibular nuclei

Vestibular-Ocular Reflex (Abnormal if Extra Saccade)

Vestibulo-Ocular Motor Screening

- Asks the patient if they have symptom provocation after various eye movements
- Neuro-ophth expertise is required, thus not possible for most teams and levels of play
- Takes 5 to 7 minutes to do
- Mostly a subjective test - symptoms provoked in 33 to 61% (VOR best)
- Misses motility problems that could be detected by objective exam
- Not validated on sidelines

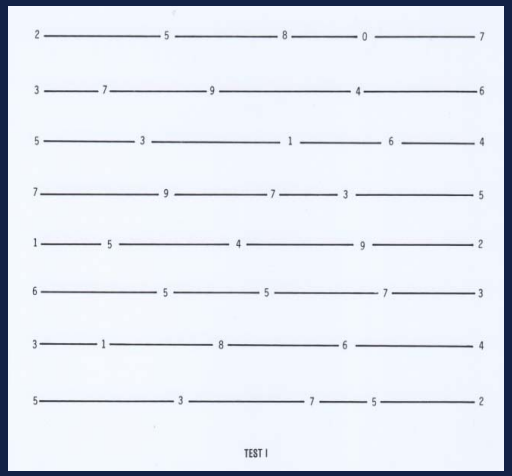
Am J Sports Med 2014

Rapid Number Naming (K-D)

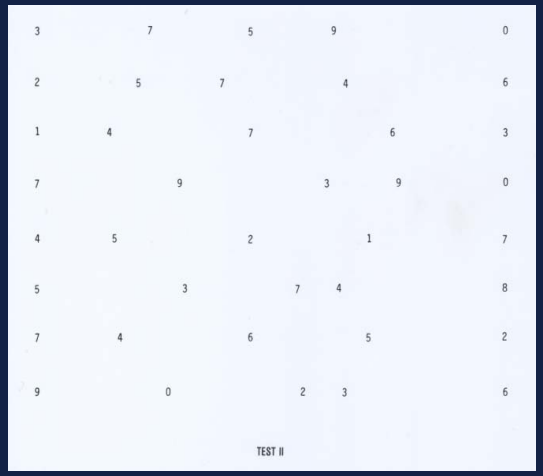
- Sideline test, takes less than a minute (tests over 100 saccades)
- Parent can administer!
- Based on saccadic eye movements, requires attention, concentration, language (DLPFC, FEF, parietal lobe)
- Lets the visual system do the work rather than the examiner

Rapid Number Naming (K-D)

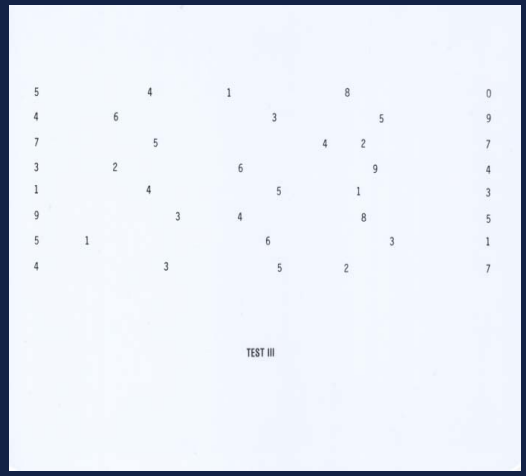
Test Card 1



Test Card 2



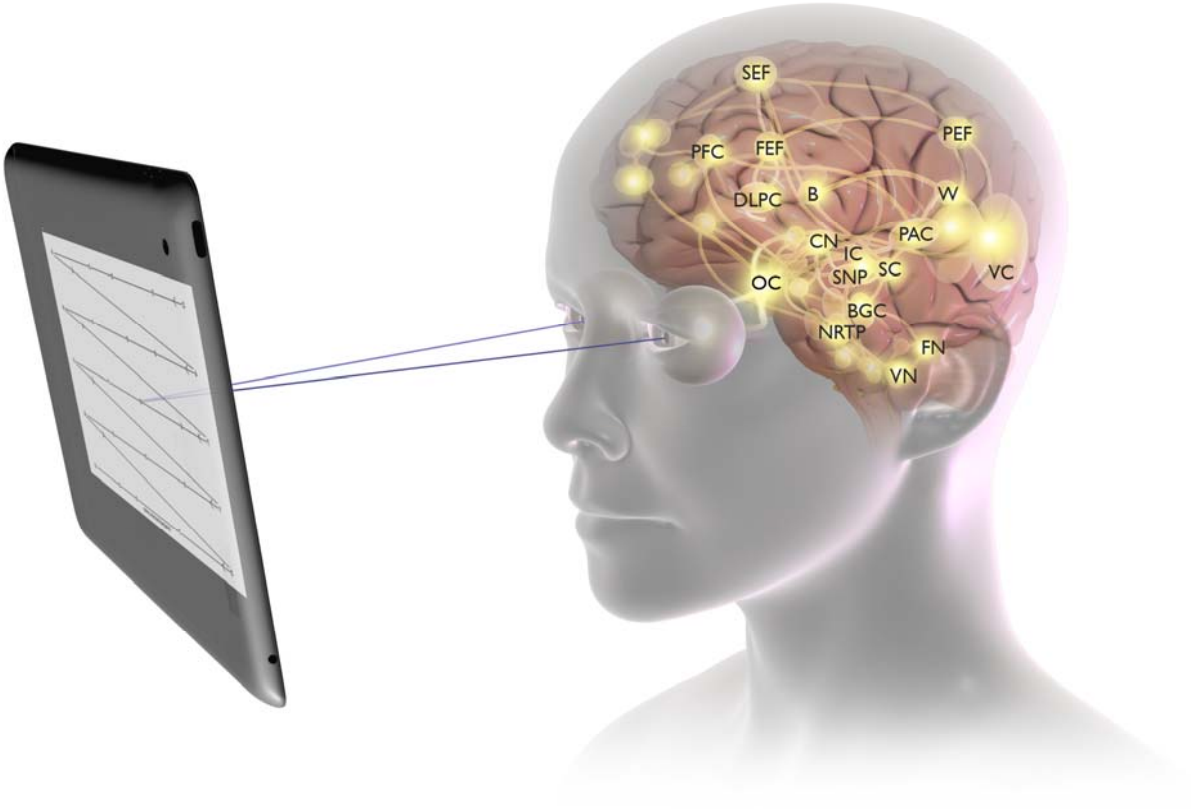
Test Card 3



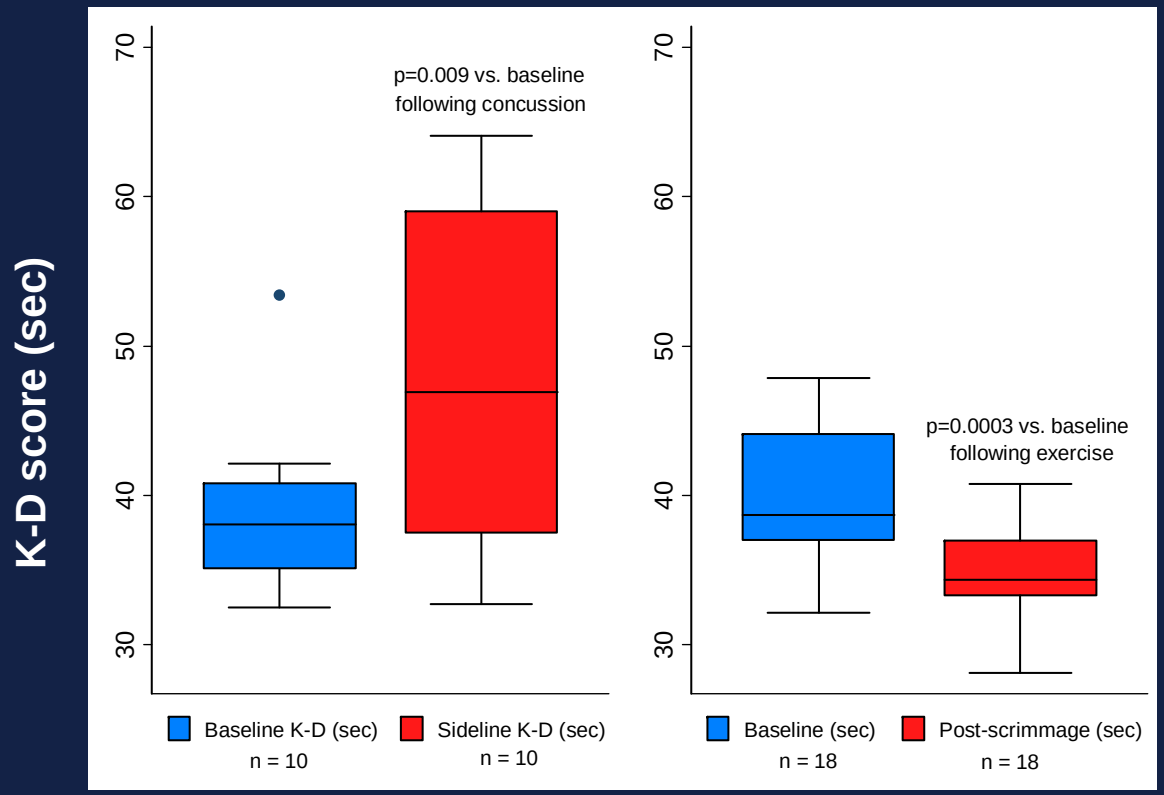
Time to read all 3 cards = baseline score

- Objective, takes <1 minute, anyone can do!
- Delay in time has been seen in concussed boxers, collegiate athletes and rugby players

The Network



The King-Devick (K-D) Test Has Been Extensively Studied



- Identified concussed athletes in boxers and MMA fighters, collegiate cohorts, New Zealand Rugby League
- Competition alone does not worsen the scores
- This test has a meta-analysis!

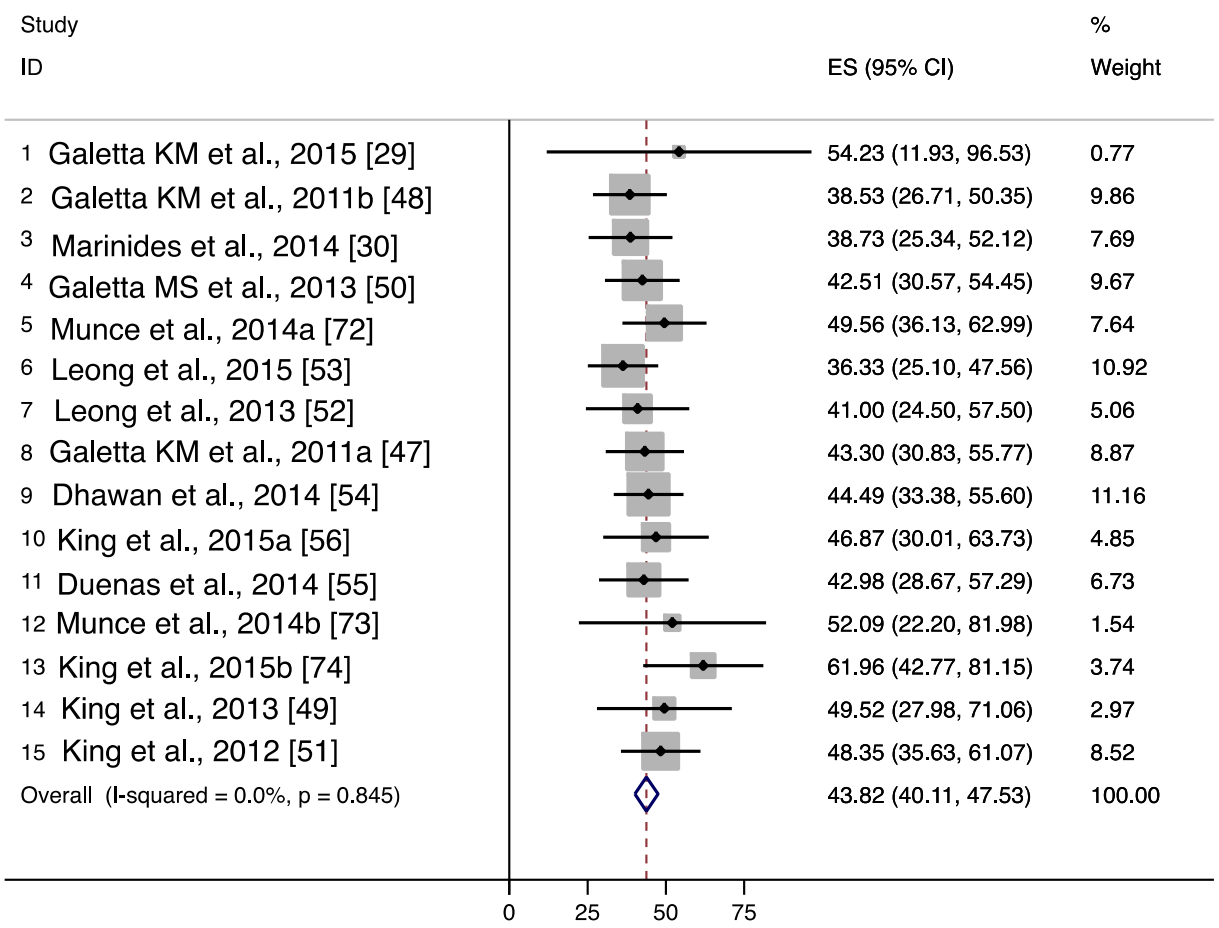
Galetta KM et al. *J Neurol Sci* 2011.

K-D Meta-Analysis

- N=1,419 athletes from 15 published studies
- De-identified participant-specific data for pooled analyses; meta-analyses using fixed-effects model techniques
- Pooled sensitivity 86% (96/112 concussed had worsening), specificity 90% (181/202 controls had no worsening of K-D)
- Relative risk of concussion if any worsening of K-D score from baseline = 4.92 (5x risk!)

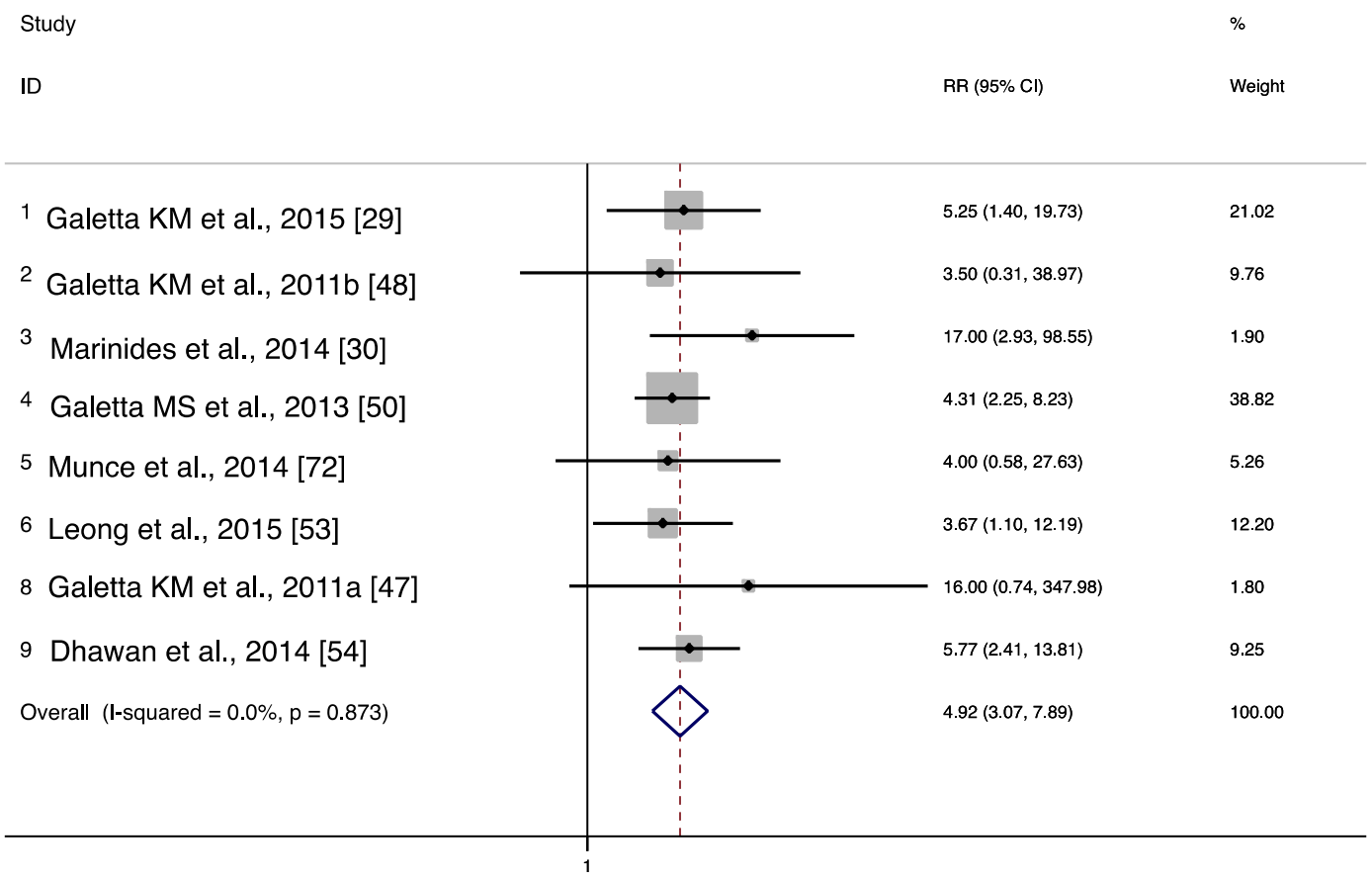
KM Galetta, et al., *Concussion* 2015

K-D Meta-Analysis (15 Studies): Weighted Average Pre-Season Baselines



KM Galetta, et al., *Concussion* 2015

K-D Meta-Analysis (15 Studies): Relative Risk of Concussion if Worse KD



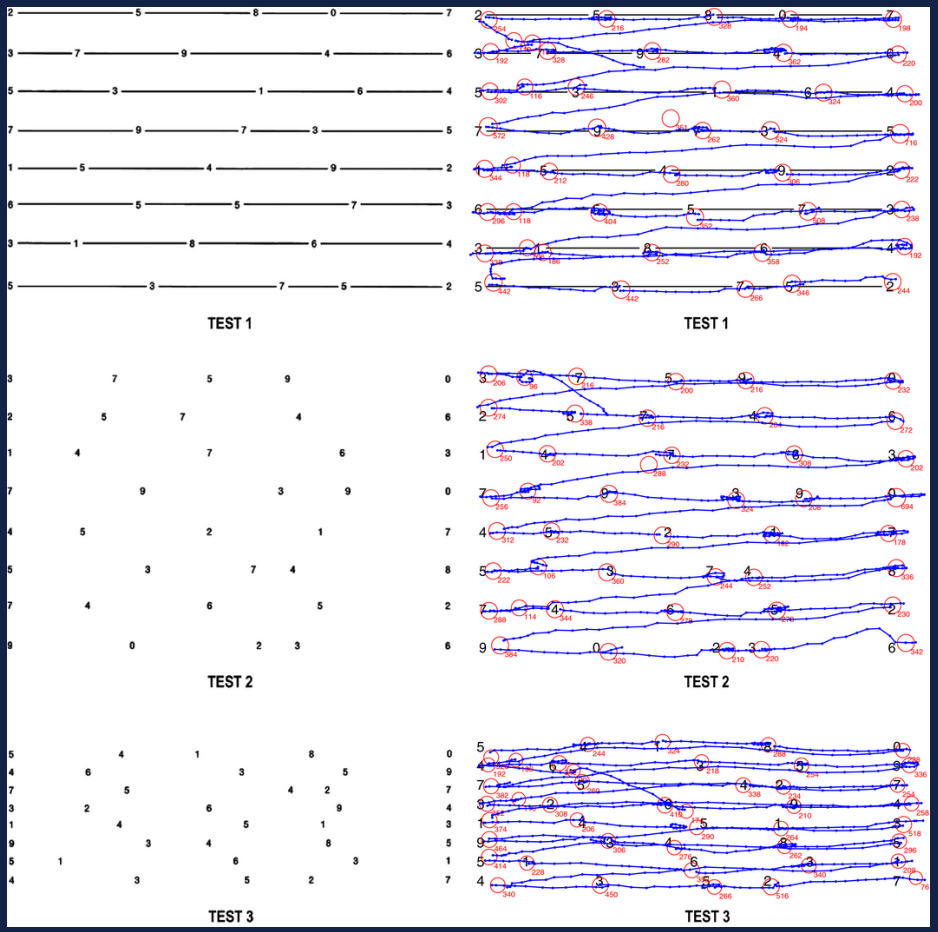
Pooled and Weighted Estimates of Relative Risk (Concussed vs. Control w/ K-D Worsening)

KM Galetta, et al., *Concussion* 2015

Rapid Number Naming in Concussion ...Digitized!

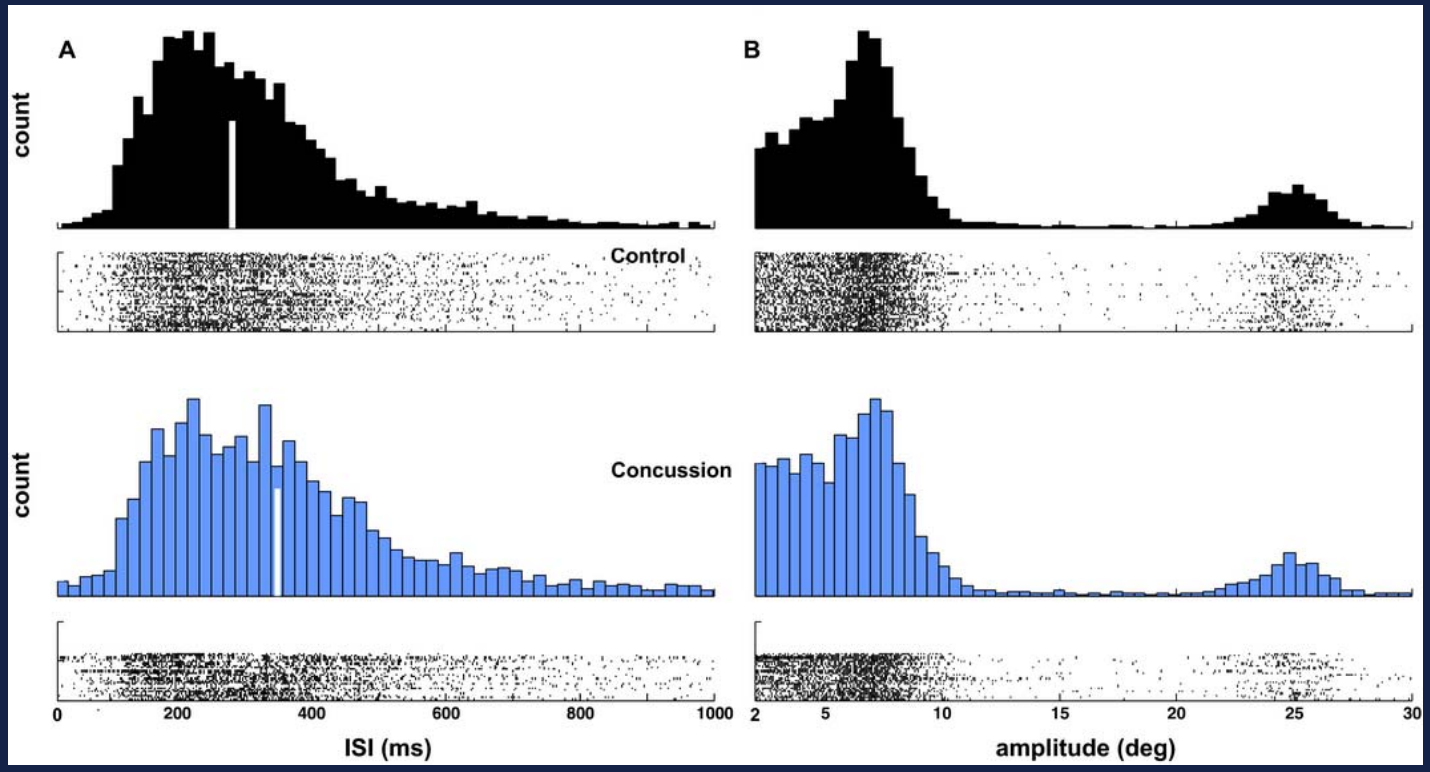
Slower times in patients compared to controls….

...and increased inter-saccadic intervals in patients with concussion



Rizzo, Rucker et al. *J Clin Translat Neurol* 2016; *J Neurol Sci* 2016.

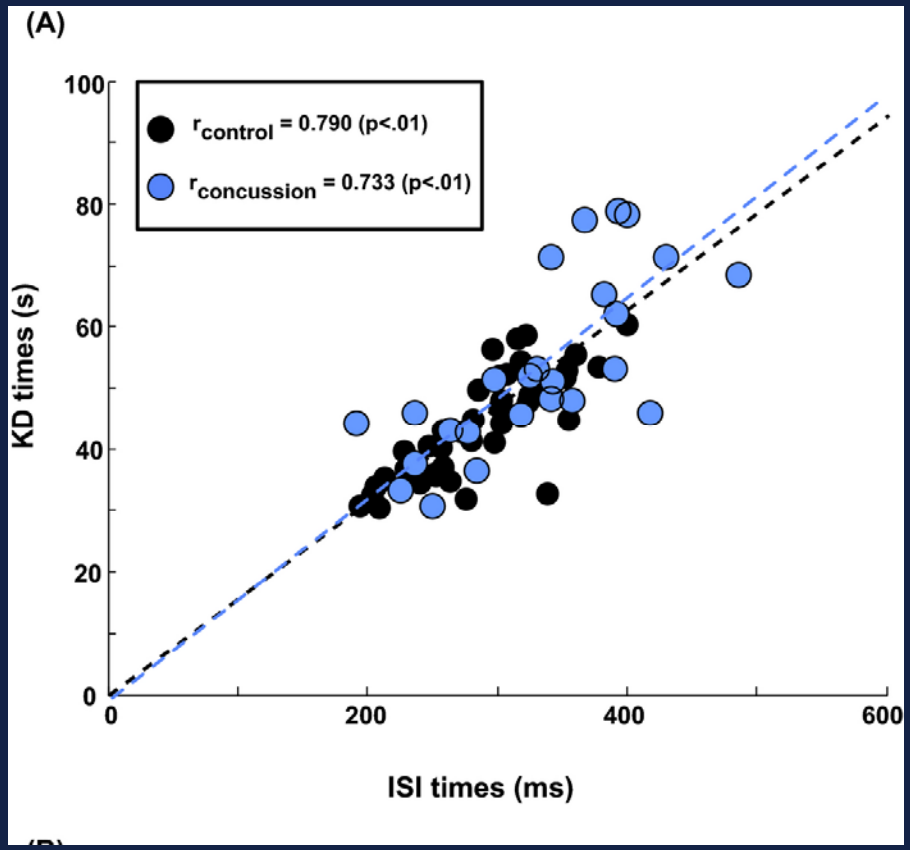
Rapid Number Naming in Concussion …Digitized!



Similar saccade amplitudes but increased inter-saccadic intervals in patients with concussion

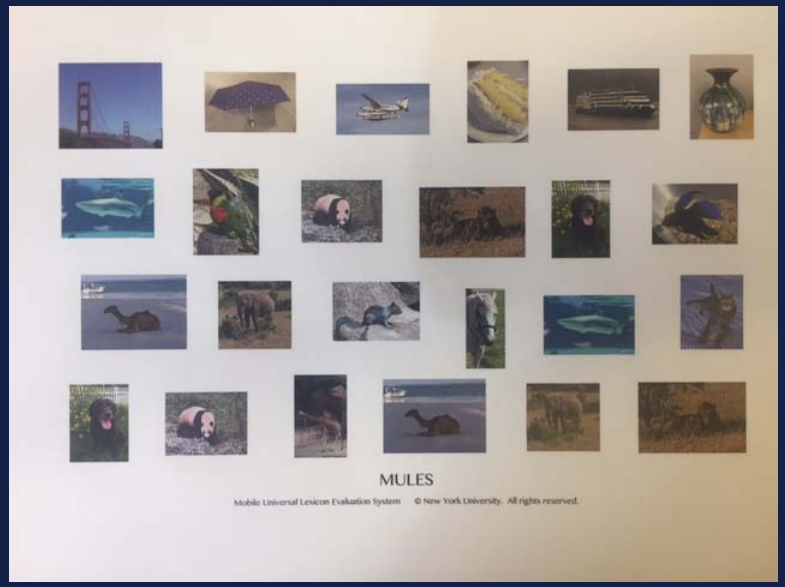
Rizzo, Rucker et al. *J Clin Translat Neurol* 2016; *J Neurol Sci* 2016.

Rapid Number Naming in Concussion …Digitized!



Longer (worse) K-D test times are associated with prolonged inter-saccadic intervals

Rizzo, Rucker et al. *J Clin Translat Neurol* 2016; *J Neurol Sci* 2016.

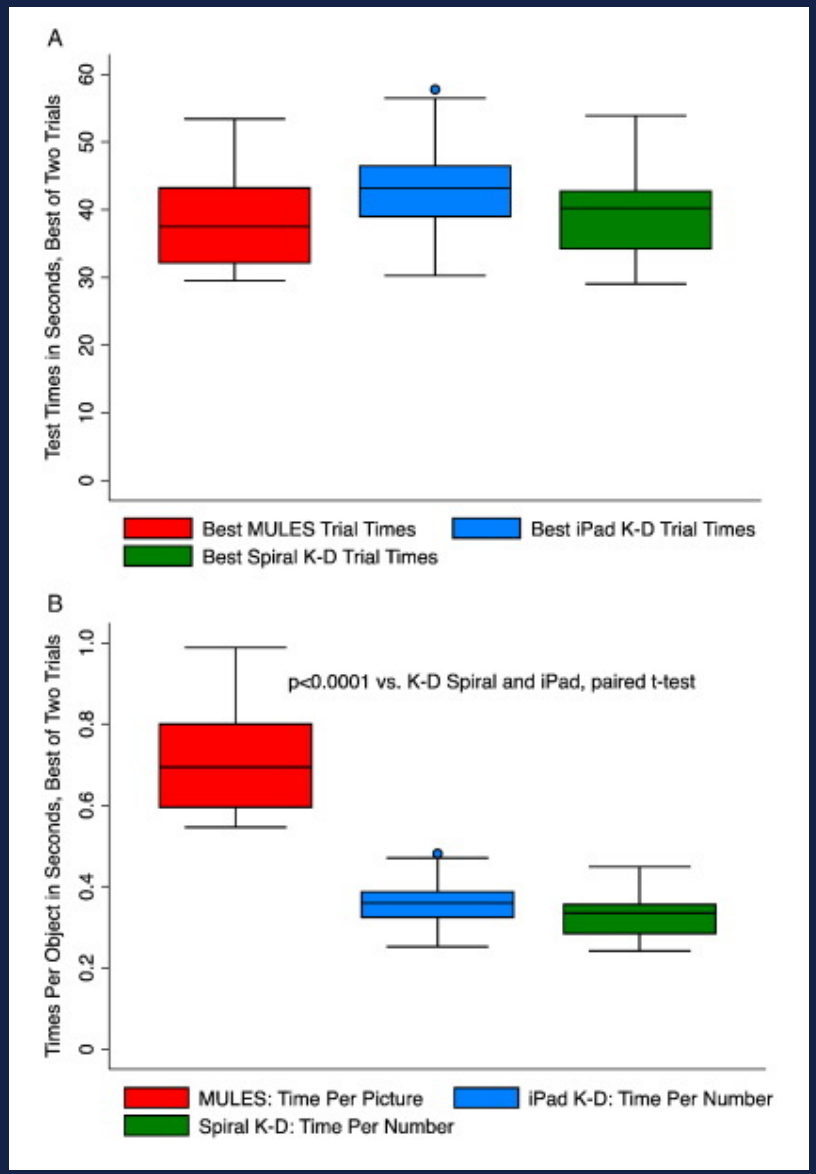


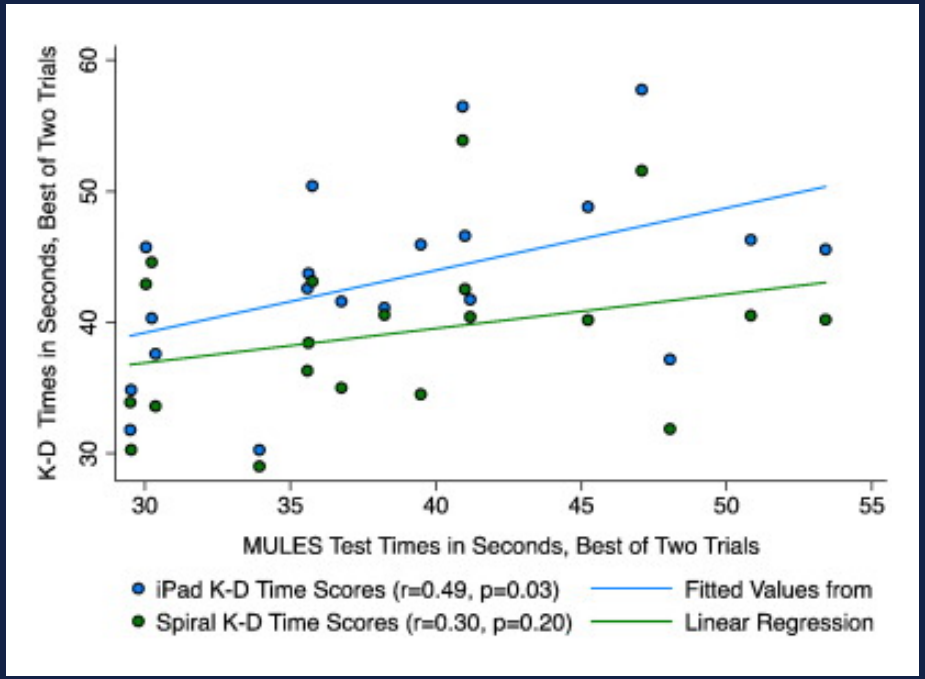
MULES Test of Rapid Picture Naming

Disease-free controls:
38.6 ± 7.3 seconds
(range 29.4 – 53.4 sec)

Cobbs et al. *J Neurol Sci* 2017.

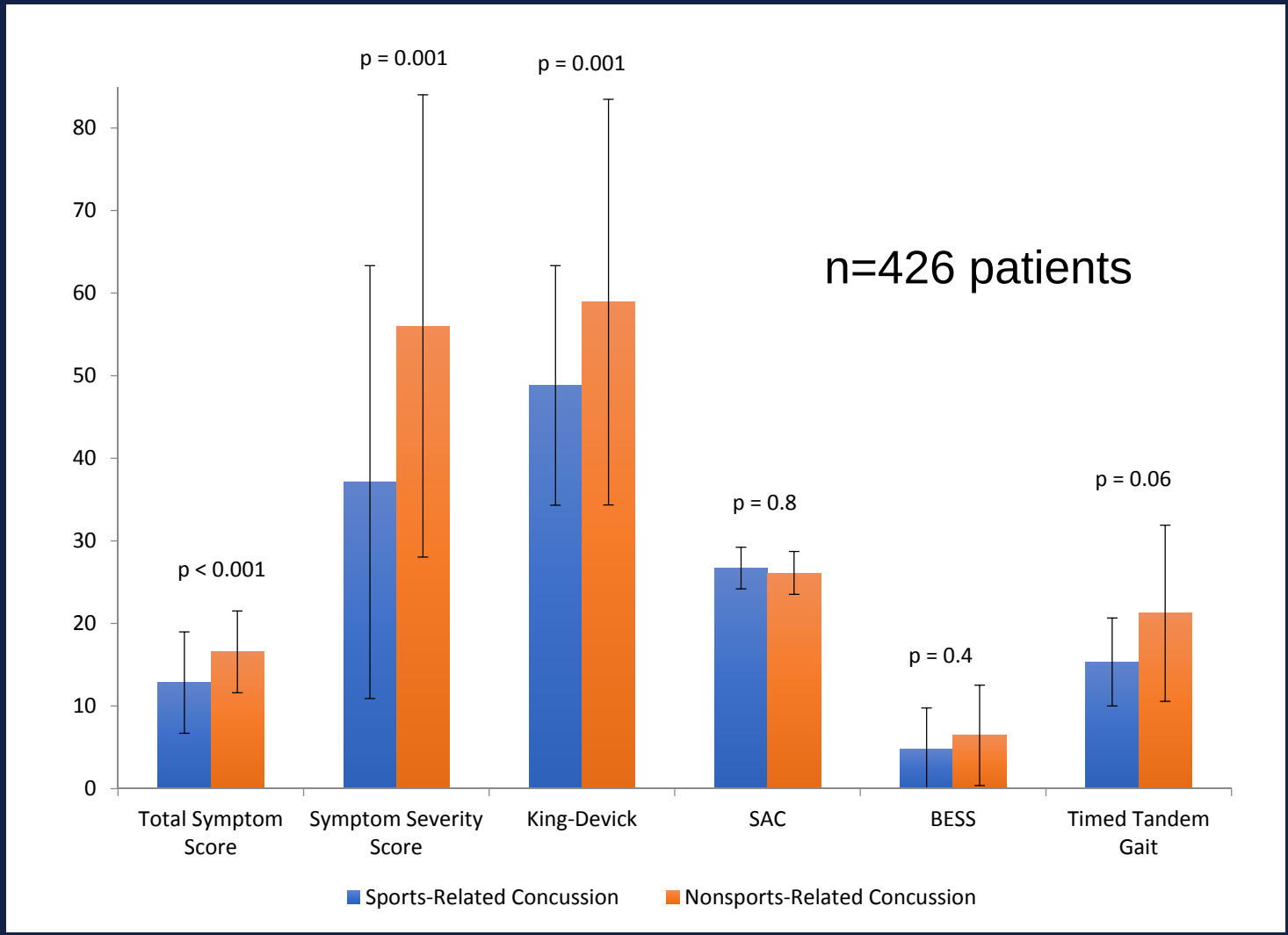
MULES and the K-D Test





Cobbs et al. *J Neurol Sci* 2017.

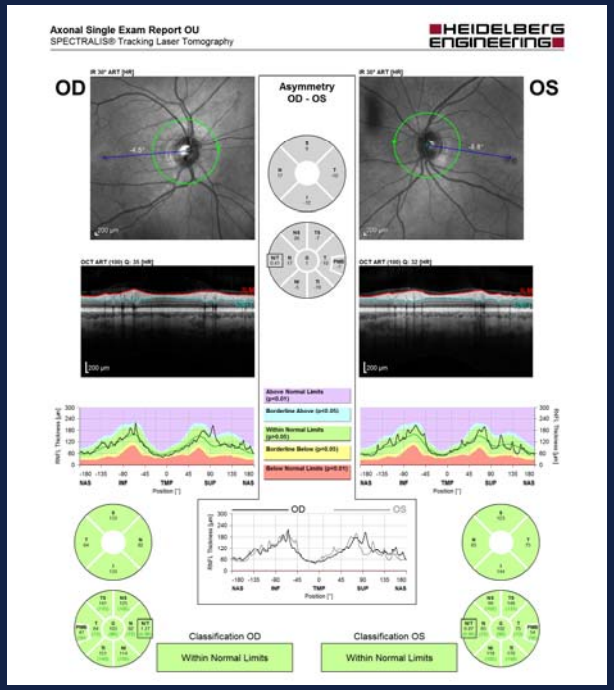
NYU Concussion Registry

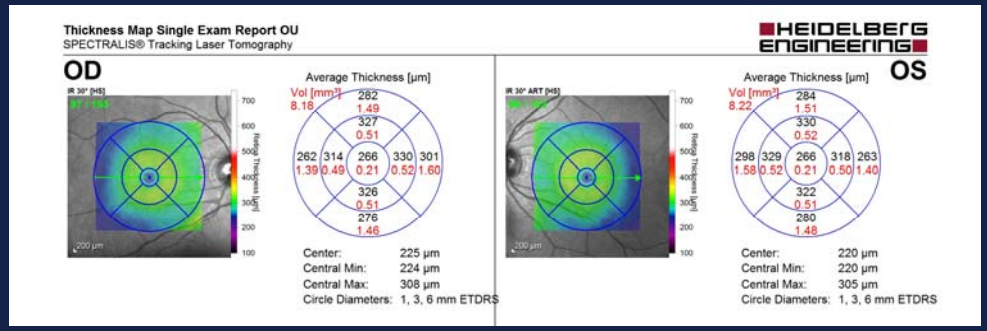


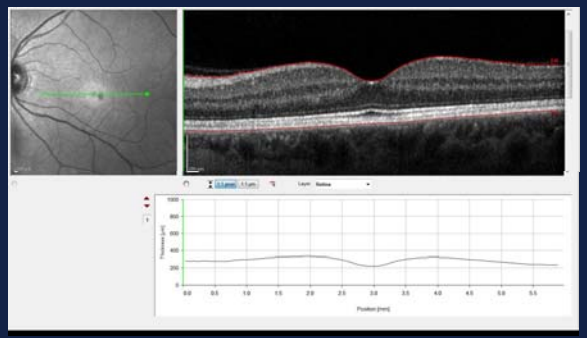
Harrold et al. Under Revision *J Neurol Sci* 2017.

At the Other End of the Age Spectrum: Vision in Chronic Traumatic Encephalopathy (CTE)

- Afferent vision is an incredibly useful tool for MS
- Can we use OCT to predict CTE? (NIH U01)

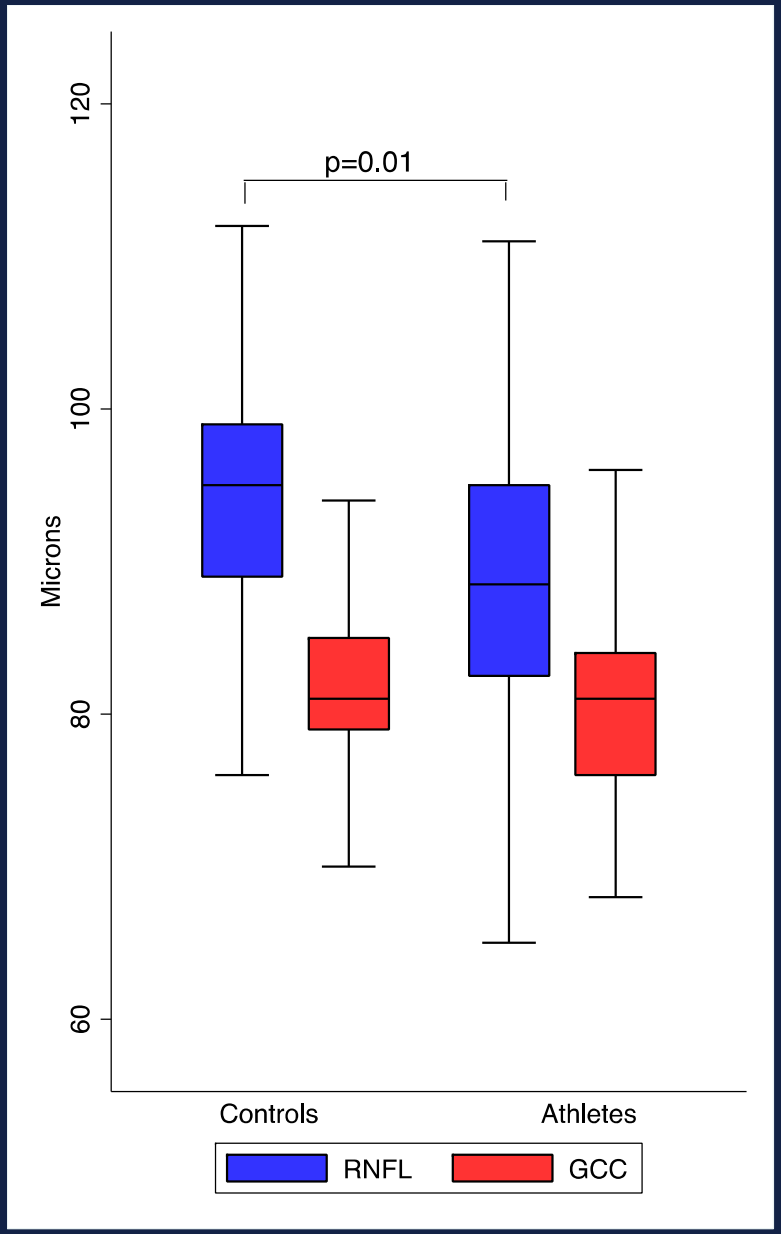






Stay Tuned!!

- OCT measures of retinal nerve fiber and ganglion cell layer thickness reduced in contact sport athletes
- Similar patterns for low-contrast acuity and quality of life!



Leong et al. To be presented at NANOS 2017.

Neuro-Ophthalmology of TBI

- Seven years of data show that rapid number naming is sensitive, additive to SCAT3
- Vision is a vulnerable system, encompasses >50% of the brain's pathways
- Simple performance measures continue to have great value and sensitivity in medicine
- Goal: establish accessible vision-based testing for sideline and clinical applications