The Concussion Conundrum:
an opportunity to explore the last frontier, TIME

Jam Ghajar MD PhD
Director, Stanford Concussion and Brain Performance Center
Founder, SyncThink
President, Brain Trauma Foundation
Research Contracts and Conflicts

Brain Trauma Evidence-based Consortium:

Director of: SyncThink®
No accepted definition or diagnostic criteria

The fog of concussion
Concussion concerns families.
Should my 8 year old play Football?
Concussion subtypes draft categories

1) Vestibular
2) Ocular-motor
3) Cognitive
4) Post-traumatic migraine
5) Anxiety/mood

Associated conditions: Sleep and Cervical

The use of subtypes to characterize symptoms and impairment provides the framework for targeted treatments to match specific concussion subtypes and recovery trajectories.
# Concussion as a disorientation disorder

## Concussion disorientation disorders

<table>
<thead>
<tr>
<th>Type 1: Ocular-motor</th>
<th>Spatial-Temporal disorientation of Self in interactions with world</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2: Vestibular</td>
<td></td>
</tr>
</tbody>
</table>

## Concussion Trigger Disorders

<table>
<thead>
<tr>
<th>Type 1: Migraine</th>
<th>Often overlaps with disorientation as a byproduct or can be isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2: Anxiety/mood</td>
<td></td>
</tr>
<tr>
<td>Type 3: Cognitive fatigue</td>
<td></td>
</tr>
</tbody>
</table>
Using Subtypes for concussion management: Stanford Sideline and Clinic Protocols
Sideline Evaluation of Concussion
Purpose of Side Line Assessment: detect impaired Brain Performance from concussion

1. Identify behavior that may indicate compromised brain performance using:
   - Spotter technology
   - Head accelerometer technology
   - Sideline view

2. Measure brain performance indicators of vulnerability for injury:
   - **Visual attention**- Orientation to moving world
   - **Vestibular/balance**- Orientation to moving self

3. You are not making a **DIAGNOSIS**, you are **SCREENING** for suboptimal brain performance from possible concussion
Suspected Concussive Event
MD present?

Yes

EYE-SYNC available?

Yes

AT performs EYE-SYNC

MPE score < 0.5?
SDTE score < 1.0?

No

Ocular-motor dysfunction confirmed. No RTP

Yes

Athlete taken to locker room for SCAT3

SAC and BESS normal

Cervical spine exam normal

Consider other differential diagnosis (e.g., dehydration, sleep deprivation, anxiety/mood, migraine headache).
Consult MD for RTP

No

SAC and/or BESS abnormal

Cognitive fatigue and/or vestibular balance dysfunction suspected. Consult MD for RTP

Yes

Cervicogenic origin confirmed. Treat accordingly. Consult MD for RTP

No

No RTP

No

EYE-SYNC available?

Yes

AT performs EYE-SYNC and SCAT3

Impairment suspected

No RTP

No

AT performs SCAT3

RTP Protocol

AT notifies academic advisor within 24 hours of incident

Refer to team MD and PT for vestibular evaluation within 24 hours or first available appointment

Team MD to follow up to confirm diagnosis, with concussion neuro MD. Additional tests and referrals as needed.

AT follow up daily or as directed by team MD. Begin progression per MD

Upon completion of stepwise progression. MD re-evaluation to determine RTP

No RTP
### Components of concussion assessment

<table>
<thead>
<tr>
<th>Component</th>
<th>Assessment tools</th>
<th>Targeted treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01. Ocular-motor impairment</strong></td>
<td>• EYE-SYNC Eye Tracking</td>
<td>Visual tracking training using rapid eye-target synchronization</td>
</tr>
<tr>
<td>The inability to synchronize visual information with motor and cognitive functions.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>02. Vestibular-balance dysfunction</strong></td>
<td>• EYE-SYNC Vestibular</td>
<td>Visual fixation on a fixed location while making rapid head movements</td>
</tr>
<tr>
<td>Impairments to the vestibular system — the balance center of the brain — affecting the ability to coordinate head and eye movements.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>03. Cognitive fatigue</strong></td>
<td>• EYE-SYNC SCAT5</td>
<td>Improved sleep habits, reduction in stress, and cognitive strategies</td>
</tr>
<tr>
<td>Decreased working memory, recall, and reaction time. Becoming distracted or fatigued following prolonged periods of concentration.</td>
<td>• Computerized Neurocognitive Testing</td>
<td></td>
</tr>
<tr>
<td><strong>04. Cervical spine</strong></td>
<td>• Clinical Assessment of the Cervical Spine</td>
<td>Standard manual therapies</td>
</tr>
<tr>
<td>Non-concussive injuries, such as neck whiplash, can also cause concussion-like symptoms.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>05. Migraine headaches</strong></td>
<td>• Migraine Headache Symptom Assessment</td>
<td>Standard migraine treatments</td>
</tr>
<tr>
<td>Recurring, often throbbing headaches that can be accompanied by nausea and disturbed vision.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>06. Anxiety and altered mood</strong></td>
<td>• Psychological assessment</td>
<td>Standard depression and cognitive behavior therapies</td>
</tr>
<tr>
<td>Depression or anxiety.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Sleep**

Sleep disruption is common in concussed patients and can amplify concussion symptoms. Sleep should be monitored and good sleep hygiene advocated.
Key to fast recovery from concussion

1. Cardio exercise
   20min 130bpm 4days/week

2. Sleep (REM)

3. Patient education
   Not a brain injury
   Full recovery expectation

4. Visual orientation training
EYE-SYNC® by SyncThink

Is the first tool to objectively screen for ocular-motor/vestibular synchronization, a key impairment in concussion.
Over 4 million concussions occur each year (CDC)

Attention impairment or Disorientation is the most common cognitive impairment
Attention = spatial and temporal orientation to content

- 80% of our attention is visual, requiring spatial and temporal (timing) prediction

- Disruption of spatial or timing prediction produces disorientation and a feeling of being in a “brain fog”, “dazed”, “out-of-sync”
Orientation requires predictive timing

250 msec delay in processing

220 msec delay in swing

100 mph ball velocity

How does the brain do real time interactions (conversation, everyday actions) when it has multiple delays in processing the sensory information and delays in motor output?

Spatial and temporal prediction
Attention and memory deficits observed in traumatic brain injury are postulated to result from the shearing of white matter connections between the prefrontal cortex, parietal lobe, and cerebellum that are critical in the generation, maintenance, and precise timing of anticipatory neural activity.
Attention/Orientation brain network vulnerable to concussion
# Table 2. Attention-based categorization of postconcussive symptoms

<table>
<thead>
<tr>
<th>Primary symptoms related to predictive timing deficit</th>
<th>Secondary symptoms related to PFC compensation and error signaling</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decreased concentration</td>
<td>• Headache</td>
</tr>
<tr>
<td>• Memory difficulties</td>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Decreased processing speed</td>
<td>• Sleep disturbances</td>
</tr>
<tr>
<td>• Decreased awareness</td>
<td>• Irritability</td>
</tr>
<tr>
<td>• Balance and coordination problems</td>
<td>• Depression</td>
</tr>
<tr>
<td>• Blurred vision</td>
<td>• Anxiety</td>
</tr>
<tr>
<td>• Dizziness</td>
<td></td>
</tr>
<tr>
<td>• Tinnitus</td>
<td></td>
</tr>
<tr>
<td>• Hypersensitivity to light or noise</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Ghajar and Ivry. 76
Cerebellar feed-forward **Cognition** and **Motor** control loops “jitter” control
Inconsistency in Reaction Time Across the Life Span

Benjamin R. Williams, David F. Hultsch, Esther H. Strauss, and Michael A. Hunter
University of Victoria

Rosemary Tannock
The Hospital for Sick Children

Figure 1. Line graphs for three age groups depicting choice reaction time (CRT; residual T scores) for each participant across 32 trials.

Figure 2. Scatter plot of inconsistency (intraindividual standard deviation [ISD] of residualized choice reaction time) across the life span.

VARIANCE
Increase in performance “jitter”
Measuring Orientation

Variability in eye movements

Need to move eyes to keep image on fovea – prediction needed
Smooth Pursuit

Cerebral / Cerebellar – Orientation / Attention

Fovea has only 2 degrees of visual angle – Need predictive smooth pursuit/saccades
Why use eye-tracking to assess attention performance?

Smooth pursuit eye tracking and attention share similar neural networks: Prefrontal cortex- Parietal lobe- cerebellum

Damage to white matter connections in mTBI are most likely in anterior tracts that are in the attention/eye tracking network

Variability in performance is a hallmark of mTBI, which can be measured by reaction time or eye movement variability

Eye tracking is a more reliable metric for performance variability than computerized reaction time testing

Eye tracking test can be done in less than 1 minute as opposed to 20-30 minutes for current computerized testing

Portable eye tracker can be used in the field
Visual tracking \sim Attention-dependent sensorimotor function

- Target selection
- Sustained engagement
- Spatio-temporal memory
- Prediction of the temporal course of the stimulus
- Synchronization of the prediction and the required action (predictive timing)

Without spatio-temporal prediction, visual interception of the target is impossible because the gaze can only be directed where the target was in some past point.
Visual Orientation

Orientation of **self** (1,0) to **world** (0,1)

- Static (0,0)
- Dynamic (0,1)
- Vestibular (1,0)
- Interactive (1,1)

Metrics: Eye-world variance

Delays in brain processing require **prediction** to **synchronize** with the outside world
• 60-seconds to fast, objective results
• FDA-cleared for eye tracking impairment detection
• Clear communication tool
• 10K subject database
Measuring attention/orientation quickly and reliably
Gaze position error variability

Tracking paradigm

30 second test with immediate report
Braking the *predictive eye movement drive* to synchronize with the target of attention

**Brakes don’t work in concussion**
Braking the future
to be in the present
Clinical evaluation of concussion: the evolving role of oculomotor assessments

Eric S. Sussman, MD, Allen L. Ho, MD, Arjun V. Pendharkar, MD, and Jamshid Ghajar, MD, PhD
Department of Neurosurgery, Stanford University School of Medicine, Stanford, California
Concussion: improving eye tracking recovery

Week 0

Week 4

Week 6
Visual Tracking Synchronization as a Metric for Concussion Screening

Jun Maruta, PhD; Minah Suh, PhD; Sumit N. Niogi, PhD; Pratik Mukherjee, MD, PhD; Jamshid Ghajar, MD, PhD

Figure 4. Relationships between fractional anisotropy (FA) values and visual tracking performance variability. (a) Right anterior corona radiata (ACR). (b) Genu of the corpus callosum (CC). (c) Left superior cerebellar peduncle (SCP). Top panels: radial
EYE PERFORMANCE

Athletes - best

Military - near best

Civilians - next best

SDTE - Standard Deviation of Tangential Error

Perfect score
Sleep deprivation

Baseline

Concussion

Predictive Visual Tracking: Specificity in Mild Traumatic Brain Injury and Sleep Deprivation

Jun Maruta, PhD; Kristin J. Heaton, PhD; Alexis L. Maule, MPH; Jamshid Ghajar, MD, PhD
The child subject had H and V gains of 0.78 and 0.58, respectively. The adult subject had H and V gains of 0.90 and 0.83, respectively.
AGE effect


143 subjects aged 7 to 82 years old (53 male)


Visual Tracking in Development and Aging.

Maruta J1,2,3, Spielman LA1, Rajashekar U1, Ghajar J1,2.
Anticipatory saccades
We found that the strongest difference between AD patients and the controls involved the number and the total amplitude of anticipatory saccades. Most importantly, 8 AD patients had more than 15 anticipatory saccades while these movements were present in very low amount in the majority of the healthy volunteers (and were frequent in only 1 volunteer).

Fig. 1. AD patient: the target velocity is 5 deg/sec; the patient brings the eyes from the center to the target with a delay of almost 1 sec; several large amplitude anticipatory saccades are present, which in the first part of the record are made toward the target direction.
Reliability and Associated Risk Factors for Performance on the Vestibular/Ocular Motor Screening (VOMS) Tool in Healthy Collegiate Athletes.

Cerebral / Cerebellar – Orientation / Attention

Total time to administer is 5 minutes

- Baseline Symptoms assessed via a post concussion symptom scale.
- Patient rates changes in symptoms on 0 – 10 scale for symptom provocation during any of the following:

  **Record:** Symptom provocation for Headache, Dizziness, Nausea, Fogginess on a 0-10 scale.

Smooth Pursuit, Saccades Horizontal, Saccades Vertical, Convergence, VOR Horizontal, VOR Vertical and Visual Motion Sensitivity
Vestibular-ocular synchronization in horizontal movement: Concussion

Normal-horizontal

Normal-vertical
How the Brain deals with Time

FEED FORWARD INHIBITORY CONTROL - model is cerebellar blink reflex
More Brain Cells = Better Prediction

About 75% of all brain cells are granule cells. The human cerebellum contains about 80 billion granule cells, making this single cell type by far the most numerous neuron in the brain.
Seeking a unified framework for cerebellar function and dysfunction: from circuit operations to cognition

Egidio D'Angelo¹,²* and Stefano Casali*
Cerebellar Blink Reflex- Feed-forward inhibitory timing
Shearing at level of cerebellar SCP causing: oculo-motor, vestibular and sleep impairments?

The cerebello-thalamo-cerebro-cortical circuits

Figure 6. Figure showing predominant focal areas of diffuse axonal injury (DAI).
Shearing at level of cerebellar SCP causing: oculo-motor, vestibular and sleep impairments?
Measuring visual orientation – life timeline of Brain Health and Performance analytics
Questions?