ADVANCED NEUROIMAGING IN CONCUSSION: A TRANSLATIONAL COLLABORATION OPPORTUNITY

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FINANCIAL DISCLOSURES

• None

• Unpaid consultant
  • IOC workgroup on psychiatric aspects of sports concussion
  • CDC Safety in Youth Sports, concussion group
  • Co-director, ENIGMA Sports Concussion Section
  • NCAA/ PAC 12 concussion research review panel
LEARNING OBJECTIVES:
AT THE CONCLUSION OF THIS PRESENTATION THE LEARNER WILL BE ABLE TO;

• Compare and contrast TBI and Concussion

• Discuss the role of biomarkers, specifically neuroimaging in concussion assessment and management

• List the challenges and opportunities for future research and collaboration in concussion neuroimaging
TBI VS CONCUSSION

- Kissing cousins, not identical twins
- Baron *Sunburn Analogy*
- Sensitization kindling model
  - Post et al
- Different role of neuroimaging
  - White matter vs grey matter impact
ROLE OF BIOMARKERS

• Despite ongoing research in imaging and proteomics
  • GFAP, NFL, SB100, UCH-L1 (and others)
  • DTI, NIS
  • Balance
  • Eye-tracking

• No approved, FDA endorsed Biomarkers for Concussion
NEED FOR LARGE INTERPROFESSIONAL COLLABORATIONS

• Puzzle with many pieces
  • Need for translational approach - *Molecules to Mainstreet*
    • *Basic neuroscience/neuroimaging/neurogenetics*
    • *Clinical perspective*
    • *Public health/public policy*
  • *Osteopathic approach*
EXAMPLE OF COLLABORATION

• ENIGMA
• NHSCA-ISSP
• NCAA-IOC-FIFA
ENIGMA

- Started in 2009 – increased power for GWAS with brain measures
  - Brain measures as intermediate phenotype between genetics and psychiatric and neurological disorders
- 28+ working groups dedicated to psychiatric, neurological, and developmental disorders
  - Working groups dedicated to methods as well
ENIGMA Brain Injury

- Working group PIs: Emily Dennis (USC), David Tate (UMSL), Elisabeth Wilde (Utah)
- 38 groups across 9 countries so far

ENIGMA Military Brain Injury
  - David Tate (UMSL) & Elisabeth Wilde (Utah)

ENIGMA Pediatric msTBI
  - Emily Dennis (USC), Karen Caeyenberghs (ACU), Elisabeth Wilde (Utah)

ENIGMA Sports Concussion
  - David Baron (USC) & Inga Koerte (Harvard and LMU)

ENIGMA Adult msTBI
  - Alexander Olsen (NTNU) & Frank Hillary (Penn State)

ENIGMA ED Civilian mTBI
  - Pratik Mukherjee (UCSF) & Andrew Mayer (UNM)

ENIGMA Intimate Partner Violence
  - Carrie Esopenko (Rutgers)
3 sites

- Total: n=54 Repetitive Head Impacts (RHI); n=13 Controls

Diffusion MRI

Results in RHI compared to controls

- Lower FA in fronto-occipital fasciculus and borderline lower FA in the tapetum.
- Borderline higher MD in the posterior thalamic radiation and tapetum
- Higher RD in the tapetum, borderline higher RD in the superior fronto-occipital fasciculus
- Higher AD in RHI in the corona radiata.
ENIGMA Sports-Related Brain Injury: Framework and Preliminary dMRI Meta-analysis

Ingrid K. Bodagb, Emily L. Dennis, David Kaufman, Elizabeth Hart, Jeffrey J. Buzar, Ross Mercheson, Thomas A. Buxton, Paul Robins, Martha Shenton, Elizabeth A. Willer, David P. Town, Paul M. Thompson, Peter Kochunov, Nadir Afshar, and Dave Baron

Introduction
Athletes participating in contact sports are exposed to repetitive head impacts (RHI). Prior research suggests a link between RHI and impaired cognitive function in adolescents and young adults. It is not clear how persistent these effects may be. Differences in RHI exposure have been attributed to differences in the age of onset of RHI exposure and to variations across the ENIGMA 2.0 (dMRI) data; however, the effect size is not small enough to be considered negligible. In this study, we investigate differences in cognitive function and brain structure across multiple cohorts.

Methods
Data from the ENIGMA 2.0 database were used. The data were divided into three main categories: RHI, former concussions, and matched controls. The RHI group was divided into three subgroups: childhood, adolescence, and adulthood. The cognitive function was assessed using a battery of tests, including the scores from the Short-Form 8 (SF-8) and the Mini-Mental State Examination (MMSE). The brain structure was assessed using diffusion tensor imaging (DTI) and diffusion-weighted imaging (DWI). The analysis was performed using statistical software, including R and SPSS.

Results
The results showed significant differences in cognitive function and brain structure across the RHI groups. The childhood RHI group showed the most significant differences, with lower scores on the SF-8 and higher scores on the MMSE compared to the matched controls. The adolescent and adult RHI groups showed less significant differences, but still demonstrated impairments compared to the matched controls.

Discussion
This study demonstrates the impact of RHI on cognitive function and brain structure. The results highlight the importance of early intervention and the need for further research on the long-term effects of RHI. The findings also suggest that different age groups may respond differently to RHI, highlighting the need for targeted interventions.

Future Directions
Future research will include larger samples to further examine the location and extent of brain injuries following RHI and their association with negative outcomes. A longitudinal study will assess the effects of concussions on cognitive function and brain structure over time.
Discussion

- MOU
- Harmonizing outcome scales
- Secondary proposals
- Grant possibilities
- Workflows for new modalities
Harmonizing outcome scales

- Common test data across cohorts
- Common domains; use or create standard scores to compare
  - Working memory
  - Memory
  - Processing speed
  - Executive function
- Set impairment threshold, use categorical grouping
- Other approaches?
CHALLENGES/ OPPORTUNITIES

• *Speak the same language*
  • Defend the clinical phenotype
• Stay focused on the *Science*, not the politics/economics
• View this as PH issue, as well as pt. issue
• Prospective, longitudinal trials
  • Consider confounding B-P-S factors Type 1 and 2 error
• Emerging science
REFERENCES: 2017 AND NEWER


QUESTIONS/COMMENTS

• Thank you for your time and attention!!
• Enjoy OMED
REFERENCES—CONT.


