# ADVANCED NEUROIMAGING IN CONCUSSION: A TRANSLATIONAL COLLABORATION OPPORTUNITY

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OMED /ACONP OCT.  $18^{TH}$ , 2018





### 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

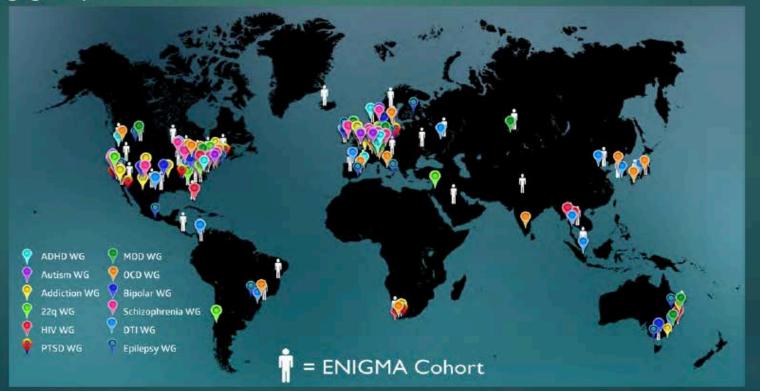
- Puzzle with many pieces
  - Need for translational approach- Molecules to Mainstreet
    - Basic neuroscience/neuroimaging/neurogenetics
    - Clinical perspective
    - Public health/public policy
  - Osteopathic approach

### 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 Pls: 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)

# ENIGMA Sports

- 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

Poster tomorrow: PS2.04.174



### ENIGMA Sports-Related Brain Injury: Framework and Preliminary dMRI Meta-analysis



inga K. Koorto<sup>- I</sup>, Emily L. Dennis<sup>74</sup>, David Kaufmann<sup>- 27</sup>, Elisabeth Harti<sup>1,6</sup>, Jeffrey J. Bazarian<sup>7</sup>, Kinn Merchant Berna<sup>7</sup>, Thomas A. Buckley<sup>9</sup>, Paul Echlin<sup>9</sup>, Martina Shenton 1-36, Elizabeth A. Wilde 11-31, David F. Tacal<sup>1</sup>, Paul M. Thompson 1-16, Peter Kochunov<sup>12</sup>, Nada Jahanshad<sup>2</sup>, Dave Baron<sup>21</sup>

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### introduction

Athletes participating in contact sports are expected to reportive head impacts IRH ), assignment suggests a link service. KHI and impacted cognitive function in adolescents and young adults but the underlying nathomechanism remains to be elucidated. Diffusion MRI (dMRI) is highly sensitive, but imaging shudy colours, revestigating RHI are periors small and results are mixed. Here, we used the mera-ameninic approach of the ENISMA conscribing to analyze the effect of RIII on white matter microstructure across multiple cohorts.

### Methods

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### Cohorts

- Rochester (corbell IP Bezarian)
- \* Mar all Ser need Michaelte )
- Hockey Concussion sought on Project (4) Schling
- Special Fern userum Fil Buckley)

presentor was included in the meta-probability



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### Results

- significantly lower F4 in the RHI group or the augment fronte-occided fasciculus. (Cohon's D- 1,13, 3-0,0009) and
- borderline inwer FA in the taperum

### MD

bor derline higher MD in the ouster or thaternic radiation and talgeton in the RHI group.

- sgrif cartly higher HD in the 8-4 group in the tabetum.
- borderline higher 8D is the superior regres-north fall face quart

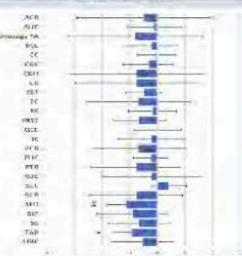
Significantly higher AD in the full encors in the corona radiata.

### Discussion

this meta analysis of pre-existing data revealed decreased -4 one increased MD acrass multiple studies based in different countries and including participants from different contact again with exposure with Results are in ma with previously published reports from singlepenter studies. Decreased FA and increased MD in the white matter support, e.g., neurodegenerative and neuroinflammatory processes.

### **Future Directions**

Fature work will include a larger sample to further examine the location and extent of WW. alteretions following BHI and their associations with agentive function. Further, we will assets the effect of female sers is male servage, sports played, and amount of exposure to Bi-



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# 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

- McCrea, M., Meier, T., Huber, D., Ptito, A., Bigler, E., Debert, C. T., ... & Schneider, K. J. (2017). Role of advanced neuroimaging, fluid biomarkers and genetic testing in the assessment of sport-related concussion: a systematic review. Br J Sports Med, bisports-2016.
- Henry, L. C., Tremblay, S., & De Beaumont, L. (2017). Long-term effects of sports concussions: bridging the neurocognitive repercussions of the injury with the newest neuroimaging data. *The Neuroscientist*, 23(5), 567-578.
- McCrory, P., Meeuwisse, W., Dvorak, J., Aubry, M., Bailes, J., Broglio, S., ... & Davis, G. A. (2017). Consensus statement on concussion in sport—the 5th international conference on concussion in sport held in Berlin, October 2016. *Br J Sports Med*, bjsports-2017.
- Qandeel, M., & Walker, M. T. (2017). Neuroimaging in concussion. In Sports-Related Concussion (pp. 181-194). CRC Press.
- Haller, S. (2017). Advance Mr imaging in sports-related concussion and mild traumatic brain injury–ready for clinical use?(commentary on Tremblay et al. 2017). European Journal of Neuroscience, 46(4), 1954-1955.
- Hasan, K. M., Keser, Z., Schulz, P. E., & Wilde, E. A. (2017). Multimodal advanced imaging for concussion. Neuroimaging clinics
  of North America.

# QUESTIONS/COMMENTS

- •Thank you for your time and attention!!
  - Enjoy OMED

# REFERENCES-CONT.

- Hasan, K. M., Keser, Z., Schulz, P. E., & Wilde, E. A. (2017). Multimodal advanced imaging for concussion. *Neuroimaging clinics of North America*.
- Di Battista, A. P., Churchill, N., Schweizer, T. A., Rhind, S. G., Richards, D., Baker, A. J., & Hutchison, M. G. (2018). Blood biomarkers are associated with brain function and blood flow following sport concussion. *Journal of* neuroimmunology, 319, 1-8.
- Mustafi, S. M., Harezlak, J., Koch, K. M., Nencka, A. S., Meier, T., West, J. D., ... & LaConte, S. M. (2017). Acute white-matter abnormalities in sports-related concussion: a diffusion tensor imaging study from the NCAA-DoD CARE Consortium. *Journal of neurotrauma*, (ja).
- Chamard, E., & Lichtenstein, J. D. (2018). A systematic review of neuroimaging findings in children and adolescents with sports-related concussion. *Brain injury*, 1-16.