Aging with a prior history of sport-related concussions

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PRESENTATION OUTLINE

• Where I come from
  – Previous work on sports concussions in youth
  – Previous work on sports concussion & aging

• Where I am going
  – Early intervention methods to alleviate chronic concussion-related impairments
Long-term effects of concussions

• The paradox
  – The effects of concussions are transient
    • Negative post-concussion symptoms 10 days after the accident
    • Normal neuropsychological test results at 10-14 days after the injury
  
  IN THE MEANTIME

  – The effects of concussions are cumulative
    • Higher vulnerability to subsequent concussions
    • More severe / longer-lasting post-concussion symptomatology
    • Prevalence of MCI is fivefold in retired athletes with a history of 3+ concussions
Long-term effects of concussions

• Cross-sectional design rationale
  – Assuming that the cumulative effects of concussions are reflective of incomplete post-trauma recovery, we hypothesized that:
    • Cognitive and motor system functions impairments found in the acute post-concussion phase could persist but at a subclinical level beyond the acute post-concussion phase
    • The combined, detrimental effects of aging and a prior history of sports concussion could be associated with decline in both spheres of cognition and motor system functions (5X prevalence of MCI)
Long-term effects of concussions

• Objectives
  – In young athletes
    • To investigate: (1) Long-term & (2) cumulative effects of sports concussions on cognitive and motor system functions in young athletes
  – In former, late adulthood athletes
    • To investigate whether aging with a remote history of concussions is associated with cognitive/motor function decline in otherwise healthy former athletes
Concussion in youth: Experiment 1

Long-term electrophysiological changes in athletes with a history of multiple concussions

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Concussion in youth: Experiment 1

Participants

• 3 groups
  1. University football players with 1 concussion (n = 15)
  2. University football players without concussion (n = 15)
  3. University football players with 2+ concussions (n = 15)

  – Time since last concussion was > 9 mo
  – Athletes were asymptomatic on the PCS scale
Concussion in youth: Experiment 1

• Methods
  – ERP recordings when athletes performed a visual-spatial attention task
  – Previous concussion data showed persistent P3 amplitude reductions in asymptomatic athletes tested a few weeks post-concussion [14]
Concussion in youth: Experiment 1

• Results

Subtracted P3 component (Rare - Frequent)

Neuropsychological tests
- 3 groups performed equally
Concussion in youth: Experiment 2

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LONG-TERM AND CUMULATIVE EFFECTS OF SPORTS CONCUSSION ON MOTOR CORTEX INHIBITION
Concussion in youth: Experiment 2

- Participants
  - 3 groups (different players than in Experiment 1)
    1. University football players without concussion (n = 17)
    2. University football players with 1 concussion (n = 16)
    3. University football players with 2+ concussions (n = 15)

- Time since last concussion was > 9 mo
- Athletes were asymptomatic on the PCS scale
Concussion in youth: Experiment 2

• Methods
  
  – TMS was used to investigate motor cortex excitability changes after sports concussions.
  
  – Previous mTBI data showed prolonged cortical silent period (CSP) in the acute post-trauma phase [15]
Concussion in youth: Experiment 2

**TMS measures**

- Resting motor threshold (rMT)
- Paired-pulse
- Input-output curve
- CSP
  - TMS pulse is delivered to the vertex and participants contract the targeted hand muscle at about 10% max strength
  - MEP is momentarily interrupted by concurrent TMS
  - The duration of this pause reflects $GABA_B$-mediated intracortical inhibition of M1
Concussion in youth: Experiment 2

• Results
Concussion in youth: Experiment 3

Persistent Motor System Abnormalities in Active Concussed Athletes

RUNNING HEAD: Motor Dysfunctions After Sports Concussions

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• Data will later be presented in relation with those of Experiment 5
Brain function decline in healthy retired athletes who sustained their last sports concussion in early adulthood

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Concussion & Aging: Experiment 1

• Participants
  – 2 groups
    1. Former University-level football/hockey players without concussion (n = 20)
    2. Former University-level football/hockey players with concussion(s) (n = 20)
  – Inclusion criteria
    • No medication affecting CNS
    • Still engaging in physical activities 3 times/week
    • MMSE score ≥ 27
    • No prior psychiatric disorder or neurological history
    • No TBI unrelated to contact sports
    • No history of alcohol/substance abuse
Concussion & Aging: Experiment 1

• Methods
  – Cognitive functions
    • ERPs (P300 (P3a & P3b) components known to reflect attention/memory and executive functions efficiency)
    • Neuropsychological tests (episodic memory & executive functions tests)
  – Motor system functions
    • TMS (Cortical silent period)
    • Rapid alternating movement task (used to assess age-related changes in motor execution speed)
Concussion & Aging: Experiment 1

- ERP / Neuropsychology Results

**ERPs**
- We found significant P3a / P3b amplitude reductions in former concussed athletes

**Neuropsychology**
- Significant response inhibition reduction in former concussed athletes
- Significant recognition memory decline on RCFT in former concussed athletes
Concussion & Aging: Experiment 1

- **TMS**
  - We used the same TMS protocols as in Experiment 2
    - Resting motor threshold
    - Paired-pulse paradigm
    - Input/Output curve
    - Cortical silent period
Concussion & Aging: Experiment 1

• **Rapid alternating movement (RAM) task**
  - RAM task allows the detection of pre-Parkinson’s disease motor slowing [20]
  - Participants were seated on a straight back chair with elbows flexed at an angle of 90°
  - They had to rotate two hand-held spheres as fast as possible with maximal movement amplitude
  - Two periods of 15 seconds were recorded for each of the three conditions: both hands, left hand only, right hand only
  - Hand position and orientation in 3D space was recorded
Concussion & Aging: Experiment 1

• TMS / RAM task results

TMS results
• Prolonged CSP duration in former concussed athletes

RAM task results
• Slowness in former concussed athletes

Correlation CSP / RAM task
• CSP duration strongly correlated with motor execution velocity
CONCUSSION SEQUELAE:
From a cross-sectional perspective

<table>
<thead>
<tr>
<th>Measures</th>
<th>Conditions</th>
<th>Younger</th>
<th>Older</th>
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<tbody>
<tr>
<td><strong>Cognition</strong></td>
<td><strong>ERPs</strong></td>
<td>P3a</td>
<td>√</td>
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<td></td>
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<td>P3b</td>
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<td><strong>Neuropsy</strong></td>
<td>Executive fcts</td>
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<td>Episodic memory</td>
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<td><strong>Motor</strong></td>
<td><strong>CSP</strong></td>
<td>Duration</td>
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<td></td>
<td><strong>RAM</strong></td>
<td>Execution velocity</td>
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Sports Concussions and Aging: A Neuroimaging Investigation

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Concussion & Aging: Experiment 2

– To combine neuroimaging and neuropsychology to explore:

• The effects of aging with a remote history of concussions on brain atrophy patterns and associated functional repercussions
SIENAX
Protocole d'analyse de l'atrophie globale des tissus GM, WM et du cerveau

GM - Peripheral GM - Ventricular CSF
vCSF «-» Delayed recall Taylor

$r = -0.55 \quad p = 0.033 \quad N = 15 \quad Inter = 0.024$
Cortical thickness

Group * Age interaction
DTI study on concussion in youth

DTI study (48hrs to 6 months post-concussion)
Diffuse white matter tract abnormalities in clinically normal ageing retired athletes with a history of sports-related concussions

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Concussion and Aging: Experiment 3

DTI study (white matter integrity markers)

Figure 1. Diffuse decrease in fractional anisotropy following remote concussions.

Figure 2. Diffuse increase in mean diffusivity following remote concussions. Sagittal
Concussion and Aging: Experiment 3

DTI study

Figure 3. Diffuse increase in radial diffusivity following remote concussions. Sagittal (A, B, C, D, E, F).

Figure 4. Decreases in visual memory correlate with increases in mean diffusivity in...
Magnetic resonance spectroscopy
Acute post-concussion phase
Motor system alterations in retired former athletes: the role of aging and concussion history

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Concussion and Aging: Experiment 4

- Magnetic Resonance Spectroscopy

Figure 2: Region of interest for H-MRS examination

Figure 5. M1 Glutamate/H$_2$O concentration ratio difference between former concussed athletes and controls with age

Figure 6: Correlation M1 glutamate and sequence-specific learning in concussion group
Summary

• Concussion exerts chronic effects on the brain

• Concussion + Aging = Abnormal aging

• LTP mechanisms alterations contribute to functional losses after concussion
Societal and Clinical issues

- To raise public awareness on the long term risks associated with sports concussions
- To develop early intervention procedure to counteract insidious brain integrity/function decline in late adulthood former athletes
Where I am going

Clinical Trials

• First treatment for sports concussions
  – Brain stimulation techniques (rTMS, theta burst, TDCS) aiming to improve brain plasticity mechanisms
  – Aerobic training program to improve cognitive functions
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TDCS & concussion application

- DC modulation of LTP mechanisms in M1
- Very weak current intensity (20 minutes)
- High tolerability, FDA approved
- Only perceptible during the first 30 sec of stimulation
- DC is applied during SRT task performance

In controls
- Associated with motor learning improvements
- Optimal efficiency when TDCS is combined to task execution
- Five, 20-min sessions over successive weekdays induced significant motor learning improvements via enhanced M1 synaptic efficacy
Concussion & Aerobic training

- Concussion & Aging project
  - Aging population most benefit from aerobic training
    - Significant cognitive response
    - Improved LTP, brain metabolism, insulin resistance & increased BDNF expression
    - In MCI, 6mo training 4X/wk reversed cognitive decline and decreased AD conversion
Concussion & Aerobic training

• Participants
  – Mild TBI patients from HSCM (1995-2005)
    • Age 55-70 (last TBI more than 7 years ago)
    • TBI effects in aging are exacerbated with the number years of sedentarity
    • No chronic post-TBI symptoms

• 6mo, 3X/wk aerobic training program

• Aerobic training effects (PRE vs POST training):
  – Neuropsychological, SRT and olfactory functions tasks
  – Synaptic plasticity PAS *(paired associative stimulation)*
  – BDNF blood levels
  – Cardiovascular condition
  – Neuroimaging (VBM, DTI, Cortical thickness, PET (FDG/PIB))