Neuropsychiatric symptoms in adults with Tuberous Sclerosis Complex (TSC)

Andy Liu, M.D., M.S.
Adult Neurologist
Duke University School of medicine
Department of Neurology
Outline

• Physical manifestations
• Medical and Surgical advancements in TSC
• Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)
• Age related disorders
• Understand the relationship between TAND and age related disorders
Outline

• Physical manifestations
  • Medical and Surgical advancements in TSC
  • Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)
• Age related disorders
• Understand the relationship between TAND and age related disorders
Physical traits of TSC throughout life

Kingwood et al. 2017
Outline

• Physical manifestations

• Medical and Surgical advancements in TSC

• Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)

• Age related disorders

• Understand the relationship between TAND and age related disorders
Medical advancement: EXIST-3 trial

French et al. 2016
Medical and Surgical advancement

Magnetic Resonance Imaging (MRI) FLAIR  Positron Emission Tomography (PET)  MRI T1

Wu et al 2010
Outline

• Physical manifestations
• Medical and Surgical advancements in TSC
• Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)
• Age related disorders
• Understand the relationship between TAND and age related disorders
### TAND

<table>
<thead>
<tr>
<th>Cognitive</th>
<th>Behavioral</th>
<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>Aggressive outbursts</td>
<td>Depressed mood</td>
</tr>
<tr>
<td>Visuospatial function</td>
<td>Temper tantrums</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Attention</td>
<td>Self-injury</td>
<td>Mood swings</td>
</tr>
<tr>
<td>Multi-tasking</td>
<td>Repeating words</td>
<td>Obsessive compulsive disorder</td>
</tr>
<tr>
<td>Planning</td>
<td>Difficulty getting along</td>
<td>Psychotic disorder</td>
</tr>
<tr>
<td>Organizing</td>
<td>Inflexible</td>
<td></td>
</tr>
<tr>
<td>Language difficulties</td>
<td>Over/hyperactive</td>
<td></td>
</tr>
</tbody>
</table>

DeVries et al. 2015
## TAND

<table>
<thead>
<tr>
<th>Cognitive</th>
<th>Behavioral</th>
<th>Psychiatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>Aggressive outbursts</td>
<td>Depressed mood</td>
</tr>
<tr>
<td>Visuospatial function</td>
<td>Temper tantrums</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Attention</td>
<td>Self-injury</td>
<td>Mood swings</td>
</tr>
<tr>
<td>Multi-tasking</td>
<td>Repeating words</td>
<td>Obsessive compulsive behaviors</td>
</tr>
<tr>
<td>Planning</td>
<td>Difficulty getting along</td>
<td>Psychotic disorder</td>
</tr>
<tr>
<td>Organizing</td>
<td>Inflexible</td>
<td></td>
</tr>
<tr>
<td>Language difficulties</td>
<td>Over/hyperactive</td>
<td></td>
</tr>
</tbody>
</table>

DeVries et al. 2015
Outline

- Physical manifestations
- Medical and Surgical advancements in TSC
- Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)
- Age related disorders
- Understand the relationship between TAND and age related disorders
Frontotemporal Dementia (FTD)

- Early-onset age related disorder with 3 subtypes
- Behavioral variant Frontotemporal Dementia
- Semantic variant Primary Progressive Aphasia
- Nonfluent variant Primary Progressive Aphasia

Olney et al 2017
MRI T1: TSC1 mutation and FTD

Olney et al 2017
MRI FLAIR: *TSC1* mutation and FTD

Olney et al 2017
MRI T1: *TSC1* mutation and FTD

Liu et al 2019 (accepted)
Outline

• Physical manifestations
• Medical and Surgical advancements in TSC
• Tuberous sclerosis Associated Neuropsychiatric Disorder (TAND)
• Age related disorders

• Understand the relationship between TAND and age related disorders
UCSF TSC study 2017-2019

Inclusion Criteria

• Over age 18
• Can complete neuropsychological testing

Exclusion Criteria

• Other genetic diseases
Clinical evaluation

3 groups
- TSC
- FTD
- Normal cognition

Clinical testing
- TAND checklist
- Neuropsychological testing
Objective analysis

Imaging

- MRI brain
- PET scan

Cerebral spinal fluid (CSF)

- Phosphorylated Tau (p-tau)
- Neurofilament light (NfL)
- Amyloid beta 42 (Aβ42)
- Total Tau (t-tau)
Results

• 18 TSC participants were evaluated
• Age ranged from 27-66
• 72% were female
• Genetic testing was finalized in 10 participants
• Equal number of TSC1 and TSC2 mutations were identified
TAND checklist

• Behavioral and cognitive domains
• Psychiatric domain

Liu et al 2019 (accepted)
Neuropsychological testing results

• Executive and language domains
• Memory
• Visuospatial domain

Liu et al 2019 (accepted)
Flortaucipir (FTP) PET results

- 3 TSC participants
- Focal uptake of FTP in all participants
- Focal uptake of FTP was seen in the structural changes of the brain in 2 of out 3 participants

Liu et al 2019 (accepted)
MRI T1

Liu et al 2019 (accepted)
Liu et al 2019 (accepted)
FTP-PET

Liu et al 2019 (accepted)
CSF results

A

B

p-Tau Level (pg/mL)

NfL Level (pg/mL)

Controls  TSC  FTD

Controls  TSC  FTD

Liu et al 2019 (accepted)
CSF results (cont)

A

**Aβ₁-₄₂ Level (pg/mL)**

- Controls
- TSC
- FTD

B

**T-Tau Level (pg/mL)**

- Controls
- TSC
- FTD

Department of Neurology
Duke University School of Medicine
Findings in adults diagnosed with TSC

- TAND symptoms vary
- TAND and FTD symptoms significantly overlap
- Imaging suggests deposition in specific areas of the brain that may explain cognitive symptoms
- Elevated CSF p-tau levels may be causing cognitive symptoms
Future direction

• Longitudinal studies with adults diagnosed with TSC is necessary to characterize the clinical trajectory

• Begin analyzing how imaging and fluid markers change over time in adults with TSC
Acknowledgements

• Bruce Miller, MD
• Aimee Kao, MD, PhD
• Adam Staffaroni, PhD
• Nick Olney, MD
• Carolina Alquezar-Burillo, PhD
• UCSF Memory and Aging Center
• Duke School of Medicine
Thank you

Andy.liu@duke.edu

https://www.dukehealth.org/find-doctors-physicians/andy-liu-md-ms
References


