NEUROPSYCHOLOGY AND NEUROIMAGING OF ALCOHOL USE DISORDER WITH AND WITHOUT KORSAKOFF’S SYNDROME:
A BETTER UNDERSTANDING FOR A BETTER TREATMENT

Anne Lise PITEL
CONFLICT OF INTEREST

No conflict of interest to declare.
ALCOHOL USE DISORDER (AUD): EPIDEMIOLOGY

- 10% of French population with disastrous health, psychological, social and professional consequences (Rehm et al. 2011).

- Alcohol is the cause of 49,000 deaths per year and 18% of the premature deaths in the 35-64 year-old people in France (Guerin et al. 2013).

- 17% of the admissions in the emergency department in France.

- Worldwide, alcohol is the third risk factor for morbidity after high blood pressure and tobacco (Moller 2013).

- Alcohol is the cause of more than 60 diseases (dependence, cirrhosis, psychosis, fetal alcohol syndrome, …) (World Health Organization 2014).

- Alcohol contributes to the development of more than 200 diseases (cancer, heart disease, pancreatitis, liver disease, …) (Moller 2013).

- The life expectancy is reduced of 20 years in a man with alcohol dependence (John et al. 2013).

- The cost related to alcohol or tobacco use disorders is 349 billion euros for Europe, knowing that it is 105 for dementia and 64 for strokes (Effertz et al. 2013).

- Tremendous social cost: first cause of hospital admission, sick leave and premature death.
ALCOHOL USE DISORDER (AUD): DSM-5 CRITERIA

Changes in the concepts:

- Alcoholism
- Alcohol dependence (DSM IV)
- Alcohol Use Disorder (DSM V)

A problem pattern of alcohol use, leading to clinically significant impairment or distress, manifested by 2 or more of the following in a 12-month period:

- Alcohol drunk in larger amounts or for longer time
- Persistent desire or unsuccessful efforts to cut down
- Inordinate time spent obtaining alcohol
- Craving (strong desire to use alcohol)
- Failure to fulfill work, school, home obligations
- Continued use despite social or interpersonal problems
- Societal, occupational, recreational activities reduced
- Recurrent use when physically hazardous
- Continued use despite physiological or psychological problems
- Tolerance
- Withdrawal

WHY?
Because alcohol changes the brain…
Acute alcohol intoxication reversibly affects brain function.

Chronic alcohol abuse affects the brain in enduring ways, and these effects themselves may contribute to the loss of control.
Sergei Korsakoff (1887, 1889, 1891): «polyneuritic psychosis» observed in 30 cases of chronic and excessive alcohol consumption and 16 patients in whom alcohol had not played a role. Main feature: severe and enduring memory disorders.

Korsakoff’s syndrome (KS)

50’s + Thiamine (Vit B1) deficiency + = KS

Kopelman et al. 2009
Arts et al. 2017
QUESTIONS

1. Are there neuropsychological deficits in AUD before the development of KS?

2. What are the clinical consequences of neuropsychological deficits observed in AUD?

3. What are the differences between altered brain structure and function in AUD and KS?
ARE THERE BRAIN ABNORMALITIES AND COGNITIVE DEFICITS IN AUD BEFORE THE DEVELOPMENT OF KS?

Question 1
NEUROPSYCHOLOGICAL PROFILE IN AUD

Sullivan et al. 2000

Oscar-Berman et al. 2014 (review)
# Executive Functions in AUD

<table>
<thead>
<tr>
<th></th>
<th>VFT</th>
<th>TMT: B-A</th>
<th>CET</th>
<th>MCST: categories achieved</th>
<th>SCW</th>
<th>GNT: passed switch trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic patients</td>
<td>40.5 (16.0)</td>
<td>74.5 (75.2)</td>
<td>5.94 (4.24)</td>
<td>4.38 (1.89)</td>
<td>89.9 (24.9)</td>
<td>3.92 (2.36)</td>
</tr>
<tr>
<td>Controls</td>
<td>46.4 (15.7)</td>
<td>30.5 (14.7)</td>
<td>4.06 (2.75)</td>
<td>5.82 (0.39)</td>
<td>107.4 (8.39)</td>
<td>5.59 (0.62)</td>
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<tr>
<td>Mann-Whitney U between alcoholic patients and controls</td>
<td>122.5</td>
<td>76.0</td>
<td>108.0</td>
<td>73.0</td>
<td>77.0</td>
<td>65.5</td>
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<tr>
<td>Asympt significance (2 tailed)</td>
<td>0.448</td>
<td>0.018*</td>
<td>0.204</td>
<td>0.008**</td>
<td>0.014*</td>
<td>0.039*</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01; Mann-Whitney U test.

VFT = Verbal fluency test (Miller*); TMT = trail making test (Reitan*); CET = cognitive estimates test (Shallcross and Evans*); MCST = modified card sorting test (Nelson*); SCW = Stroop test (Treasure et al*); GNT = goal neglect test (Duncan et al*).

## Results

<table>
<thead>
<tr>
<th>Rule shift cards</th>
<th>Action programme</th>
<th>Key search</th>
<th>Time judgement</th>
<th>Zoo map</th>
<th>Modified six elements</th>
<th>BADS total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic patients</td>
<td>3.47 (1.07)</td>
<td>3.59 (1.00)</td>
<td>3.24 (1.15)</td>
<td>1.59 (1.00)</td>
<td>2.71 (1.21)</td>
<td>3.24 (1.20)</td>
</tr>
<tr>
<td>Controls</td>
<td>3.82 (0.32)</td>
<td>3.82 (0.39)</td>
<td>3.33 (0.72)</td>
<td>2.65 (0.61)</td>
<td>3.47 (0.62)</td>
<td>4.00 (0.00)</td>
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<tr>
<td>Mann-Whitney U between alcoholic patients and controls</td>
<td>119.0</td>
<td>141.5</td>
<td>130.0</td>
<td>59.5</td>
<td>95.0</td>
<td>85.0</td>
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<tr>
<td>Asympt sig (2 tailed)</td>
<td>0.213</td>
<td>0.876</td>
<td>0.565</td>
<td>0.002**</td>
<td>0.068</td>
<td>0.004**</td>
</tr>
</tbody>
</table>

**p < 0.01; Mann-Whitney U test.

BADS = Behavioural assessment of dysexecutive syndrome (Wilson et al*).

## Tasks

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Executive functions</th>
<th>Control subjects (N = 55)</th>
<th>Alcoholic patients (N = 40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal fluencies</td>
<td>Organization</td>
<td>54.42 ± 14.48</td>
<td>45.29 ± 14.52†</td>
<td>&lt; 0.01†</td>
</tr>
<tr>
<td>Stroop test</td>
<td>Inhibition</td>
<td>41.75 ± 12.16</td>
<td>31.52 ± 10.85†</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>Alternate response task*</td>
<td>Flexibility</td>
<td>90.80 ± 10.85</td>
<td>85.15 ± 10.39†</td>
<td>&lt; 0.01†</td>
</tr>
<tr>
<td>n-Back task</td>
<td>Updating</td>
<td>90.20 ± 12.70</td>
<td>79.40 ± 15.70†</td>
<td>&lt; 0.001†</td>
</tr>
<tr>
<td>Integration task</td>
<td>Integration</td>
<td>70.10 ± 12.70</td>
<td>56.00 ± 18.70†</td>
<td>&lt; 0.001†</td>
</tr>
</tbody>
</table>

Ihara et al. 2000

Pitel et al. 2007
EPISODIC MEMORY IN AUD

<table>
<thead>
<tr>
<th>Tasks</th>
<th>Episodic memory processes</th>
<th>Variable</th>
<th>Control subjects (N = 55)</th>
<th>Alcoholic patients (N = 40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCSR Test</td>
<td>Learning abilities</td>
<td>FR$_{1+2+3}$</td>
<td>33.43 ± 4.88</td>
<td>27.95 ± 7.43</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Spondee test</td>
<td>Retention abilities</td>
<td>Rate of forgetting</td>
<td>0.01 ± 0.20</td>
<td>−0.02 ± 0.23</td>
<td>0.41</td>
</tr>
<tr>
<td>ECM test</td>
<td>Encoding and retrieval processes</td>
<td>Encoding score</td>
<td>84.32% ± 13.39</td>
<td>76.25% ± 15.77</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrieval score</td>
<td>53.84% ± 17.50</td>
<td>40.47% ± 17.73</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td></td>
<td>Contextual memory</td>
<td>Factual recognition</td>
<td>99.09% ± 3.82</td>
<td>97.50% ± 8.05</td>
<td>0.20</td>
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<tr>
<td></td>
<td></td>
<td>Temporal recognition</td>
<td>92.12% ± 11.93</td>
<td>77.92% ± 19.38</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spatial recognition</td>
<td>88.48% ± 16.31</td>
<td>80.00% ± 20.04</td>
<td>0.02†</td>
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<tr>
<td></td>
<td></td>
<td>Total recognition</td>
<td>83.03% ± 20.41</td>
<td>62.08% ± 26.14</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td></td>
<td>R answers</td>
<td>2.25 ± 0.62</td>
<td>1.92 ± 0.82</td>
<td></td>
<td>0.02†</td>
</tr>
<tr>
<td></td>
<td>K answers</td>
<td>0.45 ± 0.40</td>
<td>0.47 ± 0.50</td>
<td></td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>G answers</td>
<td>0.29 ± 0.40</td>
<td>0.57 ± 0.61</td>
<td></td>
<td>&lt;0.01†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Verbal fluencies</th>
<th>Stroop test</th>
<th>Alternate response task</th>
<th>n-Back task</th>
<th>Integration task</th>
</tr>
</thead>
<tbody>
<tr>
<td>FR$_{1+2+3}$</td>
<td>0.61†</td>
<td>0.47</td>
<td>0.47</td>
<td>0.41</td>
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<tr>
<td>Rate of forgetting</td>
<td>−0.17</td>
<td>0.06</td>
<td>0.04</td>
<td>0.004</td>
</tr>
<tr>
<td>Encoding score</td>
<td>0.44</td>
<td>0.34</td>
<td>0.31</td>
<td>0.27</td>
</tr>
<tr>
<td>Retrieval score</td>
<td>0.34</td>
<td>0.25</td>
<td>−0.02</td>
<td>0.19</td>
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<tr>
<td>Factual recognition</td>
<td>0.18</td>
<td>0.04</td>
<td>0.21</td>
<td>0.39</td>
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<tr>
<td>Temporal recognition</td>
<td>0.46</td>
<td>0.17</td>
<td>0.30</td>
<td>0.10</td>
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<tr>
<td>Spatial recognition</td>
<td>0.08</td>
<td>0.08</td>
<td>0.24</td>
<td>0.26</td>
</tr>
<tr>
<td>Total recognition</td>
<td>0.43</td>
<td>0.23</td>
<td>0.36</td>
<td>0.28</td>
</tr>
<tr>
<td>R answers</td>
<td>0.50</td>
<td>0.29</td>
<td>0.25</td>
<td>0.22</td>
</tr>
<tr>
<td>K answers</td>
<td>−0.22</td>
<td>−0.14</td>
<td>0.07</td>
<td>−0.04</td>
</tr>
<tr>
<td>G answers</td>
<td>−0.46</td>
<td>−0.37</td>
<td>−0.41</td>
<td>−0.28</td>
</tr>
</tbody>
</table>

†Significant correlations after Bonferroni’s correction.
METAMEMORY IN AUD

**Objective measure:** Recognition task/FOK

**Subjective measure:** MIA questionnaire

- No difference on the Strategy, Tasks, Capacity, or Achievement subscores
- Limited awareness of memory deficits

• AUD group less accurate than the control group
• Tendency to overestimate their memory capacities, believing themselves capable of recognizing the correct word when in fact they subsequently fail to do so.

Le Berre et al. 2010

Le Berre and Sullivan, 2016

Mild form of mnemonic anosognosia?
Denial?
Not only for memory.
SOCIAL COGNITION IN AUD

Decoding emotions in facial expression, body postures and prosody

D'Hondt et al. 2014; Maurage 2008; Maurage et al. 2013; Rupp et al. 2017

Theory of Mind

**NEW SEMANTIC LEARNING IN AUD**

**Day 1:** Pre-learning assessment

**Day 2:** Learning session 1

**Day 3:** Learning session 2

**Day 9:** Learning session 8

"What is this? Does the ratel belong to the family of insectivorous, carnivorous or herbivorous animals? Does the ratel attack buffaloes, gazelles or rodents?…"

"This animal is a ratel, it belongs to the family of carnivorous animals, it attacks buffaloes…"

"What is this? Which family of animal does the ratel belong to? Which type of animal does it attack?…"

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Pitel et al. 2007
NEW PROCEDURAL LEARNING IN AUD

Day 1/Session 1: 10 trials of the Tower of Toronto
Day 2/Session 2: 10 trials of the Tower of Toronto
Day 3/Session 3: 10 trials of the Tower of Toronto
Day 4/Session 4: 10 trials of the Tower of Toronto

Pitel et al. 2007
DECISION-MAKING IN AUD (1)

Iowa Gambling task

Le Berre et al. 2014
Emotionally and cognitively unable to anticipate risky situations

Les situations à risques

**DECISION-MAKING IN AUD (2)**

Ventromedial cortex: emotional and social components

Cingulate cortex: cognitive component

Hippocampus: memory and learning

Le Berre et al. 2014
QUESTIONS

1. Are there neuropsychological deficits in AUD before the development of KS?

YES!!!
WHAT ARE THE CLINICAL CONSEQUENCES OF ALTERED BRAIN STRUCTURE AND FUNCTION OBSERVED IN AUD?
MOTIVATION

Prochaska and Di Clemente. 2013

Awareness

LOW EPISODIC MEMORY ABILITIES

Precontemplation
No intention of changing behaviour

Contemplation
Aware a problem exists. No commitment to action

Maintenance
Sustained change - new behaviour replaces old

Action
Active modification of behaviour

Relapse
Fall back into old patterns of behaviour

RTC questionnaire, neuropsychological performance and brain structure

LOW EXECUTIVE ABILITIES

Preparation
Intent upon taking action

Decisional balance

HIGH DECISION-MAKING ABILITIES

(p<0.005 FDR; k>150)

Le Berre et al. 2013
ALCOHOL TREATMENT

Semantic learning
Procedural learning
Metamemory
Metacognition
Motivation
Decision-making
Executive functions
Episodic memory

NEUROPSYCHOLOGICAL DEFICITS = HIGH RISK OF RELAPSE!!!
All AUD patients may not be cognitively able to benefit fully from treatment

A systematic assessment of cognitive abilities is required in recently detoxified AUD patients

To assess (ideal!)

To detect (pragmatic…)

To identify risk factors
- subclinical signs of WE
- thiamine deficiency
- liver dysfunction
- denutrition

To favor spontaneous recovery

To adjust treatment
SCREENING TOOLS

**MMSE (Folstein, 1975)**

Not sensitive
Not specific

**MOCA (Nasreddine et al. 2005)**

Sensitive
Not specific
Useful for differential diagnosis

**BEARNI**

Only in French
Sensitive (too much?)
Specific
SUBCLINICAL SIGNS OF WERNICKE ENCEPHALOPATHY (WE)

Clinical criteria of Caine et al. 1997:

- Dietary deficiency: > 30 missed-meals over lifetime
- Oculomotor abnormalities: nystagmus
- Cerebellar dysfunction: lower limb ataxia
- Altered mental state: DRS<123

1 criterion = risk for WE  \(\geq 2\) criteria = signs of WE


Pitel et al. 2011
SUBCLINICAL SIGNS OF WERNICKE ENCEPHALOPATHY (WE)

Pitel et al. 2011
BIOLOGICAL FACTORS

TDP (active form of thiamine)

alcoholics = controls

Correlation between poorer memory scores and lower TDP levels

Alcohol-related clinical and biological comorbidities

- Fibrosis score > 0.22
- % fibrosis > 7.03
- Fibrosis score > 0.22
- Fibrosis score > 0.15

- Cushman score ≤ 4
- > 13 years of alcohol misuse and Cushman score > 3
- Metabolic ratio ≤ 0.89
- Metabolic ratio ≤ 0.86
- ≤ mild

- Risk of memory impairments
- Risk of executive impairments
- Risk of ataxia
- Risk of visuospatial impairments
- Risk of moderate impairments
- Risk of severe impairments

Pitel et al. 2011
Ritz et al. 2016
# Recovery of Brain Function

## 6 months of sobriety

<table>
<thead>
<tr>
<th>Cognitive functions</th>
<th>Tasks</th>
<th>Variables</th>
<th>Baseline M</th>
<th>Baseline SD</th>
<th>Follow-up M</th>
<th>Follow-up SD</th>
<th>Comparison with controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic memory</td>
<td>FCSR</td>
<td>Free recalls</td>
<td>28.58</td>
<td>3.75</td>
<td>32.33</td>
<td>6.08</td>
<td>0.47</td>
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<tr>
<td></td>
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<td>Delayed free</td>
<td>11.33</td>
<td>1.97</td>
<td>12.92</td>
<td>2.31</td>
<td>0.73</td>
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<tr>
<td>Executive functions</td>
<td>Stroop test</td>
<td>CW</td>
<td>39.92</td>
<td>9.65</td>
<td>44.25</td>
<td>8.04</td>
<td>0.51</td>
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<td>Alternate response task</td>
<td>CA</td>
<td>86.00</td>
<td>10.00</td>
<td>88.73</td>
<td>7.98</td>
<td>0.47</td>
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<tr>
<td></td>
<td></td>
<td>RT</td>
<td>1,308.29</td>
<td>433.50</td>
<td>1,123.17</td>
<td>290.96</td>
<td>0.52</td>
<td></td>
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<tr>
<td></td>
<td>2-Back task</td>
<td>CA</td>
<td>82.12</td>
<td>12.23</td>
<td>85.04</td>
<td>14.76</td>
<td>0.25</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>RT</td>
<td>4,217.53</td>
<td>1,765.53</td>
<td>2,794.41</td>
<td>1,850.09</td>
<td>0.49</td>
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</tr>
</tbody>
</table>

**Oscar-Berman et al. 2014 (review)**

## Relapse within 6 months (>1 drink)

<table>
<thead>
<tr>
<th>Cognitive functions</th>
<th>Tasks</th>
<th>Variables</th>
<th>Baseline M</th>
<th>Baseline SD</th>
<th>Follow-up M</th>
<th>Follow-up SD</th>
<th>Comparison between baseline and follow-up</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Episodic memory</td>
<td>FCSR</td>
<td>Free recalls a</td>
<td>29.89</td>
<td>9.58</td>
<td>29.78</td>
<td>10.84</td>
<td>1</td>
<td>0.83</td>
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<td>Delayed free recall</td>
<td>11.00</td>
<td>3.84</td>
<td>11.11</td>
<td>2.93</td>
<td>0.81</td>
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<tr>
<td>Executive functions</td>
<td>Stroop test</td>
<td>CW</td>
<td>39.78</td>
<td>12.26</td>
<td>39.67</td>
<td>11.98</td>
<td>0.81</td>
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<tr>
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<td>Alternate response task</td>
<td>CA</td>
<td>88.78</td>
<td>13.23</td>
<td>77.44</td>
<td>18.94</td>
<td>0.03*</td>
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<td>1,524.78</td>
<td>1,152.92</td>
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<td>590.96</td>
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<td>82.87</td>
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<td>3,446.59</td>
<td>1,952.78</td>
<td>2,329.10</td>
<td>952.82</td>
<td>0.24</td>
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</tr>
</tbody>
</table>

**Pitel et al. 2009**

**Improvement**

Return to normal

**No improvement**

Deterioration

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Oscar-Berman et al. 2014 (review)
TREATMENT ADJUSTMENTS

Treatment delay

Screening and neuropsychological assessment

- Preserved NP abilities
  - Regular alcohol treatment
  - Neuropsychological recovery

- Mild-to-moderate NP deficits
  - Reassessment
  - Persistent NP deficits

- Severe NP deficits
  - «Mid-term» care unit
  - «Mid-term» care unit
  - Nursing home
  - Specialized unit (when available...)

Preserved NP abilities

Mild-to-moderate NP deficits

Severe NP deficits
TREATMENT ADJUSTMENTS

Treatment delay

Cognitive remediation/rehabilitation

Bates et al. 2013
Rupp et al. 2012

Modification of attentional bias toward alcohol

Wiers et al. 2006
Schoenmakers et al. 2007, 2010
Boffo et al. 2015, 2017
QUESTIONS

1. Are there neuropsychological deficits in AUD before the development of KS?

2. What are the clinical consequences of neuropsychological deficits observed in AUD?

- Limit the benefit of treatment
- Increase the risk of relapse
- Evaluate
- Identify risk factors
- Favor recovery
- Adjust treatment
WHAT ARE THE DIFFERENCES BETWEEN ALTERED BRAIN STRUCTURE AND FUNCTION IN AUD AND KS?

Question 3
GRAY MATTER (GM) ABNORMALITIES

AUD<CS

KS<CS

Pitel et al. 2009

KS: variability in the individual pattern

Conjunction

KS<CS and AUD<CS

FDR p<0.05

Pitel et al. 2012

Pitel et al. 2009
GM: SPECIFICITY OF KS COMPARED WITH AUD

KS<AUD

* significant difference compared to controls
† significant difference compared to alcoholics

P<0.001 unc.

KS<AUD and France vs US

Le Berre et al. 2015

Pitel et al. 2012
WHITE MATTER (WM) ABNORMALITIES

AUD<CS

KS<CS

Conjunction
KS<CS and AUD<CS

KS: variability in the individual pattern

FDR p<0.05

Pitel et al. 2009

Pitel et al. 2012
WM: SPECIFICITY OF KS COMPARED WITH AUD

KS<AUD

P<0.001 unc.

KS<AUD and France vs US

*: significant difference compared to controls
†: significant difference compared to alcoholics

Pitel et al. 2012

Le Berre et al. 2015
WM MICROSTRUCTURE (1)

Voxel-by-voxel comparisons of FA values (TBSS)

5,000 permutations, FWE \( P<0.05 \)
TFCE for cluster-wise correction

Segobin et al. 2015
Cluster analysis on certain fiber tracts

- Fronto-cerebellar circuit
- Papez circuit

Between-group comparisons of episodic memory results

- Fornix
- Cingulum

Significance:
- * sig different from HC (p<0.05)
- ** sig different from HC (p<0.001)
- § sig different from UA_LOW (p<0.05)
- §§ sig different from UA_LOW (p<0.001)
- ¥ sig different from UA_HIGH (p<0.001)

Segobin et al. 2015
MEMORY DISORDERS (1)

Continuity between AUD and KS

AUD patients at risk for KS

Similar profiles

Pitel et al. 2008
MEMORY DISORDERS (2)

SOURCE MEMORY: temporal confusion

Continuous recognition task

⇒ Temporal confusion in KS only
⇒ Confabulations?

Brion et al. 2017
QUESTIONS

1. Are there neuropsychological deficits in AUD before the development of KS?

2. What are the clinical consequences of neuropsychological deficits observed in AUD?

3. What are the differences between altered brain structure and function in AUD and KS?

Papez circuit  Episodic memory  Temporal confusion/confabulation  Recovery
QUESTIONS

1. Are there neuropsychological deficits in AUD before the development of KS?
   YES!!!!

2. What are the clinical consequences of neuropsychological deficits observed in AUD?
   - Limit the benefit of treatment
   - Increase the risk of relapse
   - Evaluate
   - Identify risk factors
   - Favor recovery
   - Adjust treatment

3. What are the differences between altered brain structure and function in AUD and KS?
   - Papez circuit
   - Episodic memory
   - Temporal confusion/confabulation
   - Recovery
TWO BRAIN CIRCUITS PREDOMINANTLY AFFECTED

Working memory
Executive functions
Motor abilities

Episodic memory

Pitel et al. 2014
THALAMIC SEGMENTATION IN AUD AND KS

Frontal executive target
- BA9, BA46

Cerebellar executive: Crus I et II

Frontal motor: precentral gyrus

Cerebellar motor: Lobs IV-VI

Hippocampus target
- Morel Atlas
  70% of MD

Atrophy MD: AUD=KS
No disconnexion between MD and frontal

Atrophy ANT in KS only

Disconnexion between ANT and hippocampus in both groups
Mild-to-moderate atrophy

Mild-to-moderate dysfunction of the FCC

Mild-to-moderate WM and executive deficits

Mild-to-moderate disconnection

Mild-to-moderate dysfunction of the PC

Mild-to-moderate episodic memory deficits

AUD

Reversible
Mild-to-moderate disconnexion of the PC

Mild-to-moderate dysfunction of the FCC

Mild-to-moderate WM and executive deficits

Mild-to-moderate episodic memory deficits

Mild-to-moderate atrophy

Severe atrophy

+ altered thiamine metabolism or thiamine deficiency
Mild-to-moderate disconnexion

WM and executive deficits

Mild-to-moderate atrophy

Mild-to-moderate dysfunction of the FCC

Mild-to-moderate WM and executive deficits

Mild-to-moderate disconnexion

Severe atrophy

Severe dysfunction of the PC

Amnesia

+ altered thiamine metabolism or thiamine deficiency

KORSAKOFF SYNDROME
Persistent
ALCOHOL-INDUCED NEUROCOGNITIVE DISORDER (DSM-5 CRITERIA)

- A. Clinical criteria for **mild** neurocognitive disorder
- B. Does not occur exclusively during the course of a delirium and persists beyond the usual duration of intoxication and acute withdrawal
- C. Duration and extent of use are capable of producing the neurocognitive impairment
- D. The temporal course of the neurocognitive deficits is consistent with the timing of alcohol use and abstinence
- E. The neurocognitive disorder is not attributable to another medical condition or is not better explained by another mental disorder

- A. Clinical criteria for **major** neurocognitive disorder
- B. Does not occur exclusively during the course of a delirium and persists beyond the usual duration of intoxication and acute withdrawal
- C. Duration and extent of use are capable of producing the neurocognitive impairment
- D. The temporal course of the neurocognitive deficits is consistent with the timing of alcohol use and abstinence
- E. The neurocognitive disorder is not attributable to another medical condition or is not better explained by another mental disorder

- **Amnestic-confabulatory type**
- Persistent: Neurocognitive impairment continues to be significant after an extended period of abstinence

ACKNOWLEDGEMENT OF ALCOHOL-RELATED NP DEFICITS
CONTINUUM BETWEEN ALCOHOLICS AND KORSAKOFF PATIENTS
AUD is a major health issue worldwide!

- The detection of alcohol-related NP deficits is clinically relevant
  - for the treatment of alcohol addiction
  - to prevent neurological complications such as KS

- The comparison between AUD and KS gives insight on the physiopathology of these diseases

Interesting model to examine:
- neuropsychological/brain recovery
- the role of the thalamus in memory (ANT versus MD)