ADHD-Index
Neuroalgorithms in adults with ADHD
Development, reliability and application in clinical practice

Andreas Müller, Sarah Vetsch
IPEG 2018
Brain and Trauma Foundation Grison/Switzerland

Foundation purpose:
- Support for people with strokes
- Research in the field of neurobiology
- Publications

applied science, research and development
- Criteria for diagnosis and treatment of mental disorders for precise medicine

Giusep Nay
Pius Baschera
Erich Seifritz
Paul Ruschetti
Monika Bobbert
Andreas Müller
systemic model of self regulation for mental diseases

History of life

- Pregnancy
- Birth
- Early childhood
- Childhood
- Preschool
- School

Behaviour
Emotion
Cognition
Biology

Person

Individul adaption processes

Disorder

Structural-physical env.

Adaptation process in social life and in community (culture)

Biosocial env.

Systemic organisation- and transactions patterns

Genes
Neuroanatomy
Neurochemistry
Neuropsychology
Neurophysiology

Individul adaption processes
ADHD as a disturbance of contradictions and discrepancies

- **Subjectivity of diagnosis**, because as with all mental disorders, mainly questionnaires and interviews are used (questionnaire according to DSM-5, ICD-10)
- **Interview**: mix of subjective worlds of patient and interviewer
- **Unclear clinical picture**, depending on behavior, emotions and cognitions that come into focus, different perspectives emerge. The diversity of perspectives is confusing
- **There is no reliable ADHD test**: neuropsychology, behavioral questionnaires and biochemical processes achieve insufficient reliability
- **ADHD symptoms are continuously distributed** in the population (e.g. control)
- **In children, it is difficult to distinguish between immaturity symptoms and ADHD symptoms** because some of the symptoms that lead to ADHD are developmentally dysfunctional

Jenni (2016)
Often incorrect diagnoses

Of interest are false diagnoses, of which mainly the overdiagnosis was discredited, as a diagnosis usually requires treatment with stimulants and psychotherapy (Merten et al., 2017).

According to the authors such false-positive diagnoses are more often than false-negative diagnoses. In the latter case, the diagnosis is not made, even though the criteria are met.
Who of them has ADHD?
From Biomarkers to neuroalgorithms

Biomarkers:
There is not a single biomarker that can explain the variance between patient groups even approximately.

Reliability and objectivity
Neuromarkers are highly reliable and have high objectivity.

Validity of the markers
Individual EEG-neuromarkers map important aspects of a disorder, e.g. sensitivity, impulse control, drive.

Healthy and patient groups can be separated mathematically.

Combination of markers is crucial!
Project: ‘Biomarker-oriented diagnostics of ADHD and comorbidity – children, adolescents and adults’

• Brain and Trauma Foundation Grisons/Switzerland
  • Between July 2014 and July 2017
  • 5 different locations (Zurich, Chur, Lausanne, Lucerne and Rapperswil)

• Bio-/Neuromarkers/Genetics on ADHDs and comorbidities over live span of 6 - 60 years

• Change markers over two years

• Outcome markers in a naturalistic design
Project: ADHD-Study: Design

Research group

- Monthly survey 5 min
- MBF 1, MBF 2, MBF 3, MBF 4, MBF 5
- Investigation 1
- Questionnaires
- Interview
- Comorbidities Interview
- Neuropsychological examination (candit/IQ)
- Biomarker (eo/ec, event-related potentials)
- Report

- 「Mood survey」5 min on 4 consecutive days

- Monthly survey 5 min
- MBF 1, MBF 2, MBF 3, MBF 4, MBF 5
- Investigation 2
- Questionnaires
- Interview
- Comorbidities Interview
- Biomarker (eo/ec, event-related potentials)

- 「Mood survey」5 min on 4 consecutive days

- Monthly survey 5 min
- MBF 1, MBF 2, MBF 3, MBF 4, MBF 5
- Investigation 3
- Questionnaires
- Interview
- Comorbidities Interview
- Biomarker (eo/ec, event-related potentials)

- 「Mood survey」5 min on 4 consecutive days

- Monthly survey 5 min
- MBF 1, MBF 2, MBF 3, MBF 4, MBF 5
- Investigation 4
- Questionnaires
- Interview
- Comorbidities Interview
- Biomarker (eo/ec, event-related potentials)

- 「Mood survey」5 min on 4 consecutive days

- Monthly survey 5 min
- MBF 1, MBF 2, MBF 3, MBF 4, MBF 5
- Investigation 5
- Questionnaires
- Interview
- Comorbidities interview
- Neuropsychological examination (candit/IQ)
- Biomarker (eo/ec, event-related potentials)
- Reports

Timeline:
- 0 months
- 6 months
- 12 months
- 18 months
- 2 years
**Project: ADHD-Study: Design**

**Control group**

- Questionnaires
- Interview
- Comorbidities interview
- Neuropsychological examination (candit/IQ)
- Biomarker (eo/ec, event-related potentials)
- Report

**Blood**

**Investigation 1**
- Questionnaires
- Interview
- Comorbidities interview
- Biomarker (eo/ec, event-related potentials)
- Report

**Investigation 2**
- Questionnaires
- Interview
- Comorbidities interview
- Biomarker (eo/ec, event-related potentials)
- Report

**Investigation 3**
- Questionnaires
- Interview
- Comorbidities interview
- Neuropsychological examination (candit/IQ)
- Biomarker (eo/ec, event-related potentials)
- Report

**Timeline**
- 0 months
- 12 months
- 2 years
Project: ADHD-Study - Samplesize

Research group: ADHD
age 6 - 60
Subjects:
Children and adolescents : 250
adults: 250

Control group:
age: 6 - 60
subjects 250
Sub-project: ADHD-Index

Research group: ADHD
  age 18-60
  Subjects: 181

Control group
  age: 18-60
  Subjects: 147

EEG-Data: Signal power: Eyes-closed, eyes-open, VCPT (Go-/Nogo-Task)/ ERP peak amplitudes and latencies/ ICA

Timeline:
- t1: Basis for formation of classification models
- t2: Re-Test
- t3: Re-Test

Timeline:
- t1: 12 months
- t2: 12 months
- t3: 24 months
Methodical Work - Framework for Big Data

Main functions of the framework:

Model selection to find the best models/classifiers, reliable evaluation of the resulting model is enabled.

The framework allows to play through as many variations as possible economically thanks to the different methods applied.

A separate hold-out data set is used to control overfitting after model selection.
## Results classification adults

<table>
<thead>
<tr>
<th>Model</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>ROC-AUC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 SVM</td>
<td>0.83</td>
<td>0.75</td>
<td>0.85</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 Logistic regression</td>
<td>0.75</td>
<td>0.77</td>
<td>0.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3 Logistic regression</td>
<td>0.81</td>
<td>0.72</td>
<td>0.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4 Logistic regression</td>
<td>0.82</td>
<td>0.73</td>
<td>0.85</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>5 SVM</td>
<td>0.82</td>
<td>0.71</td>
<td>0.84</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
### Results reliability adults

<table>
<thead>
<tr>
<th></th>
<th>t1</th>
<th>t2 (after 12 months)</th>
<th>t3 (after 24 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.75</td>
<td>0.72</td>
<td>0.76</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.77</td>
<td>0.64</td>
<td>0.67</td>
</tr>
</tbody>
</table>

ICC, two-way mixed, absolute agreement 0.560 - 0.683

\[ p < .001 \]
From science to clinical work

Scientific data (hundreds of datasets all loaded in the same format)

Individual Data (standard format: Filters, aso)

Loader

EEG/ERP Statistics (ERPSA)

- Normative Database
  - Healthy People 6-69

- Algorithms
  - ADHD
  - Stress

- Indexes
  - Arousal/CSI
  - T/B Ratio

HRV

Interfaces

Reportgenerator

- Normative Database
- Algorithms
  - ADHD
  - Stress
  - Subtypes
  - MPH

- Indexes
  - Arousal
  - CSI
  - T/B Ratio

HRV

Scientific papers
Application in clinical praxis

Age Group Adults: ADHD: 79%

Control group compared to ADHD group: significant features

- Chan T6 (VCPT: A-A)
- FS of Chan C4
- FS of Chan P3
- Chan Fz (VCPT A-P)
- Chan Pz (VCPT: A-P-A-A)
- Chan T6 (VCPT: A-P)
- Chan Pz (VCPT: A-A EP)
- Chan O2 (VCPT: A-A)
- Chan Cz (VCPT: A-P)
- Chan Pz (VCPT: A-A)

Influence of the features in the single case
Who benefits from biomarkers/neuralgorithms?

• The MD, Psychotherapist - more safety for diagnoses and treatment

• The patient - more clarity

• Healthcare - Fewer Blind Flights - Lower Costs

• The psychiatric-psychological subject - evidence-based discipline
The End – thank you!