

Title of the planned thesis project:

Identifying neuropsychological subgroups in patients with bipolar disorder and evaluation of a cognitive remediation program

Bipolar disorder is a severe, chronic and recurrent illness, which affects nearly 5% of the population. Recent research points at the relevance and persistence of cognitive dysfunctions in bipolar patients even beyond the acute phases, although cognitive impairment has been classically associated with schizophrenia and not bipolar disorder. The clinical experience shows, that some bipolar patients don't receive their former level of cognitive performance, while others get well without any deficits after an acute episode of depression or mania. In this study we want to investigate several moderator variables and their relation to the cognitive performance of the bipolar patients (identifying a deficit- vs. non-deficit subgroup).

Current findings suggest furthermore that some intervention is needed in order to improve not only affective symptoms but also cognitive dysfunctions, so that patients could benefit from cognitive remediation techniques to improve cognitive impairment and the functional outcome. There is only little previous research on the efficacy of cognitive remediation programs on bipolar disorder. Cognitive remediation (CR) is a new psychological treatment, which aims to improve cognitive function and coping skills. Several studies have recently demonstrated that CR improves cognitive and occupational function in patients with schizophrenia and with depression. However, it is unclear whether CR improves cognitive and socio-occupational function in individuals with bipolar disorder (BD) and, if so, what impact this might have on these people's abilities in terms of work, coping strategies, quality of life, and everyday safety.

The aims of the planned study are:

1. Identifying subtypes of bipolar disorder by neuropsychological methods (deficit vs. non-deficit subgroup).
2. Development and implementation of a tailored cognitive remediation (CR) program for those bipolar patients with cognitive deficits.

The **hypotheses** of the present study are that CR (in comparison to usual medical treatment) will:

- 1) improve cognitive functions (attention, memory, executive functions), social function and life quality of the patients.
- 2) increase neuroplasticity, measured by Near-infrared spectroscopy (NIRS).

Intervention (CR):

The cognitive remediation program is composed of 12 weekly sessions of 75 minutes, each aimed at improving the following cognitive domains: attention, memory and executive functions and psychosocial functioning. The program will be performed

in an 5-8-patient group conducted by an experienced neuropsychologist with previous experience with bipolar patients and specific training on patients' group management. The CR program consists of a computerized training of cognitive functions via exercises of happyneuron.de. Furthermore each group session comprised a cognitive-skills part. This Skills-Group is intended to bridge what is exercised on the computer tasks to everyday tasks. It will follow the computer activity and is about techniques to problem solving, verbal reasoning and solving logical problems. Furthermore there will be group sessions about improvement attention, planning and organization in daily life and effective communication.

Outcome Measures:

1) Total scores of attention, memory and executive functions with manual and computerised neuropsychological tests:

Cognitive domain	Test	Test duration (minutes)
<i>Processing speed</i>	Stroop- test (colour / word condition)	15
<i>Attention</i>	Tests of attentional performance (TAP): subtests "alertness" and "divided attention"	5 2,5-6
<i>Long-Term verbal memory</i>	California Verbal Learning Test (CVLT)	30-40
	Rey Complex Figure Test (CFT)	
<i>Executive Functions</i>		
Problem solving	TL-D	10
Interference tendency	Stroop- test (interference condition)	s.o.
Word fluency	Regensburger Wortflüssigkeitstest (RWT)	5
Working memory	N-Back	10
Cognitive flexibility	Cogshift	18

2) Changes of neuronal functions measured via NIRS (while CogShift exercise)

3) Changes in scores of questionnaires:

Concept	Questionnaires
Life Quality	WHOQOL-BREF
Psychosocial Functioning	GAF-Skala /SOFAS, Mini-ICF-APP
Subjective cognitive complaints	FLEI

Estimated Enrollment for Identifying neuropsychological subgroups: 75 bipolar patients (75 healthy controls, matched for age)

Estimated Enrollment for CR program: 40 bipolar patients (40 bipolar patients as control group)

Inclusion Criteria:

- Diagnosis of bipolar disorder type I or II, according to DSM-IV-TR 4 criteria Adult patients
- aged between 18 and 55 years old
- Euthymic (YMRS < 6, HDRS < 8) for at least three months prior to study entry.
- Signed informed consent

Inclusion criteria for the CR:

- euthymic (MADRS ≤ 12 ; YMRS ≤ 5) for at least three months prior to the remediation program
- stabile Medikation

Exclusion Criteria:

- IQ < 85
- Neurological illness
- Present diagnosis of substance abuse or dependence according to DSM-IV criteria the last three months
- Significant medical illness considered as severe by the study that may interfere with assessments
- having been enrolled in any kind of cognitive rehabilitation intervention the last two years

The study will be performed in the university hospital of Würzburg, department psychiatry. The Bipolar Disorder Program (a specialized bipolar ward) has been established at the University hospital of Würzburg in April 2009 by Prof. Andreas Reif.

Study Start Date: April 2012

Estimated Study Completion Date: April 2015

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