Trial Description

Title

Searching New Physiological Markers for the Prognosis of Memory Decline in Mild Cognitive Impairment and Temporal Lobe Epilepsy

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

Against our scientific background, we found an analogy in one of their most disabling symptoms between the two different clinical groups that form the focus of our research interest: Epilepsies, especially temporal lobe epilepsies (TLE) and degenerative dementia in its earliest stage, mild cognitive impairment (MCI). While it is obvious that memory problems are the main concern of people with MCI, they are also a major predictor of impaired quality of life and social disability in TLE. Moreover, memory impairments are not only a link between MCI and TLE, but may also act as a starting point from which researchers in each field may add innovative aspects to the corresponding research area.
Specifically, the cause of memory disturbance in both conditions is unclear when patients of each clinical group perform normally on standard neuropsychological tests of memory. This is the case in early stages of MCI. However, memory problems may be detectable with physiological tests.
Thus, the overall aims of our study are:
1. To identify eventual analogies in the pattern of memory impairments in TLE and MCI and to better understand the mechanisms of memory problems in both conditions. This objective will be addressed by comparing these groups by several measures.
2. To make a more accurate prognosis of memory decline by use of modern examinations.
In this study, MCI patients will be divided into a subgroup of evidenced memory impairment, as assessed by standardized tests, and in a subgroup of patients with subjective cognitive complaint, but without objectively measurable abnormality. Additionally we include pharmacoresistant TLE-patients. By entering the study, each patient undergoes several neuropsychological tests, and an electroencephalography. On the second appointment an another electroencephalography will be conducted in addition to a a magnetic resonance imaging. The acquired data will be analyzed with modern techniques. The clinical groups will be compared with a sample of healthy controls in order to determine abnormalities. After 1.5 years, a second session of neuropsychological testing will reveal the degree of memory decline.

Brief Summary in Scientific Language

Against our scientific background, we found an analogy in one of their most disabling symptoms between the two different clinical groups that form the focus

of our research interest: Epilepsies, especially temporal lobe epilepsies (TLE) and degenerative dementia in its earliest stage, mild cognitive impairment (MCI). While it is obvious that memory problems are the main concern of people with MCI, they are also a major predictor of impaired quality of life and social disability in TLE. Moreover, memory impairments are not only a link between MCI and TLE, but may also act as a starting point from which researchers in each field may add innovative aspects to the corresponding research area.
Specifically, the pathogenesis of memory disturbance in both conditions is unclear when patients of each clinical group perform normally on standard neuropsychological tests of memory. This is the case in early stages of MCI. However, correlates of the subjective observation of memory problems would be detectable with neuroimaging and neurophysiology.
Thus, the overall aims of our study are:
•To identify eventual analogies in the pattern of memory impairments in TLE and MCI and to better understand the mechanisms of memory problems in both conditions. This objective will be addressed by comparing these groups by several measures.
•To increase the validity for prognosis of memory decline by implementing multimodal examination on a single subject base.
In this study, MCI patients will be divided into a subgroup of evidenced memory impairment, as assessed by standardized tests, and in a subgroup of patients with subjective cognitive complaint, but without objectively measurable abnormality. Additionally we include pharmacoresistant TLE patients. By entering the study, each patient undergoes several neuropsychological tests on memory performance, document confounding variables, event-related electroencephalography and magnetic resonance imaging. In order to find individual abnormalities, we will use innovative data-processing techniques and single-subject non-parametric statistics. The extracted features of the clinical groups will be compared with those of a sample of healthy controls in order to determine abnormalities. Specifically, we will assess features which were shown to be of diagnostic or predictive value in one of the two assessed disorders (MCI or TLE). After 1.5 years, a second session of neuropsychological testing will reveal the degree of memory

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00003314**
- Date of Registration in DRKS: **2011/11/14**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

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Investigator Sponsored/Initiated Trial (IST/IIT): **yes**

- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **1429 , Amt der Salzburger Landesregierung Ethikkommission für das Bundesland Salzburg**

Secondary IDs

Health condition or Problem studied

- ICD10: **F06.7 - Mild cognitive disorder**
- Free text: **temporal lobe epilepsy**
- ICD10: **G40 - Epilepsy**

Interventions/Observational Groups

- Arm 1: <style fontName='DejaVu Sans' isBold='true'>healthy subjects
  begin:
  EEG,
  neuropsychological diagnostics;

  2 weeks after begin:
  structural & functional MRI,
  EEG;

  18 months after begin:
  neuropsychological diagnostics;</style>
- Arm 2: <style fontName='DejaVu Sans' isBold='true'>temporal lobe epilepsy - chronic course and resistance to medication

  begin:
  EEG,
  neuropsychological diagnostics;

  2 weeks after begin:
  structural & functional MRI,
  EEG;

  18 months after begin:
  neuropsychological diagnostics;</style>

- Arm 3: <style fontName='DejaVu Sans' isBold='true'>mild cognitive impairment; amnestic subtype

  begin:
  EEG,
  neuropsychological diagnostics;

  2 weeks after begin:
  structural & functional MRI,
  EEG;

  18 months after begin:
  neuropsychological diagnostics;
  </style>
- Arm 4: <style fontName='DejaVu Sans' isBold='true'>subjective memory complaints; performance 1 standard deviation below average

  begin:
  EEG,
  neuropsychological diagnostics;

  2 weeks after begin:
  structural & functional MRI,
  EEG;

  18 months after begin:
  neuropsychological diagnostics;
  </style>

Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Non-randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Other**
- Purpose: **Prognosis**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

prognosis of memory decline by markers in EEG and MRI

EEG: begin: Synchronicity, complexity and frequency distribution during encoding of information (word-pair-learing and watching a movie) and during recall of information(word-pair-recall: free recall and recognition)
EEG: 2 weeks after begin: synchronicity, complexity and frequency distribution

during recall of information(word-pair-recall: free recall and recognition; questions about the movie)
MRI: 2 weeks after begin: volumetry, shape, cortical thickness of hippocampus, rhinal and entorhinal cortex and global intensity and deformation.

The validity of the prognosis according to these markers will be evaluated according to the neuropsychologically measured decline of memory (difference between begin and 18 months later).

Secondary Outcome

Basic research: analogies in the pattern of physiological changes related with memory decline in MCI and TLE

group comparisons according to the markers:
EEG: begin: synchronicity, complexity and frequency distribution during encoding of information (word-pair-learing and watching a movie) and during recall of information(word-pair-recall: free recall and recognition)
EEG: 2 weeks after begin: synchronicity, complexity and frequency distribution during recall of information(word-pair-recall: free recall and recognition; questions about the movie)
MRT: 2 weeks after begin: volumetry, shape, cortical thickness of hippocampus, rhinal and entorhinal cortex and global intensity and deformation.

tecnical aspects of the analysis: Which algorithms perform best for segmenting the relevant brain regions? Which protocol for segmentation yields the most accurate prognosis?

Countries of recruitment

- AT **Austria**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2012/01/01**
- Target Sample Size: **180**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**

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- Minimum Age: **18 Years**
- Maximum Age: **100 Years**

Additional Inclusion Criteria

MCI: We include 20 level 2 patients (subjective cognitive complaints of memory-related nature) and 20 level 3 patients (mild cognitive impairment; amnestic subtype) according to the “global deterioration scale for aging and dementia” (Reisberg et al., 1982). Level 2 patients are included if they have subjective cognitive complaints of memory-related nature, not reaching the diagnostic criteria on neuropsychological scales for MCI but scoring at least 1 standard-deviation below normative data (Gauthier et al., 2006). Level 3 patients are diagnosed with the CERAD-tests according to Petersen et al. (1999). Patients are included if they report duration of the problems for at least 0.5 and maximal 5 years.
TLE : We include 20 patients with chronic, medication resistant, i.e. not controllable seizures, unilateral TLE. Patients are included regardless presence or severeness of memory deficits.
Healthy controls: 20 subjects will participate in the pre-evaluation of the EEG-paradigms. 80 subjects will serve as control-group for the MCI/TLE groups. The control group will be recruited among the non-genetically connate relatives or friends of the patients to ensure similar demographic factors.

Exclusion criteria

MCI: Patients are excluded if aged below 50 or if vascular, metabolic, traumatic, or psychiatric pathologies as well as pharmacological treatment may better explains the impairment. Thus, only patients with probable degenerative aetiology will be considered.
TLE: Patients with progressive lesions or immune-mediated TLE will be excluded.
Healthy controls: Subjects with psychiatric or neurologic diseases will be excluded.

Addresses

- **Primary Sponsor**

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Sources of Monetary or Material Support

■ **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

Fonds zur Förderung der wissenschaftlichen Forschung (FWF)
Haus der Forschung, Sensengasse 1
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Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)

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- **Private sponsorship (foundations, study societies, etc.)**

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Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2016/10/31**

Trial Publications, Results and other documents

- Approval of ethics comm. (mandatory for transfer to Studybox) **Approval of last amendment to study by Ethikkommission für das Bundesland Salzburg.**
- trial protocol (mandatory for transfer to Studybox) **Last version of study protocol as submitted to ethical committee**
- Further trial documents <style fontName='DejaVu Sans' isBold='true'>Höller, Y., & Trinka, E. (2014). What do temporal lobe epilepsy and progressive mild cognitive impairment have in common?. Frontiers in systems neuroscience, 8.</style>
- Paper <style fontName='DejaVu Sans' isBold='true'>Höller, Y., Butz, K., Thomschewski, A., Schmid, E., Uhl, A., Bathke, A. C., ... & Höller, P. (2017). Reliability of EEG interactions differs between measures and is specific for neurological diseases. Frontiers in human neuroscience, 11, 350.</style>
- Paper <style fontName='DejaVu Sans' isBold='true'>Liedlgruber, M., Butz, K., Höller, Y., Kuchukhidze, G., Taylor, A., Tomasi, O., ... & Uhl, A. (2016, June). Variability Issues in Automated Hippocampal Segmentation: A study on out-of-the-box software and multi-rater ground truth. In Computer-Based Medical Systems (CBMS), 2016 IEEE 29th International Symposium on (pp. 191-196). IEEE.</style>
- Paper <style fontName='DejaVu Sans' isBold='true'>Höller, Y., Uhl, A., Bathke, A.,

Thomschewski, A., Butz, K., Nardone, R., ... & Trinka, E. (2017). Reliability of EEG Measures of Interaction: A Paradigm Shift Is Needed to Fight the Reproducibility Crisis. Frontiers in Human Neuroscience, 11, 441.</style>

- Paper <style fontName='DejaVu Sans' isBold='true'>Höller, Y., Bathke, A.C., & Uhl, A. (2019). Age, Sex and Pathology Effects on Stability of Electroencephalographic Biometric Features Based on Measures of Interaction. IEEE Transactions on Information Forensics and Security, 14, 459-471.</style>

- Paper <style fontName='DejaVu Sans' isBold='true'>Yvonne Höller and Andreas Uhl. 2018. Do EEG-Biometric Templates Threaten User Privacy?: Full Paper. In IH&MMSec ’18: 6th ACM Workshop on Informa- tion Hiding and Multimedia Security, June 20–22, 2018, Innsbruck, Austria. ACM, New York, NY, USA, 10 pages. https://doi.org/10.1145/3206004.3206006</style>

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