Trial Description

Title

Understanding the interplay of the mixed pathologies of the aging brain - longitudinal multimodal imaging studies

Trial Acronym

MIZERA

URL of the trial

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Brief Summary in Lay Language

Cerebral aging and mixed dementia are related to several mixed pathologies accumulating in the elders' brains, including cerebral small vessel disease (CSVD), protein depositions and neurodegeneration. There is, however, a lack of knowledge, how those pathologies interact, especially whether there is a causal link. Moreover, while both, vascular pathologies and protein depositions impact on cognitive decline, it remains to be elucidated whether this happens through common or distinct mechanisms. We moreover aim to understand, how lifestyle (including physical activity, cognitive activity, socioeconomic status, education, vascular health) impact on each of those mixed pathologies and on their interaction. Our research questions will be addressed by applying several methods, including multimodal imaging and cerebrospinal fluid (CSF) markers, using a longitudinal study-design in a cohort of patients displaying CSVD as identified by cerebral microbleeds (MRI). We overall aim to increase the pathophysiological understanding of cerebral aging, to open the gate for specific prevention and therapies against mixed dementia.

Brief Summary in Scientific Language

Cerebral aging and mixed dementia development is related to several pathologies accumulating in the elders' brains, including cerebral small vessel disease (CSVD), cerebral amyloid angiopathy (CAA), parenchymal Abeta and neurodegeneration. There is, however, a lack of knowledge, whether those pathologies occur just co-incidentally or whether they are causally related to one another. Moreover, while both, vascular pathologies and protein depositions impact on cognitive decline, it remains to be elucidated whether this happens through common or distinct mechanisms. The study will moreover focus on the understanding how lifestyle, such as cognitive activity, modifies the interaction between the mixed pathologies of the aging brain. Our research questions will be addressed by applying a multimodal biomarker approach, including structural and functional MRI, PET and cerebrospinal fluid (CSF), using a longitudinal study-design. We overall aim to increase the pathophysiological understanding of cerebral aging, to open the gate for specific prevention and therapies against mixed dementia.

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

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[---]*

Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00010532**
- Date of Registration in DRKS: **2016/05/20**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **28/16 , Ethikkommission der Medizinischen Fakultät der Otto-von-Guericke-Universität Magdeburg**

Secondary IDs

Health condition or Problem studied

- ICD10: **F01.3 - Mixed cortical and subcortical vascular dementia**
- ICD10: **F00.2 - Dementia in Alzheimer disease, atypical or mixed type**
- ICD10: **I68.0 - Cerebral amyloid angiopathy**

Interventions/Observational Groups

- Arm 1: **Baseline diagnostics in patients with cerebral microbleeds will be conducted as a part of clinical routine, and medical history, neurological and cognitive status, lifestyle variables, data on cerebrospinal fluid (CSF) as well as neuroimaging (including MRI and PET) will be assessed. After 6 to 12 months, patients will come to follow-up visits, which will comprise the following procedures: after 6 months, assessment of medical history, neurological status, lifestyle variables; after 12 months, assessment of medical history, neurological/cognitive status, lifestyle variables; after 24 months, assessment of medical history, neurological/cognitive status, lifestyle variables, CSF data, MRI, PET; after 36 months, assessment of medical history, neurological/cognitive status, lifestyle variables; after 48 months, assessment of medical history, neurological/cognitive status, lifestyle variables, CSF data, MRI, PET; after 60 months, assessment of medical history, neurological/cognitive status, lifestyle variables**

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Characteristics

- Study Type: **Non-interventional**
- Study Type Non-Interventional: **Other**
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Basic research/physiological study**
- Assignment: **Single (group)**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

We aim to understand, whether cerebral small vessel disease and amyloid depositions act together on certain neurodegeneration patterns, network disturbances, cognitive impairment and dementia development. We will further examine how lifestyle impacts on the interactions between the mixed pathologies of the aging brain.

To answer our research questions voxelwise analysis will be conducted using MRI and PET data, and methods of pattern recognition need to be established to quantify microangiopathic lesions. Imaging data will be related to the patients' cognitive state, lifestyle and CSF variables, using distinct statistical models (including e.g. structural equation models and mixed effects linear models) and taking the availability of a longitudinal dataset into account.

Secondary Outcome

We further aim to answer the question, whether there is a relationship between cerebral small vessel disease and cerebral amyloid angiopathy.

Again, voxelwise imaging analysis will be conducted taking several follow-up data into account. Imaging data will then be related to the patients' vascular risk

factors, cognition and demographics.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Klinik für Neurologie, Otto-von-Guericke Universität, Magdeburg**

Recruitment

- Planned/Actual: **Planned**
- (Anticipated or Actual) Date of First Enrollment: **2016/06/01**
- Target Sample Size: **300**
- Monocenter/Multicenter trial: **Monocenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **60 Years**
- Maximum Age: **90 Years**

Additional Inclusion Criteria

• Microbleeds detectable using MRI (according to STRIVE criteria)
• Ages of 60 to 90 years
• Agreement to attend the study and to take part in follow-up visits

Exclusion criteria

• Macroinfarctions, intracerebral hemorrhages
• Severe stenoses of the extracerebral arteries
• Severe vascular risk profile
• Severe chronic kidney disease, heart failure
• Severe dementia
• Cancer (palliative stage)
• Neurodegeneration from other diseases (parkinson disease, motor neuron disease, temporal lobe epilepsy, multiple sclerosis, mitochondrial disorders, storage diseases)
• Primary psychiatric diseases (schizophrenia, bipolar disorder)

Addresses

■ **Primary Sponsor**

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■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

■ **Institutional budget, no external funding (budget of sponsor/PI)**

Klinik für Neurologie, Otto-von-Guericke Universität Magdeburg
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Status

- Recruitment Status: **Recruiting planned**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*