



MEDIZINISCHE  
FAKULTÄT

# Forschungsbericht 2018

Institut für Kognitive Neurologie und Demenzforschung

# INSTITUT FÜR KOGNITIVE NEUROLOGIE UND DEMENZ-FORSCHUNG

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## 1. Leitung

Prof. Dr. med. Emrah Düzel

## 2. Forschungsprofil

- Erforschung höherer Mechanismen kognitiver Hirnfunktionen (Gedächtnis, Motivation, zielgerichtetes Handeln, Entscheidungsfindung, Verhaltenskontrolle)
- Erforschung neurodegenerativer Erkrankungen (Demenz, Parkinson'sche Erkrankung)

## 3. Methodik

Funktionelle Bildgebungverfahren (Kernspintomographie, Magnetenzephalographie und EEG)

## 4. Forschungsprojekte

**Projektleitung:** Prof. Dr. Emrah Düzel  
**Förderer:** Stiftungen - Sonstige - 01.07.2015 - 30.06.2020

### **Energi: Verbundprojekt "Anregung des Hippocampus bei älteren Menschen" (BMBF)**

Physical and cognitive inactivity as well as metabolic dysfunction are important risk factors for cognitive decline in old age. Very little is unknown about how the benefits of physical and cognitive activity are mechanistically linked to the plastic properties and energy metabolism of the brain nor the extent to which such risks are modifiable to improve cognition in aging. This consortium aims to test hypotheses that focus on the interdependence and interaction of neural plasticity and metabolic regulatory pathways such as insulin signaling. We also hypothesize that this interaction is modified by individual risk factors such as cerebral amyloidosis found in over 20% of cognitively normal older individuals. We will focus on a specific brain region, the hippocampus, because its dysfunction impairs spatial navigation and memory precision. These functions will be boosted through plasticity-related interventions and probed using parallel behavioral assays in animals and humans. In a tightly interconnected effort we aim to relate mechanistic insights at the level of synapses and small synaptic networks, epigenetic processes including histone modifications and non-coding RNAs, to human aging, its individual variability and scope for plasticity in the face of metabolic dysregulation. Thus the participating groups aim to narrow the existing gaps in our mechanistic and clinical understanding of the crossroads between genetic, neural and metabolic effects of a physically and cognitively active lifestyle. We want to apply the novel insights provided in this consortium to develop scientifically proven novel commercial products for combined physical and cognitive training interventions in humans. Furthermore, we anticipate that mechanistic insights gained will identify novel pharmacological targets for the interaction between metabolic signaling pathways and neural plasticity.

**Projektleitung:** Dr. Martin Riemer  
**Kooperationen:** Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE) ,  
Magdeburg; Groningen University  
**Förderer:** EU - ESF Sachsen-Anhalt - 01.01.2016 - 31.12.2018

### **AGETIME - Ein neuer Ansatz zu Diagnose und Therapie kognitiver Störungen bei dementiellen Erkrankungen**

Das Projekt AGETIME zielt darauf ab, altersbedingte normale und pathologische Veränderungen in den neuronalen Prozessen zu bestimmen, die der zeitlichen Wahrnehmung zugrundeliegen. Es ist hinreichend belegt, dass zeitliche Orientierungsstörungen häufig mit Defiziten in der räumlichen Orientierung einhergehen, die als wichtige Prädiktoren für die Entstehung von Demenzerkrankungen angesehen werden. Aus diesem Grund kann die Diagnostik zeitlicher und räumlicher Wahrnehmungsverzerrungen uns dabei helfen, Informationen zur Früherkennung von Risikopatienten mit einer beginnenden demenziellen Erkrankung zu erhalten. Zusätzlich können die Ergebnisse als Grundlage für die Entwicklung entsprechender Interventionsstudien dienen.

## 5 Veröffentlichungen

### *Begutachtete Zeitschriftenaufsätze*

**Becke, Andreas; Müller, Patrick; Dordevic, Milos; Leßmann, Volkmar; Brigadski, Tanja; Müller, Notger Germar**

Daily intermittent normobaric hypoxia over 2 weeks reduces BDNF plasma levels in young adults - a randomized controlled feasibility study

Frontiers in physiology - Lausanne: Frontiers Research Foundation, Bd. 9.2018, Art.-Nr. 1337, insges. 7 S.; [Imp.fact.: 3.394]

**Berron, David; Neumann, Katja; Maass, Anne; Schütze, Hartmut; Fliessbach, Klaus; Kiven, Verena; Jessen, Frank; Sauvage, Magdalena; Kumaran, Dharshan; Düzel, Emrah**

Age-related functional changes in domain-specific medial temporal lobe pathways

Neurobiology of aging - Amsterdam [u.a.]: Elsevier Science, Bd. 65.2018, S. 86-97; [Imp.fact.: 4.454]

**Betts, Matthew J.; Ehrenberg, Alexander J.; Hämmerer, Dorothea; Düzel, Emrah**

Commentary - locus coeruleus ablation exacerbates cognitive deficits, neuropathology, and lethality in P301S tau transgenic mice

Frontiers in neuroscience - Lausanne: Frontiers Research Foundation, Bd. 12.2018, Art.-Nr. 401, insges. 3 S.; [Imp.fact.: 3.877]

**Chen, Yi; Cichy, Radoslaw Martin; Stannat, Wilhelm; Haynes, John-Dylan**

Scale-specific analysis of fMRI data on the irregular cortical surface

NeuroImage: a journal of brain function - Orlando, Fla: Academic Press, Bd. 181.2018, S. 370-381; [Imp.fact.: 5.426]

**Franzmeier, Nicolai; Düzel, Emrah; Jessen, Frank; Buerger, Katharina; Levin, Johannes Martin; Düring, Marco; Dichgans, Martin; Haass, Christian; Suárez-Calvet, Marc; Fagan, Anne M.; Paumier, Katrina; Benzinger, Tammie; Masters, Colin L.; Morris, John C.; Pernecky, Robert Georg; Janowitz, Daniel; Catak, Cihan; Wolfsgruber, Steffen; Wagner, Michael; Teipel, Stefan; Kilimann, Ingo; Ramírez, Alfredo; Rossor, Martin; Jucker, Mathias; Chhatwal, Jasmeer; Spottke, Annika; Boecker, Henning; Brosseon, Frederic; Falkai, Peter; Fliessbach, Klaus; Heneka, Michael Thomas; Laske, Christoph; Nestor, Peter; Peters, Oliver Hubertus; Fuentes, Manuel; Menne, Felix; Priller, Josef; Spruth, Eike J.; Franke, Christiana; Schneider, Anja; Kofler, Barbara; Westerteicher, Christine; Speck, Oliver; Wiltfang, Jens; Bartels, Claudia; Araque Caballero, Miguel Angel; Metzger, Coraline Danielle; Bittner, Daniel Markus; Weiner, Michael; Lee, Jae-Hong; Salloway, Stephen P.; Danek, Adrian; Goate, Alison; Schofield, Peter R.; Bateman, Randall J.; Ewers, Michael**

Left frontal hub connectivity delays cognitive impairment in autosomal-dominant and sporadic Alzheimers disease

Brain: a journal of neurology - Oxford: Oxford Univ. Press, Bd. 141.2018, 4, S. 1186-1200; [Imp.fact.: 10.848]

**Freund, Patrick; Thompson, Alan; Curt, Armin; Hupp, Markus; Weiskopf, Nikolaus; Grabher, Patrick; Altmann, Daniel; Friston, Karl; Ashburner, John; Ziegler, Gabriel**

Author response - Progressive neurodegeneration following spinal cord injury : implications for clinical trials

Neurology: official journal of the American Academy of Neurology - Philadelphia, Pa: Wolters Kluwer, Bd. 91.2018, 21, S. 985;

[Imp.fact.: 7.609]

**Graf, Heiko; Wieggers, Maïke; Metzger, Coraline Danielle; Walter, Martin; Abler, Birgit**

Differential noradrenergic modulation of monetary reward and visual erotic stimulus processing

Frontiers in psychiatry - Lausanne: Frontiers Research Foundation, Bd. 9.2018, Art.-Nr. 346, insges. 9 S.;

[Imp.fact.: 2.857]

**Henschke, Julia; Oelschlegel, Anja Maria; Angenstein, Frank; Ohl, Frank W.; Goldschmidt, Jürgen; Kanold, Patrick O.; Budinger, Eike**

Early sensory experience influences the development of multisensory thalamocortical and intracortical connections of primary sensory cortices

Brain structure & function - Berlin: Springer, Bd. 223.2018, 3, S. 1165-1190;

[Imp.fact.: 4.231]

**Henschke, Julia; Ohl, Frank W.; Budinger, Eike**

Crossmodal connections of primary sensory cortices largely vanish during normal aging

Frontiers in aging neuroscience - Lausanne: Frontiers Research Foundation, Vol. 10.2018, Art. 52, insgesamt 14 S.;

[Imp.fact.: 3.582]

**Hämmerer, Dorothea; Callaghan, Martina F.; Hopkins, Alexandra; Kosciessa, Julian; Betts, Matthew; Cardenas-Blanco, Arturo; Kanowski, Martin; Weiskopf, Nikolaus; Dayan, Peter; Dolan, Raymond J.; Düzel, Emrah**

Locus coeruleus integrity in old age is selectively related to memories linked with salient negative events

Proceedings of the National Academy of Sciences of the United States of America - Washington, DC: National Acad. of Sciences, Bd. 115.2018, 9, S. 2228-2233;

[Imp.fact.: 9.504]

**Kievit, Rogier; Brandmaier, Andreas M.; Ziegler, Gabriel; Harmelen, Anne-Laura; Mooij, Susanne M. M.; Moutoussis, Michael; Goodyer, Ian M.; Bullmore, Edward T.; Jones, Peter B.; Fonagy, Peter; Lindenberger, Ulman; Dolan, Raymond J.**

Developmental cognitive neuroscience using latent change score models - a tutorial and applications

Developmental cognitive neuroscience: a journal for cognitive, affective and social developmental neuroscience - Amsterdam [u.a.]: Elsevier, Bd. 33.2018, S. 99-117;

[Imp.fact.: 4.815]

**Knolle, Franziska; Ermakova, Anna O.; Justicia, Azucena; Fletcher, Paul C.; Bunzeck, Nico; Düzel, Emrah; Murray, Graham K.**

Brain responses to different types of salience in antipsychotic naive first episode psychosis - an fMRI study

Translational Psychiatry - London: Nature Publishing Group, Bd. 8.2018, Art.-Nr. 196, insges. 13 S.;

[Imp.fact.: 4.691]

**Koster, Raphael; Chadwick, Martin J.; Chen, Yi; Berron, David; Banino, Andrea; Düzel, Emrah; Hassabis, Demis; Kumaran, Dharshan**

Big-loop recurrence within the hippocampal system supports integration of information across episodes

Neuron - [Cambridge, Mass.]: Cell Press, Bd. 99.2018, 6, Seite 1342-1354.e6;

[Imp.fact.: 14.318]

**Lim, Lynette; Pakan, Janelle M. P.; Selten, Martijn M.; Marques-Smith, André; Llorca, Alfredo; Bae, Sung Eun; Rochefort, Nathalie; Marín, Oscar**

Optimization of interneuron function by direct coupling of cell migration and axonal targeting

Nature neuroscience - New York, NY: Nature America, Bd. 21.2018, 7, S. 920-931;

[Imp.fact.: 19.912]

**Long, Rebecca M.; Pakan, Janelle M.P.; Graham, David J.; Hurd, Peter L.; Gutierrez-Ibañez, Cristian; Wylie, Douglas R. W.**

Modulation of complex spike activity differs between zebrin-positive and -negative Purkinje cells in the pigeon cerebellum

Journal of neurophysiology - Bethesda, Md: Soc, Bd. 120.2018, 1, S. 250-262;

[Imp.fact.: 2.502]

**Pakan, Janelle M. P.; Currie, Stephen P.; Fischer, Lukas; Rochefort, Nathalie**

The impact of visual cues, reward, and motor feedback on the representation of behaviorally relevant spatial locations in primary visual cortex

Cell reports - Maryland Heights, MO: Cell Press, Bd. 24.2018, 10, S. 2521-2528;

[Imp.fact.: 8.032]

**Pakan, Janelle M.P.; Francioni, Valerio; Rochefort, Nathalie**

Action and learning shape the activity of neuronal circuits in the visual cortex

Current opinion in neurobiology: reviews of all advances : evaluation of key references : comprehensive listing of papers - Philadelphia, Pa: Current Biology, Bd. 52.2018, S. 88-97;

[Imp.fact.: 6.541]

**Spallazzi, M.; Dobisch, L.; Becke, A.; Berron, D.; Stucht, Daniel; Oeltze-Jafra, Steffen; Caffarra, P.; Speck, Oliver; Düzel, Emrah**

Hippocampal vascularization patterns - a high-resolution 7 Tesla time-of-flight magnetic resonance angiography study

NeuroImage: Clinical: a journal of diseases affecting the nervous system : open access journal - [Amsterdam u.a.]: Elsevier, 2018;

[First online]

[Imp.fact.: 3.869]

**Teipel, Stefan; Metzger, Coraline Danielle; Brosseron, Frederic; Buerger, Katharina; Brüggem, Katharina; Catak, Cihan; Diesing, Dominik; Dobisch, Laura; Fliebach, Klaus; Franke, Christiana; Heneka, Michael Thomas; Kilimann, Ingo; Kofler, Barbara; Menne, Felix; Peters, Oliver Hubertus; Polcher, Alexandra; Priller, Josef; Schneider, Anja; Spottke, Annika; Spruth, Eike J.; Thelen, Manuela; Thyrian, René J.; Wagner, Michael; Düzel, Emrah; Jessen, Frank; Dyrba, Martin**

Multicenter resting state functional connectivity in prodromal and dementia stages of Alzheimers disease

Journal of Alzheimer's disease - Amsterdam: IOS Press, Bd. 64.2018, 3, S. 801-813;

[Imp.fact.: 3.476]

**Turtaev, Sergey; Leite, Ivo T.; Altwegg-Boussac, Tristan; Pakan, Janelle M. P.; Rochefort, Nathalie; imár, Tomá**

High-fidelity multimode fibre-based endoscopy for deep brain in vivo imaging. Letter

Light: Science & Applications - London: Nature Publishing Group, Bd. 7.2018, Art.-Nr. 92, insges. 8 S.;

[Imp.fact.: 13.625]

**Ziegler, Gabriel; Grabher, Patrick; Thompson, Alan; Altmann, Daniel; Hupp, Markus; Ashburner, John; Friston, Karl; Weiskopf, Nikolaus; Curt, Armin; Freund, Patrick**

Progressive neurodegeneration following spinal cord injury - implications for clinical trials

Neurology: official journal of the American Academy of Neurology - Philadelphia, Pa: Wolters Kluwer, Bd. 90.2018, 14, Seite e1257-e1266;

[Imp.fact.: 7.609]