

# NAME: Claus Normann (\*30.06.1967)

POSITION TITLE: Professor Dr.

## EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Albert-Ludwigs-University, Freiburg Royal Free Hospital School of Medicine, London College of Physicians and Surgeons, New York	M.D.	1989	1996	Medicine
Dept. of Psychiatry and Psychotherapy, University of Freiburg		1996	1997	Internship Dept. of Psychiatry
Institute of Physiology, University of Freiburg (lab Prof. Jonas)		1997	1998	Postdoc
Dept. of Neurosurgery and Dept. of Neurology, Dept. of Psychiatry, University of Freiburg		1998	2001	Resident
Dept. of Psychiatry and Psychotherapy, University of Freiburg		2002	2010	Senior physician
Dept. of Psychiatry and Psychotherapy, University of Freiburg		2010	present	Associate professor, Managing Director Section Head Experimental Psychopharmacotherapy

## A. Expertise/Research Aims

have 1 successfully combined expertise in clinical psychiatry and psychotherapy. neuropsychopharmacology and basic science to develop a translational approach in order to understand the pathophysiology of affective disorders and to develop novel treatment strategies for major depression. Our research group was among the first to develop and to support the neuroplasticity hypothesis of depression. Starting from a basic science approach with a focus on long-term synaptic depression (LTD), we soon discovered a facilitation of LTD and an inhibition of long-term synaptic potentiation (LTP) in different animal models of depression and early stress, which were effectively restored by different classes of antidepressants. We have characterized novel targets for antidepressant action, including Ca<sup>2+</sup> channels, TrkB receptor, mGluR, NMDA receptor subunits. In a translational approach, we have developed and examined methods to assess correlates of synaptic plasticity in healthy humans and depressed patients; including the characterization of therapeutic mechanisms. A neuroplasticity approach to explain and to treat depression highlights the importance of interactions between disorder, treatment and environment. Moreover, it suggests effective ways to augment psychotherapeutical approaches by medication and brain stimulation; hereby providing a science based reconciliation between the schools of biologically and psychotherapeutically oriented psychiatrists. In my daily work, I combine clinical psychiatry and psychotherapy with advanced basic science; thus allowing real bench-to-bedside translation. My final aim is to contribute to an integrative, science-based and effective treatment of major depression.

## **B.** Positions, Scientific Appointments and Honors

## **Positions**

Current position: Managing Medical Director, Dept. of Psychiatry, University of Freiburg Head of Section Psychopharmacotherapy Previous positions: see above

## **Scientific Appointments and Honors**

2010	Associate professor
2002	ECNP/ACNP exchange award
2002	ECNP travel award
1999	Research Award of the AGNP (German Association for Neuropsychopharmacology)
1998	Glaxo Welcome Research Award for Bipolar Disorder
1990-1997	Fellowship of the Studienstiftung des Deutschen Volkes

## **C.** Contributions to Science

## Research focus

#### 1. Basic mechanisms of synaptic plasticity

Mechanism of associative LTD, role of astrocytes in LTP, calcium influx pathways, modulation of different forms of synaptic plasticity in the hippocampus.

#### 2. Synaptic plasticity in animal models of depression

Behavioral assessment and synaptic plasticity in animal models of depression and early stress.

## 3. Modulation of synaptic plasticity by antidepressants

Multidimensional approach assessing the modulation of synaptic plasticity by antidepressants and rapid-acting antidepressants, behavioural methods and electrophysiological recordings. Identification of novel targets for antidepressant action (TrkB receptor, mGluR, NMDAR subunits)

#### 4. Correlates of synaptic plasticity in humans

Translational assessment of brain plasticity in healthy controls and depressed patients by visually evoked potentials, transcranial magnetic stimulation, imaging and behavioral methods.

#### 5. Augmentation of psychotherapy and effect of environmental factors on mood disorders

D-Cycloserine in depression, social cognition and influence of positive and negative external stimuli in states of altered plasticity. Role of oxytocin in mood disorders.

#### 6. Treatment of chronic and therapy-resistant depression

Extensive research on CBASP for chronic depression, implementation of in-patient treatment programs for chronic depression and TRD, pharmacotherapy for TRD and bipolar disorder. Brain stimulation: clinical and preclinical ECT, tDCS and rTMS research

#### 7. Health economics

Funding of psychiatric care, AI-based prediction of treatment outcomes and pharmacological trajectories

#### **Funding**

- Reviewed funding by DFG (German Research foundation), BMBF (German Ministry for Health and Research), Neurex (Regional German/French/Swiss Research foundation), University of Freiburg
- Industry funds as investigator in > 20 clinical trials

## Other scientific acitivities

- Ad hoc reviewer for numerous scientific journals and DFG, SNF (German and Swiss Research Foundations)
- Supervision of >20 graduated MD students, 4 graduated PhD students
- Investigator in numerous phase II-IV clinical studies (>10 phase II, >20 phase III, >5 phase IV or postmarketing). Continuous ICH/GCP-Training received since 1996. Experimental and clinical IITs.
- Member of DMCs and Advisory boards in commercial drug development
- Regular organization of symposia at national and international scientific conferences

## Peer-reviewed publications

>130 original publications, 4280 citations, h-index 34 (Google Scholar)

Full list of publications:

https://pubmed.ncbi.nlm.nih.gov/?size=50&term=Normann+C&cauthor\_id=33606976

#### Selected peer-reviewed publications

Casarotto PC, Girych M, Fred SM, Kovaleva V, Moliner R, Enkavi G, Biojone C, Cannarozzo C, Sahu MP, Kaurinkoski K, Brunello CA, Steinzeig A, Winkel F, Patil S, Vestring S, Serchov T, Diniz CRAF, Laukkanen L, Cardon I, Antila H, Rog T, Piepponen TP, Bramham CR, Normann C, Lauri SE, Saarma M, Vattulainen I, Castrén E: Antidepressant drugs act by directly binding to TRKB neurotrophin receptors. *Cell*. 184, 1299-1313.e19 (2021).

Frase L, Mertens L, Krahl A, Bhatia K, Feige B, Heinrich SP, Vestring S, Nissen C, Domschke K, Bach M, Normann C: Transcranial direct current stimulation induces long-term potentiation-like plasticity in the human visual cortex. *Transl. Psychiatry.* 11(1):17 (2021)

Kuhn M, Maier JG, Wolf E, Mainberger F, Feige B, Maywald S, Bredl A, Michel M, Sendelbach N, Normann C, Klöppel S, Eckert A, Riemann D, Nissen C: Indices of cortical plasticity after therapeutic sleep deprivation in patients with major depression. *J. Affective Dis.* 277:425-435 (2020)

Holz A, Mülsch F, Schwarz MK, Hollmann M, Döbrössy MD, Coenen VA, Bartos M, Normann C, Biber K, van Calker D, Serchov T: Enhanced mGlu5 Signaling in Excitatory Neurons Promotes Rapid Antidepressant Effects via AMPA Receptor Activation. *Neuron* 104(2):338-352.e7 (2019).

Mauler M, Herr N, Schoenichen C, Witsch T, Marchini T, Härdtner C, Koentges C, Kienle K, Ollivier V, Schell M, Dorner L, Wippel C, Stallmann D, Normann C, Bugger H, Walther P, Wolf D, Ahrens I, Lämmermann T, Ho-Tin-Noe B, Ley K, Bode C, Hilgendorf I, Duerschmied D: Platelet serotonin aggravates myocardial ischemia/reperfusion injury via neutrophil degranulation. *Circulation.* 139(7):918-931 (2019)

Normann C, Frase S, Haug V, von Wolff G, Clark K, Münzer P, Dorner A, Scholliers J, Horn H, Vo Van T, Seifert G, Serchov T, Biber K, Nissen C, Klugbauer C, Bischofberger J: Antidepressants Rescue Stress-Induced Disruption of Synaptic Plasticity via Serotonin Transporter-Independent Inhibition of L-Type Calcium Channels. *Biol. Psychiatry*. 84, 55–64 (2018)

Brakemeier EL, Dobias J, Hertel J, Bohus M, Limberger MF, Schramm E, Radtke M, Frank P, Padberg F, Sabaß L, Jobst A, Jacob G, Struck N, Zimmermann J, Normann C: Childhood maltreatment in women with borderline personality disorder, chronic depression, episodic depression, and in healthy controls. *Psychother. Psychosom*. 87:49-51 (2018)

Wolff J, Auber G, Schober T, Schwär F, Hoffmann K, Metzger M, Heinzmann A, Krüger M, Normann C, Südkamp N, Reinhard T, Berger M: Work-Time Distribution of Physicians at a German University Hospital. *Dtsch. Arztebl. Int.* 114(42): 705-11 (2017)

Kuhn M, Wolf E, Maier JG, Mainberger F, Feige B, Schmid H, Bürklin J, Maywald S, Mall V, Jung NH, Reis J, Spiegelhalder K, Klöppel S, Sterr A, Eckert A, Riemann D, Normann C, Nissen C: Sleep recalibrates homeostatic and associative synaptic plasticity in the human cortex. *Nature Commun.* 7:12455 (2016)

Schmaal L, Veltman DJ, (...) Normann C, (..) Hibar DP: Subcortical brain alterations in major depressive disorder: findings from the ENIGMA Major Depressive Disorder working group. *Mol. Psychiatry*. 21(6):806-12 (2016)

Kuhn M, Mainberger F, Feige B, Maier JG, Mall V, Jung NH, Reis J, Klöppel S, Normann C, Nissen C: State-dependent partial occlusion of cortical LTP-like plasticity in major depression. *Neuropsychopharmacology*. 41:1521-9 (2016)

Domes G, Spenthof I, Radtke M, Isaksson A, Normann C, Heinrichs M: Autistic traits and empathy in chronic vs. episodic depression. *J. Affective Dis.* 195:144-7 (2016)

Serchov T, Clement HW, Schwarz MK, Iasevoli F, Tosh TK, Idzko M, Jacobson KA, de Bartolomeis A, **Normann C**, Biber K, van Calker D: Increased Signaling via Adenosine A1 Receptors, Sleep Deprivation, Imipramine, and Ketamine Inhibit Depressive-like Behavior via Induction of Homer1a. *Neuron*. 87, 549–562 (2015).

Brakemeier EL, Radtke M, Engel V, Zimmermann J, Tuschen-Caffier B, Hautzinger M, Schramm E, Berger M, Normann C: Overcoming treatment resistance in chronic depression: a pilot study of outcome and feasibility of the Cognitive Behavioral Analysis System of Psychotherapy as an inpatient treatment program. **Psychother. Psychosom.** 84:51-56 (2015)

Brakemeier EL, Engel V, Schramm E, Zobel I, Hauzinger M, Berger M, Normann C: Effectiveness of cognitive behavioral analysis system of psychotherapy for chronically depressed inpatients: a pilot study. *Psychother. Psychosom.* 80:191-194 (2011)

Niehusmann P, Seifert G, Clark K, Atas HC, Herpfer I, Fiebich B, Bischofberger J, Normann C: Coincidence detection and stress modulation of spike time-dependent long-term depression in the hippocampus. *J. Neurosci. Off. J. Soc. Neurosci.* 30, 6225–6235 (2010)

Nissen C, Holz J, Blechert J, Feige B, Riemann D, Voderholzer U, Normann C: Learning as a model for neural plasticity in major depression. *Biol. Psychiatry*. 68, 544–552 (2010)

Normann C, Schmitz D, Fürmaier A, Döing C, Bach M: Long-term plasticity of visually evoked potentials in humans is altered in major depression. *Biol. Psychiatry*. 62, 373–380 (2007)

Holderbach R, Clark K, Moreau JL, Bischofberger J, Normann C: Enhanced Long-Term Synaptic Depression in an Animal Model of Depression. *Biol. Psychiatry*. 62, 92–100 (2007)

Normann C, Peckys D, Schulze CH, Walden J, Jonas P, Bischofberger J: Associative long-term depression in the hippocampus is dependent on postsynaptic N-type Ca2+ channels. *J. Neurosci. Off. J. Soc. Neurosci.* 20, 8290–8297 (2000).