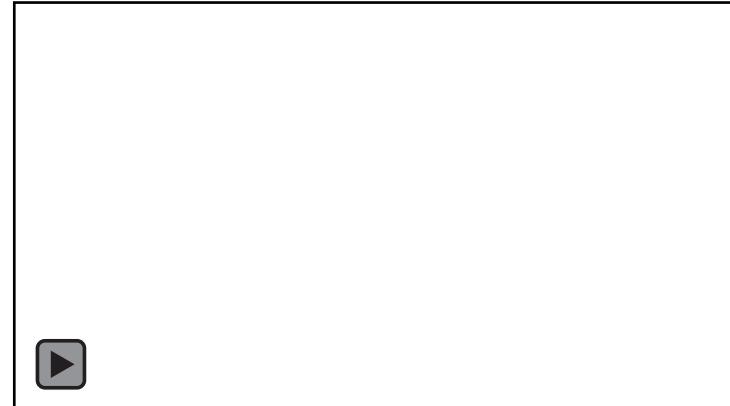


EEG und Psychiatrie: Von Hirnwellen und künstlicher Intelligenz

Sebastian Olbrich
PUK Zürich
23.10.2024

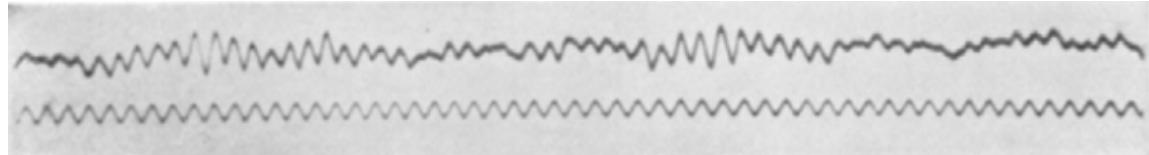


Inhalt

- Etwas Geschichte
- Pharmako-EEG
- EEG, Schlaf und die Vigilanz
- EEG in der Psychiatrie
- EEG und Prädiktion
- Etwas Zukunft

EEG und Hans Berger

- Erste Ableitungen einer „EEG“ am Menschen 1924
- „Berger-Reaktion“ mit Alpha Wellen
- Erste vermutete Korrelation zwischen Alpha Wellen und affektiven Symptomen
- Bereits 1941 konkrete Hypothesen für Korrelationen EEG und Depressionen



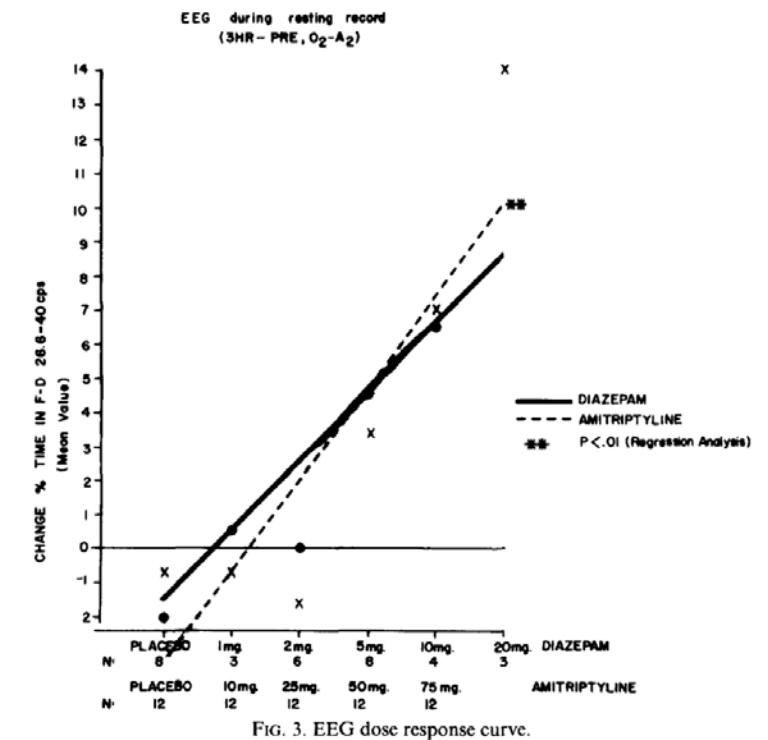
6. EEG Findings in Depression

Lemere (1941) was the first to report that manic-depressive patients tend to have a large amplitude, strongly dominant alpha rhythm. Davis (1941, 1942) confirmed Lemere's finding showing that manic-depressed individuals have more alpha-type EEGs compared with schizophrenics, and that predominantly depressed patients have more alpha-type and mixed alpha and slow activity EEGs; whereas predominantly manic patients have more mixed alpha and fast activity EEGs. Greenblatt *et al.* (1944) further discriminated the manic patients, based on the large amount of fast activity found in his manic group. Hurst *et al.*, 1954, also found that manic patients have higher alpha frequencies than the depressed patients, but they did not show a shift in alpha frequency accompanying a phase change, whenever a manic-depressive patient shifted from mania to depression or from depression to mania. On the contrary, some others observed an increase in alpha frequency during manic episodes of two manic-depressive patients.

Through visual analysis of the EEGs of 73 schizophrenics and 100 endogenous depressed patients, it was shown that there is a significant relationship between alpha dominance and depression, and beta dominance and schizophrenia (Itil, 1964). Brezinova *et al.*, 1966, reported a greater abundance of alpha rhythm in patients with endogenous depression. Volavka *et al.*, 1967, compared the EEGs of five depressed patients during the episodes of depression and during remission. The patients showed significantly more alpha and beta activities during the depressive phase.

Das Pharmako-EEG

- Bereits 1937 postulierte H. Berger, dass einen engen Zusammenhang zwischen Verhaltensänderung und EEG-Mustern
- 1957 berichtete Max Fink von engen Zusammenhängen zwischen Besserung nach EKT und EEG Veränderungen
- 1954 berichteten Itil und Bente von EEG Veränderungen unter Chlorpromazin



Das Pharmako-EEG

- 1964 berichtet Itil davon, dass antidepressive Medikamente eine Verminderung der EEG Alpha Aktivität bewirken

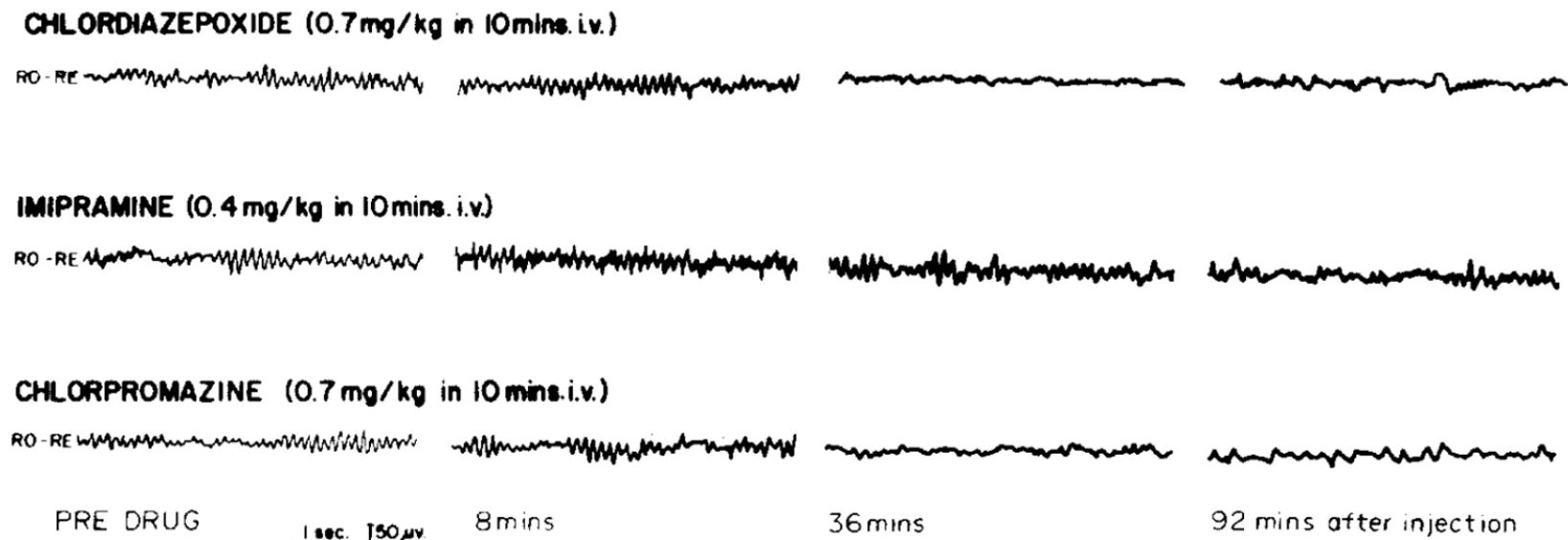


FIG. 5. EEG classification of psychotropic drugs.

Das „Key-Lock“ Prinzip

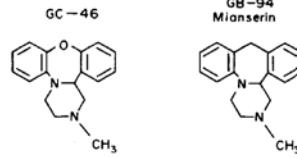


FIG. 17. Chemical structures of GB-94 (Mianserin) and GC-46.

- Entdeckung der antidepressiven Wirkung des Mianserin durch Itil aufgrund des EEG-Profils 1972

Progress in Neurobiology, Vol. 20, pp. 185 to 249 1983
Printed in Great Britain. All rights reserved

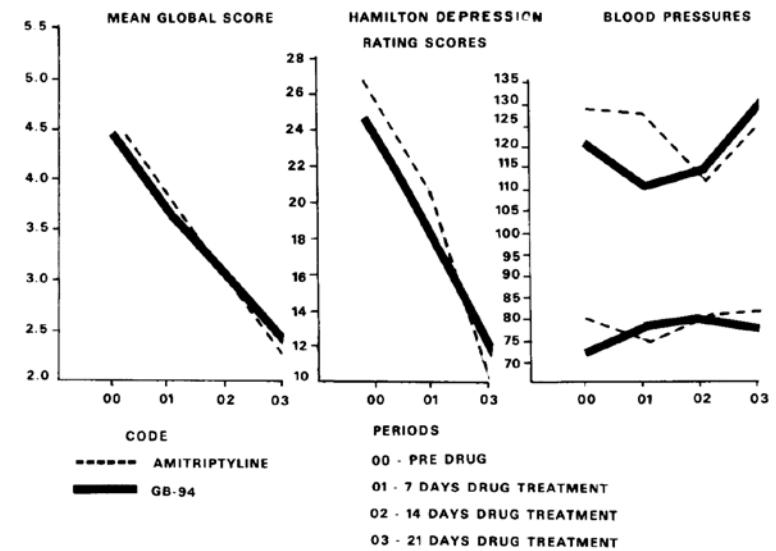
0301-0082/83/\$0.00 + .50
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THE DISCOVERY OF ANTIDEPRESSANT DRUGS BY COMPUTER-ANALYZED HUMAN CEREBRAL BIO-ELECTRICAL POTENTIALS (CEEG)

TURAN M. ITIL

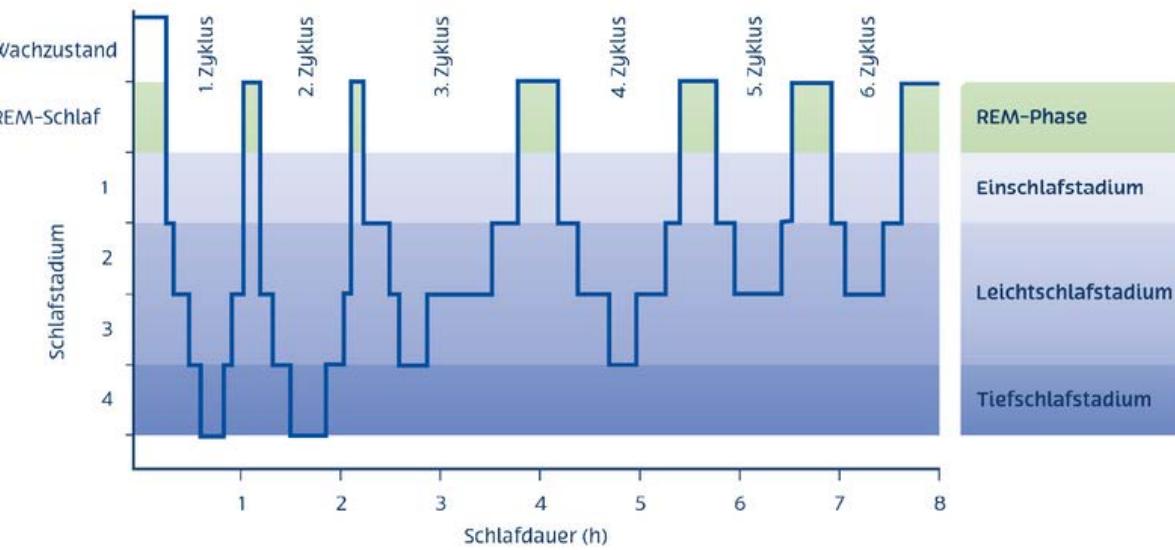
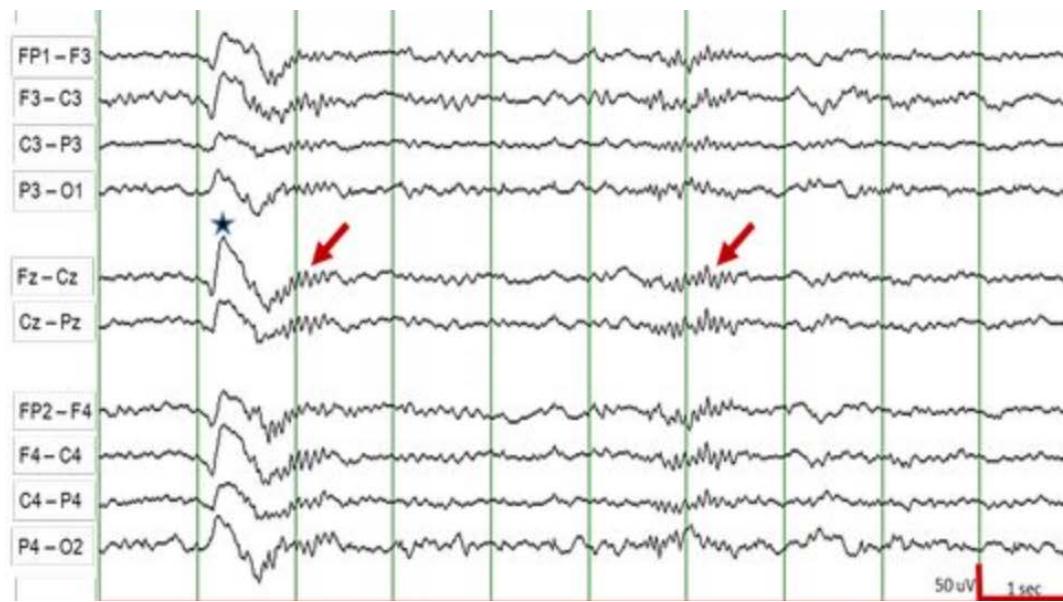
Division of Biological Psychiatry, Department of Psychiatry,
New York Medical College, Valhalla, NY 10595, U.S.A.
and HZI Research Center, Tarrytown, NY, U.S.A.

(Received 14 September 1982)



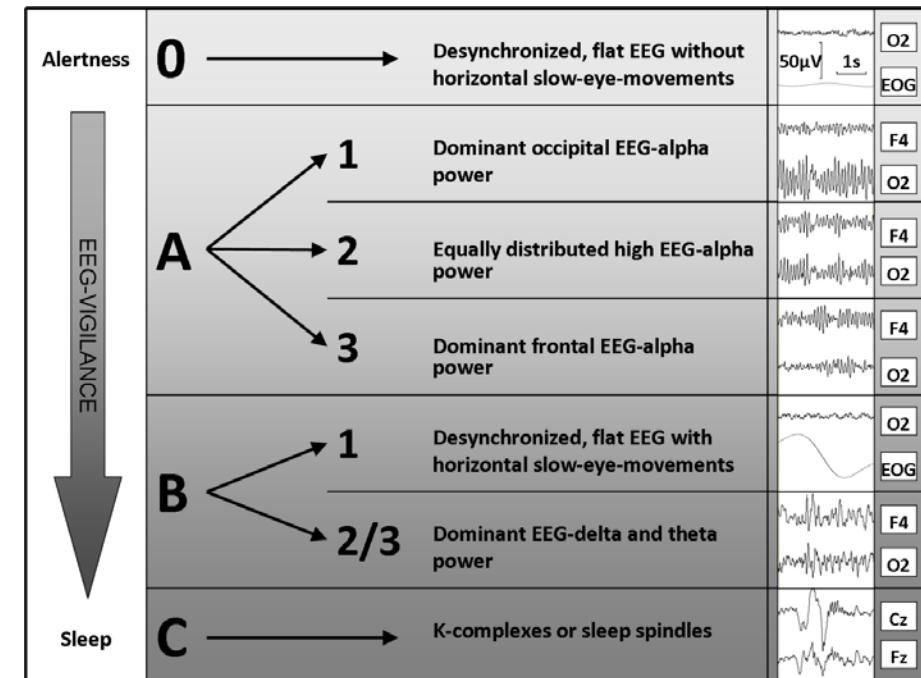
EEG und Alfred Lee Loomis

- Erstbeschreibung von K-Komplexen und Schlafspindeln 1937
- Anfänge der Polysomnographie

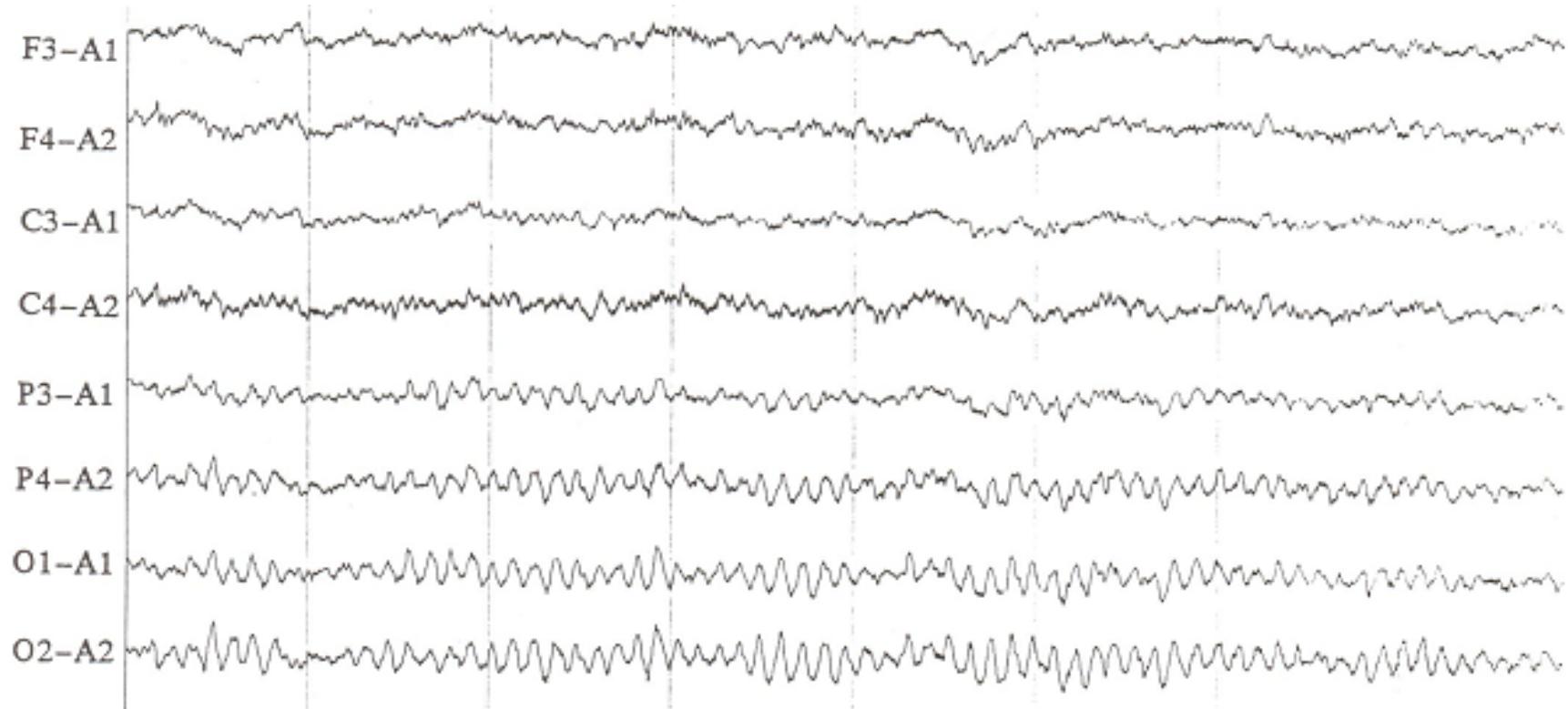


Das EEG Vigilanzmodell

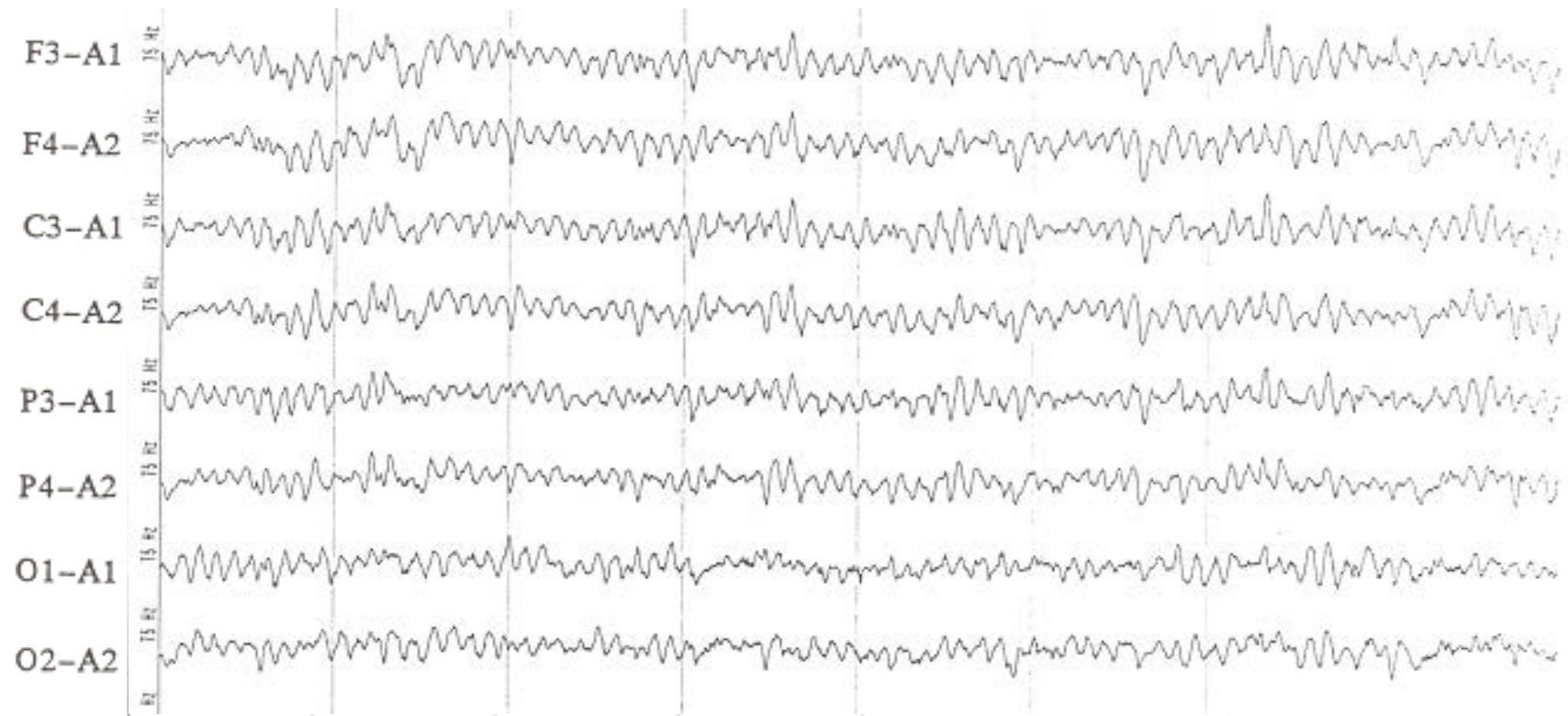
- Die Vigilanz als globaler Hirn-Funktionszustand: Reaktion auf Stimuli (Head 1923)
- Operationalisierung der EEG-Vigilanz (Loomis 1937, Bente, Roth 1967)
- Psychiatrische Syndrome und EEG-Vigilanz (Ulrich 1988)
- Das EEG-Vigilanzmodell bei psychiatrischen Erkrankungen (Hegerl 2014)



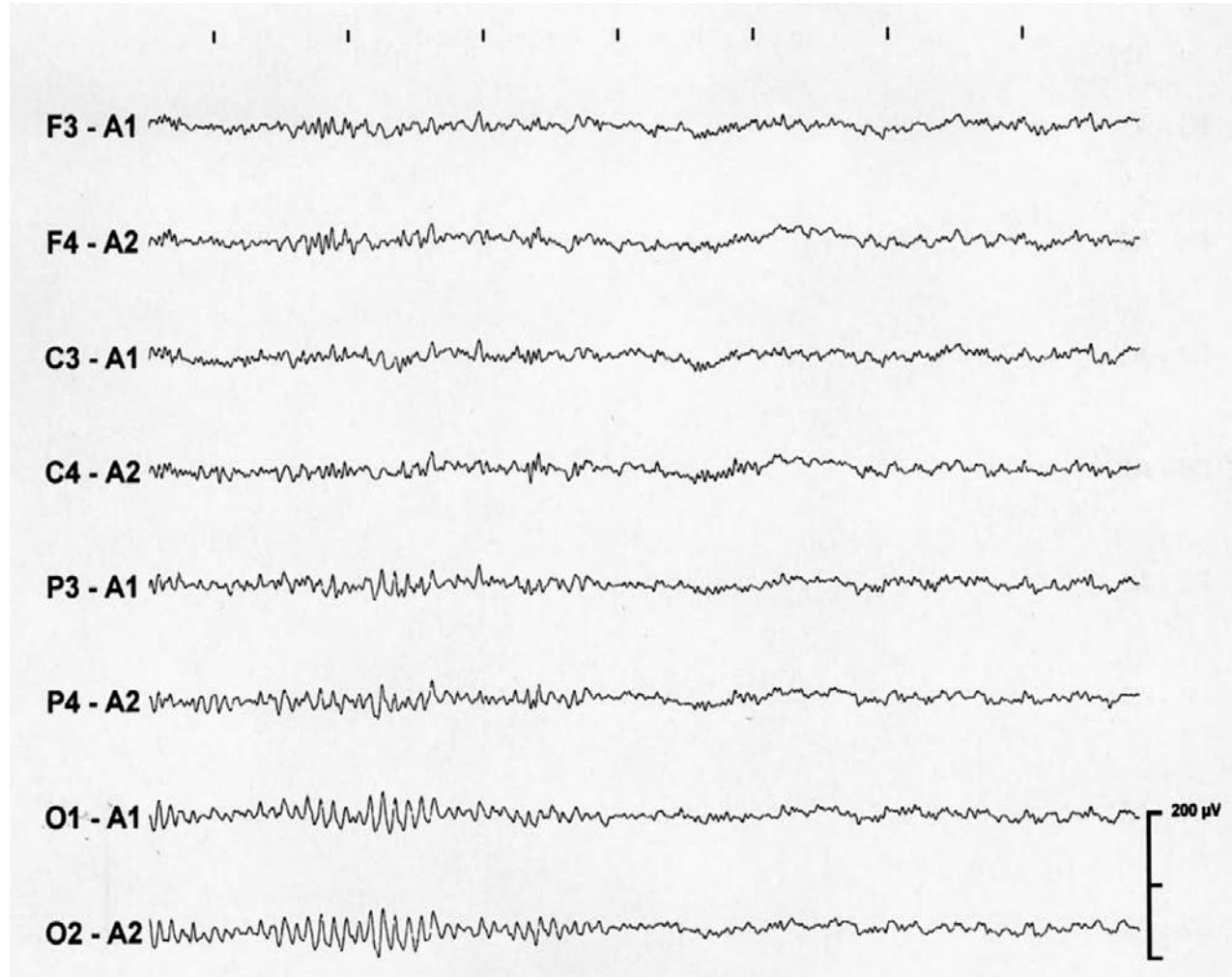
Vigilance stage A1



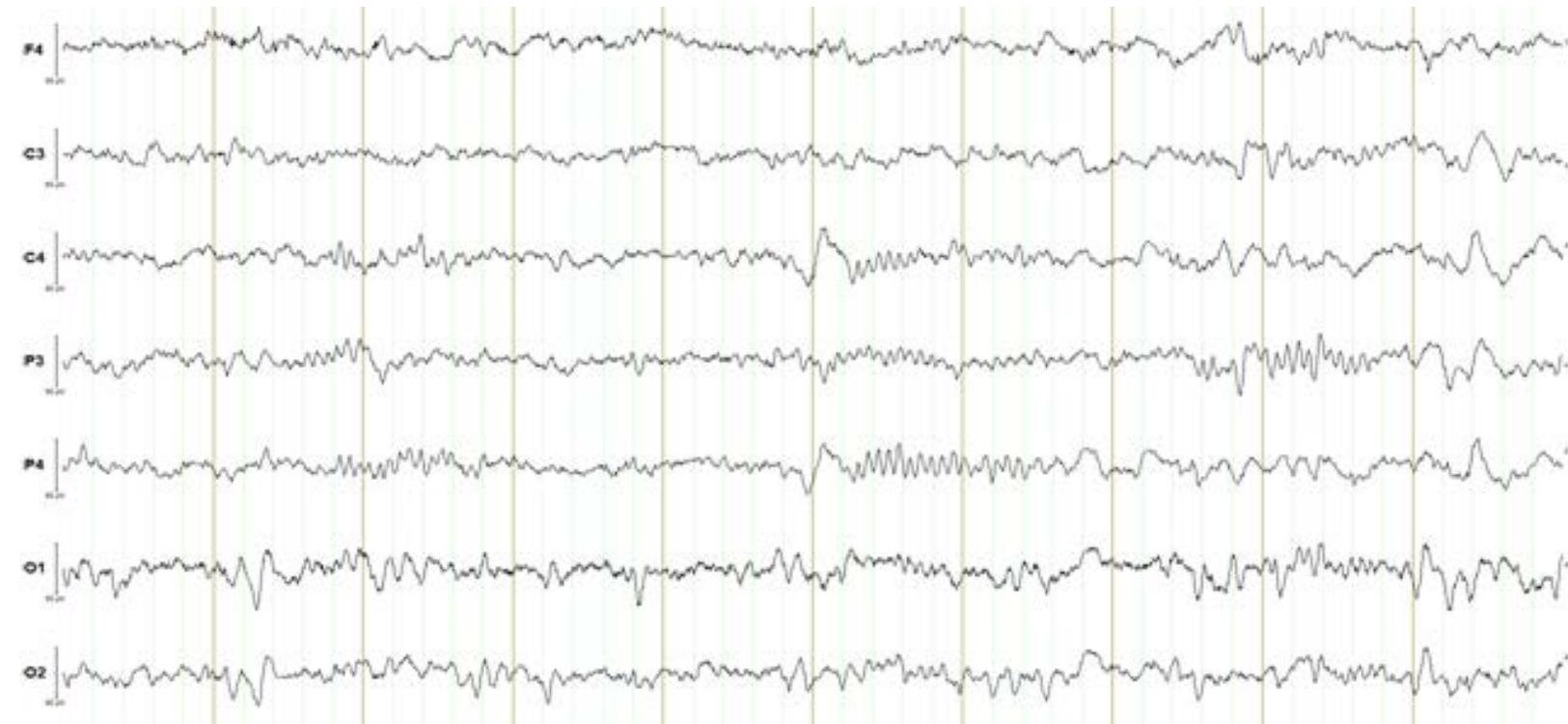
Vigilance stage A2/3



Vigilance stage A/B1

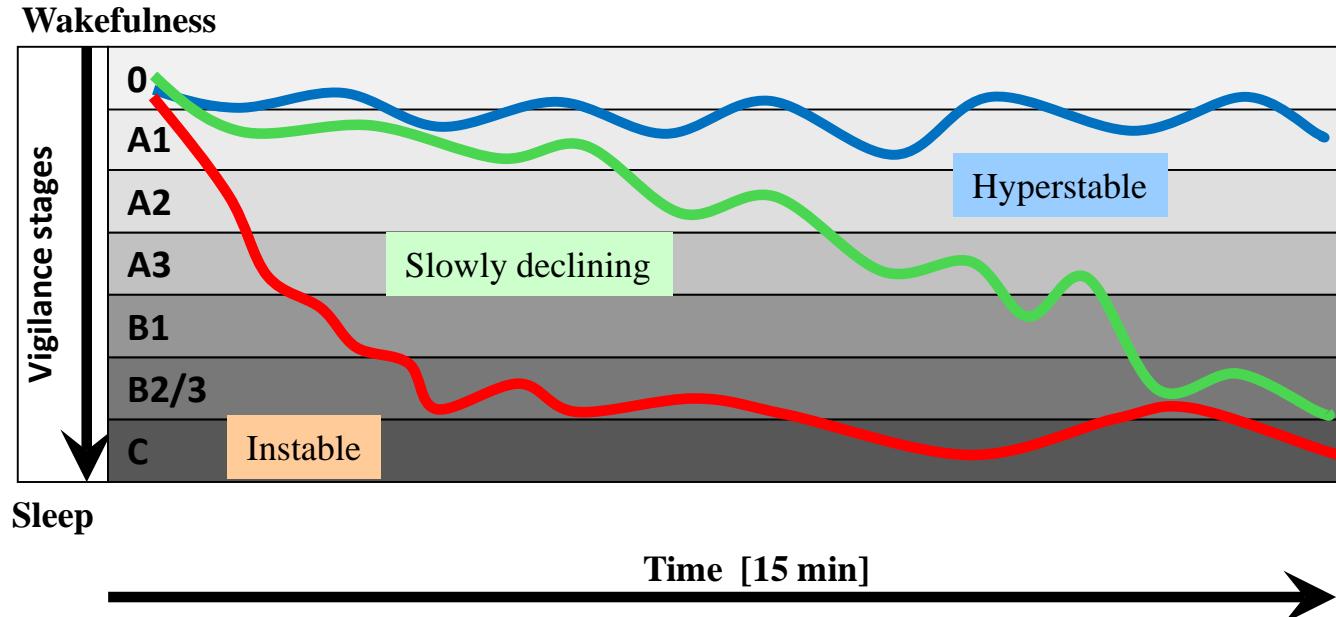


Vigilance stage C

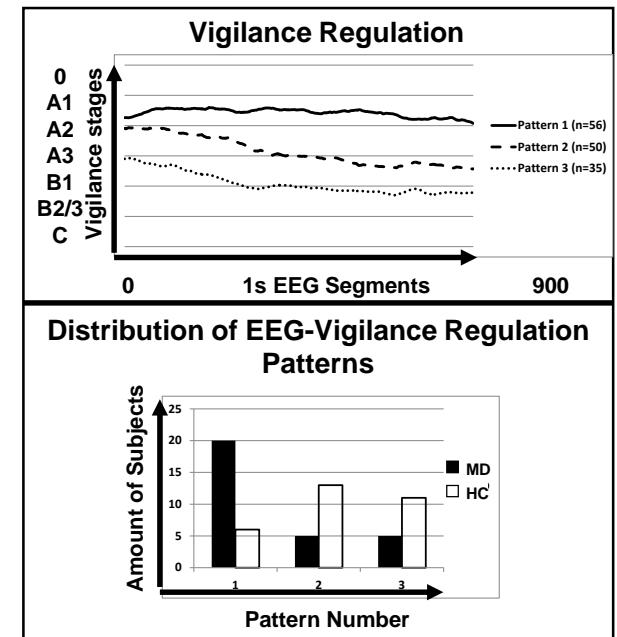


EEG-Vigilanz-Framework (Hensch&Hegerl 2014)

- Affektive Symptome als Kompensation der Vigilanzregulation

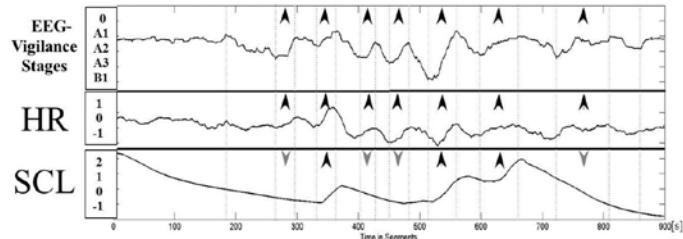
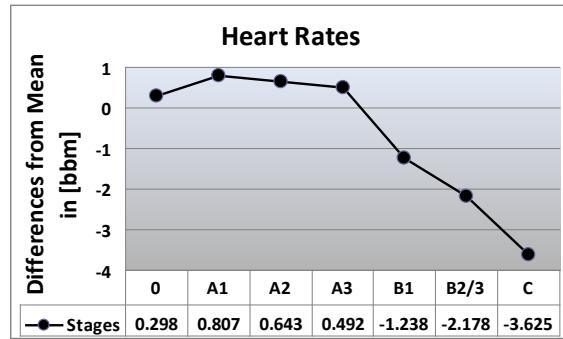


Olbrich et al. 2012



- Hyperstabile Vigilanzregulation bei Depression
- Instabile Regulation bei manischen Symptomen, ADHS und emotional instabiler PKS

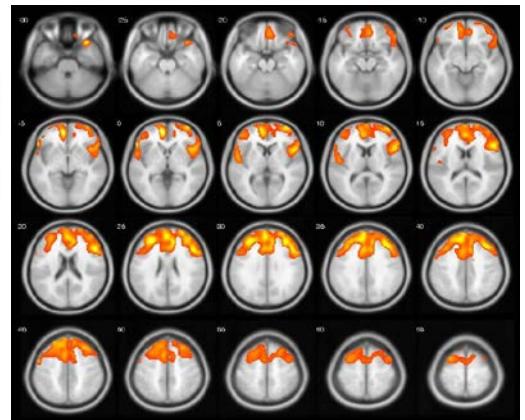
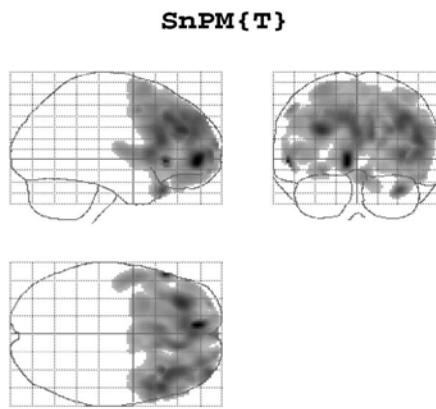
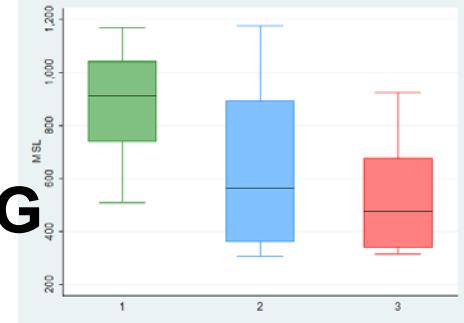
Validierung EEG - Vigilanz



Olbrich et al. 2011 Journal of Psychophysiology

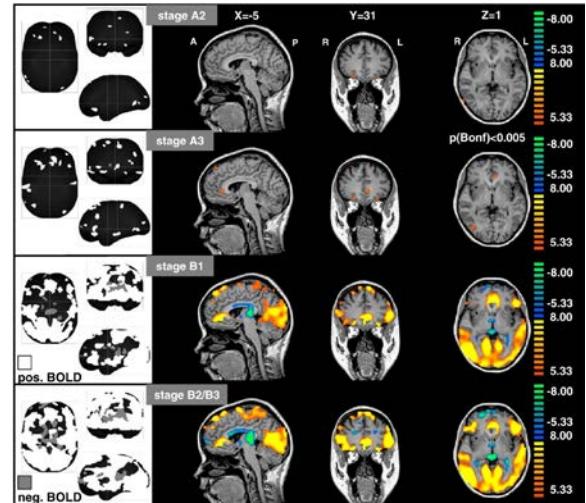
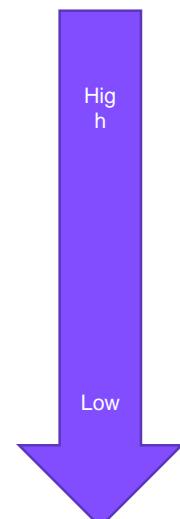
ECG&EEG

Stable Cluster 910s (n= 13)	Unstable Cluster 540s (n= 12)
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Günther et al. 2010
Neuroimage

PET&EEG



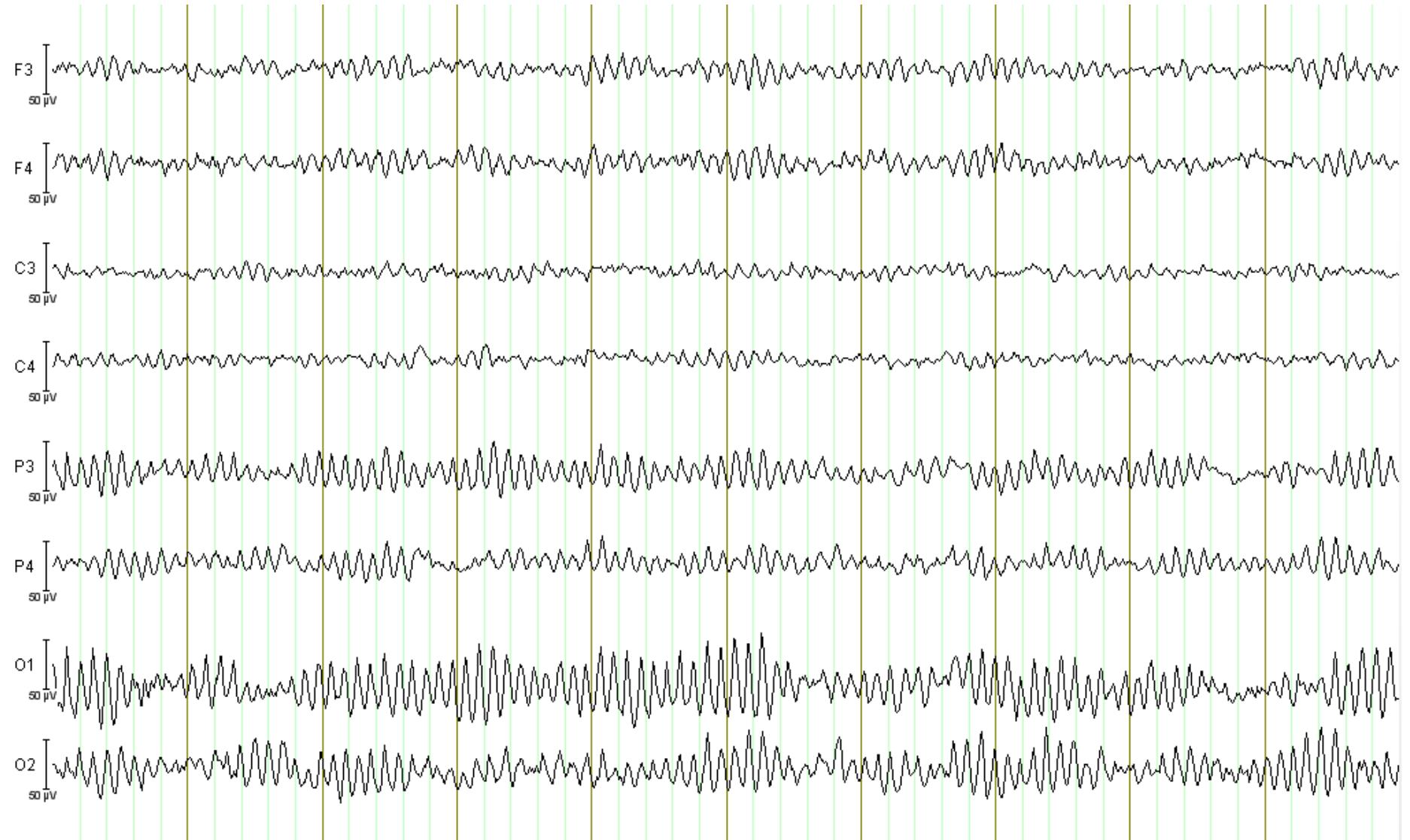
fMRI&EEG

Olbrich et al. 2009 Neuroimage

Wann EEG in der Psychiatrie?

- Medikation Baseline: Lithium und Clozapin
- Differentialdiagnostik Panikattacken vs. Anfälle vs. Dissoziation
- Differentialdiagnostik Depression (Pseudodemenz) versus Demenz
- Klinik für Anfälle (Alkoholentzug, Status epilepticus, etc)
- Ausschluss organischer Ursachen der Symptome, z.B. Erstmanifestation Psychose
- Delirante Zustandsbilder
- Ausschluss organischer Ursachen bei atypischer Präsentation oder Therapieresistenz
- Im Rahmen der individualisierten Medizin: EEG Biomarker zur Identifikation der besten Behandlungsschemata

Demenz vs. Pseudodemenz





I. EEG in der Psychiatrie: Believers

Conventional and Quantitative Electroencephalography in Psychiatry

John R. Hughes, M.D., Ph.D.
E. Roy John, Ph.D.

J Neuropsychiatry Clin Neurosci 11:2, Spring 1999

SUMMARY

Both conventional EEG and QEEG studies provide valuable information to the psychiatrist regarding diagnosis and treatment responsiveness.

Conventional EEG is most useful in the following:

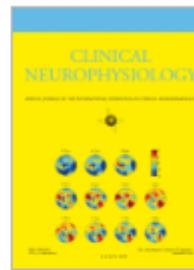
1. Identifying paroxysmal activity.
2. Identifying gross alterations in the background frequencies of the EEG.
3. Identifying intermixed slow activity that may be related to delirium or dementia.
4. Evaluating sleep disorders.

Conventional EEG assessments should be included in the diagnostic workup for the following:

1. An acute confusional state.
2. The first presentation of schizophrenia.
3. A major mood disorder or mania.
4. Refractory behavioral problems such as obsessions, violence, or panic.



Clinical Neurophysiology
Volume 127, Issue 1, January 2016, Pages 17-18



Editorial

Future of clinical EEG in psychiatric disorders: Shifting the focus from diagnosis to the choice of optimal treatment

Sebastian Olbrich  , Jan Conradi

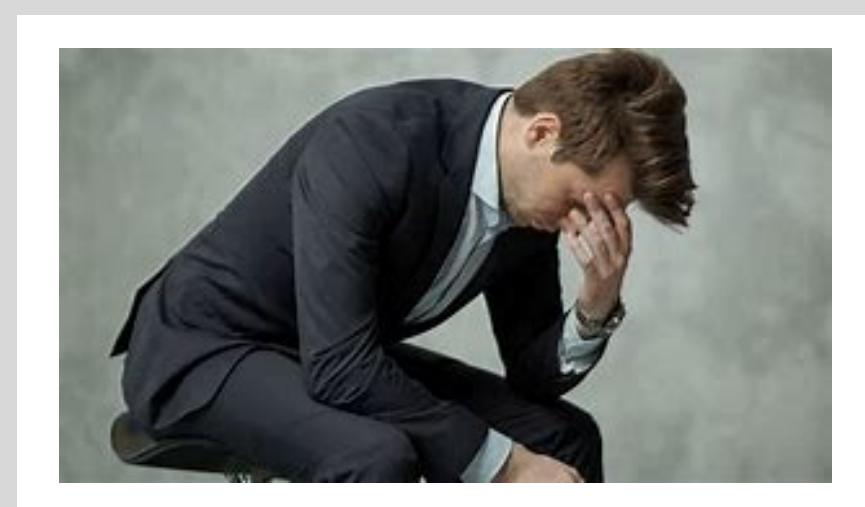
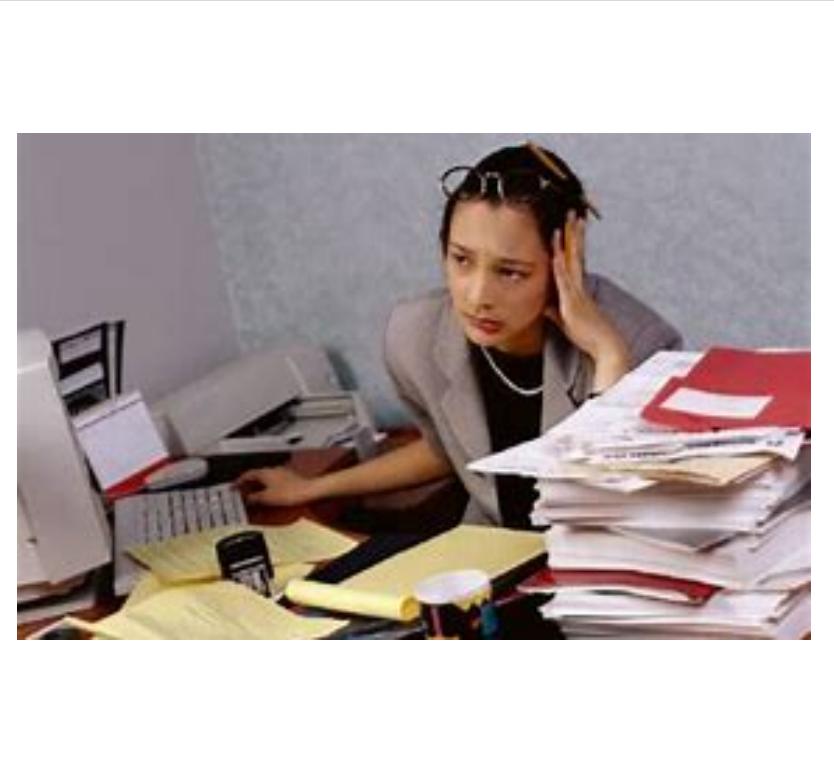
Jahr 2024

- Objektive
Untersuchungen führen
zu den richtigen
Entscheidungen in der
somaticischen Medizin

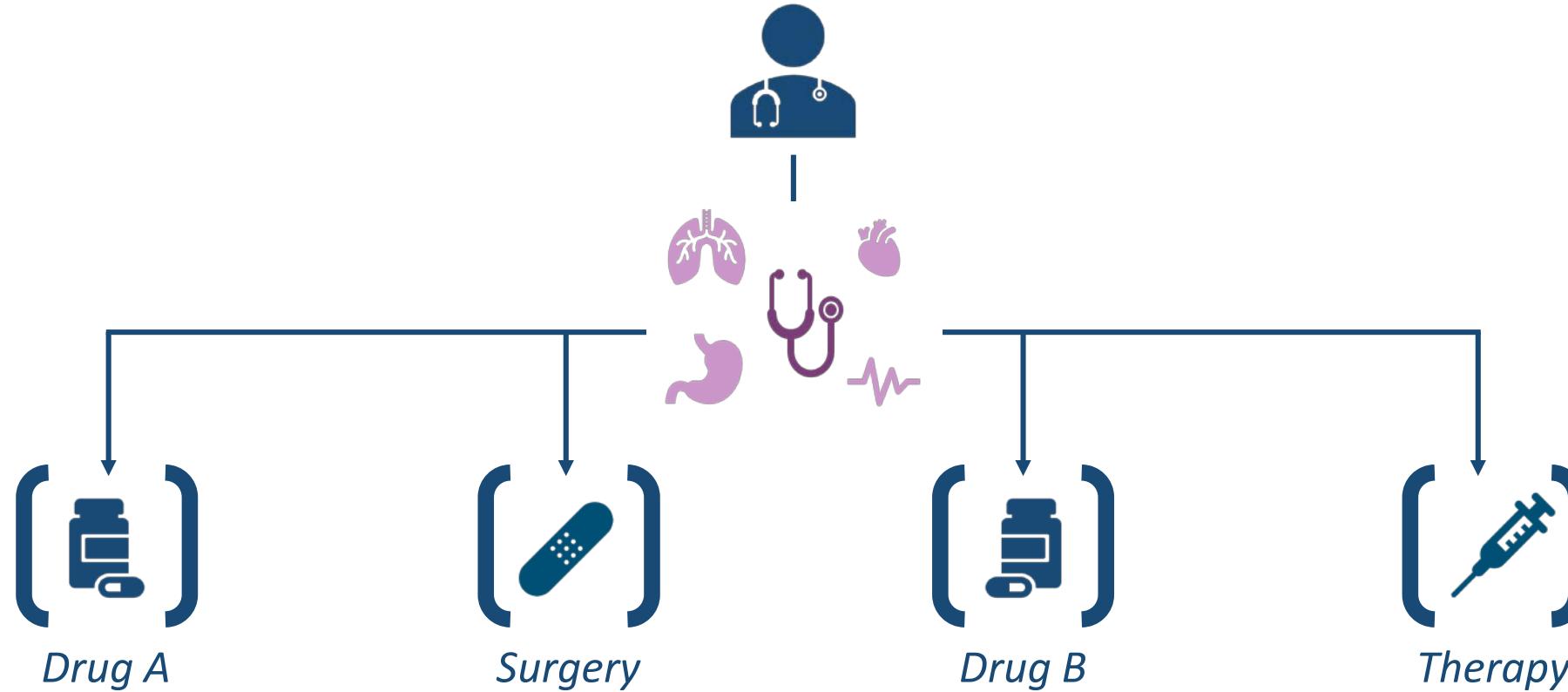


Jahr 2024

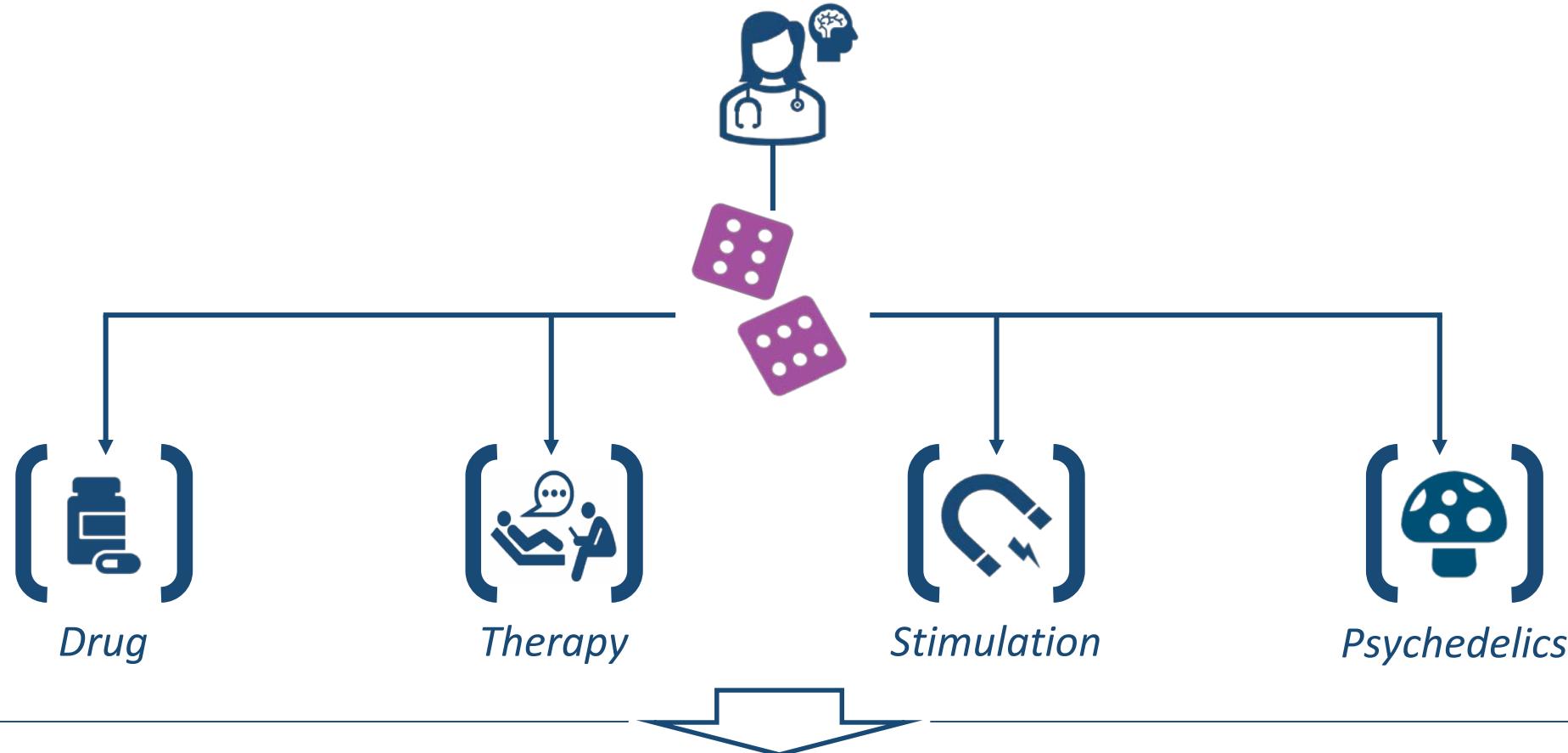
- In der Psychiatrie sind weiterhin persönliche Meinungen und subjektive Wahrnehmung entscheidend für wichtige Therapieentscheidungen



Somatische Erkrankungen werden behandelt auf Basis objektiver Informationen



“Trial-and-error” in der psychiatrischen Praxis?



Häufige Non-Response und Non-Remission: schwer zu behandelnde Depressionen

2024 Stratifizierte Psychiatrie



American College of
Neuropsychopharmacology

PERSPECTIVE OPEN

Electronic health records and stratified psychiatry: bridge to precision treatment?

Adrienne Grzenda ^{1,2} and Alik S. Widge ³

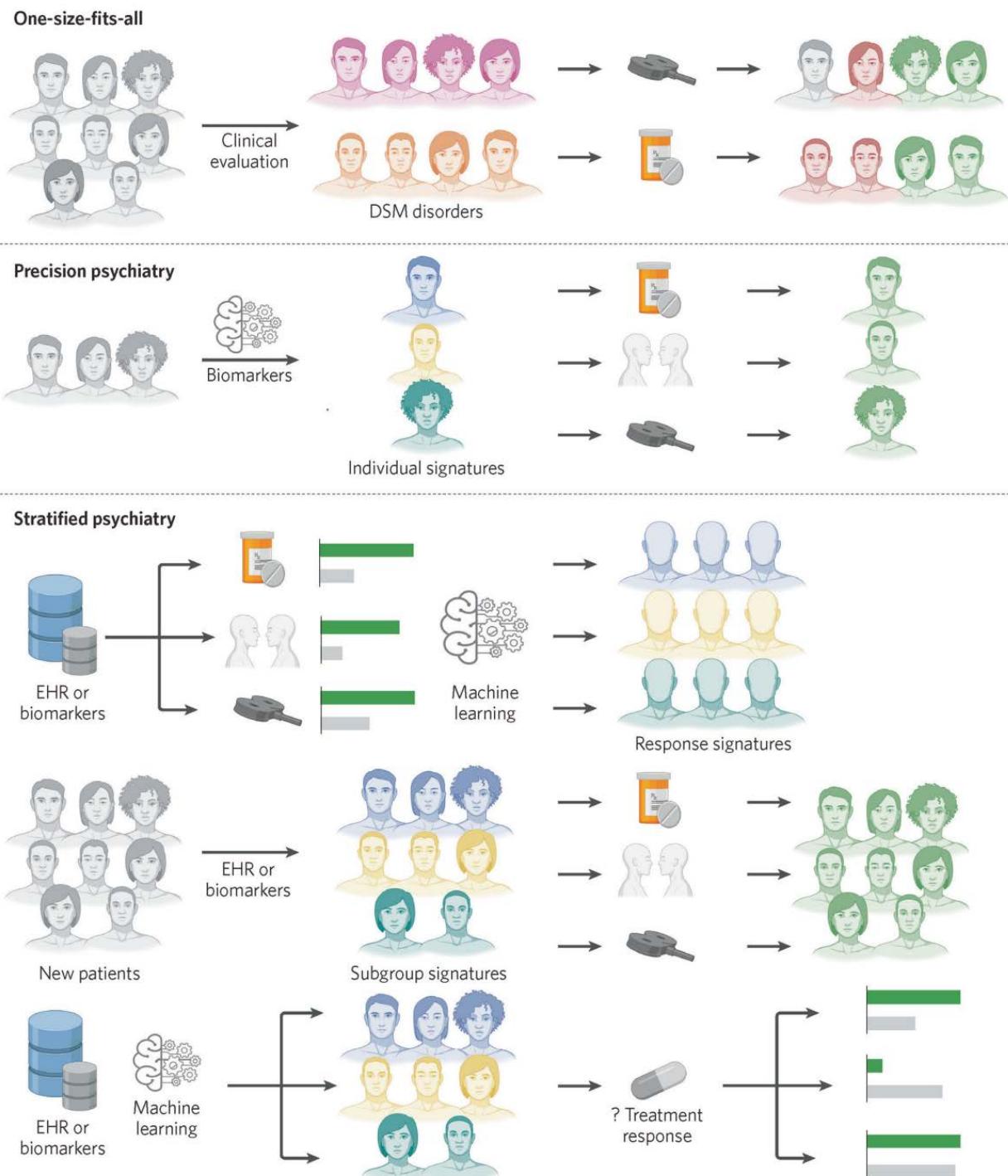
© The Author(s) 2023

The use of a stratified psychiatry approach that combines electronic health records (EHR) data with machine learning (ML) is one potentially fruitful path toward rapidly improving precision treatment in clinical practice. This strategy, however, requires confronting pervasive methodological flaws as well as deficiencies in transparency and reporting in the current conduct of ML-based studies for treatment prediction. EHR data shares many of the same data quality issues as other types of data used in ML prediction, plus some unique challenges. To fully leverage EHR data's power for patient stratification, increased attention to data quality and collection of patient-reported outcome data is needed.

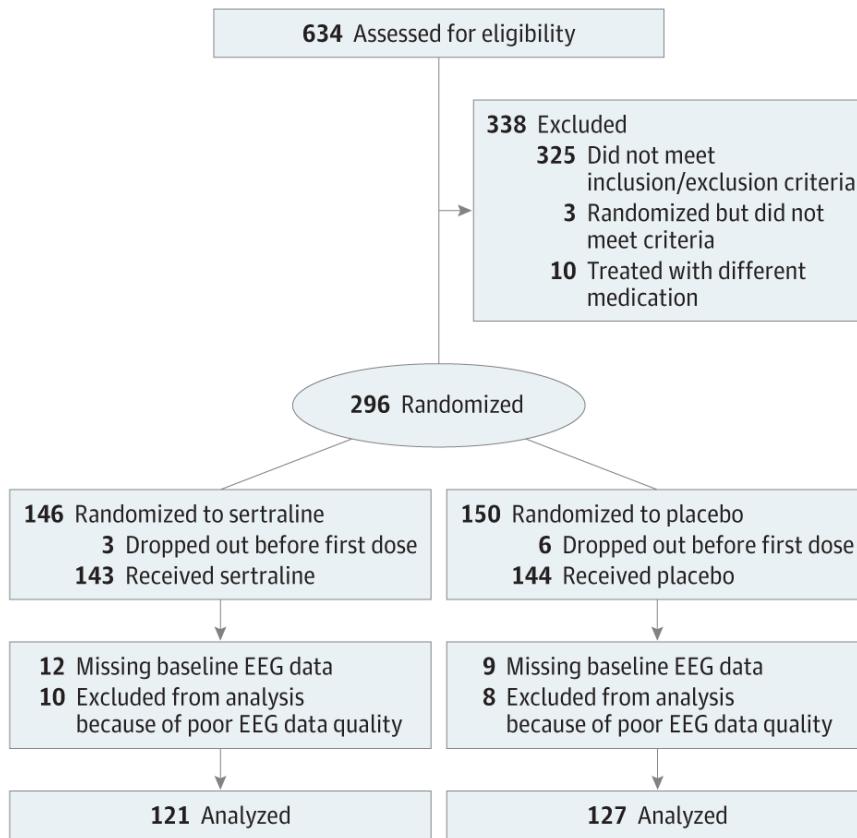
Neuropsychopharmacology: <https://doi.org/10.1038/s41386-023-01724-y>

www.nature.com/npp

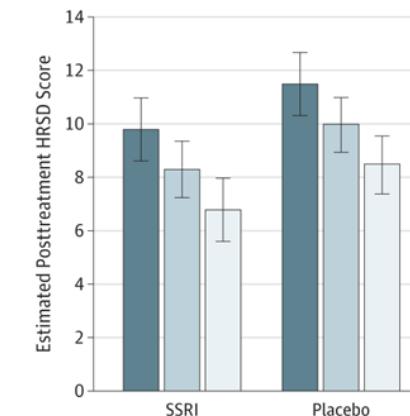
Check for updates



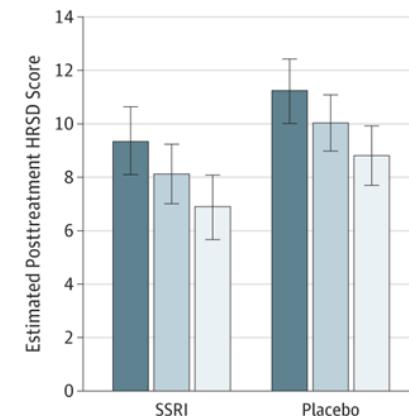
Embarc



A Baseline



B Week 1

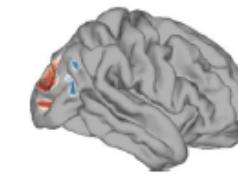
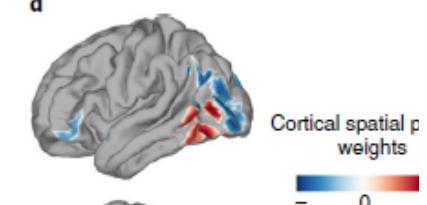
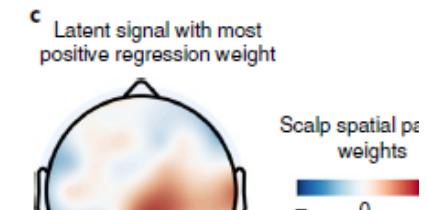
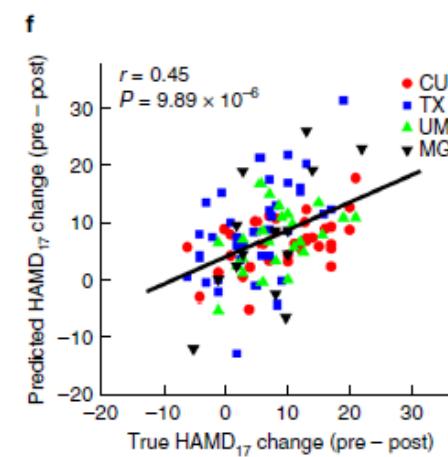
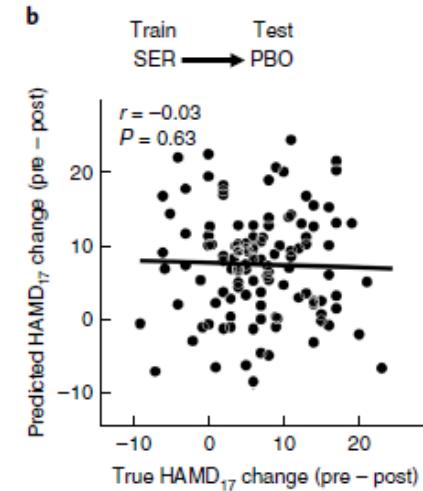
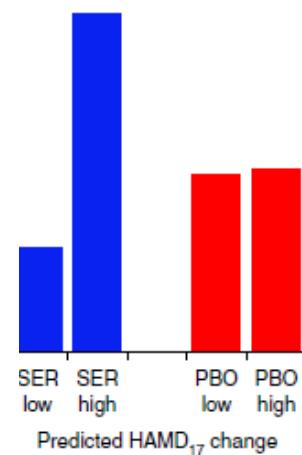
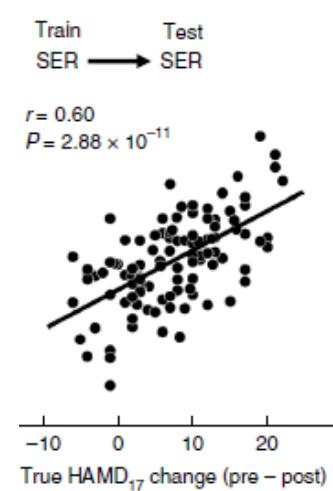


Estimated Week 8 Hamilton Rating Scale for Depression (HRSD) Scores for the Sertraline and Placebo Groups

Three values of baseline (A) and week 1 (B) rACC theta activity shown: 1 SD below the mean, the mean, and 1 SD above the mean. Error bars represent ± 1 SE. rACC indicates rostral anterior cingulate cortex; SSRI, selective-serotonin reuptake inhibitor.

Behandlungs
spezifisch:
Vorhersage Response auf SSRIs
Keine Vorhersage Placebo

RE BIOTECHNOLOGY



i-SPOT – EEG -Alpha-Asymmetry geschlechterspezifisch

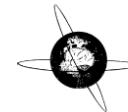


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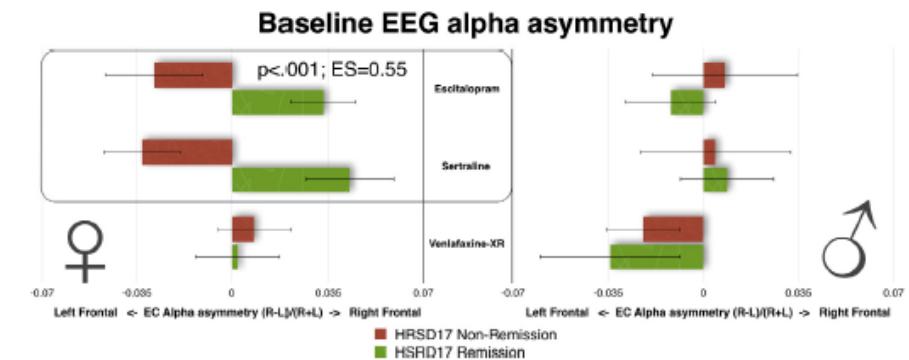
journal homepage: www.elsevier.com/locate/clinph



EEG alpha asymmetry as a gender-specific predictor of outcome to acute treatment with different antidepressant medications in the randomized iSPOT-D study

Martijn Arns ^{a,b,*}, Gerard Bruder ^c, Ulrich Hegerl ^d, Chris Spooner ^{e,f}, Donna M. Palmer ^{e,f,g}, Amit Etkin ^{h,i}, Kamran Fallahpour ^{c,j}, Justine M Gatt ^{g,k,l}, Laurence Hirshberg ^m, Evian Gordon ^{e,f}

- Vorhersage Behandlungserfolg durch „frontale Alpha Asymmetrie“
- Nur für SSRIs, nicht bei SNRIs
- Nur bei Frauen, nicht bei Männern

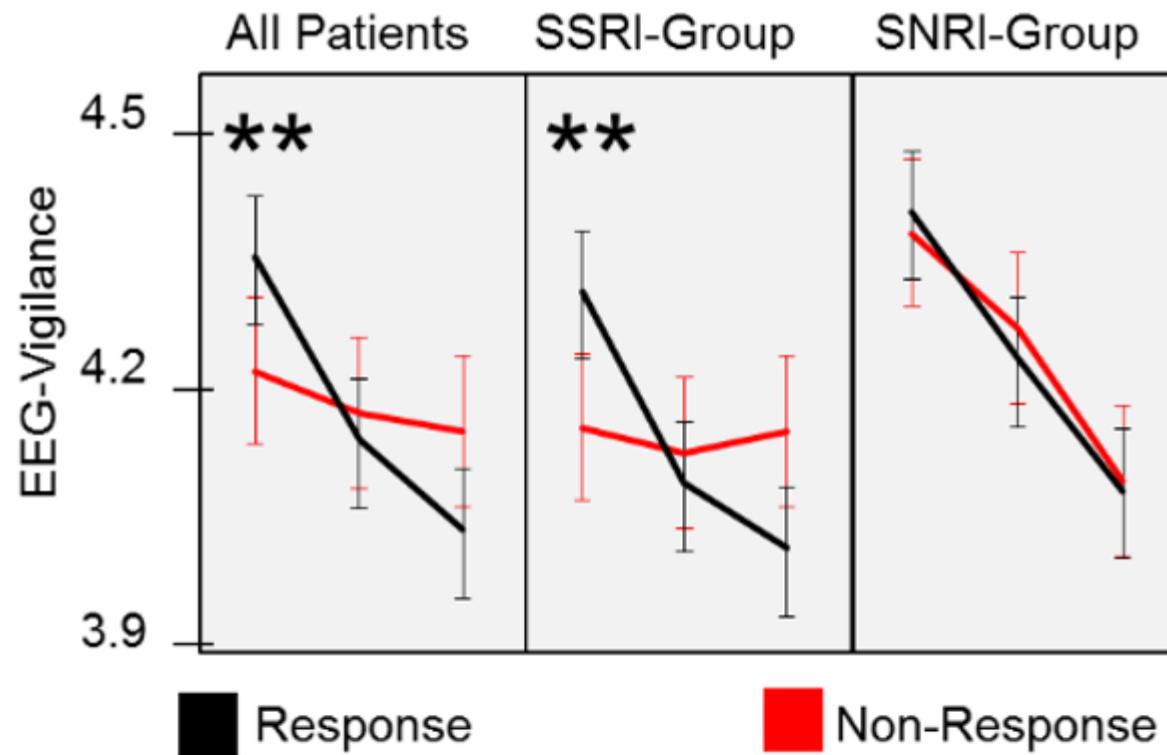


Prediction: iSPOT-D

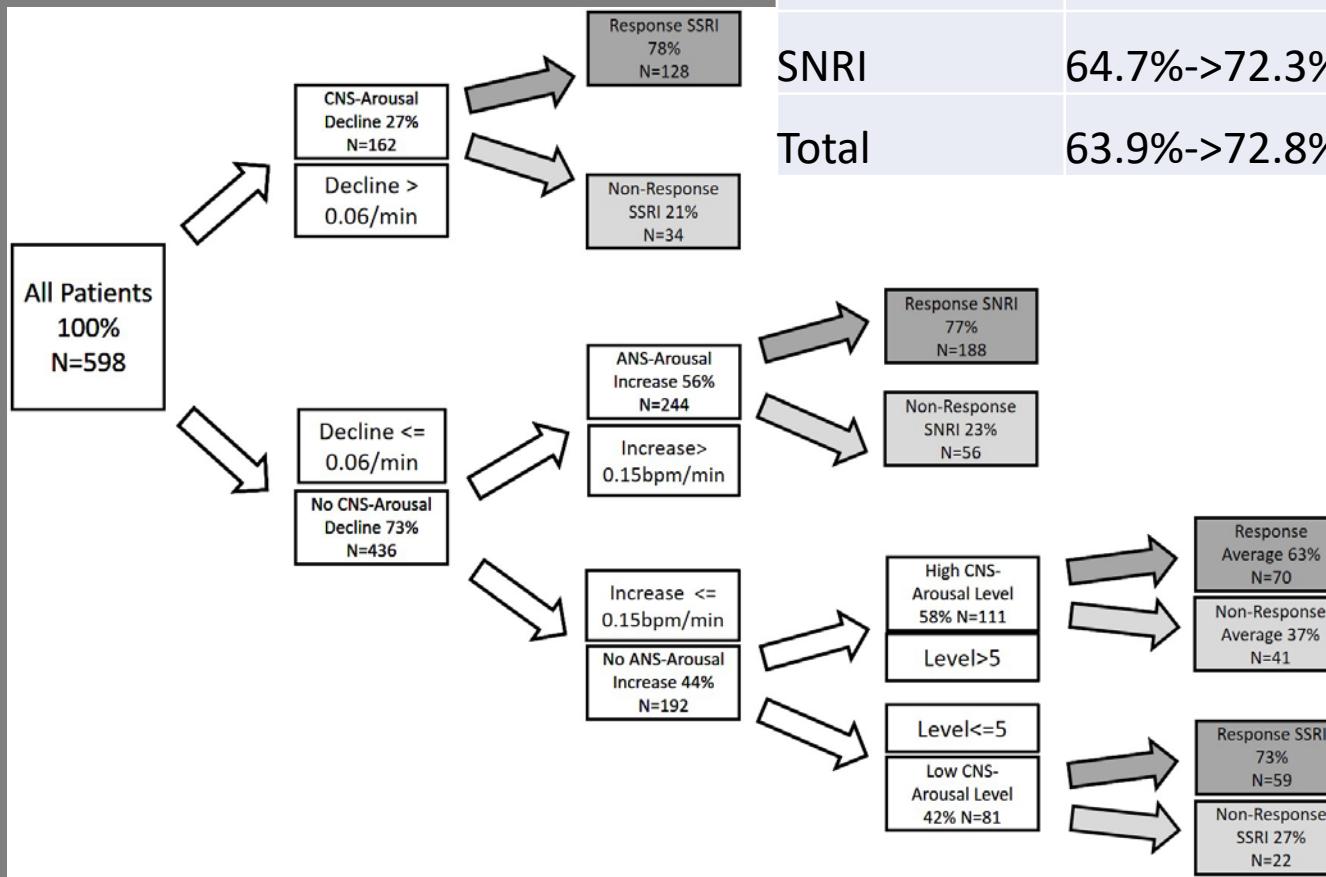
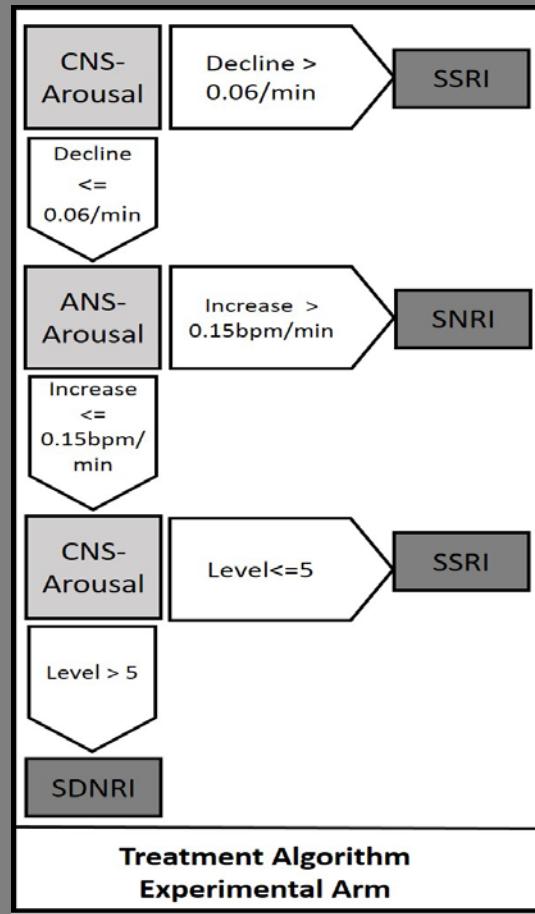
- International Study to Predict Optimal Treatment – in Depression
- Multicentre, international, prospective, randomized, open-label effectiveness trial
- 22 sites involved
- 2016 MDD subjects, 1008 included



CNS-Wakefulness Regulation

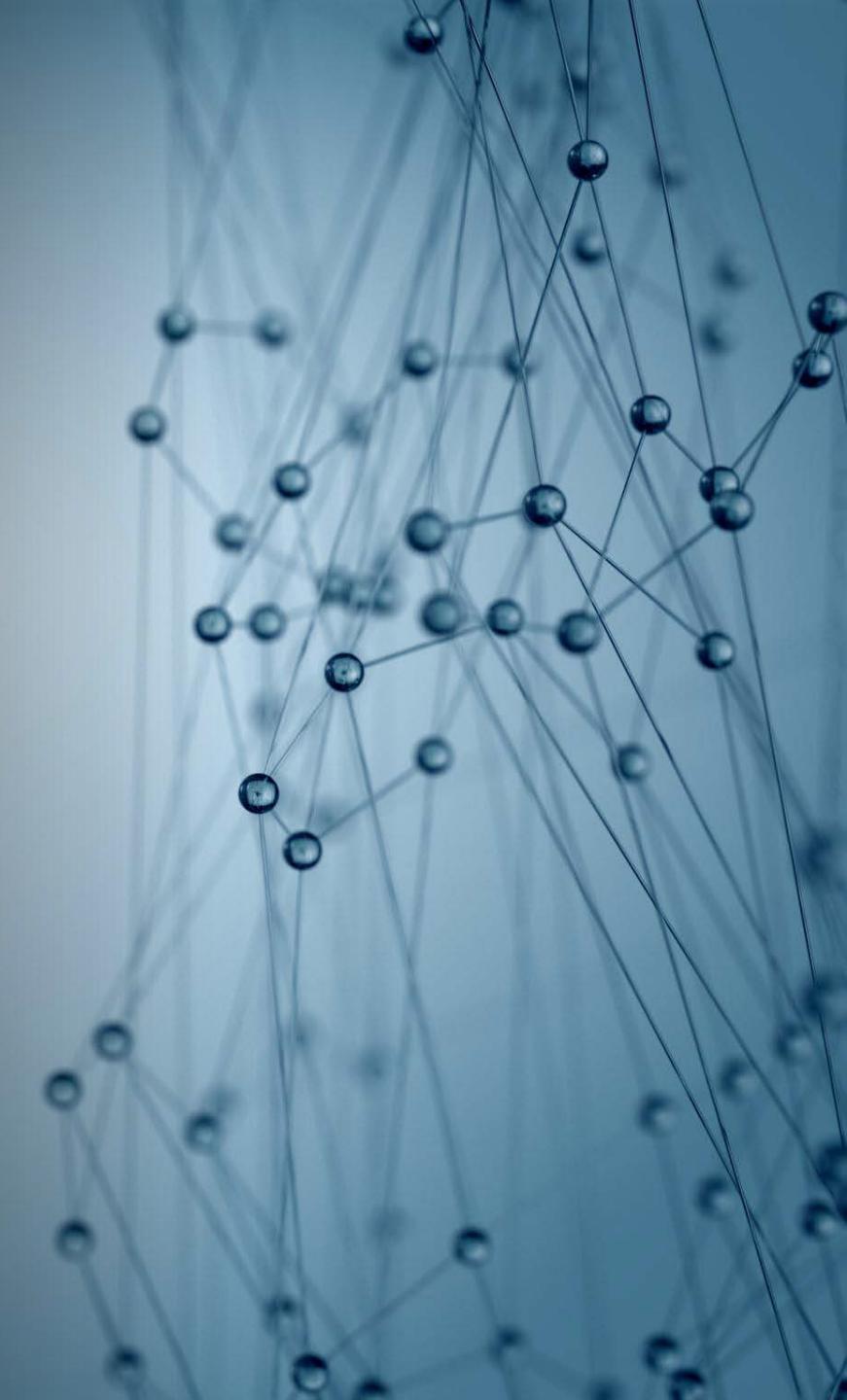


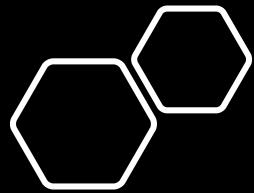
Prädiktion iSPOT-D: Algorithmus



	Response	Remission
SSRI	63.5%->73.3%	47.1%->58.4%
SNRI	64.7%->72.3%	43.2%->46.8%
Total	63.9%->72.8%	46.3%->52.5%

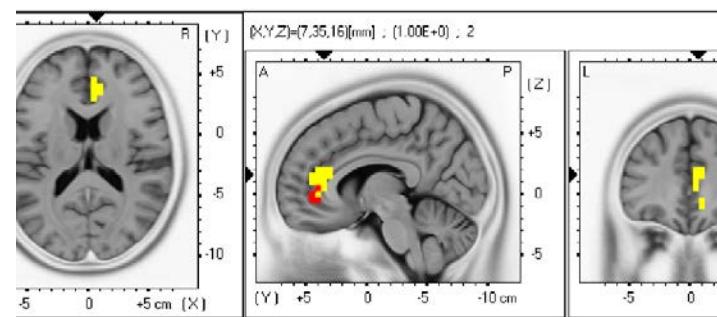
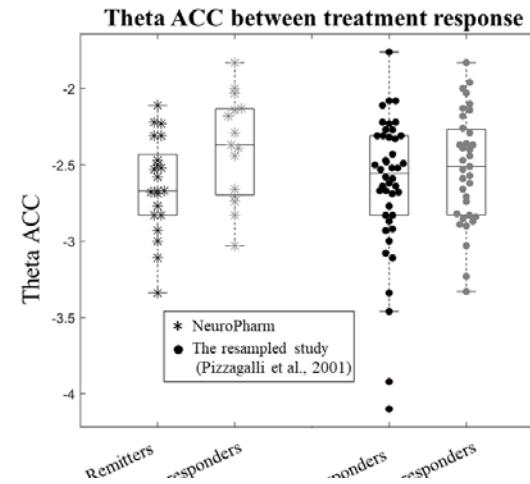
REPLIKATION

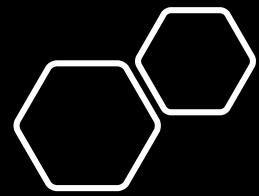




The Neuropharm Study - theta

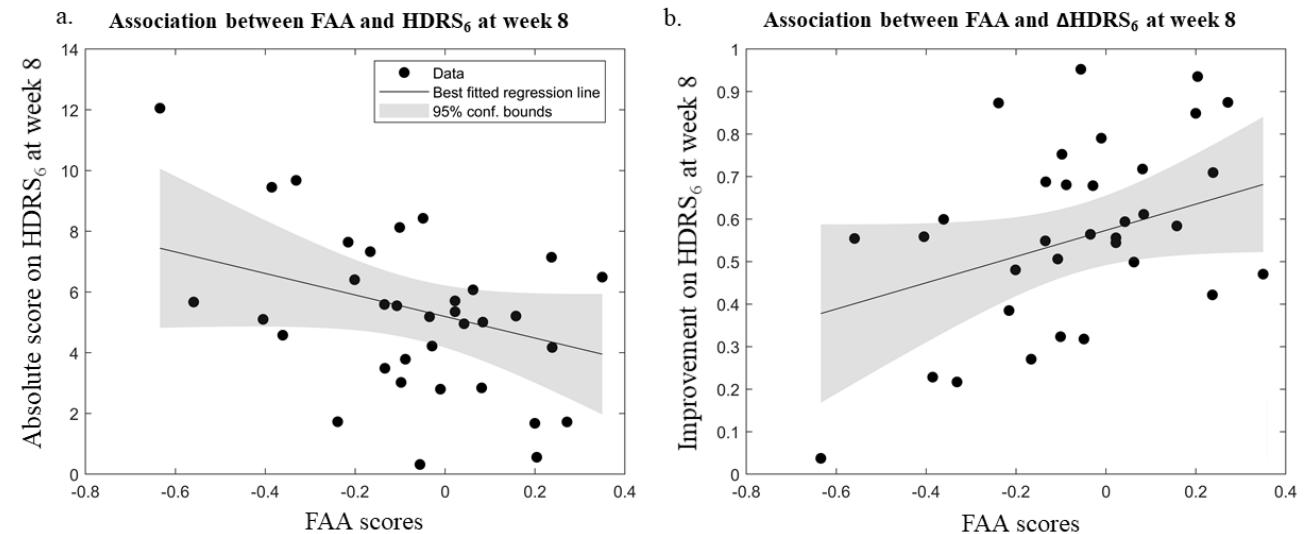
- Keine Replikation des sogenannten “Frontalen Theta” als Prädiktionsmarker





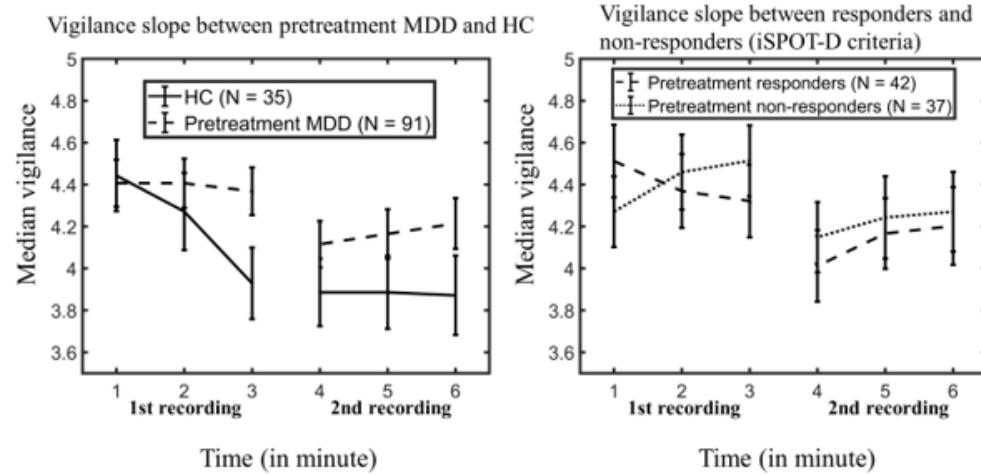
The Neuropharm study – alpha asymmetry

- Replikation der Alpha Asymmetrie als Prädiktionsmarker
- Ebenfalls nur bei Frauen
- → Rechtsfrontale Alpha Aktivität sagt Response auf SSRIs voraus



The Neuropharm Study – Vigilance

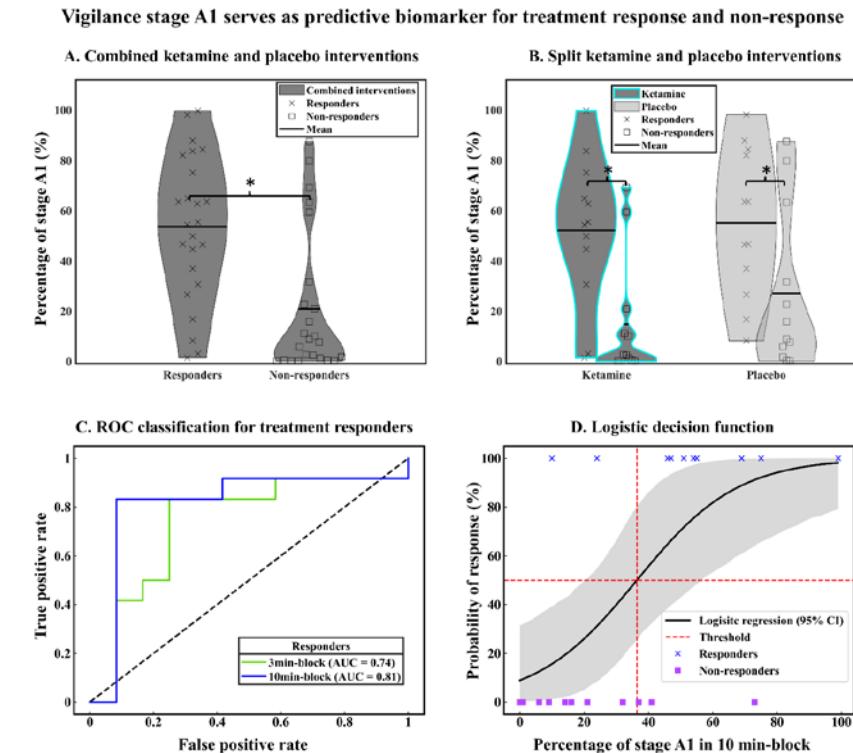
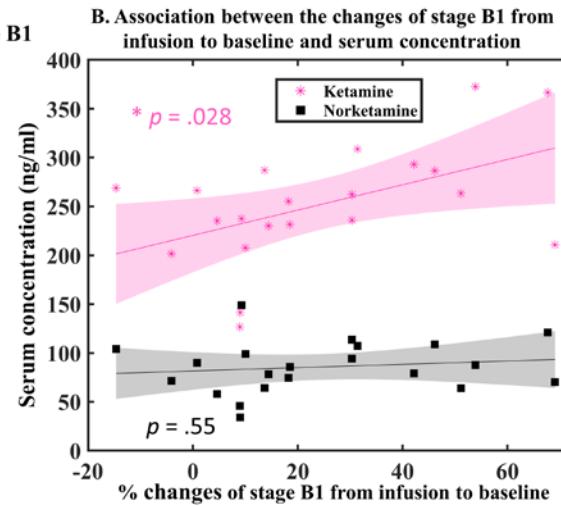
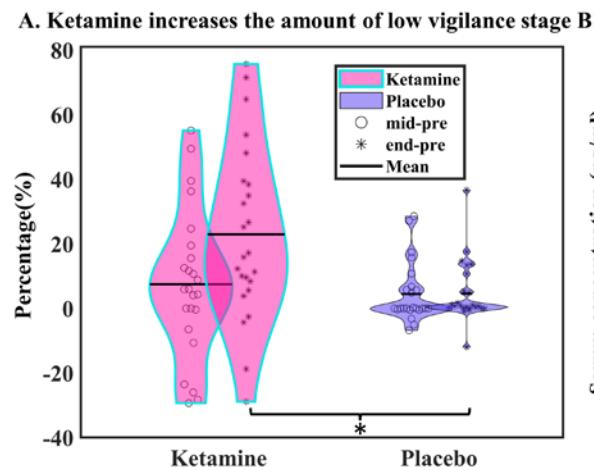
- Cheng et al. 2021, Replikation Wachheitsregulation
- Schneller Abfall der EEG-Vigilanz sagt Response auf SSRIs voraus



	PRETREATMENT VISIT		CLINICAL OUTCOME AT WEEK 8			
			NeuroPharm ¹		iSPOT-D ²	
	Healthy controls	MDD	Remitters	Non-responders	Responders	Non-responders
Stage 0 (%), Mean \pm SD	13.7 \pm 3.3	15.3 \pm 2.1	14.2 \pm 5.1	22.6 \pm 6.0	16.2 \pm 3.4	15.3 \pm 3.6
Stage A1	32.6 \pm 5.7	36.3 \pm 3.5	36.1 \pm 7.7	35.4 \pm 9.2	35.2 \pm 5.3	37.0 \pm 5.7
Stage A23	10.1 \pm 3.2	14.1 \pm 2.0	14.1 \pm 3.9	6.1 \pm 4.6	13.0 \pm 3.3	17.1 \pm 3.5
Stage B1	34.8 \pm 4.4	26.4 \pm 2.7	23.2 \pm 5.5	23.6 \pm 6.6	27.7 \pm 3.9	22.0 \pm 4.1
Stage B23	8.8 \pm 2.4	7.8 \pm 1.5	12.4 \pm 4.8	12.4 \pm 5.7	7.9 \pm 2.4	8.5 \pm 2.6
Median vigilance (Mean \pm SD)	4.07 \pm 0.15	4.27 \pm 0.93	4.24 \pm 0.25	4.31 \pm 0.30	4.28 \pm 0.15	4.30 \pm 0.16
Vigilance slope at 1 st recording (Mean \pm SD)	-0.17 \pm 0.05	-0.25 \pm 0.03*	-0.09 \pm 0.12	0.03 \pm 0.14	-0.11 \pm 0.08	0.13 \pm 0.08*
Vigilance slope at 2 nd recording (Mean \pm SD)	0.04 \pm 0.05	0.03 \pm 0.03*	0.10 \pm 0.09	0.16 \pm 0.11	0.10 \pm 0.06	0.06 \pm 0.07

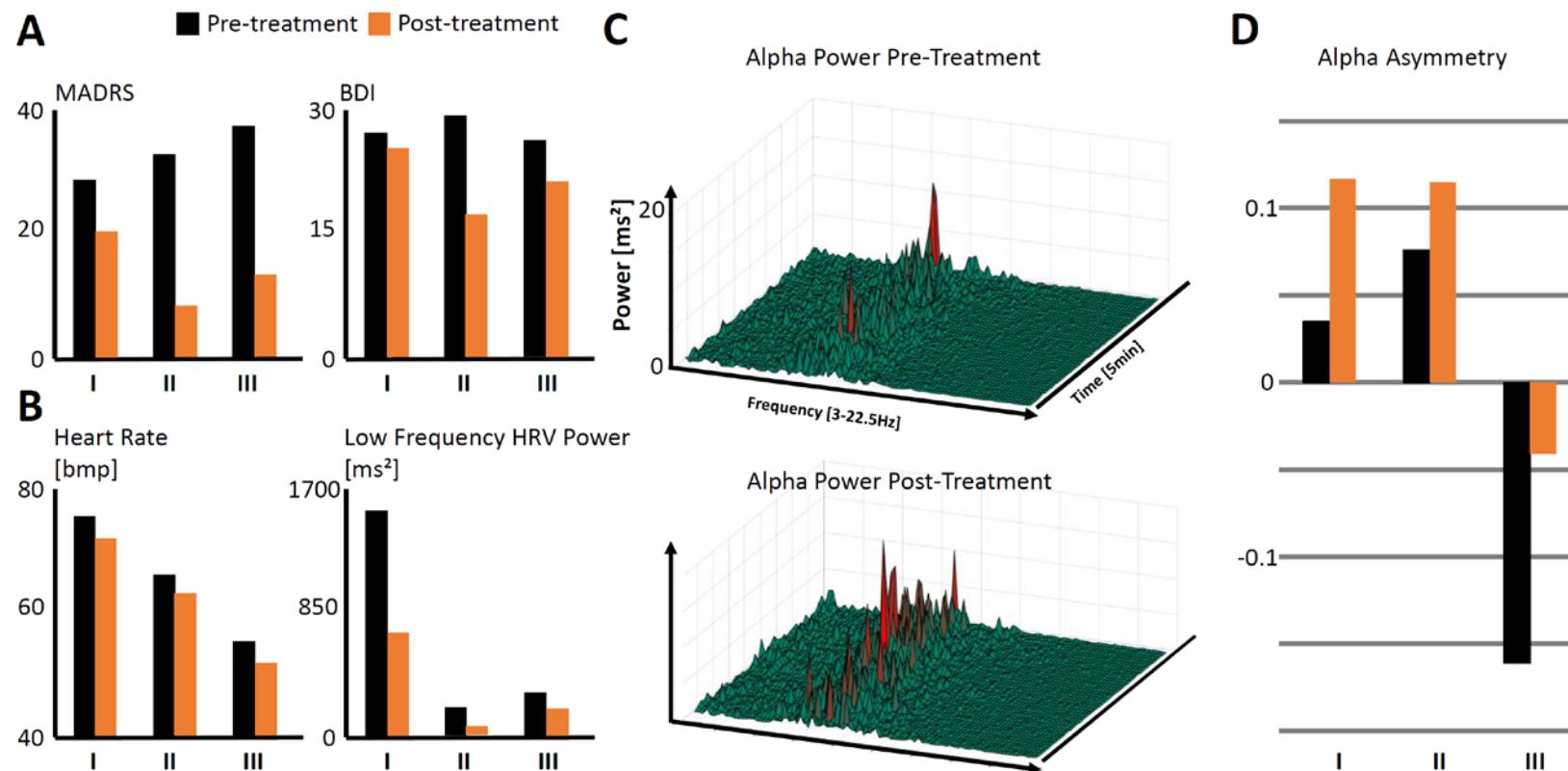
Ketamin und Prädiktion

- 2x25 Patienten, iv. Ketamine, EEG-Vigilance (Cheng et al. 2024)
- A1 Vigilanzstadien sagen Ketaminresponse voraus



Ketamin und N2O (Lachgas)

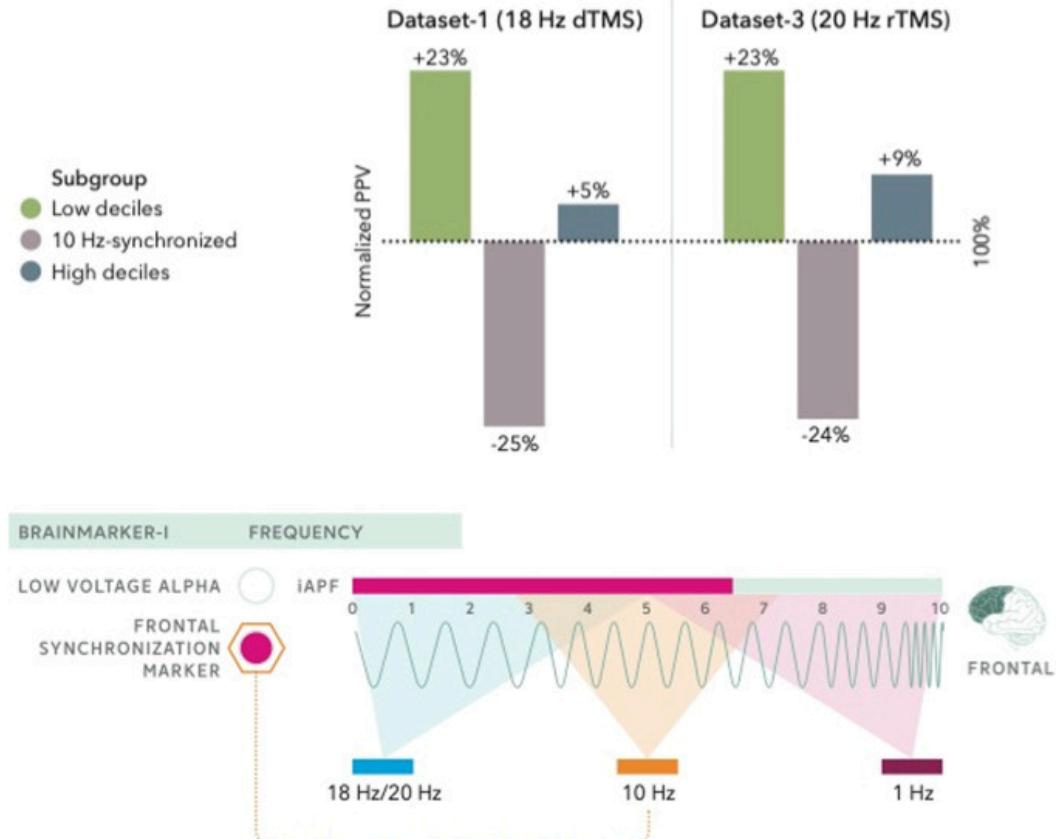
- Entgegengesetzte Effekte des Ketamin und N2O auf das ZNS und ANS(Kronenberge et al. 2022)



Verwendung eines Markers für verschiedene Behandlungen

Alpha Peak Frequenz :

- EEG mit Abnormailtäten: Sertralin
- EEG mit APF<<10Hz: EKT oder 18/20Hz TMS
- EEG mit APF = 10Hz: 10Hz TMS
- EEG mit APF >>10Hz: 1 Hz TMS



Prospektive Studie

EEG biomarker informed prescription of antidepressants in MDD: a feasibility trial



Nikita van der Vinne^{a,b,c,*}, Madelon A. Vollebregt^b,
A. John Rush^{d,e,f}, Michiel Eebe^a, Michel J.A.M. van
Putten^{c,g,1}, Martijn Arns^{b,h,i,1}

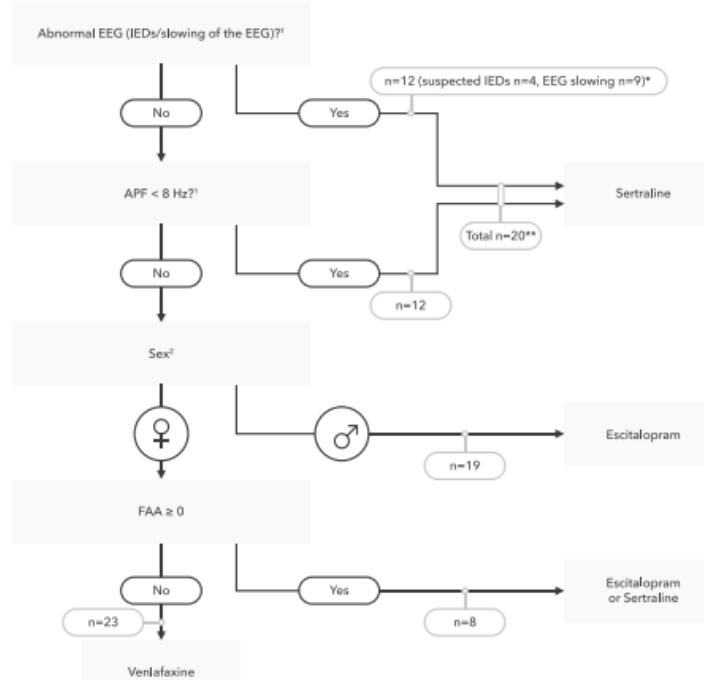


Table 3 Treatment outcomes for the two patient groups.

	TAU	EEG-informed	Total
<i>n</i>	52	70	122
BDI-II baseline to week 8	35.4-27.1	31.7-20.2	33.3-23.1
% BDI-II change (below per medication and per sex (in italic))	23.9%*	36.8%*	31.3%
<i>Escitalopram</i>	34.3% (n = 20)	35.1% (n = 24)	
<i>Sertraline</i>	23.5% (n = 8)	38.5% (n = 24)	
<i>Venlafaxine</i>	18.1% (n = 8)	36.7% (n = 22)	
<i>Duloxetine</i>	10.2% (n = 6)	—	
<i>Bupropion</i>	1.0% (n = 2)	—	
<i>Fluoxetine</i>	25.5% (n = 2)	—	
<i>Nortriptyline addition</i>	10.0% (n = 2)	—	
<i>Vortioxetine</i>	36.0% (n = 2)	—	
<i>Mirtazapine addition</i>	26.0% (n = 1)	—	
<i>Paroxetine</i>	-7.0% (n = 1)	—	
<i>Female/Male</i>	28.7% / 19.4%	38.3% / 34.3%	
<i>Normal EEG</i>	—	37.9% / 36.1%	
<i>Abnormal EEG</i>	—	39.2% / 29.3%	
Remission	17%	29%	24%
<i>Female/Male</i>	16%/19%	32%/23%	
Response	27%	39%	34%
<i>Female/Male</i>	28%/26%	39%/38%	

Verwendung in der Psychiatrie

- DeepPsy Report für EEG/EKG in Neuropsychiatrie (Michael Fischer)
„Early Adapter“
- Implementierung in der PUK Oktober 2023
- Hinweise über Behandlungsstrategien basierend auf Hirnwellen und Herzaktivität



Name:
Patienten-ID:
Alter: 38
Geschlecht: Weiblich

Fall-ID:
Bericht ID: 2147-625-9630898
Datum der Analyse: 17.10.2024
Erstellungsdatum: 17.10.2024

EEG- und EKG-Biomarker-Bericht

- Dieser Bericht darf nur von qualifizierten Mediziner/innen verwendet werden.
- Dieser Bericht hat den Zweck, die Entscheidungsfindung im Rahmen der für einen/eine Patient/in bereits indizierten Behandlungsmöglichkeiten zu verbessern.

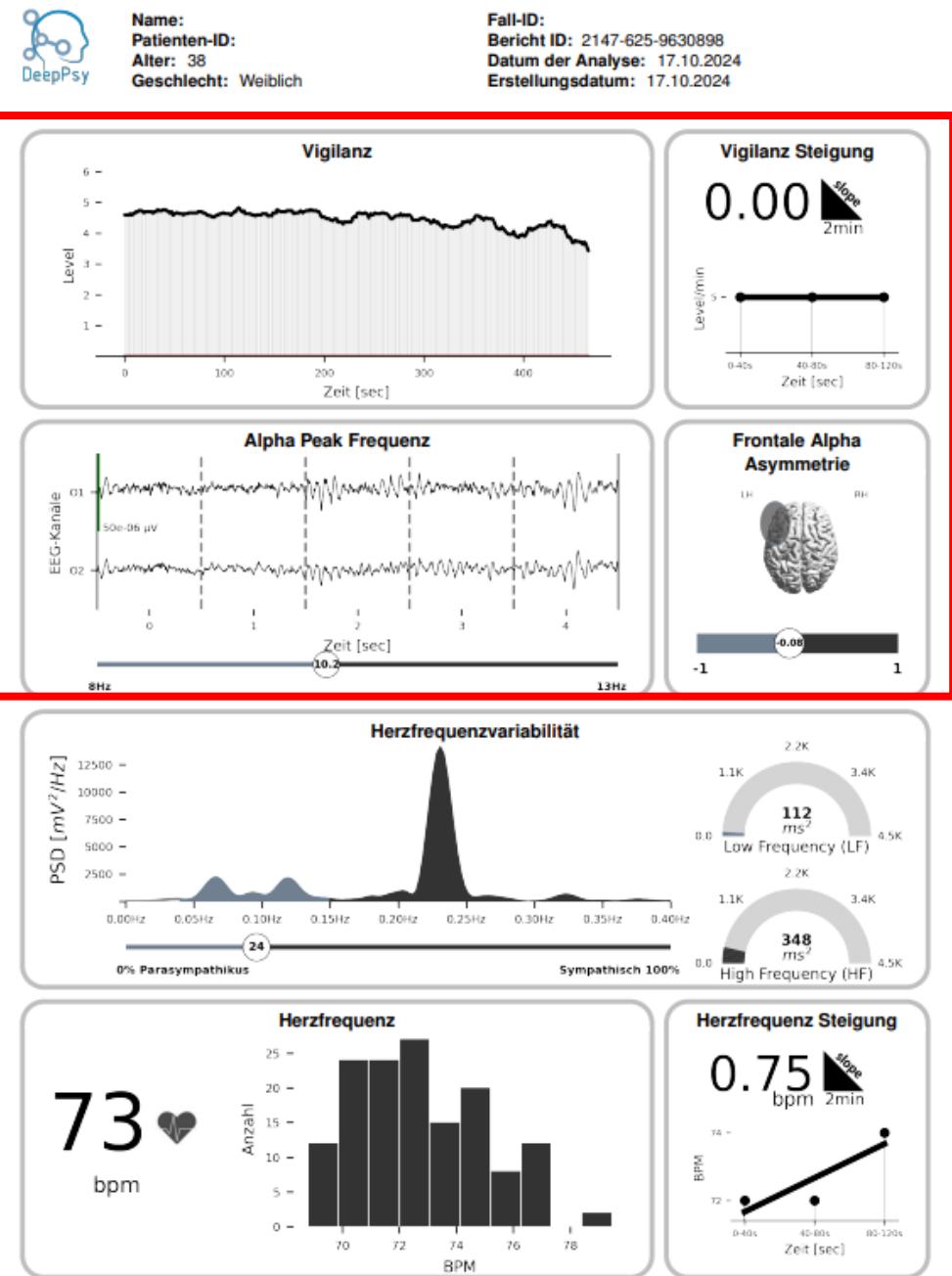
- Dieser Bericht soll nicht verwendet werden, um zu entscheiden, ob sich ein/e Patient/in einer Behandlung unterziehen sollte. Er soll auch nicht verwendet werden, um festzustellen, ob eine Behandlung für einen/eine Patient/in indiziert oder kontraindiziert ist.
- Dieser Bericht soll nicht bei neurologischen Pathologien, Kopfhautanomalien, Kopfverletzungen (im EEG) oder kardialen Pathologien (im EKG) verwendet werden.
- Dieser Bericht soll nicht zur Beurteilung von Diagnosen, zur Überwachung der Vitalparameter oder in Situationen verwendet werden, in denen die gemessenen Parameter eine unmittelbare Gefahr für den/die Patient/in darstellen könnten.

Zusammenfassung der Korrelationen von Biomarkern

Diagnose	Behandlung	Korrelation
MDD	SSRI	Schlechtere Wirksamkeit als SNRI Frontale Alpha Asymmetrie (FAA), Herzratenregulation (BPM Steigung), Vigilanz-Regulierung
	SNRI	Bessere Wirksamkeit als SSRI Frontale Alpha Asymmetrie (FAA), Herzratenregulation (BPM Steigung), Vigilanz-Regulierung
	rTMS	10Hz über linkem DLPFC hat bessere Wirksamkeit als 1Hz über rechtem DLPFC Alpha Peak Frequenz
	Ketamin (oral/i.v.)	Schlechtere Wirksamkeit für Ketamin Herzrate (BPM)
	EKT	Normale Wirksamkeit Alpha Peak Frequenz
OCD	Kombination aus SSRI und KVT	Erhöhte Wirksamkeit bei Kombination aus SSRI und KVT Vigilanz Regulation Stadium 0

Verwendung in der Psychiatrie

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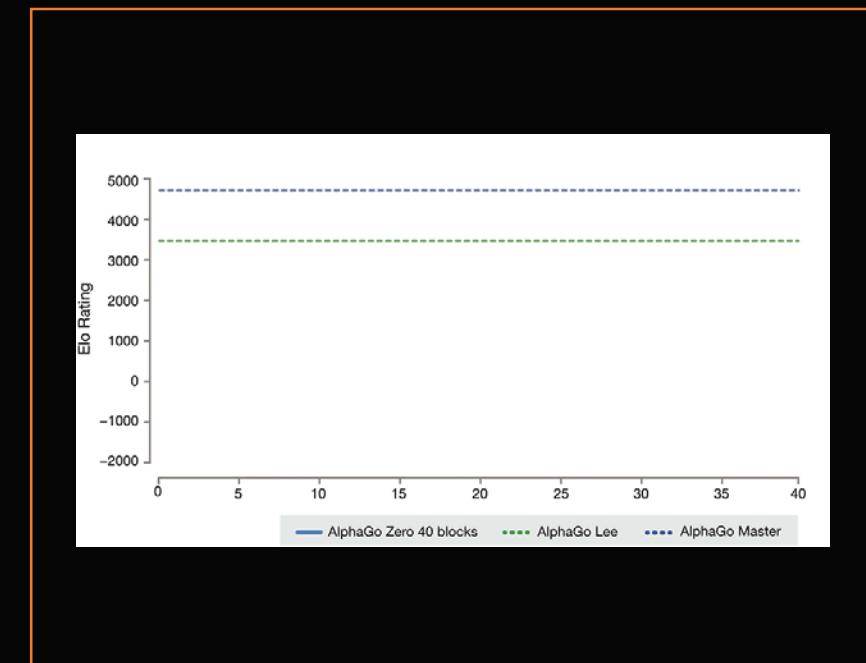
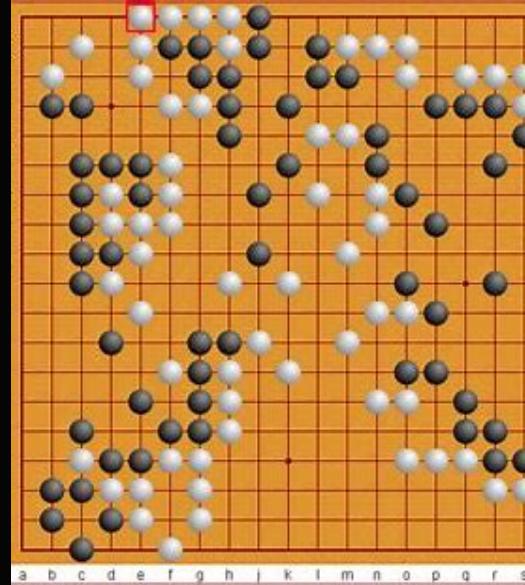


Die Zukunft mit künstlicher Intelligenz?



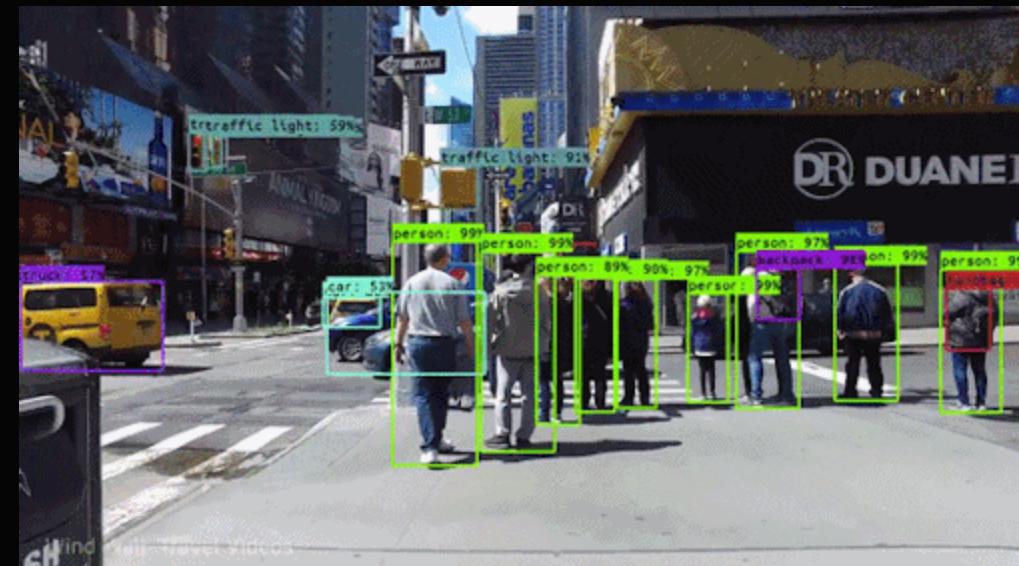
Google Alpha Go

- Wins over humans in complex games
- Learns fastest when playing against itself
- Discover new patterns that have been unknown before



Autonomous driving

- Sensors stream data
- AI integrates data online
- AI makes decisions
- Moral questions unanswered
(Who`s fault is an accident?)



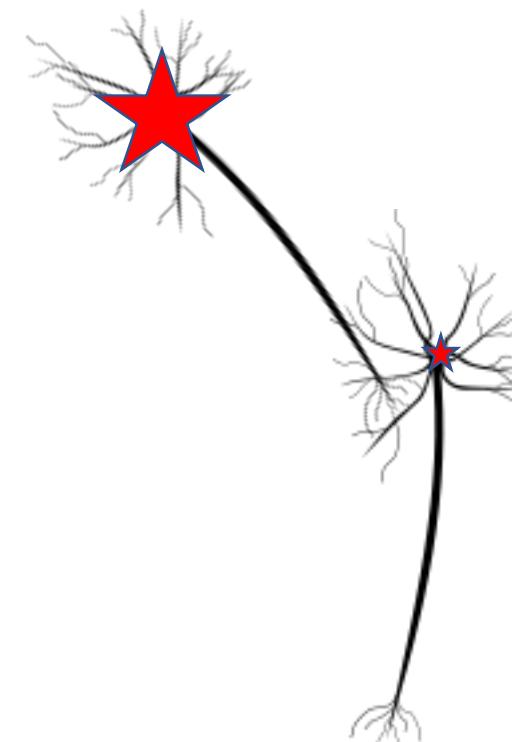
Deep Learning

- Text Generierung
 - Video Generierung
 - Stimmen Generierung
- Deep Learning

Was ist das?

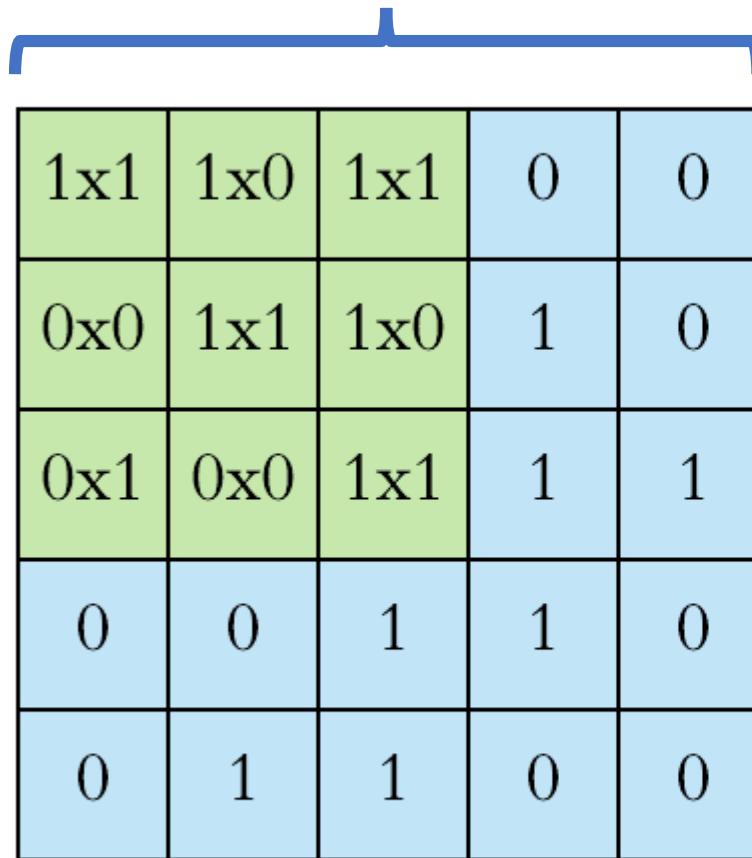


Hebb's Rule 1949



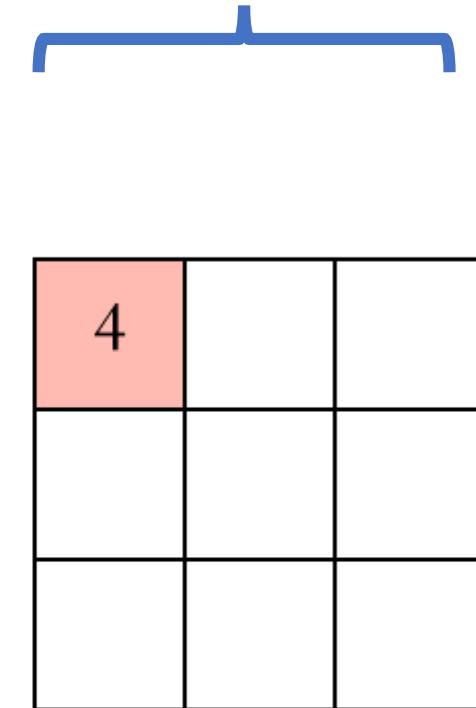
Filters

Input Data



1x1	1x0	1x1	0	0
0x0	1x1	1x0	1	0
0x1	0x0	1x1	1	1
0	0	1	1	0
0	1	1	0	0

Output Data



4		



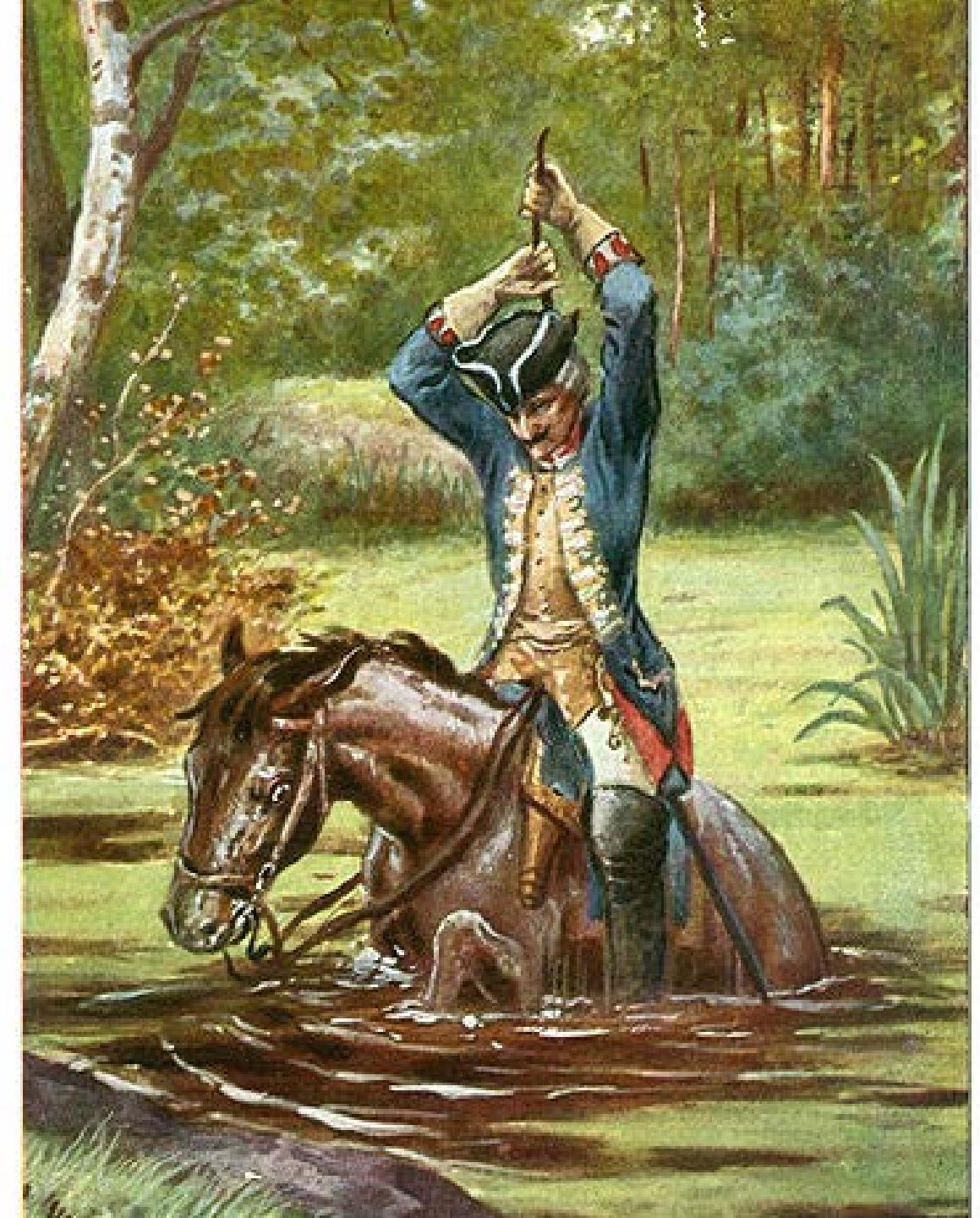
Arden Dertat [Follow](#)

ML Engineer @ Pinterest. Photography and travel enthusiast.

Nov 8, 2017 · 23 min read

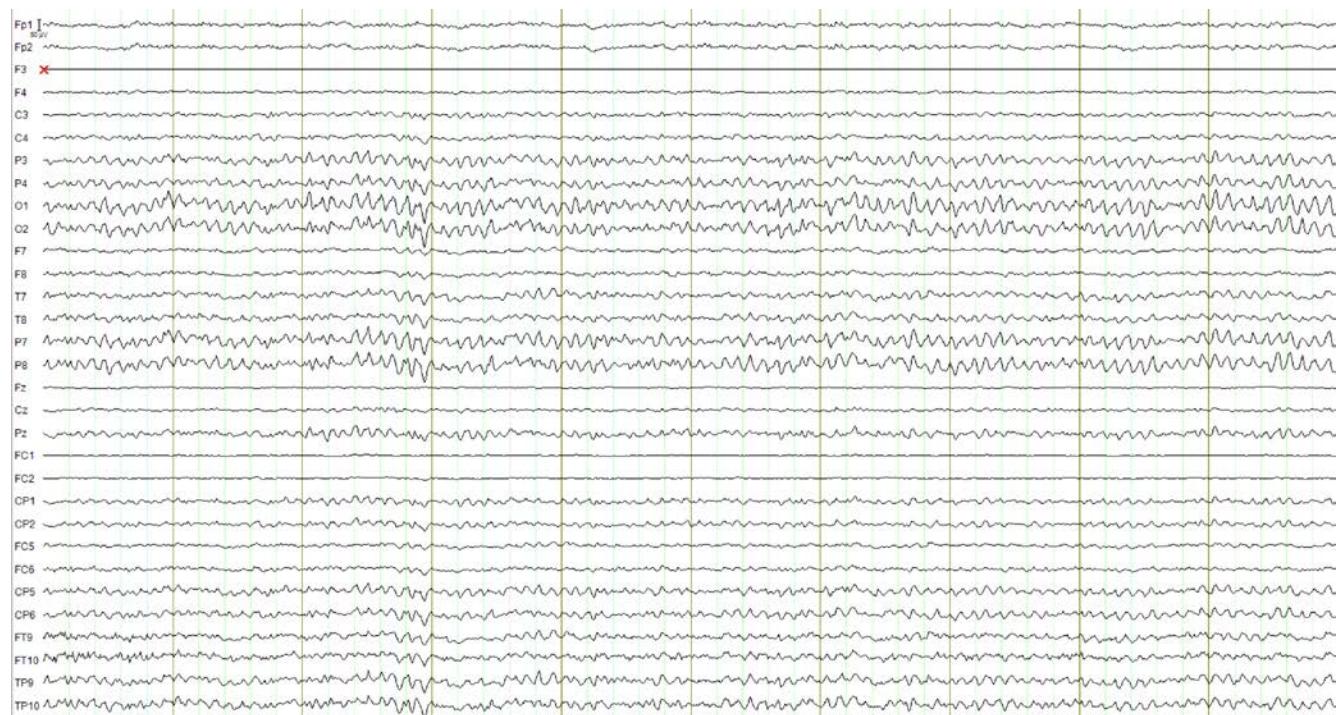
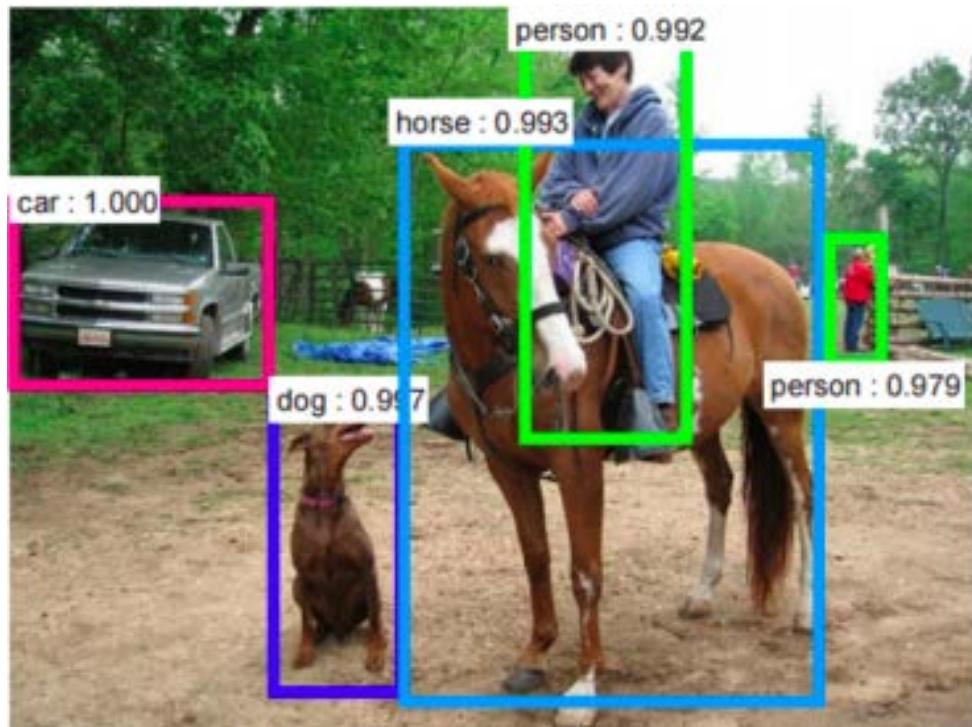
Paradoxon

- „Deep Learning“ verwendet ähnliche Methoden wie unser Nervensystem
- Im Psychiatrischen Kontext:
Kann uns so eine Methode somit überhaupt weiterbringen?

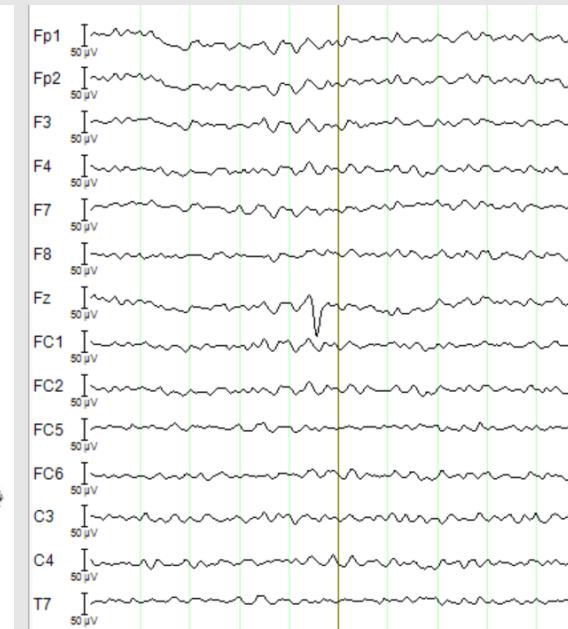
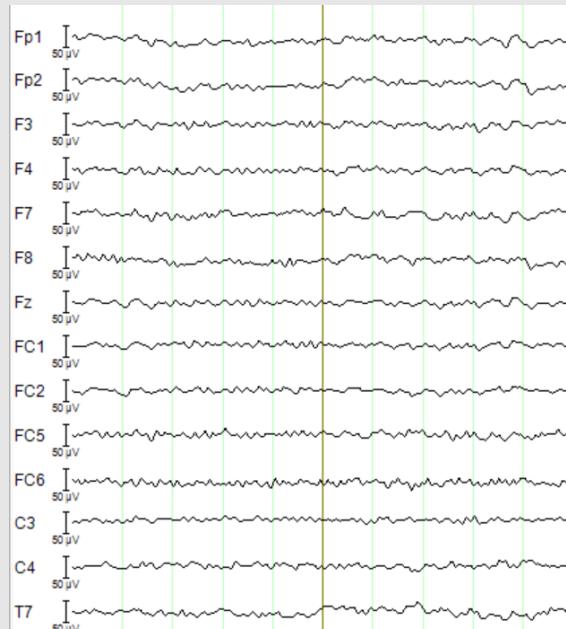


Was soll das mit dem
EEG zu tun haben?

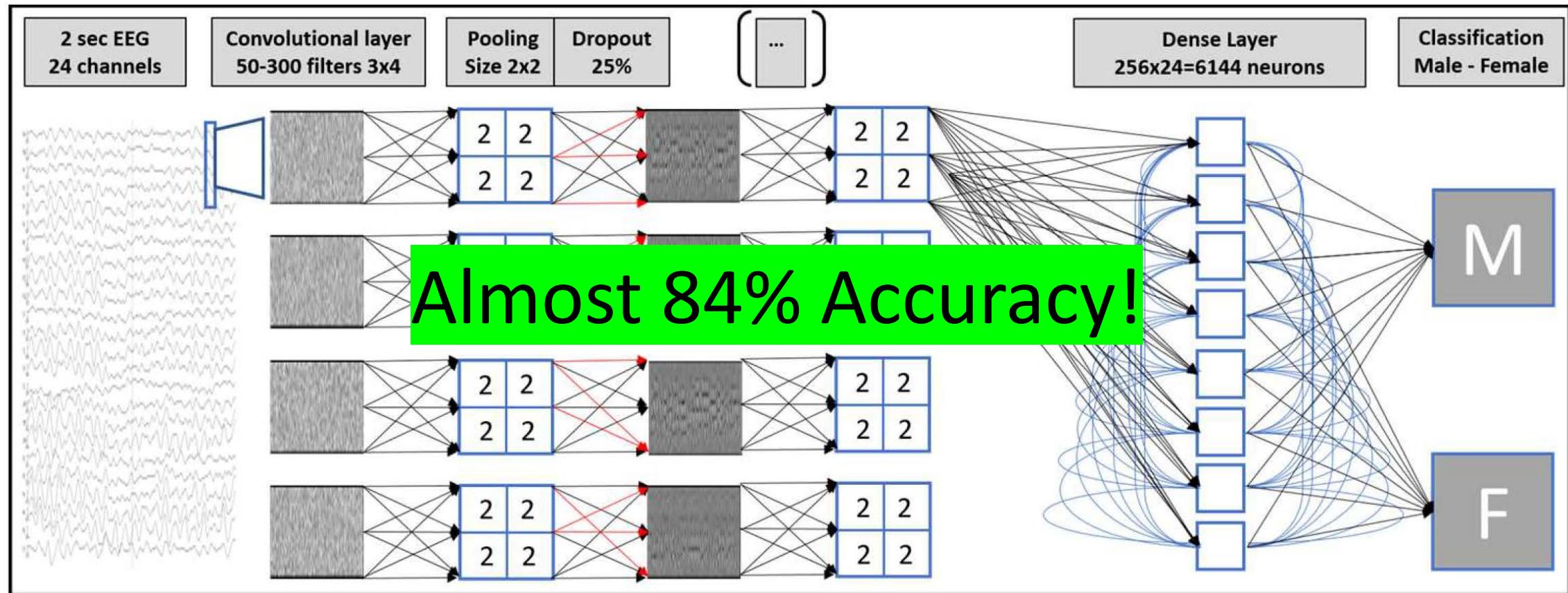
?



„Ground Truth“ MANN FRAU?



Deep Learning zur Bestimmung des biologischen Geschlechts

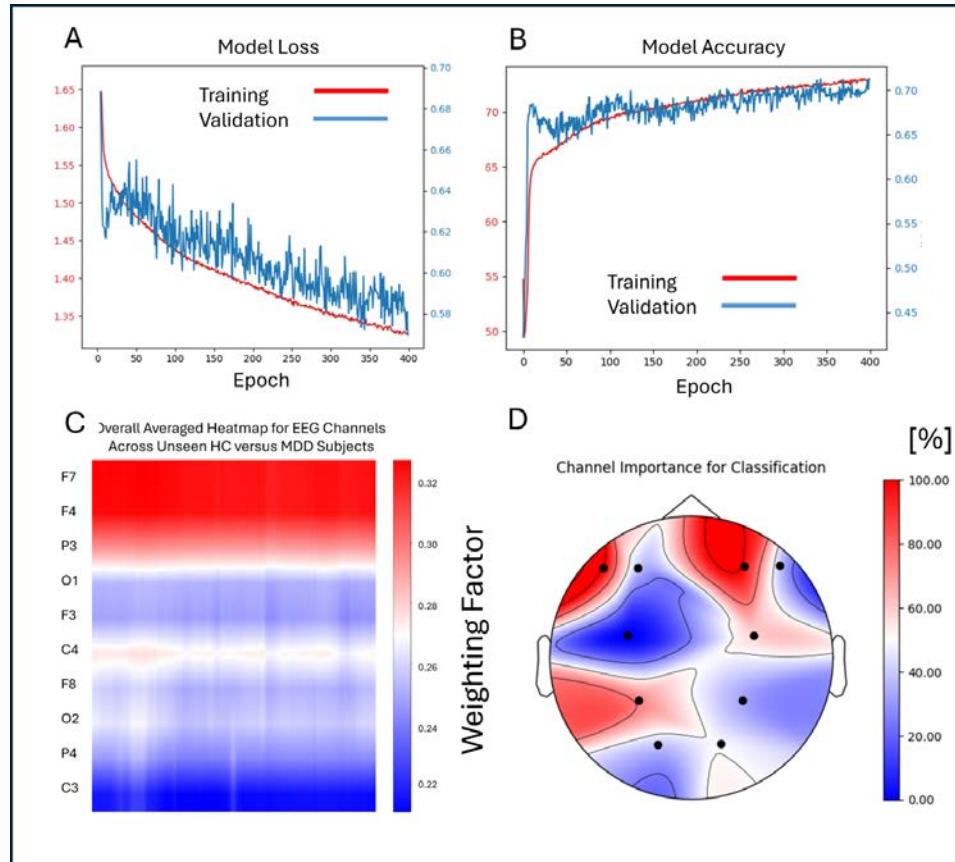


Klinische Verwendung?

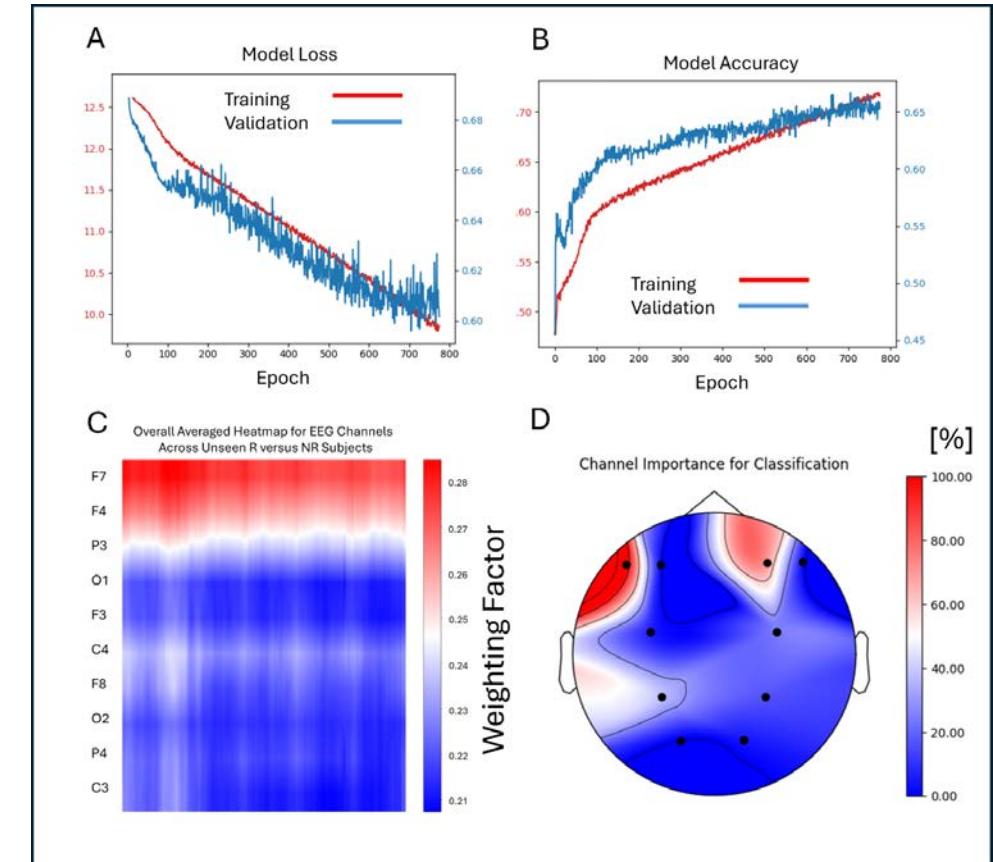
MDD around the world

- EEG datasets from 2x Canada (including Canbind), 2x Leipzig, 2 x Praha with > 250 MDD and >200 HC
 - All Patients treated with (es) citalopram
 - Outcome Data (MADRS or HDRS) available
 - Unification of EEG recordings across sites in preprocessing
-
- 1. Diagnostic Value of Deep Learning
 - 2. Prognostic Value of Deep Learning

Depression, EEG und Deep Learning



67% diagnostische Genauigkeit bei MDD versus HC



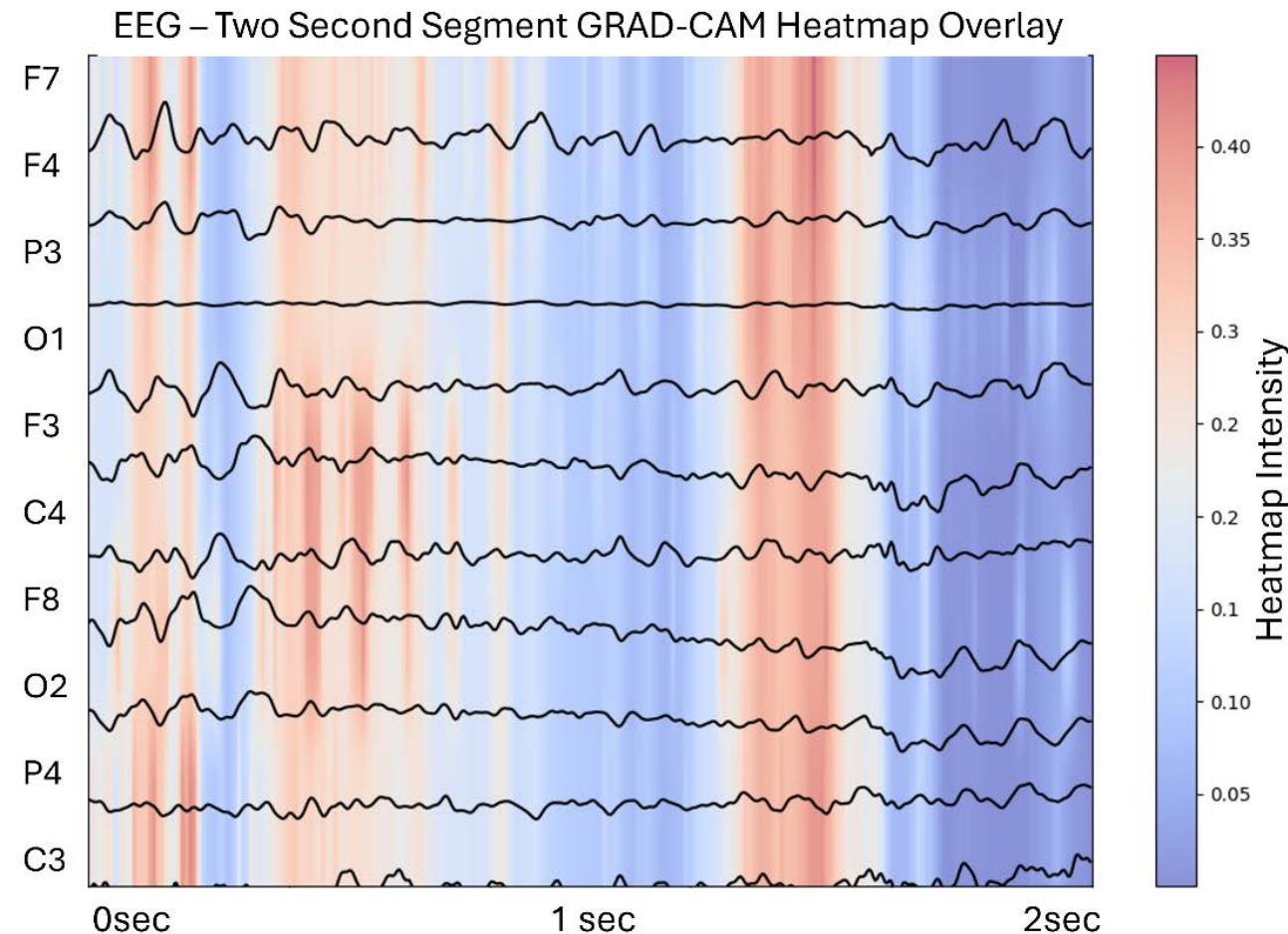
80% prädiktive Vorhersage für SSRI



Was sieht das
Netzwerk?

- „GRAD-CAM Methode“

Lernen von Deep Learning



Take Home

- Das EEG hat einen wichtigen Stellenwert in der Ausschlussdiagnostik in der Psychiatrie
 - Das EEG hat einen wichtigen Stellenwert beim Monitoring in der Psychiatrie (Medikamente, EKT)
 - Die EEG-Vigilanz korreliert mit psychopathologischen Syndromen
 - Das EEG bietet die Möglichkeit prädiktiver Marker, die eine Verbesserung der Behandlungseffizienz ermöglichen
 - Das EEG und Deep Learning bieten neue Möglichkeiten der Analyse neuronaler Aktivität
-



Merci!

Fragen?