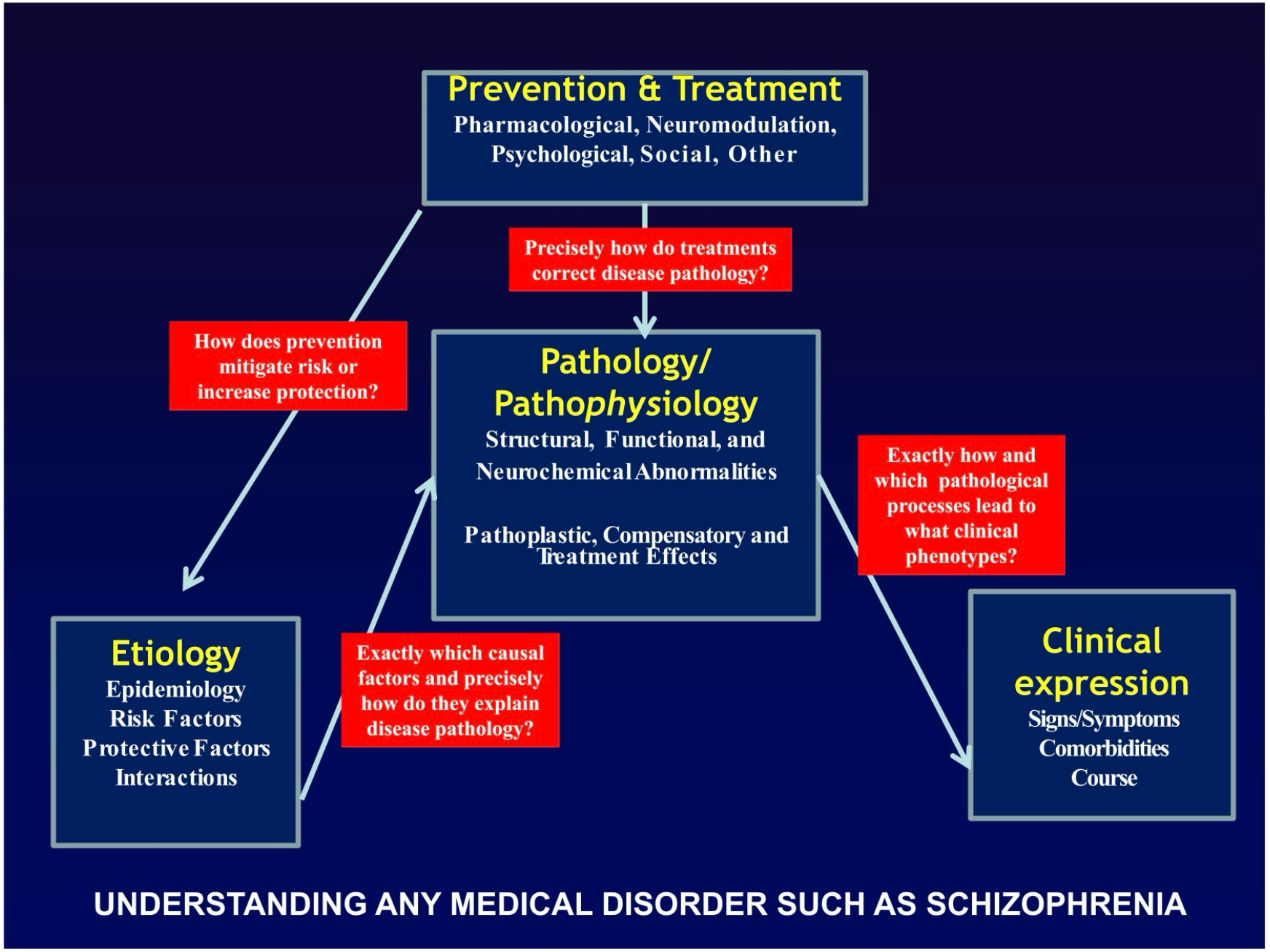
Zentralinstitut
für Seelische
Gesundheit

Biologische Grundlagen psychotischer Erkrankungen

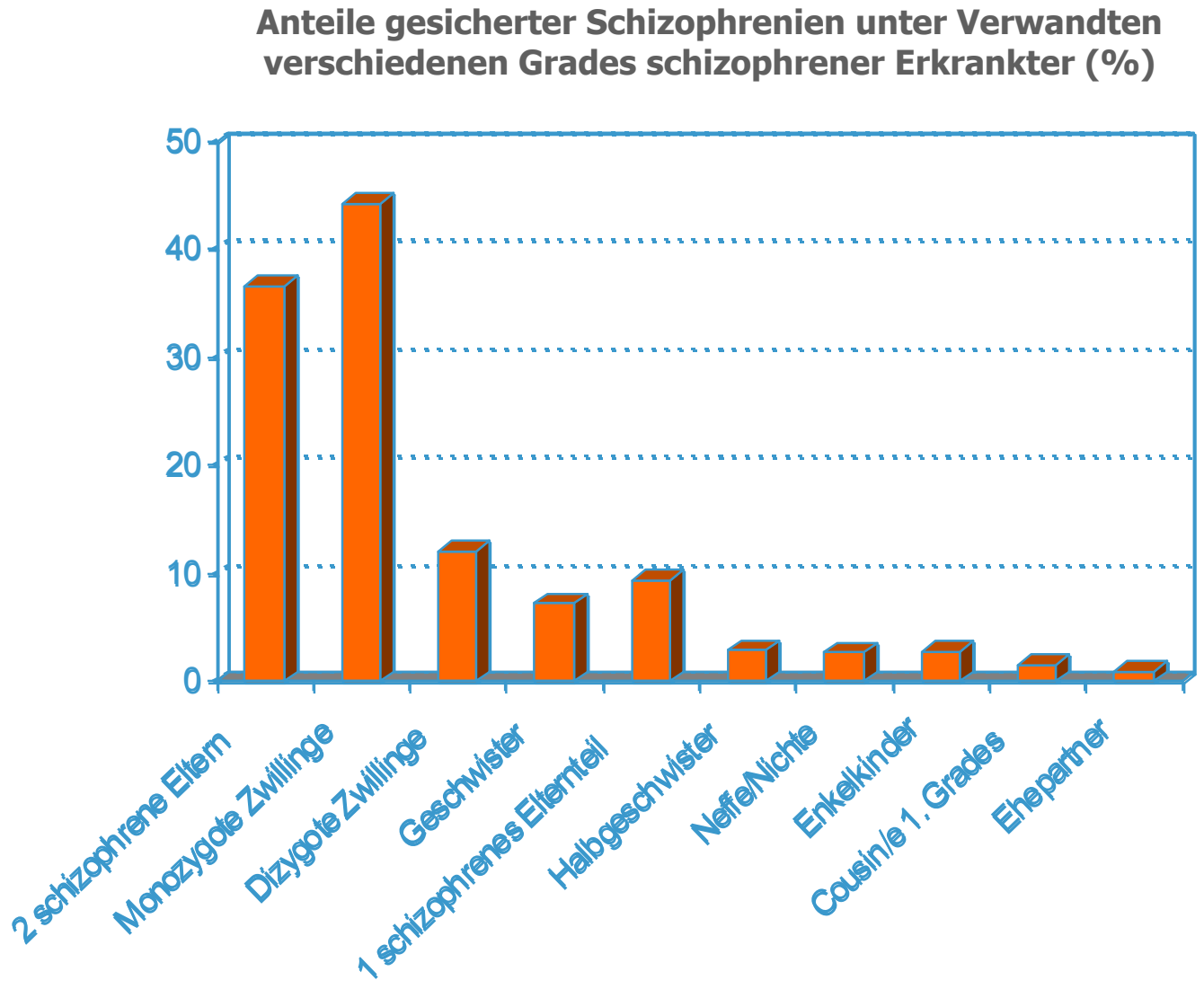
25. Vierwaldstätter Psychiatrietag, 05.2.2026

Andreas Meyer-Lindenberg



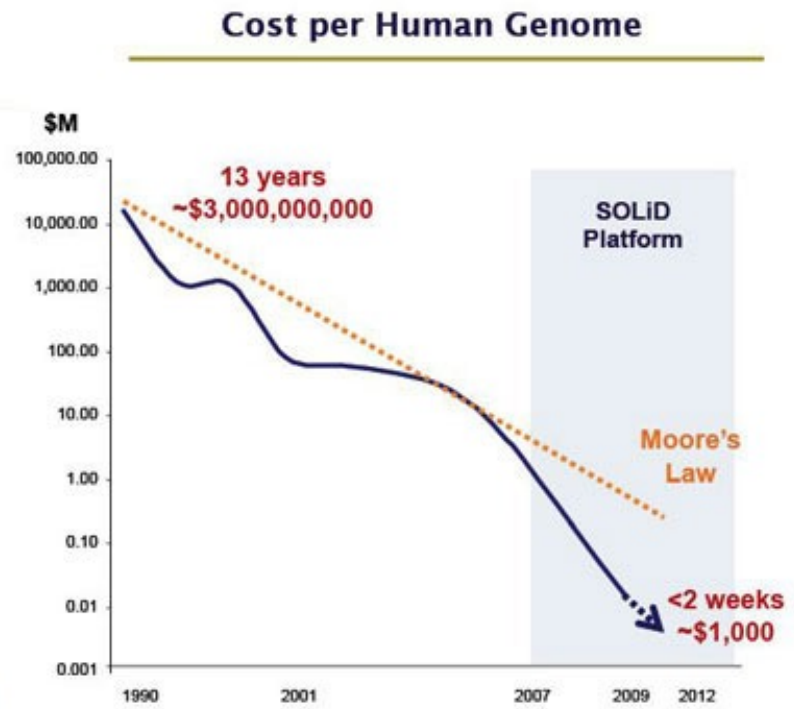
Tandon et al. **Schiz Res** 2024

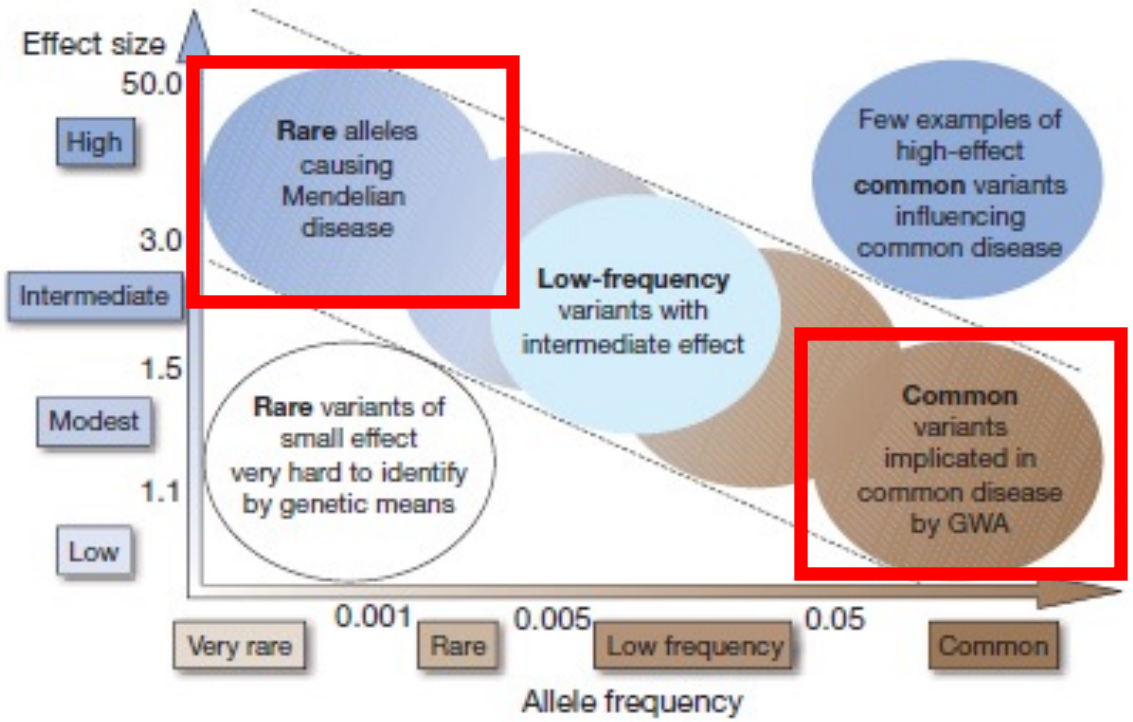
Neurogenetik



McGue & Gottesman 1991

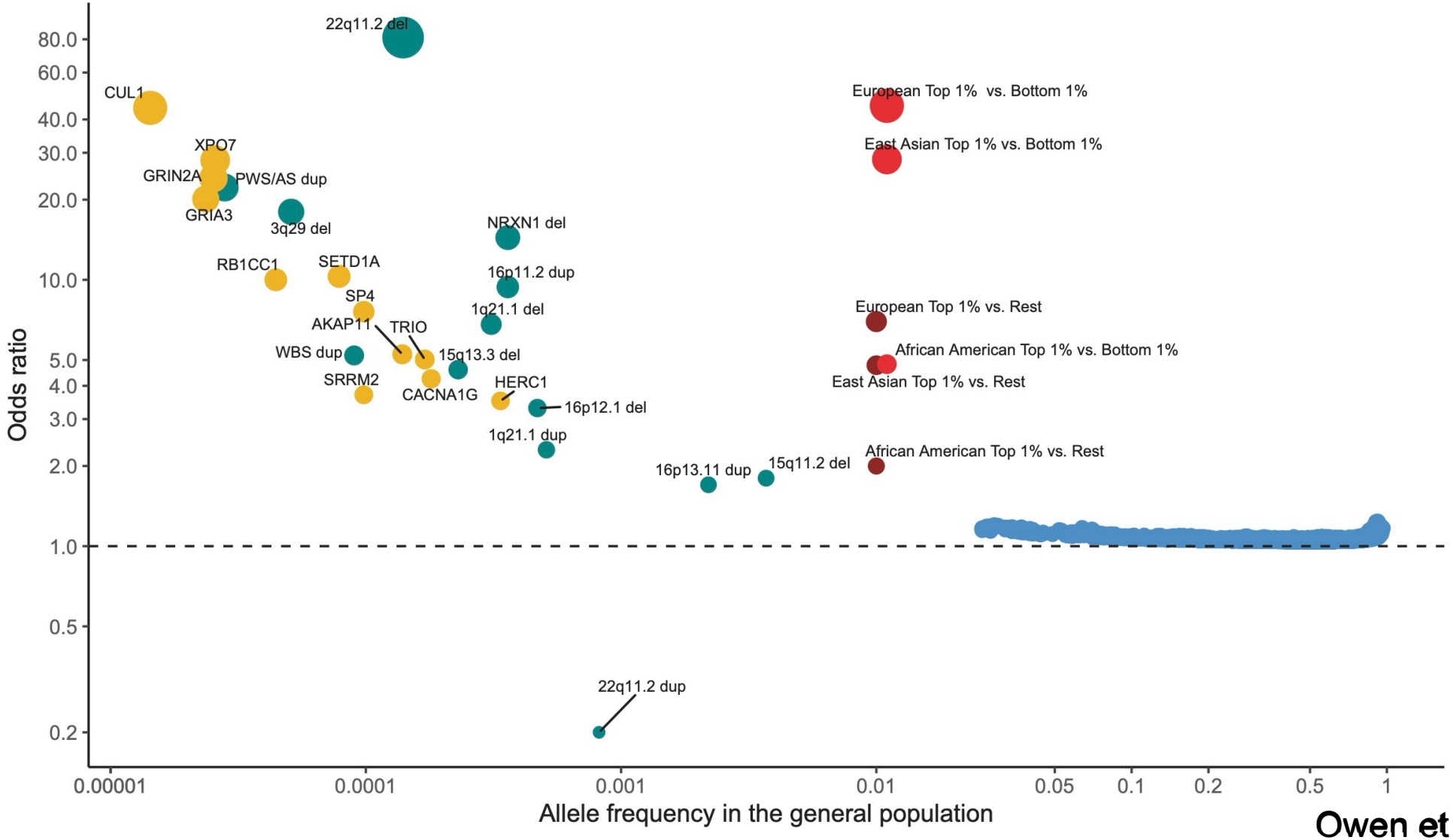
Genetik und Erkrankungsrisiko





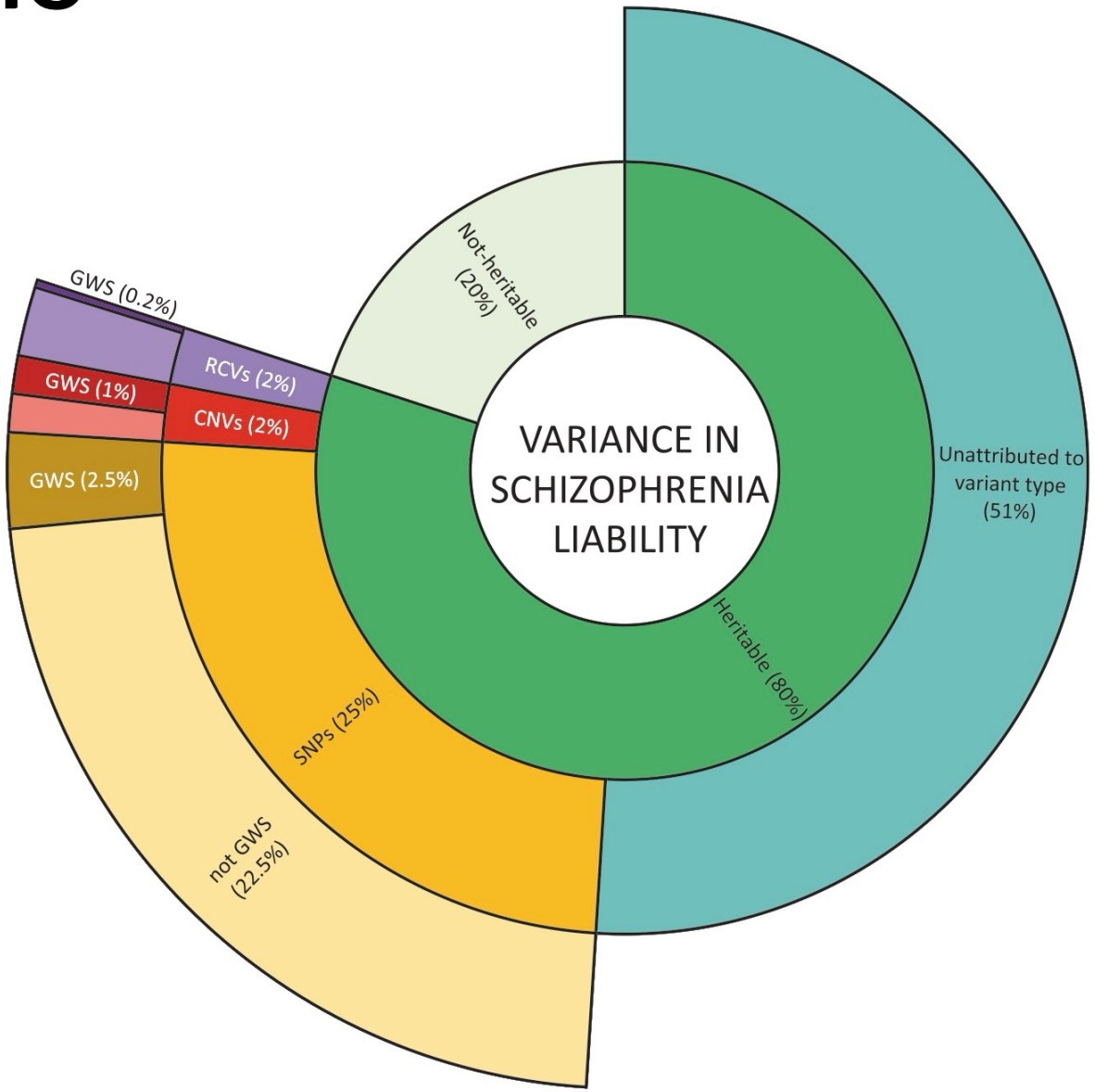
Manolio et al. **Nature** 2009

Genetische Risikoarchitektur der Schizophrenie



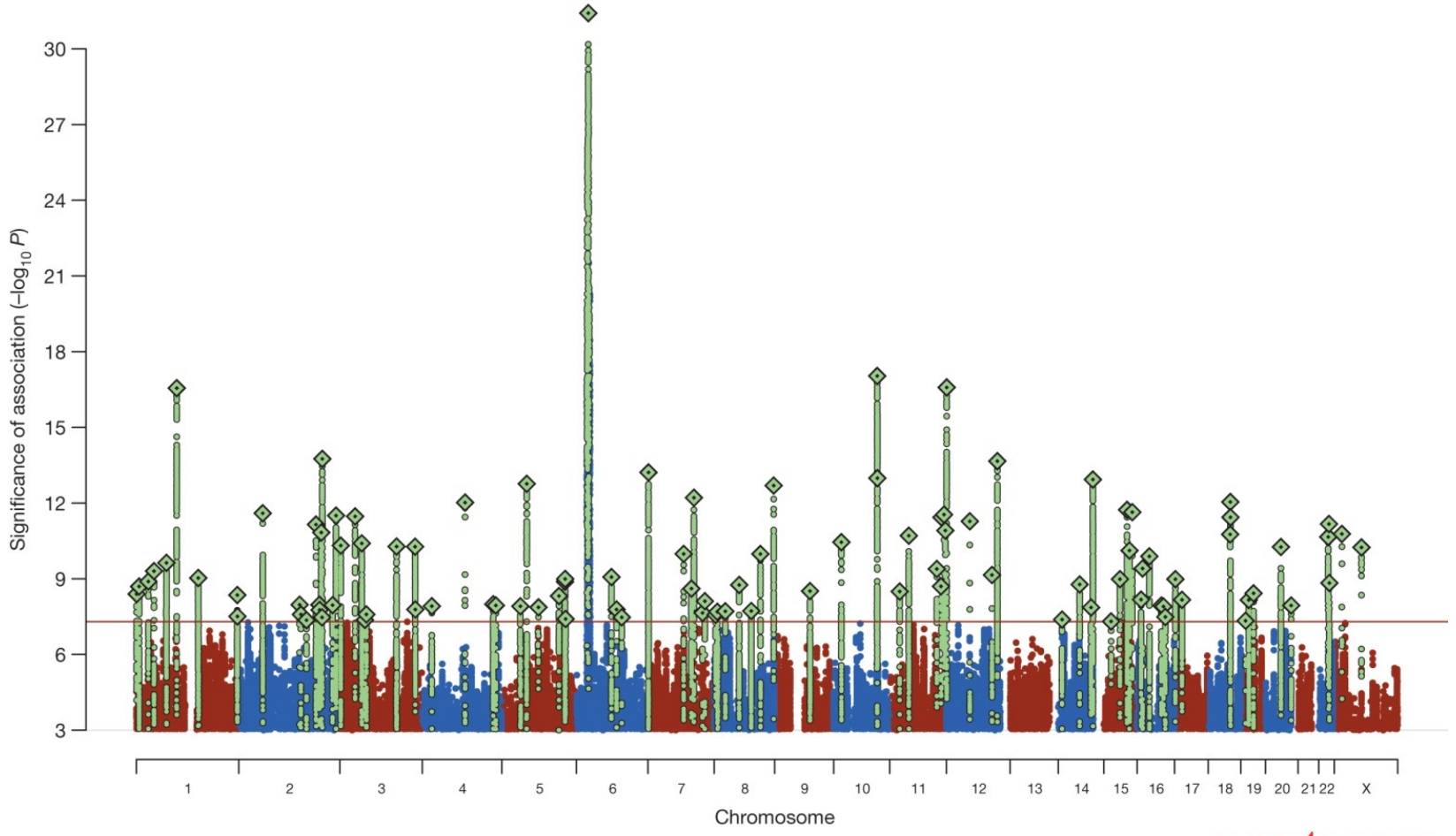
Owen et al. **Mol Psych** 2023

Genetische Risikoarchitektur der Schizophrenie



Owen et al. **Mol Psych** 2023

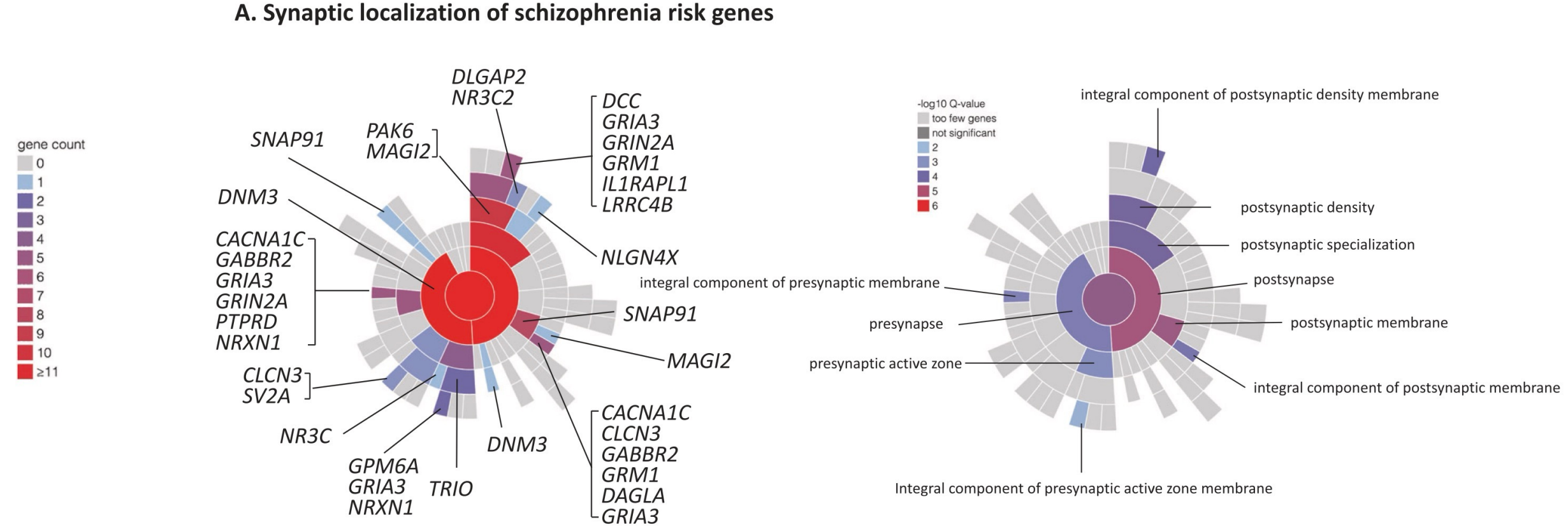
Genomweit signifikante häufige mit Schizophrenie assoziierte Varianten



S Ripke *et al. Nature* **000**, 1-7 (2014) doi:10.1038/nature13595

nature

Schizophrenie: eine Erkrankung der (Post-)synapsen



Owen et al. **Mol Psych** 2023

post mortem-Studien

- **Keine Gliose**, klinisch keine klaren Zeichen für Neurodegeneration
- **Reduziertes Neuropil**, synaptischer Apparat
- **Gestörte Zellreifung** und Zellmigration
- **Pathologie GABAerger** Interneurone
- **Differentielle Genexpression** (Regulatoren der Hirnentwicklung, Myelinisierung, synaptische Plastizität, GABAerge und glutamaterge Neurotransmission)
- CAVE: Konfundierende pharmakogene Effekte

Zelluläre Pathologie

Prenatal disturbances of nerve cell migration in the entorhinal region: a common vulnerabilitv factor in functional psvchoses?

J Neural Transm [GenSect] (1991) 84: 155–164

Rapid Communication

H. Beckmann[1] and **H. Jakob**[2]

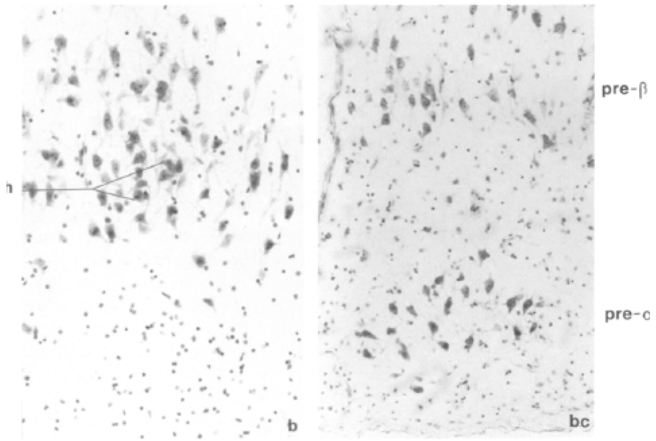


Fig. 2. *Case 2.* Coronal sections through the right temporal lobe; the parahippocampal gyrus with central and lateral fields of the entorhinal region; (**a**) view upon the superior section of the rostral fields at the level of amygdaloid nucleus. Disturbed architecture, particularly in the layers II and III. Absence of the layer II. Nissl (20 μ) × 31; (**ac**) control showing the normal cytoarchitecture at the same level; Nissl (20 μ) × 31; (**b**) magnification of the layers II pre-α, III pre-β. Disturbed architecture of the upper layers. In the layer III pre-β heterotopic group of neurons (h); the layer II pre-α does not show the characteristic neuronal insular formation; Nissl (20 μ) × 220; (**bc**) control: normal structure of the upper layers at the same level; Nissl (20 μ) × 220

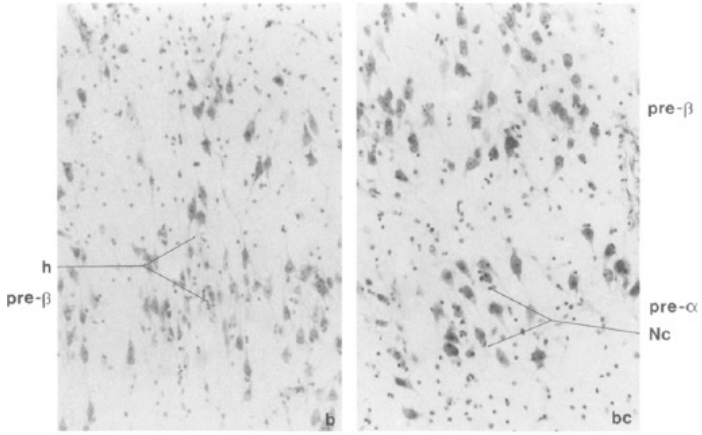


Fig. 1. *Case 4.* Coronal sections through the parahippocampal gyrus of the left temporal lobe; (**a**) rostral part of the entorhinal region at the level of the amygdaloid nucleus. Poorly developed layers and disturbed structure of the layer II pre-α. Nissl (20 μ) × 25; (**ac**) control of the cytoarchitecture at the same level; pre-α – pri-α: layers II–IV. Designation of the layers according to Rose (1927). Nissl (20 μ) × 25; (**b**) magnification of the layers pre-α, pre-β; disarranged layer pre-α. The neuronal insular formation in layer pre-α is lacking; heterotopic group of nerve cells (h) in layer pre-β. Note the diminished volume of these neurons. Nissl (20 μ) × 220; (**bc**) magnification of the layers pre-α and pre-β with normal structure. Note the island structure of nerve cells (Nc) in pre-α. Nissl (20 μ) × 220

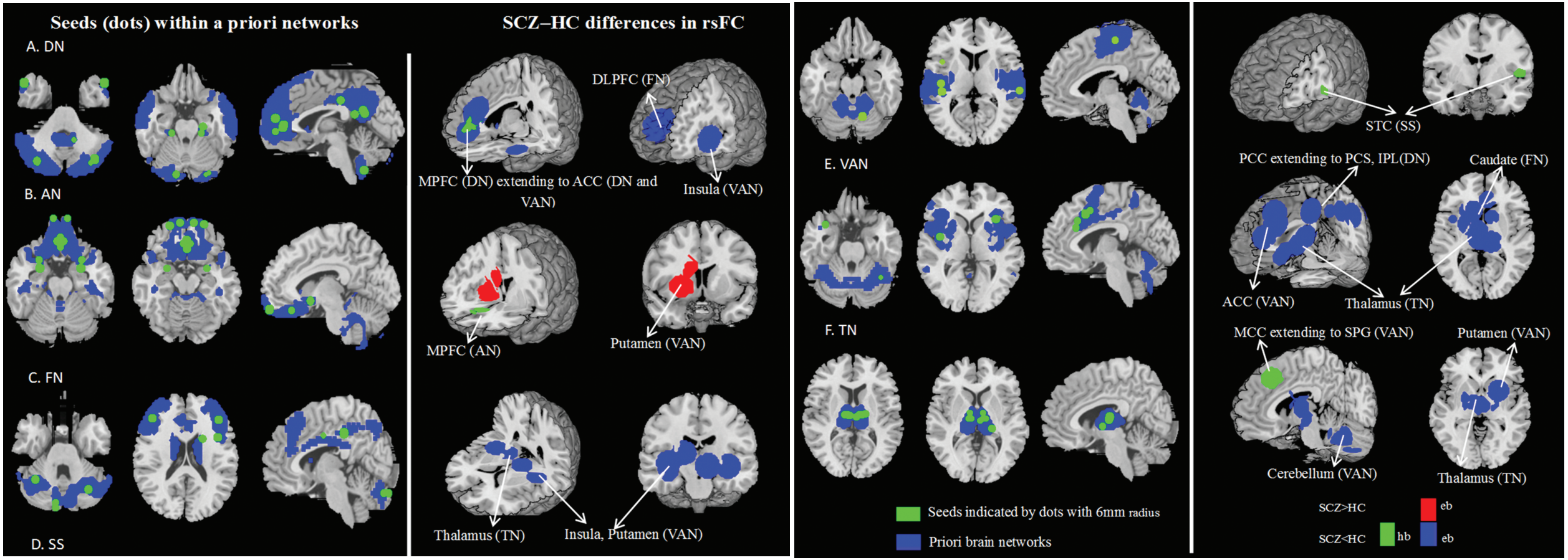
Störungen der Konnektivität bei Schizophrenie

Lokalisierte Hirnveränderungen sind subtil, aber Symptomatik meist massiv ->

Störung der Interaktion von Hirnarealen

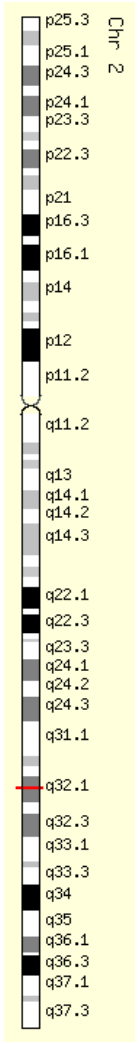
Verminderte Konnektivität

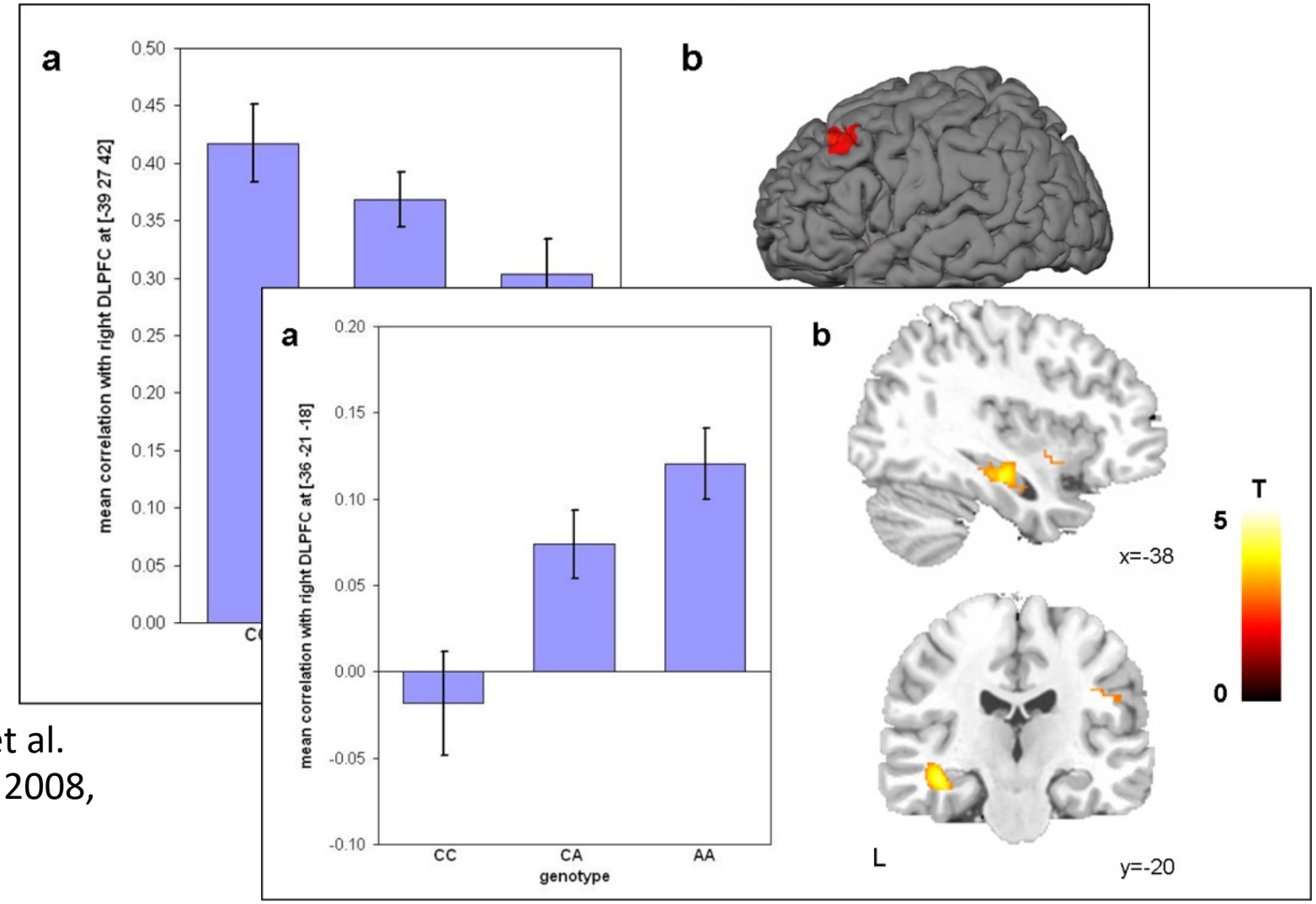
default mode (DN, self-related thought), affective network (AN, emotion processing), ventral attention network (VAN, processing of salience), thalamus network (TN, gating information) and somatosensory network (SS)



Dong et al. Schiz Bull 2017

ZNF804A und Schizophrenie

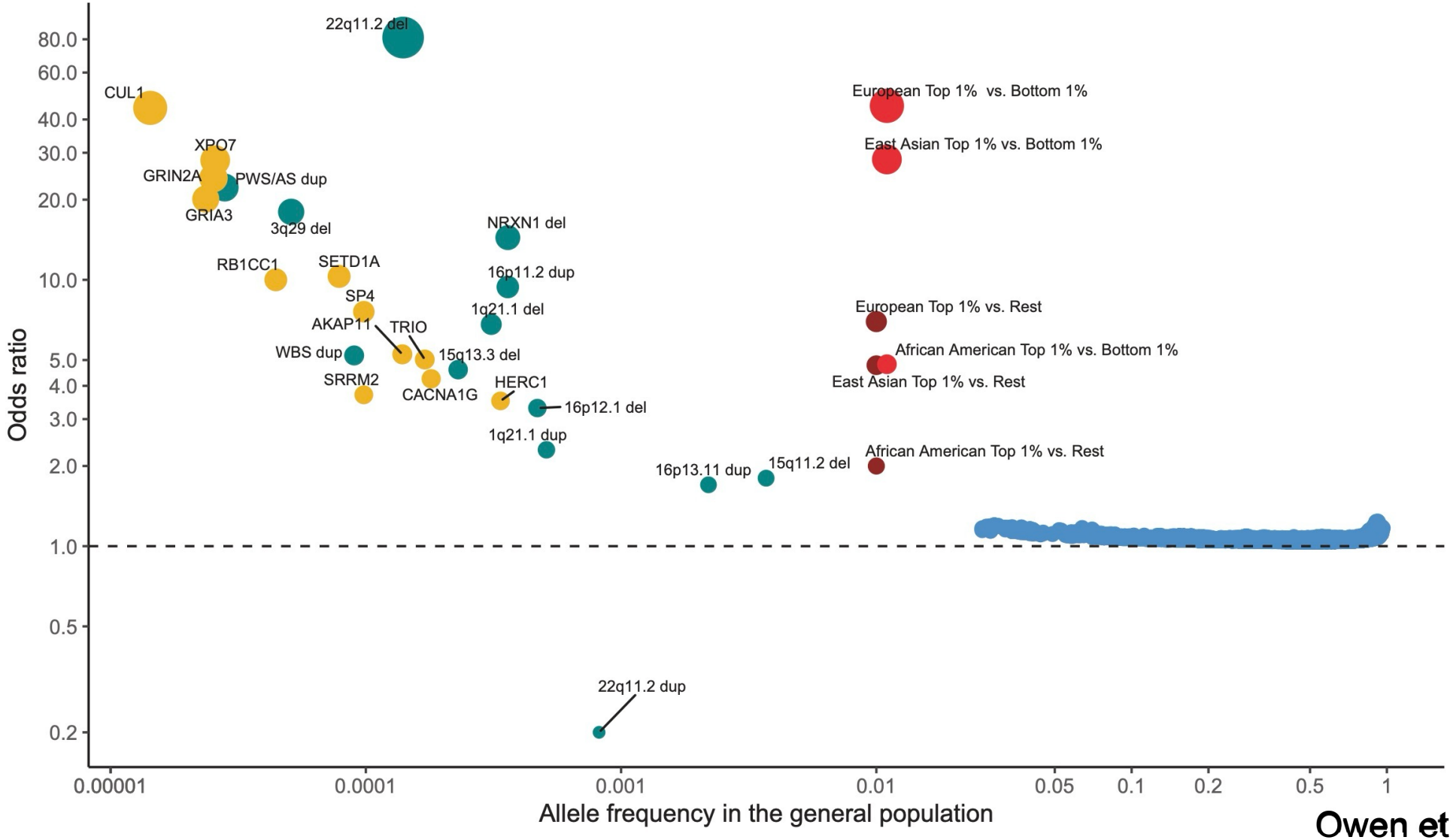




O'Donovan et al. **Nat Genetics** 2008,
Purcell et al, **Nature** 2009,
Riley et al. **Mol Psych** 2009, u.a.

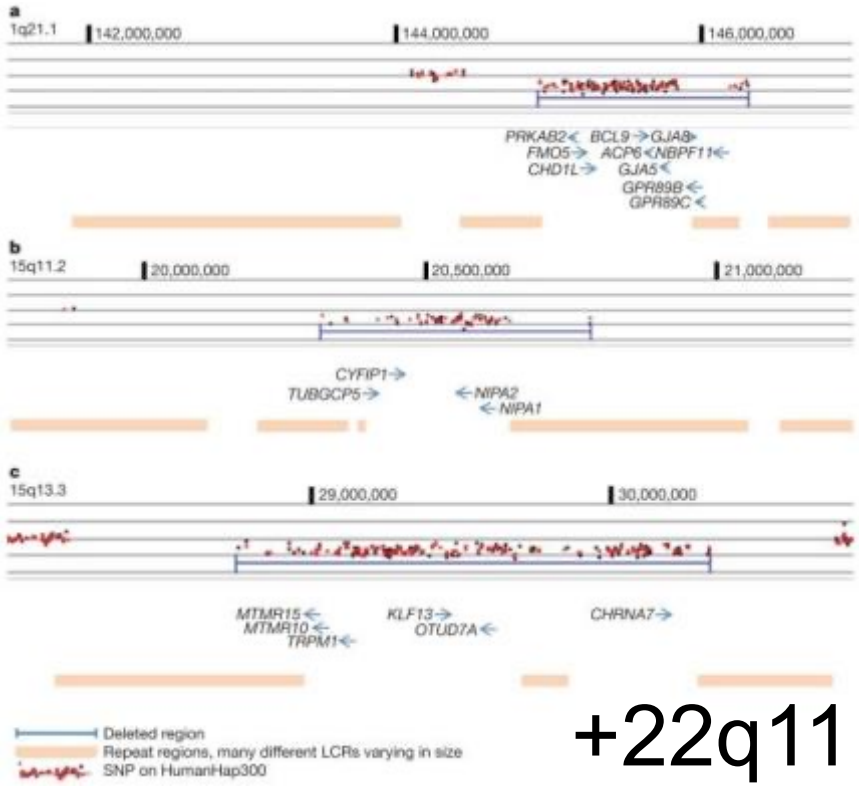
Esslinger*, Walter*, Kirsch* et al. **Science** 2009

Genetische Risikoarchitektur der Schizophrenie



Owen et al. **Mol Psych** 2023

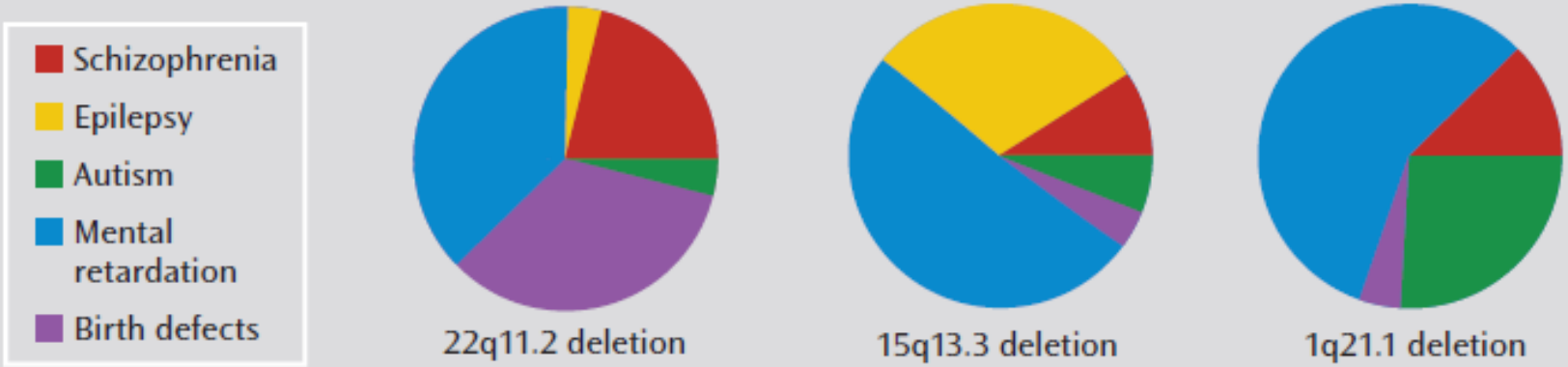
Hochrisikovarianten: CNVs



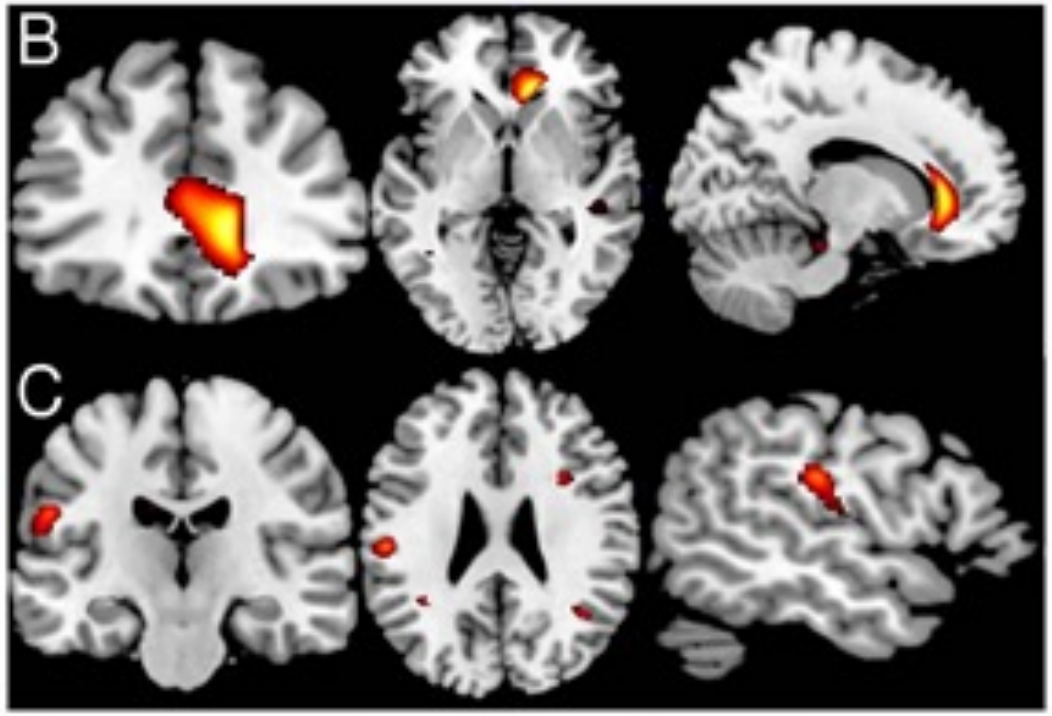
+22q11

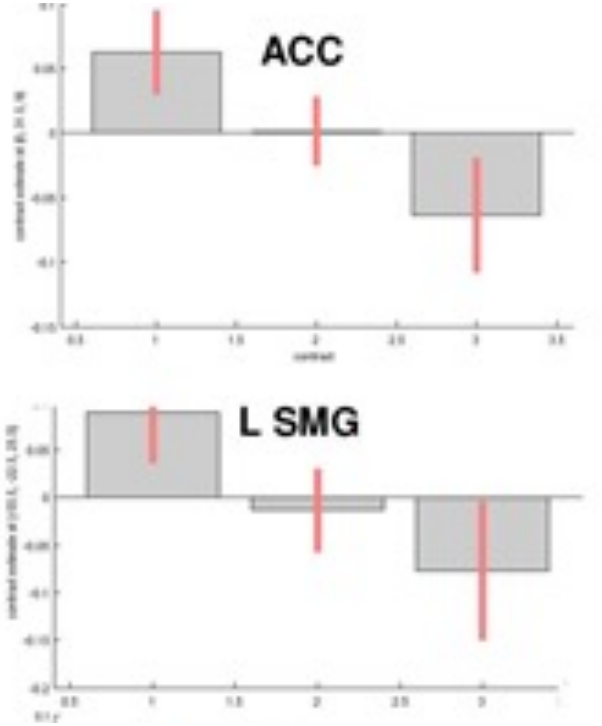
Steffanson et al. **Nature** 2008,
Walsh **Science** 2008,
International Schizophrenia Consortium **Nature** 2008

Bassett et al. **Am J Psychiat** 2010 Core phenotypes differ for specific CNVs



15q11.2 und Hirnstruktur



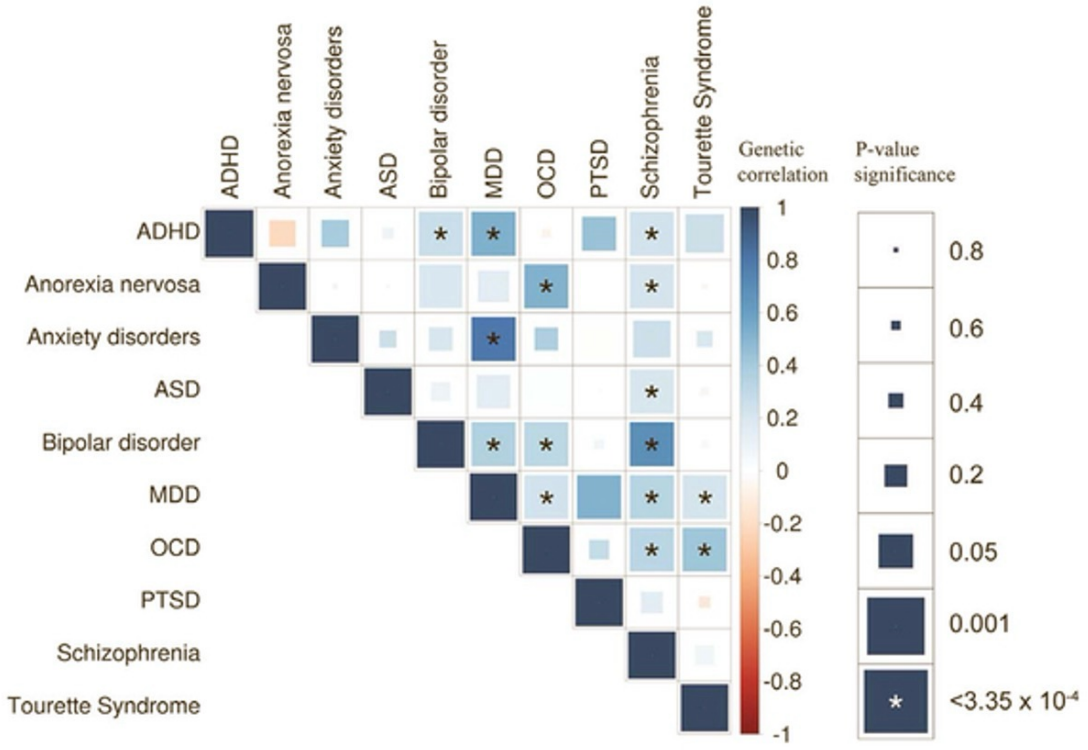


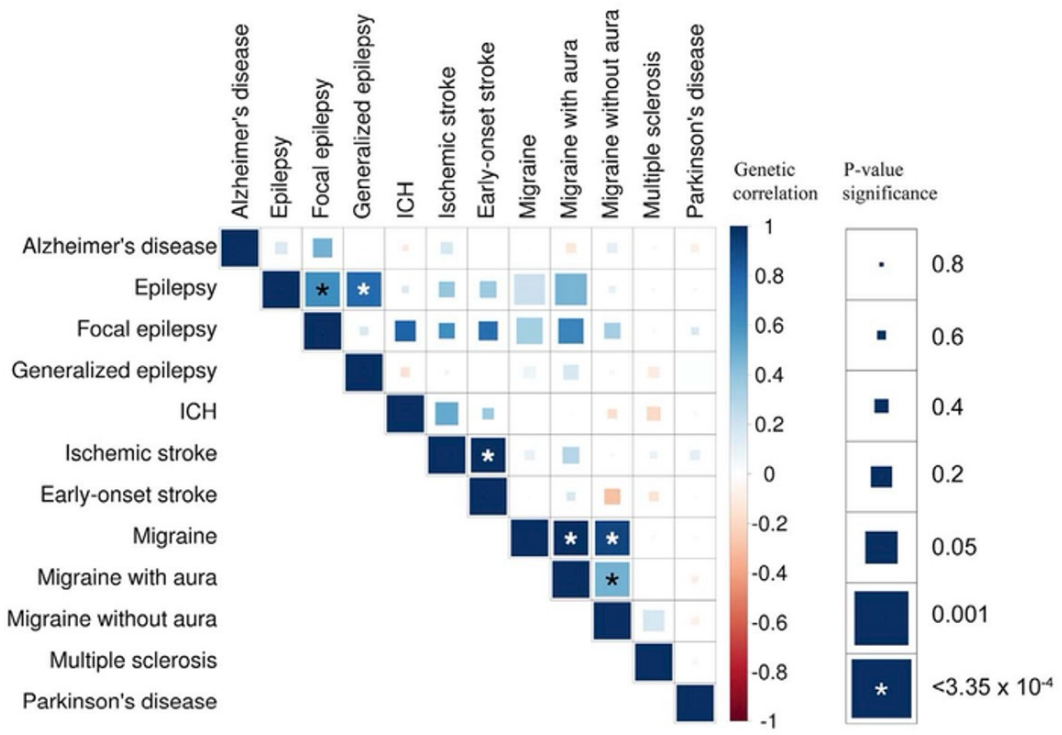
Grey matter, 15q11.2
duplication > controls > deletion

p<0.05, FWE corrected in mask (GM)

Stefansson*, Meyer-Lindenberg*, et al. **Nature** 2014

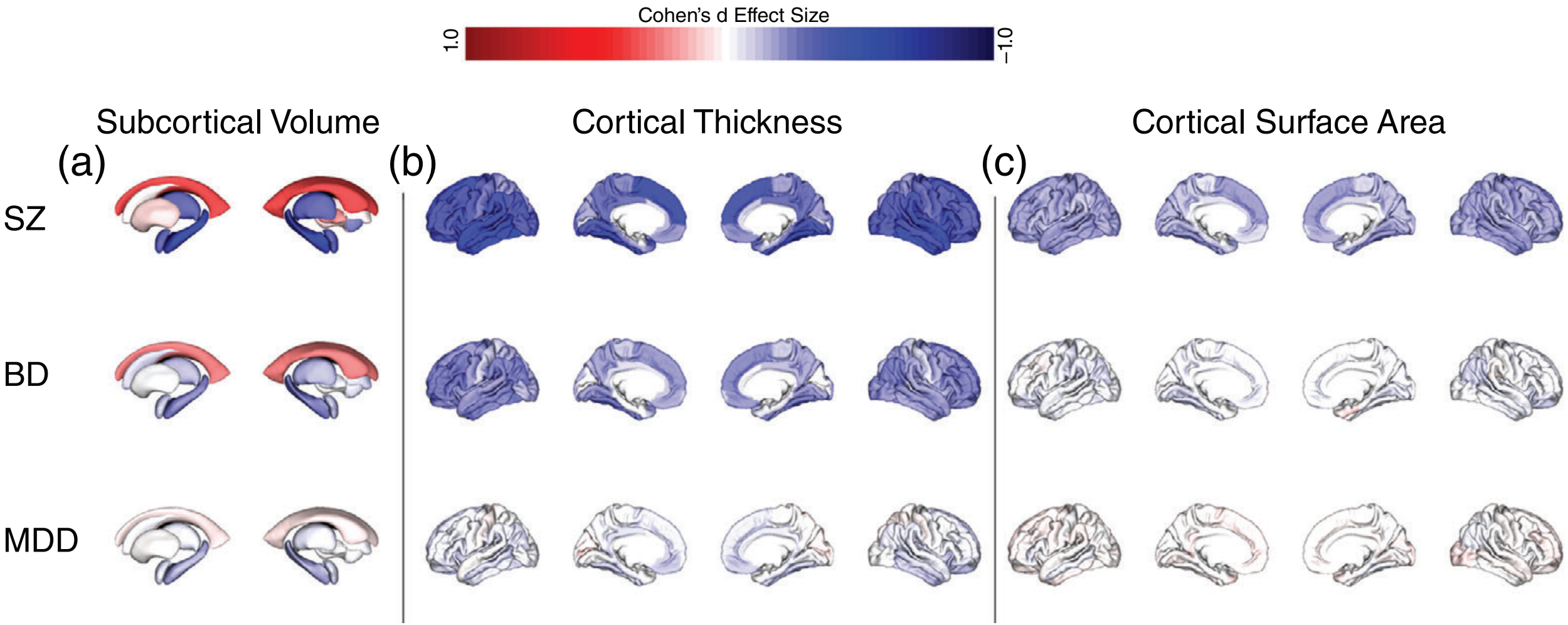
Genetisches Risiko: Pleiotropie





Brainstorm Consortium et al. **Science** 2018

Reduktion des Hirnvolumens

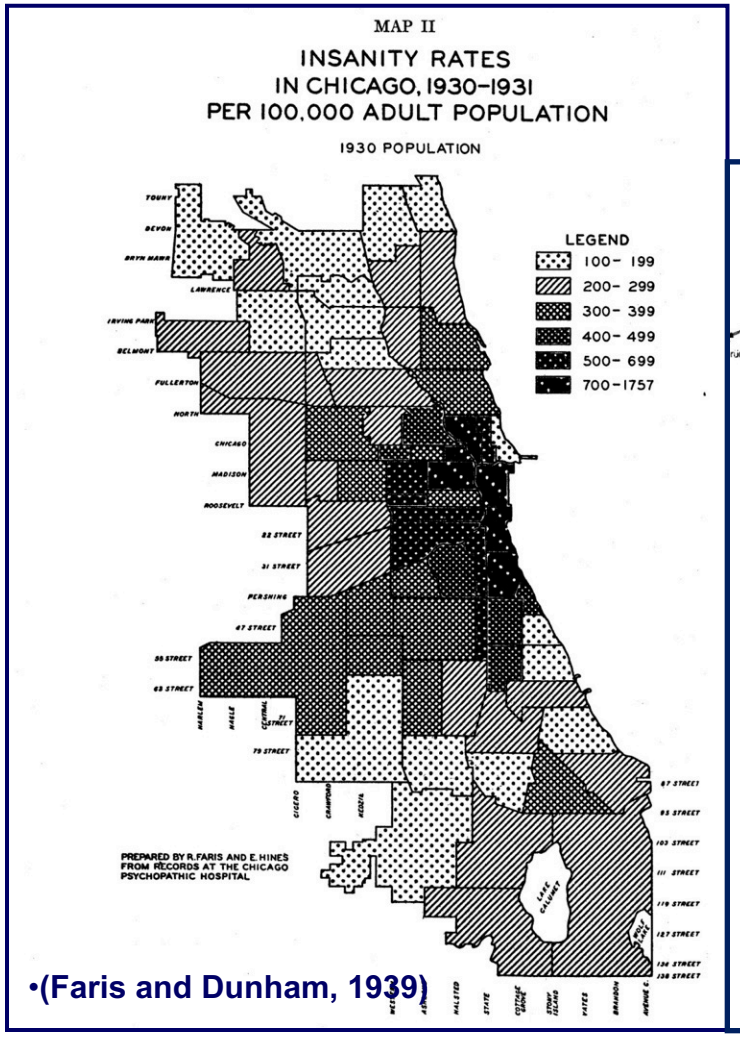


Cheon et al. Psychiat Clin Neurosci 2022

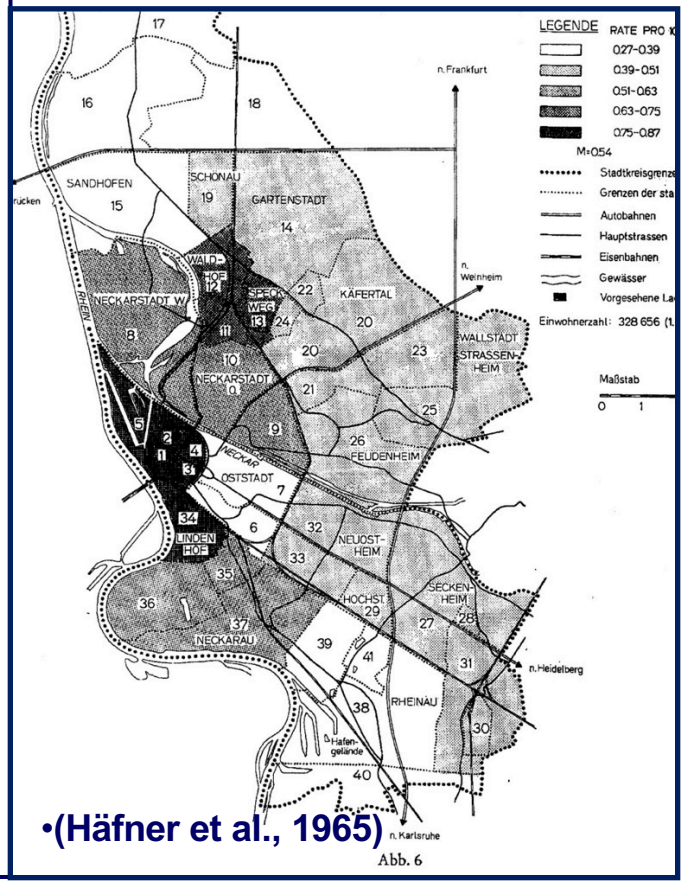
Umweltrisiken

Van Os et al., **Nature** 2010

Urbanicity and mental illness

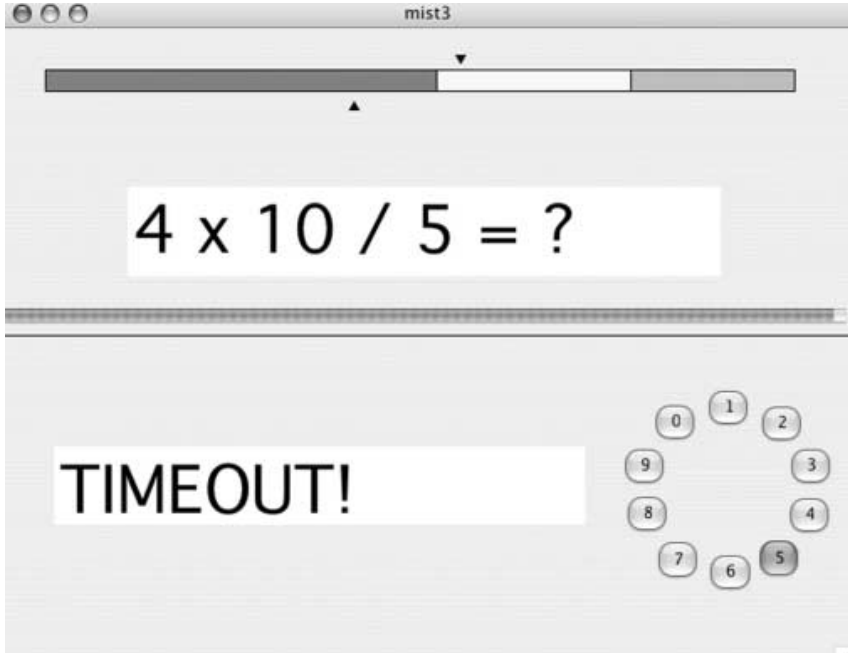


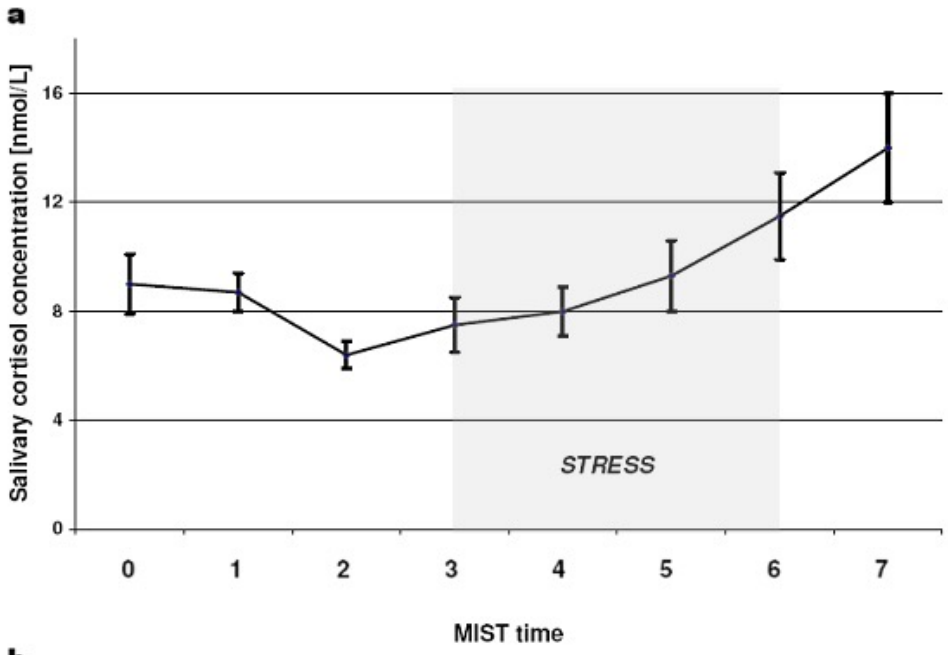
•(Faris and Dunham, 1939)

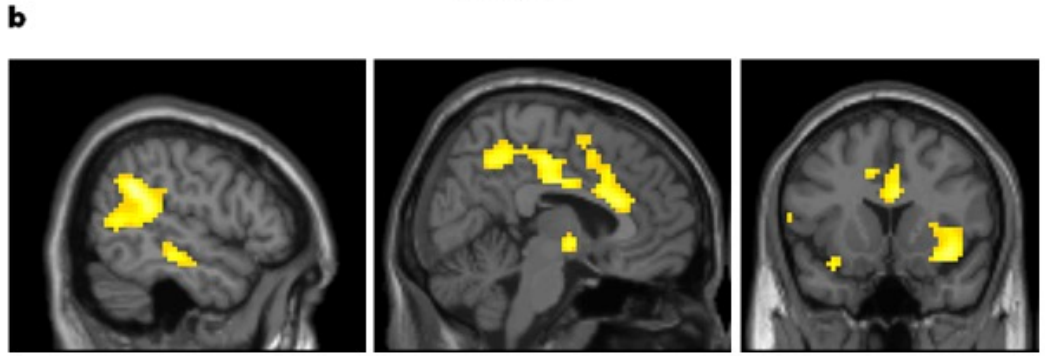


•(Häfner et al., 1965)

Montreal Imaging Stress Task

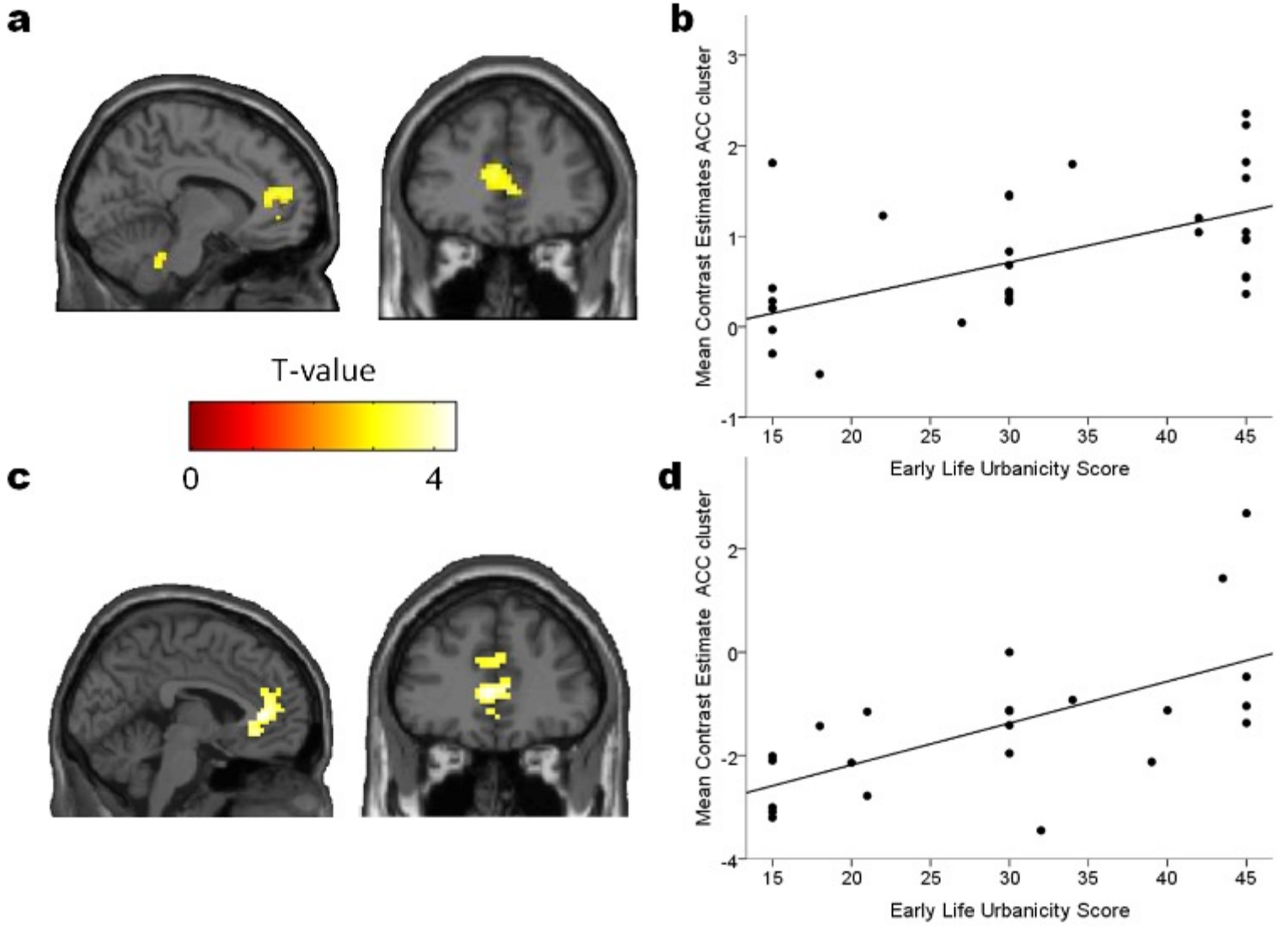






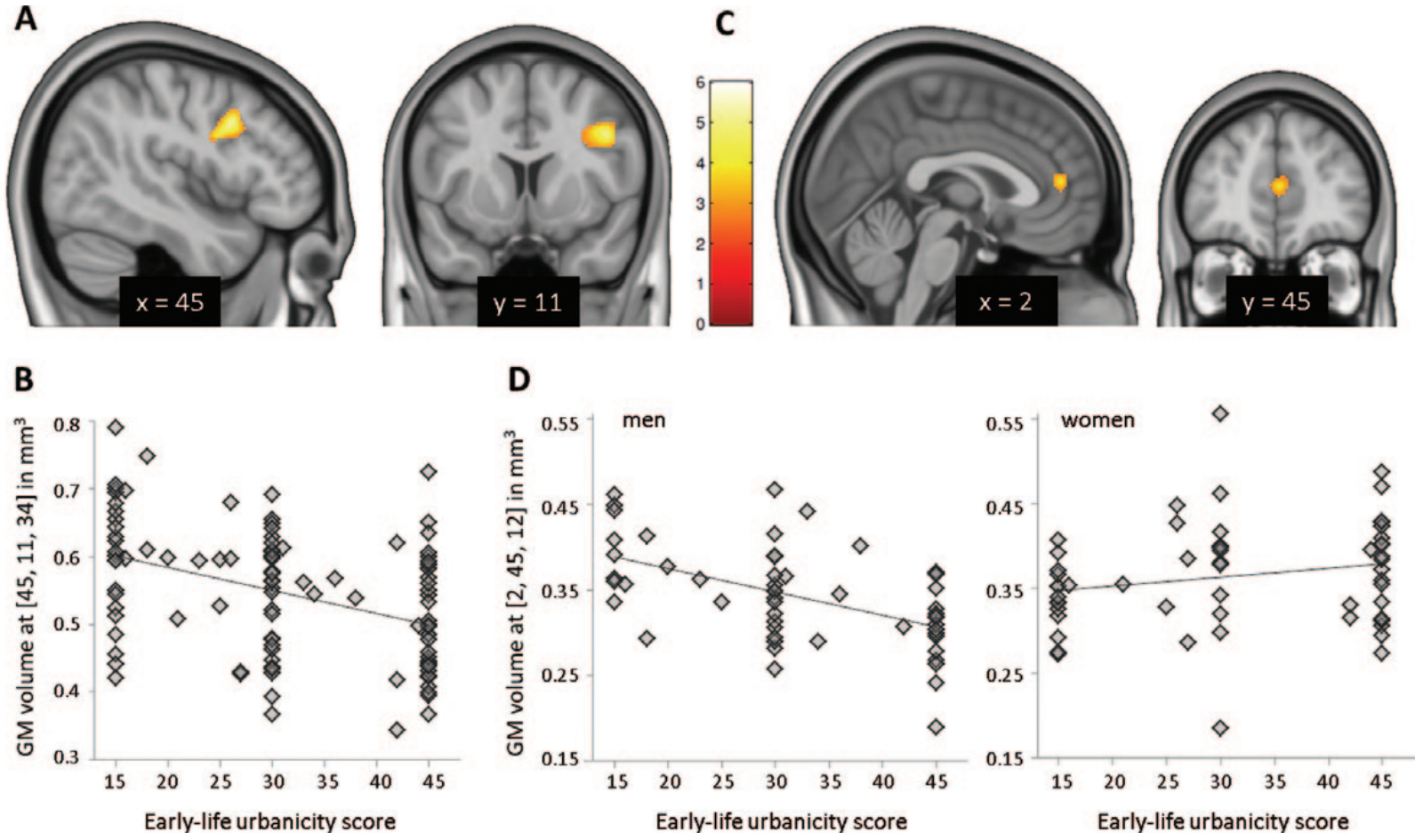
Lederbogen, Kirsch, Haddad et al., **Nature** 2011

Stadtgeburt und Zingulum



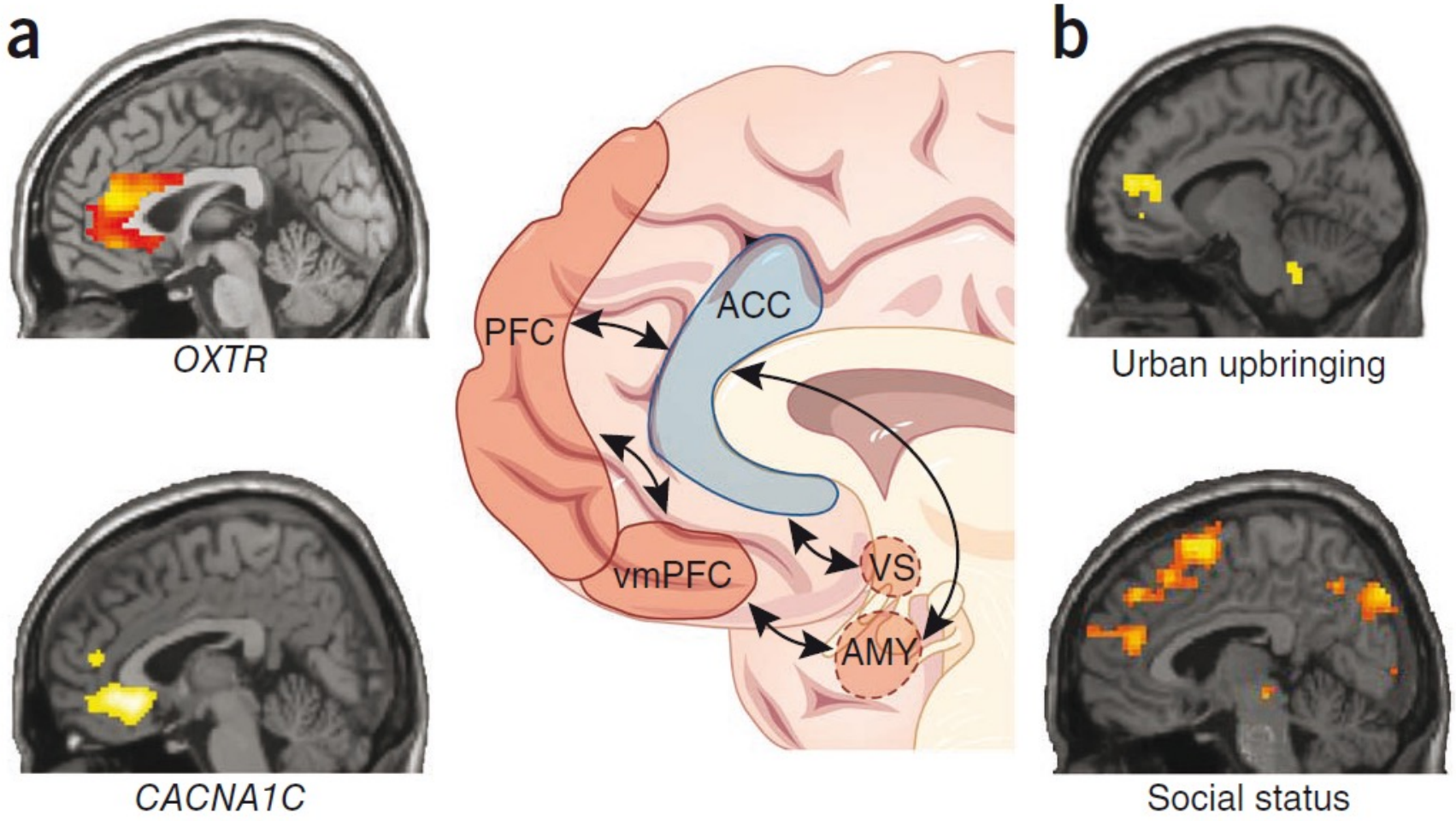
Lederbogen, Kirsch, Haddad et al., **Nature** 2011

Stadtgeburt und Hirnstruktur



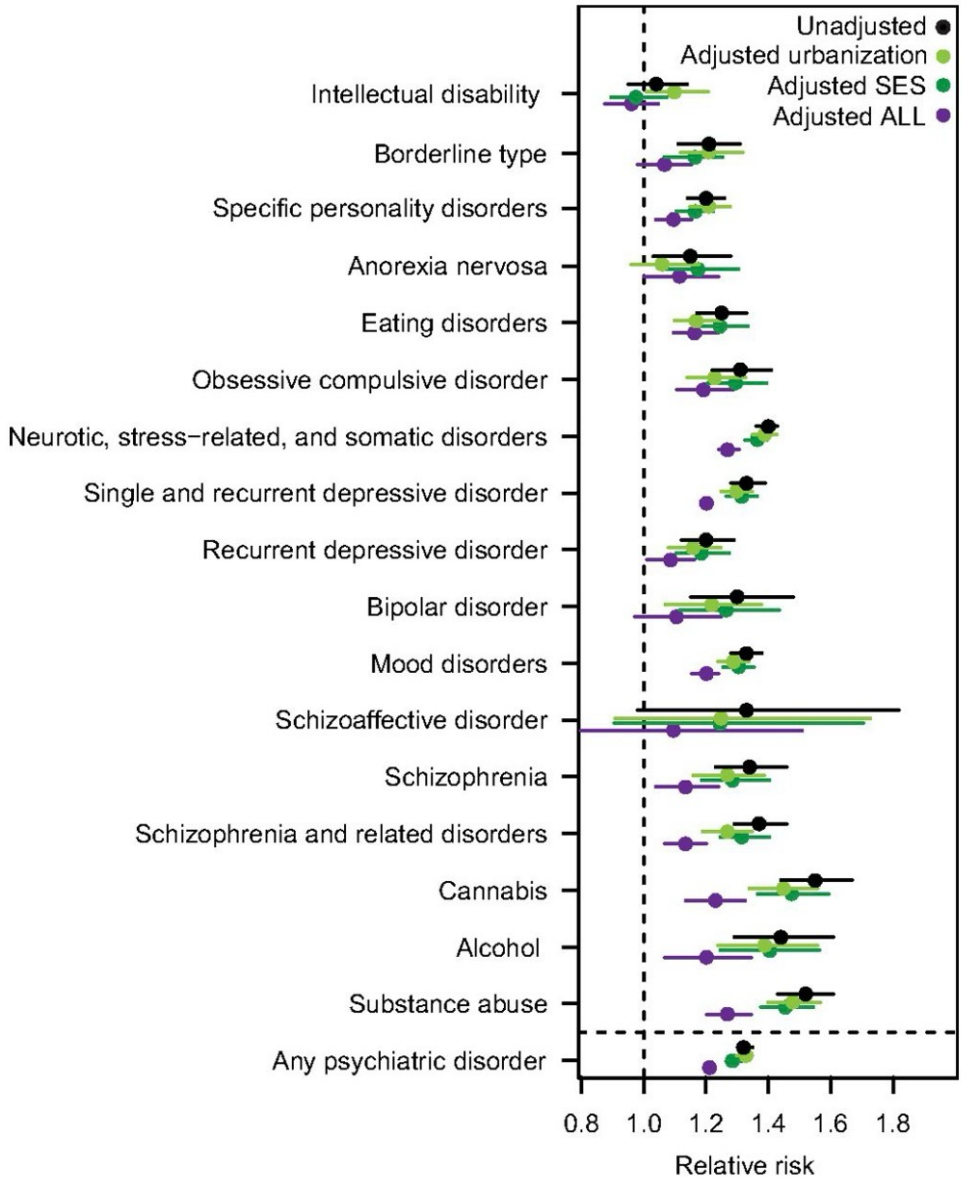
Haddad et al., **Schiz Bull** 2014

Konvergenz von genetischem- und Umweltrisiko



Meyer-Lindenberg and Tost **Nat Neurosci** 2012
Tost et al **PNAS** 2010; Erk*, Meyer-Lindenberg* et al. **Arch Gen Psychiat** 2010,
Zink et al. **Neuron** 2008; Lederbogen*, Kirsch*, Haddad* et al. **Nature** 2011

Umweltrisiko Pleiotropie



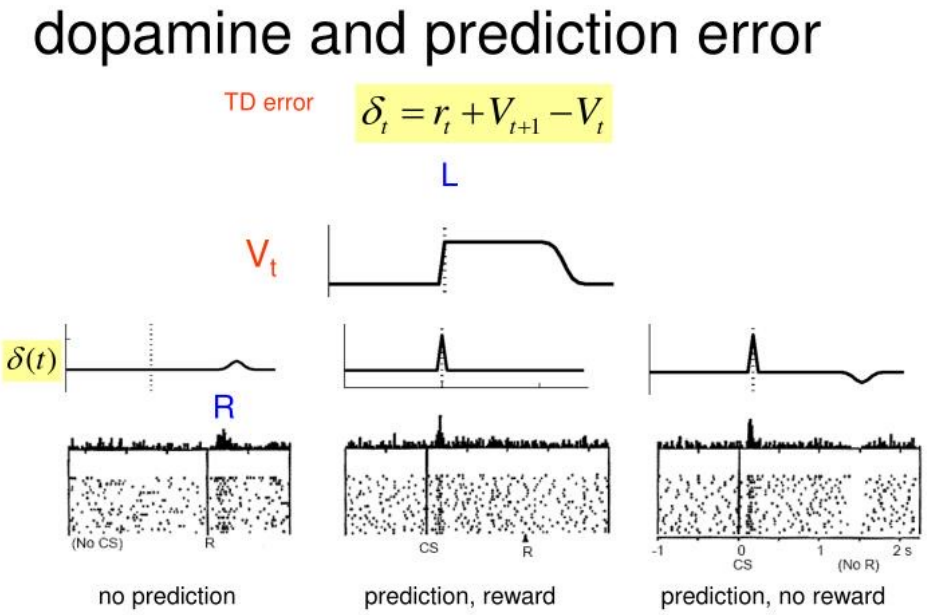
Kristine Engemann et al. PNAS 2019;116:11:5188-5193

Dopamin im Striatum

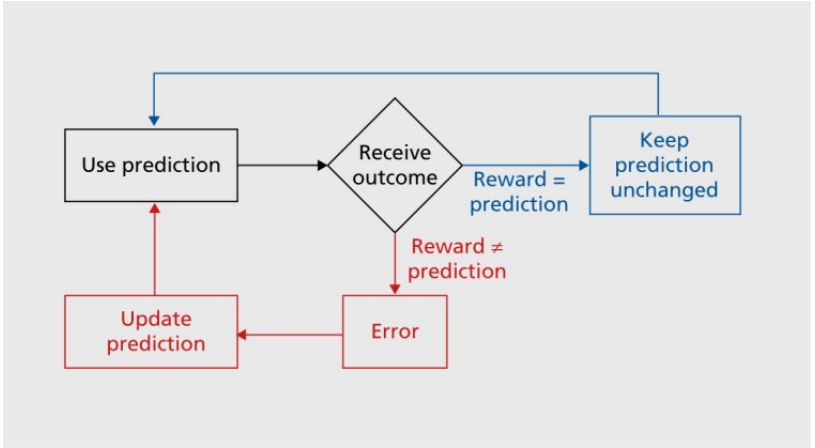
- Presynaptic: increased synthetic capacity (F-DOPA) (Effect size 0.79, $p < 0.001$) (but half of patients have normal values) with normal synaptic integrity (DAT)
- Postsynaptic:
  - increased dopamine $D_{2/3}$ occupancy (d=0.26, medication confound) (half of patients have normal occupancy)
  - Drug $D_{2/3}$ occupancy linked to antipsychotic dose
  - D_1 unclear picture

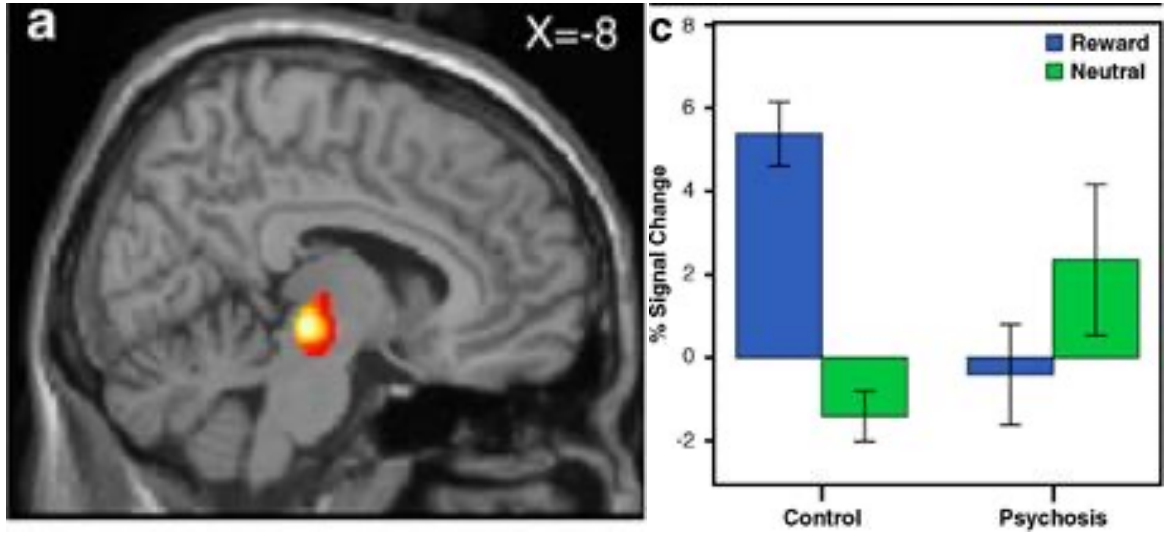
Cumming et al. Behav Brain Res 2021

Dopamin und Wahn



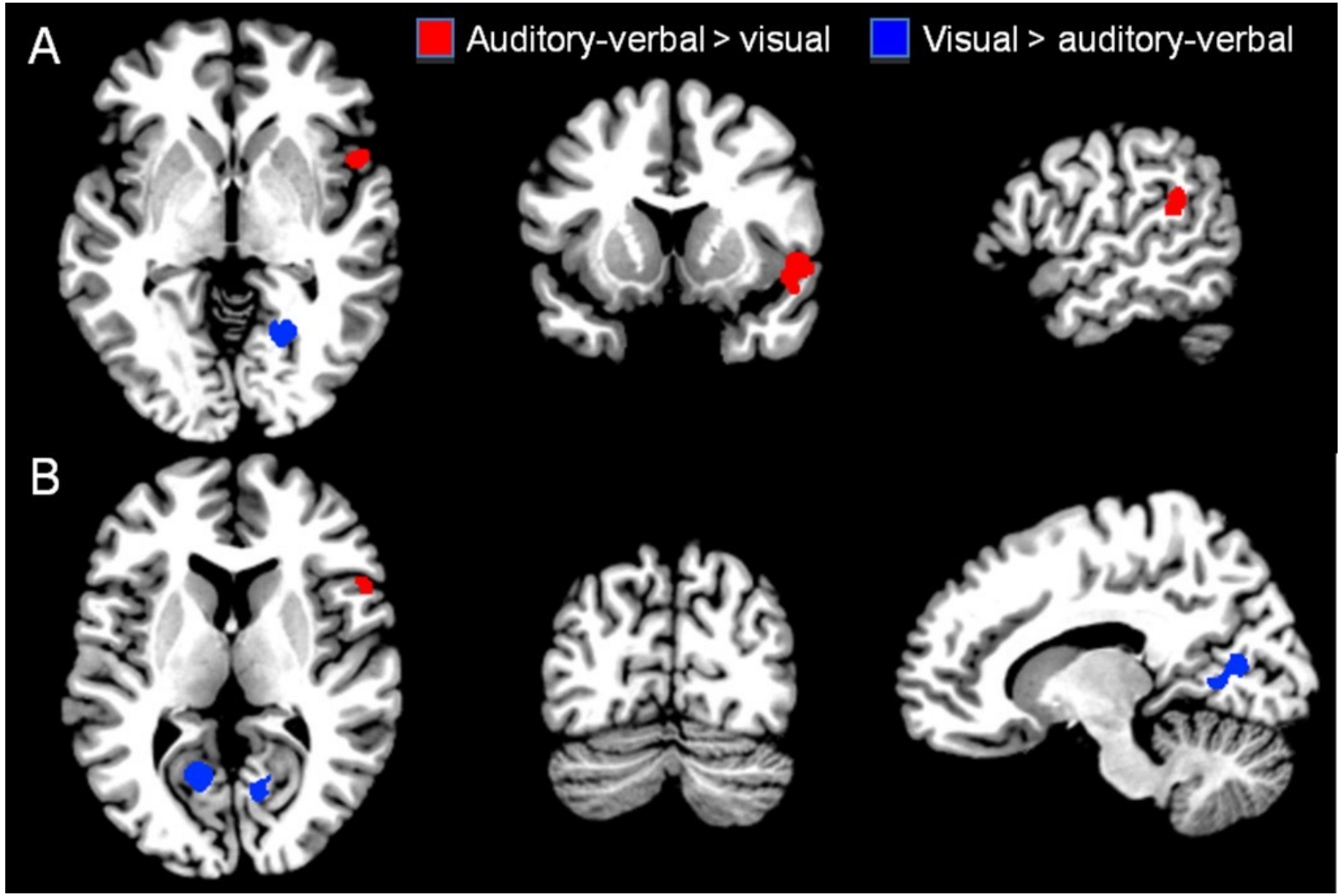
Schultz et al **Science** 1997





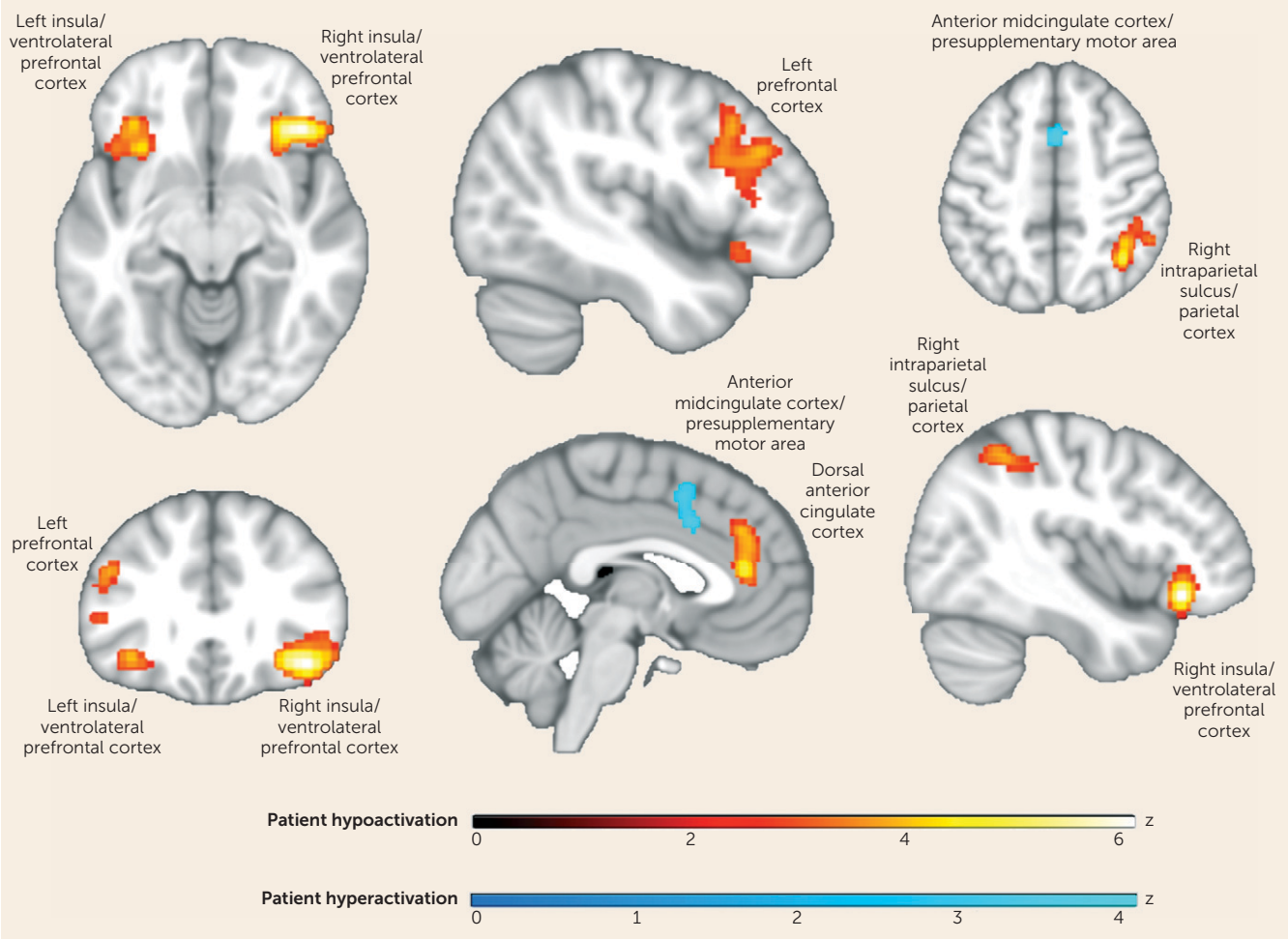
Murray et al **Mol Psychiatry** 2008

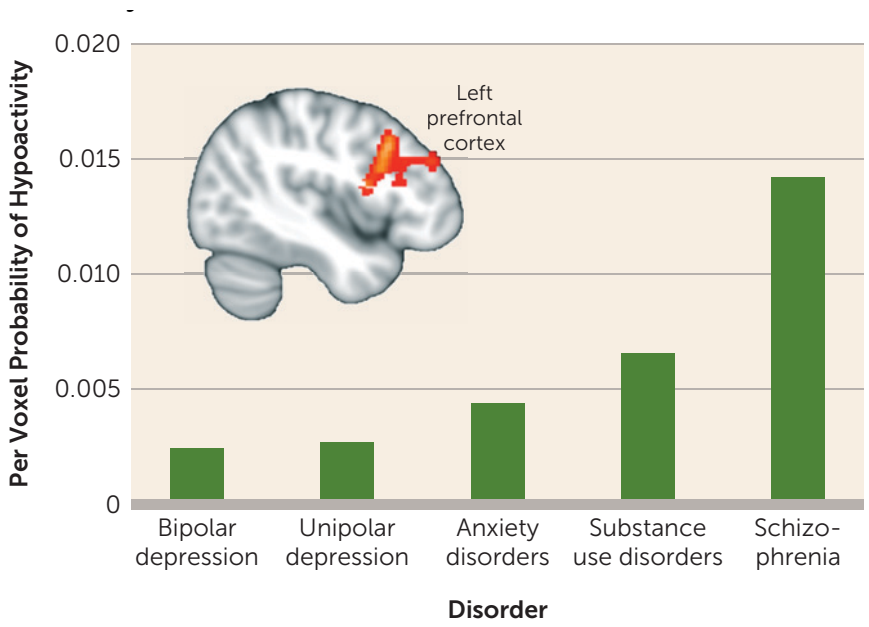
Halluzinationen und primäre sensorische Areale



Zmigrod et al.
Neuroscie Behav Rev
2016

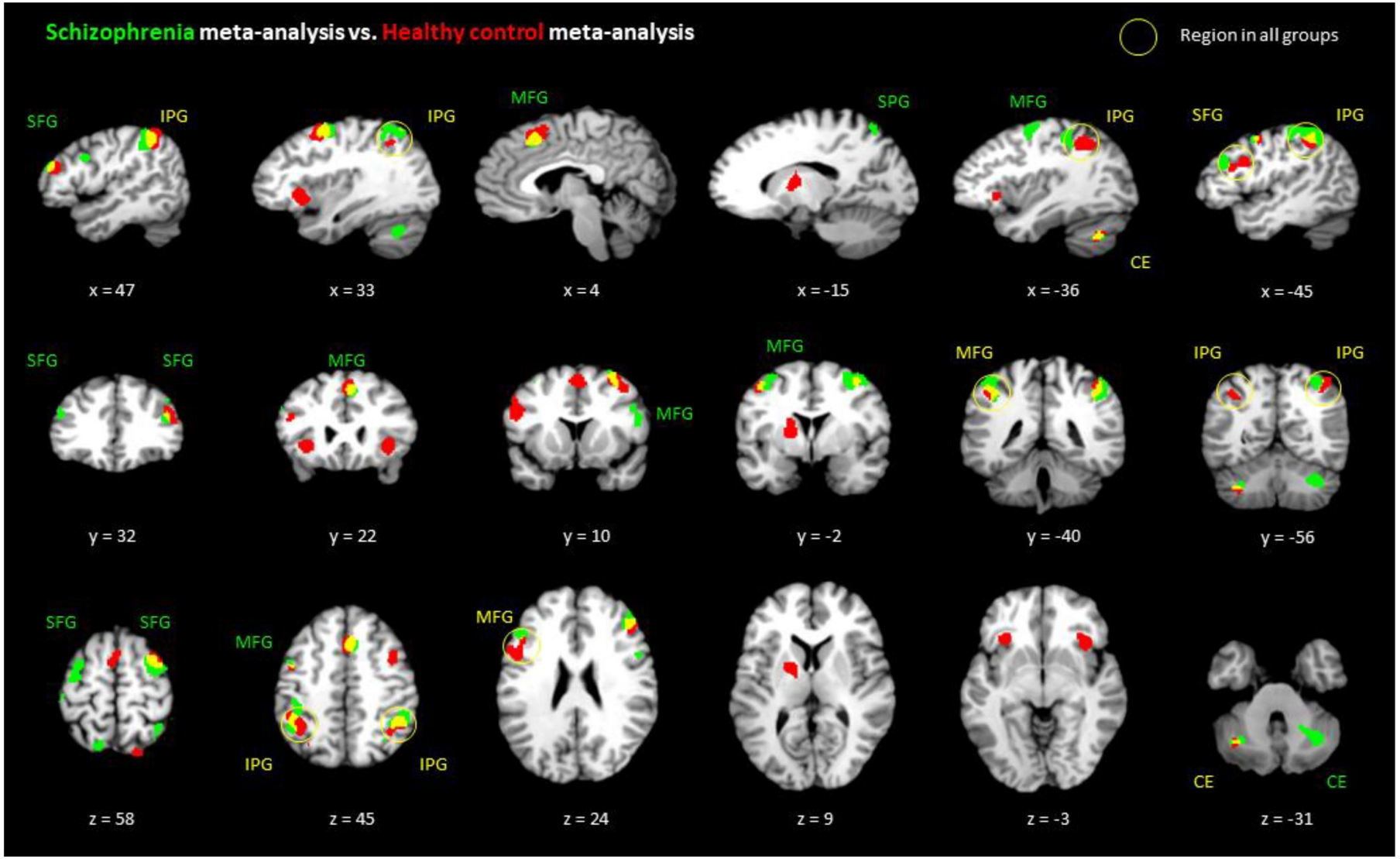
Kognitive Kontrolle





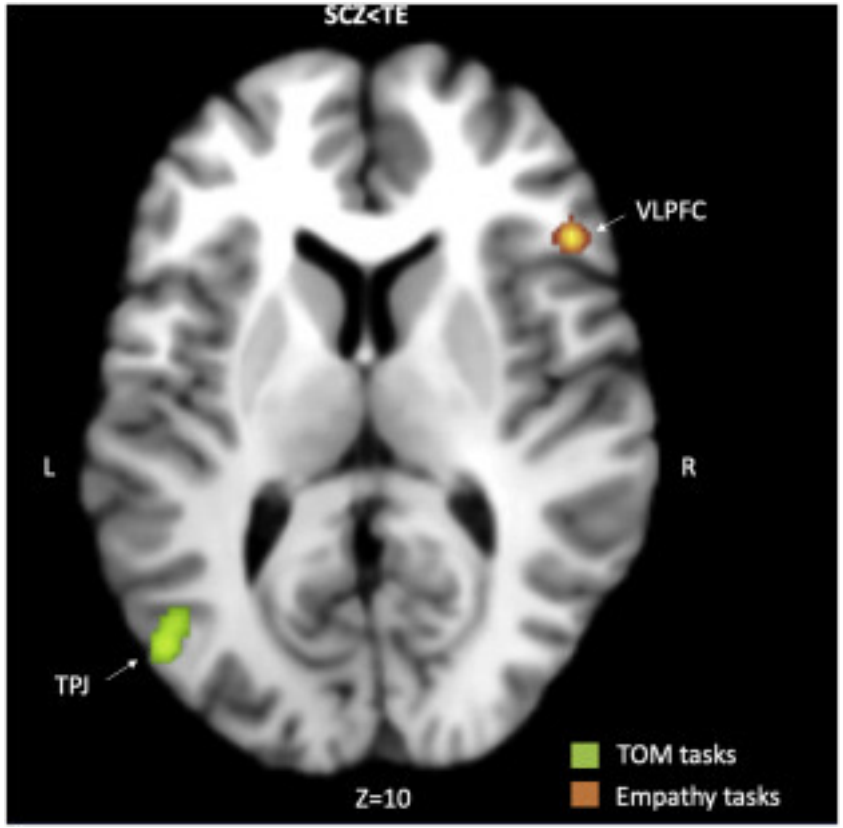
McTeague et al. Am J Psychiat 2020

Arbeitsgedächtnis

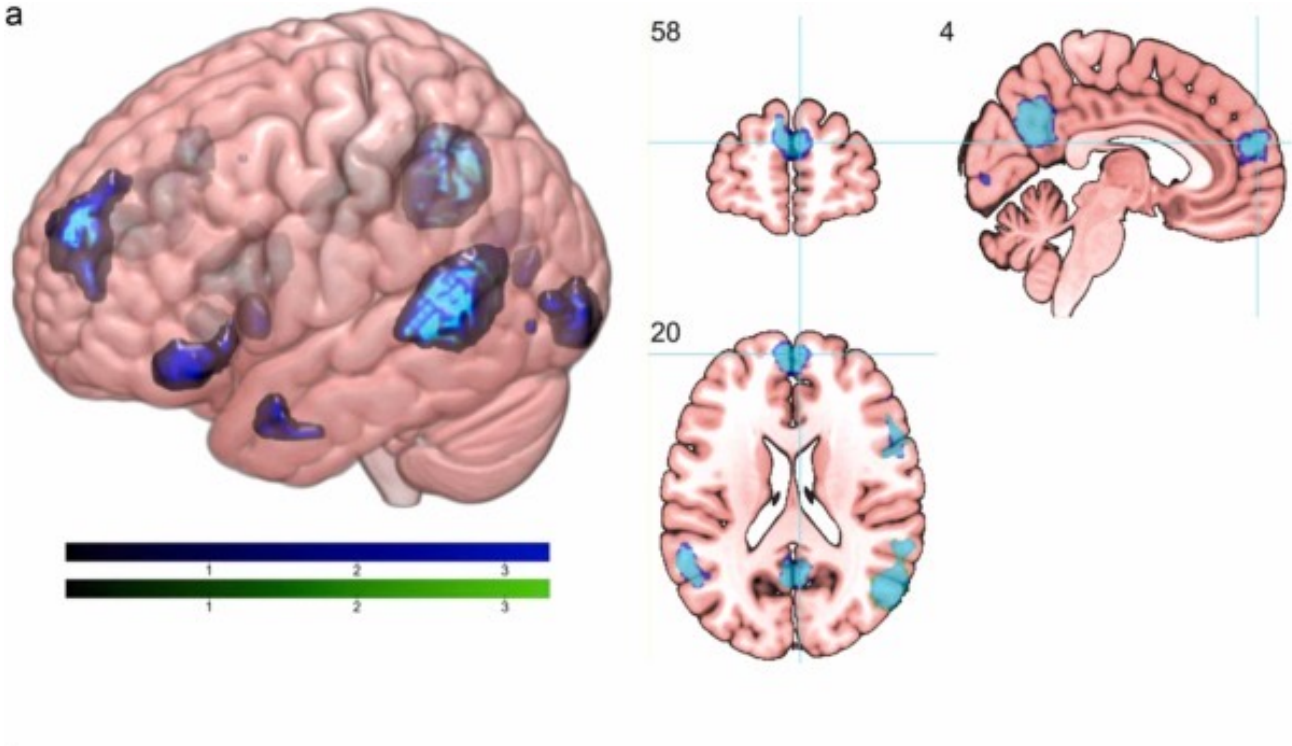


Yaple et al. Neuroimaging Clin 2021

Soziale Kognition/Theory of Mind

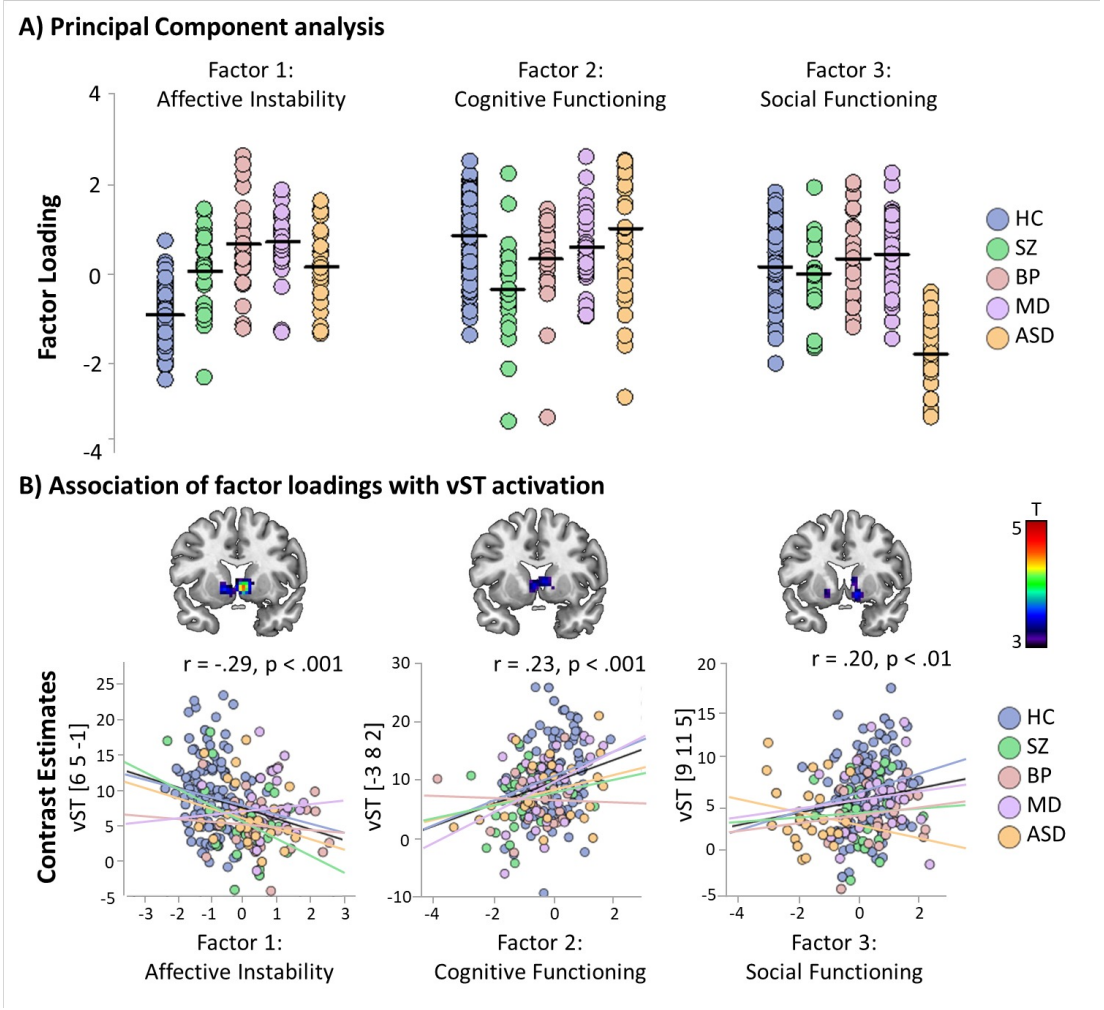


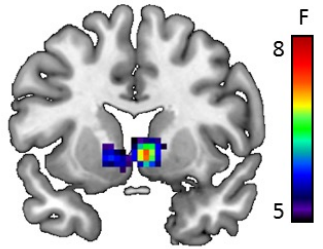
Vucorovic et al J Psychiat Rec 2020

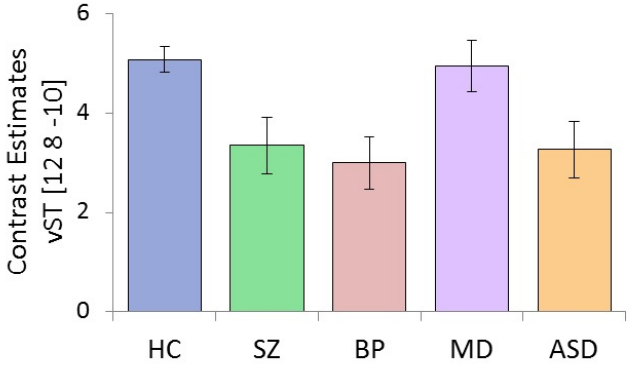


Weng et al. Neurobiol Biobehav Rev 2022

Transdiagnostische Mechanismen

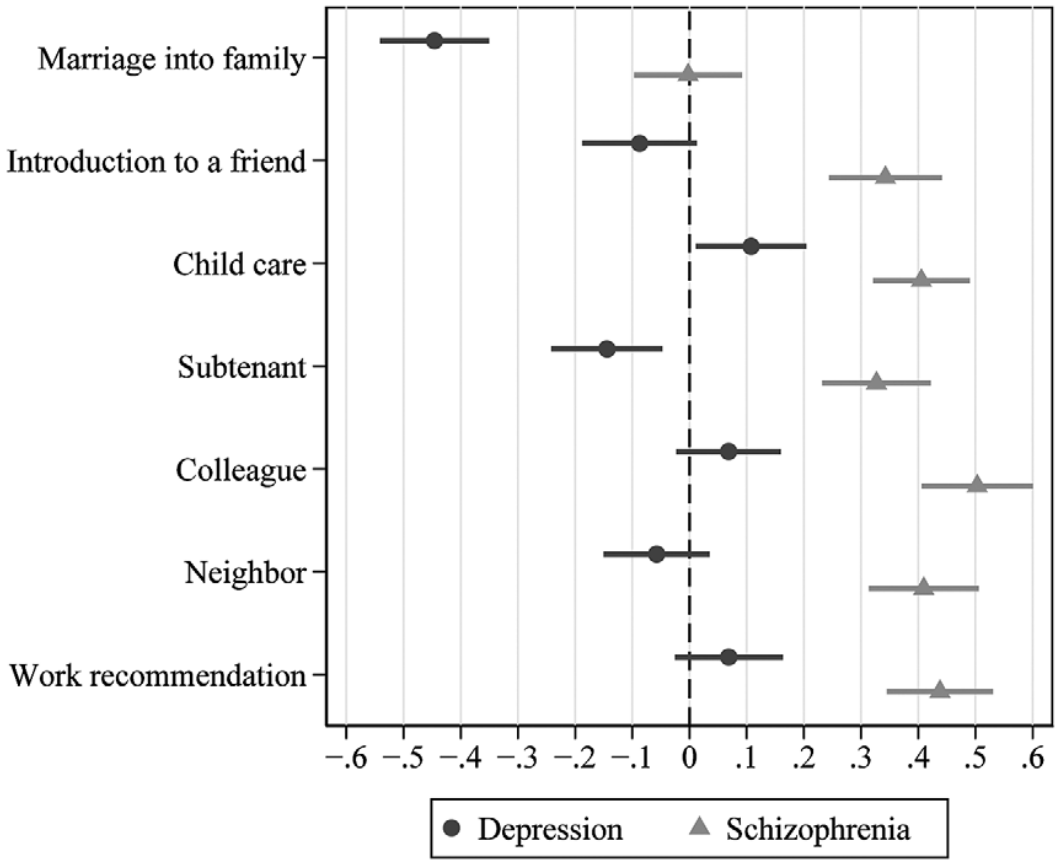


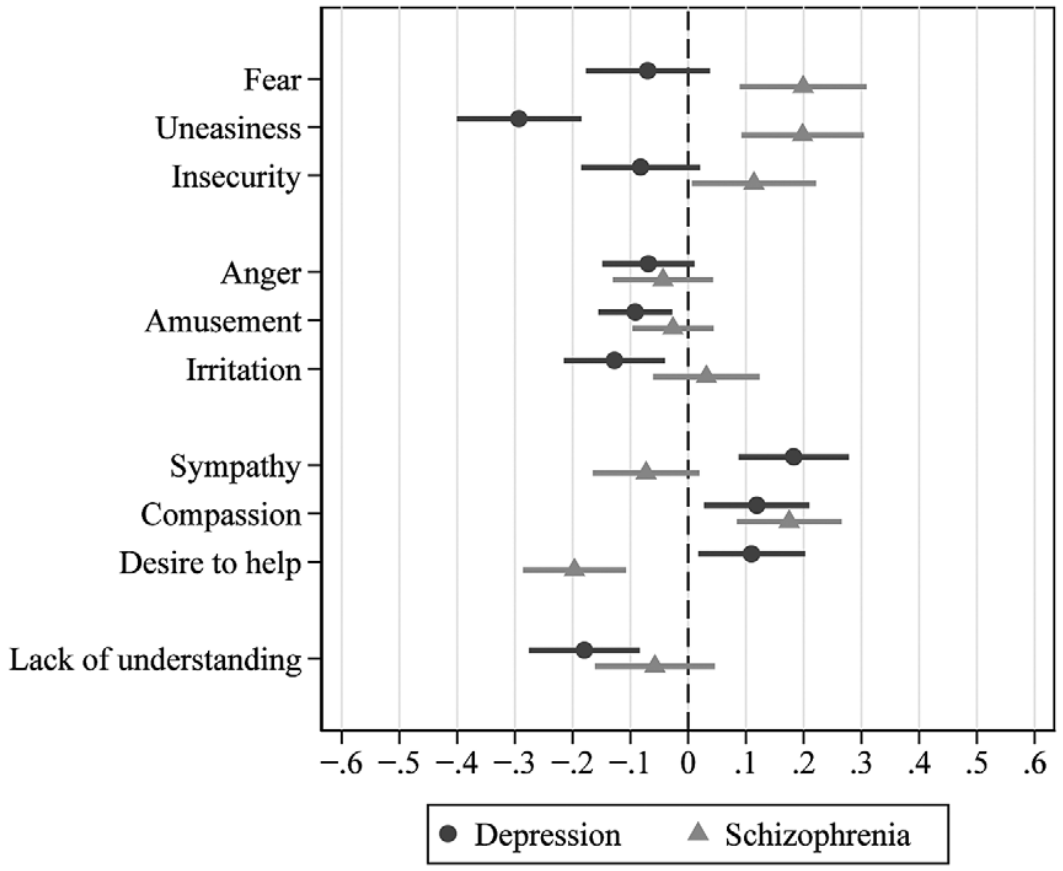




Schwarz*, Mößnang*, et al. **Schiz Bull** 2019

Stigma in Deutschland: 30 Jahre Verlauf





Schomerus et al **European Psychiat** 2022

Biologische Erklärung der Schizophrenie und Stigma

Biogenetic explanations and public acceptance of mental illness: systematic review of population studies

Matthias C. Angermeyer, Anita Holzinger, Mauro G. Carta and Georg Schomerus

Background
Biological or genetic models of mental illness are commonly expected to increase tolerance towards people with mental illness, by reducing notions of responsibility and blame.

Aims
To investigate whether biogenetic causal attributions of mental illness among the general public are associated with more tolerant attitudes, whether such attributions are related to lower perceptions of guilt and responsibility, to what extent notions of responsibility are associated with rejection of people who are mentally ill, and how prevalent notions of responsibility are among the general public with regard to different mental disorders.

Method
A systematic review was conducted of representative population studies examining attitudes towards people with mental illness and beliefs about such disorders.

Results
We identified 33 studies relevant to this review. Generally, biogenetic causal attributions were not associated with more tolerant attitudes; they were related to stronger rejection in most studies examining schizophrenia. No published study reported on associations of biogenetic causal attributions and perceived responsibility. The stereotype of self-responsibility was unrelated to rejection in most studies. Public images of mental disorder are generally dominated by the stereotypes of unpredictability and dangerousness, whereas responsibility is less relevant.

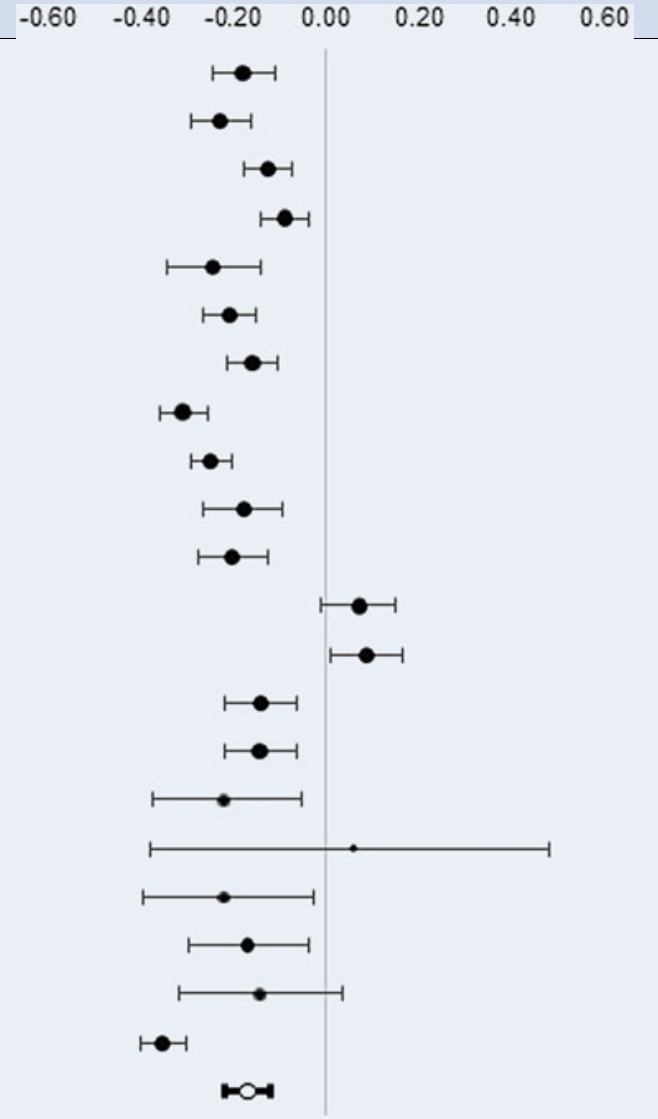
Conclusions
Biogenetic causal models are an inappropriate means of reducing rejection of people with mental illness.

Declaration of interest
None.

Angermeyer et al **Br J Psychiat** 2011

Kontinuum-Ansätze vermindern Stigma

	Study	Disorder	*r*	L CI	U CI	Weight (%)
1	Angermeyer et al. (2015)[1]	Depr.	−0.18	−0.25	−0.11	5.31
2	Angermeyer et al. (2015)[1]	Schiz.	−0.23	−0.29	−0.16	5.31
3	Makowski et al. (2016a)[1]	Depr.	−0.13	−0.18	−0.07	5.53
4	Makowski et al. (2016a)[1]	Schiz.	−0.09	−0.14	−0.04	5.54
5	Schlier et al. (2016)[1]	Schiz.	−0.25	−0.34	−0.14	4.67
6	Schomerus et al. (2013)[1]	Alc.	−0.21	−0.26	−0.15	5.48
7	Schomerus et al. (2013)[1]	Depr.	−0.16	−0.22	−0.10	5.49
8	Schomerus et al. (2013)[1]	Schiz.	−0.31	−0.36	−0.26	5.49
9	Schomerus et al. (2016)[1]	Depr., Schiz.	−0.25	−0.29	−0.20	5.61
10	Speerforck et al. (2019)[1]	ADHD	−0.18	−0.26	−0.09	5.00
11	Subramaniam et al. (2017)[1]	Alc.	−0.20	−0.28	−0.12	5.15
12	Subramaniam et al. (2017)[1]	Dement.	0.07	−0.01	0.15	5.14
13	Subramaniam et al. (2017)[1]	Depr.	0.09	0.01	0.17	5.15
14	Subramaniam et al. (2017)[1]	OCD	−0.14	−0.22	−0.06	5.15
15	Subramaniam et al. (2017)[1]	Schiz.	−0.14	−0.22	−0.06	5.14
16	Thibodeau and Peterson (2018)[2]	Schiz.	−0.22	−0.38	−0.05	3.54
17	Thibodeau et al. (2018)[2]	Schiz.	0.06	−0.38	0.48	1.10
18	Thibodeau (2017)[1]	Schiz.	−0.22	−0.40	−0.03	3.14
19	Thibodeau (2019)[1]	Depr.	−0.17	−0.30	−0.04	4.20
20	Wiesjahn et al. (2014)[1]	Schiz.	−0.15	−0.32	0.04	3.37
21	Wiesjahn et al. (2016)[1]	Schiz.	−0.35	−0.40	−0.30	5.49
			−0.17	**−0.22**	**−0.12**	



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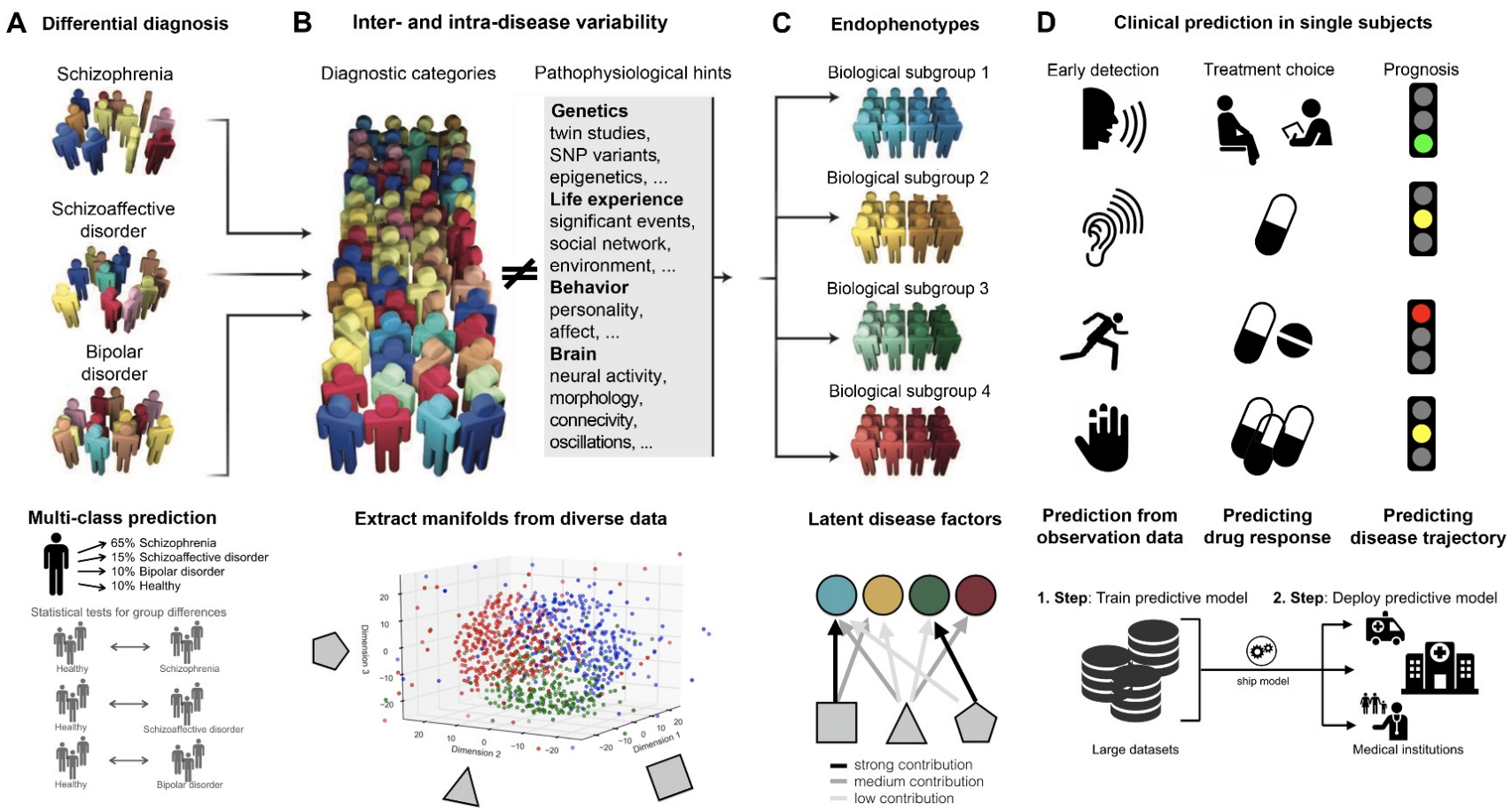

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