



Schizophrenia

(for non-clinicians)

2020 Computational Psychiatry Course



Translational Neuromodeling Unit



Universität
Zürich



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

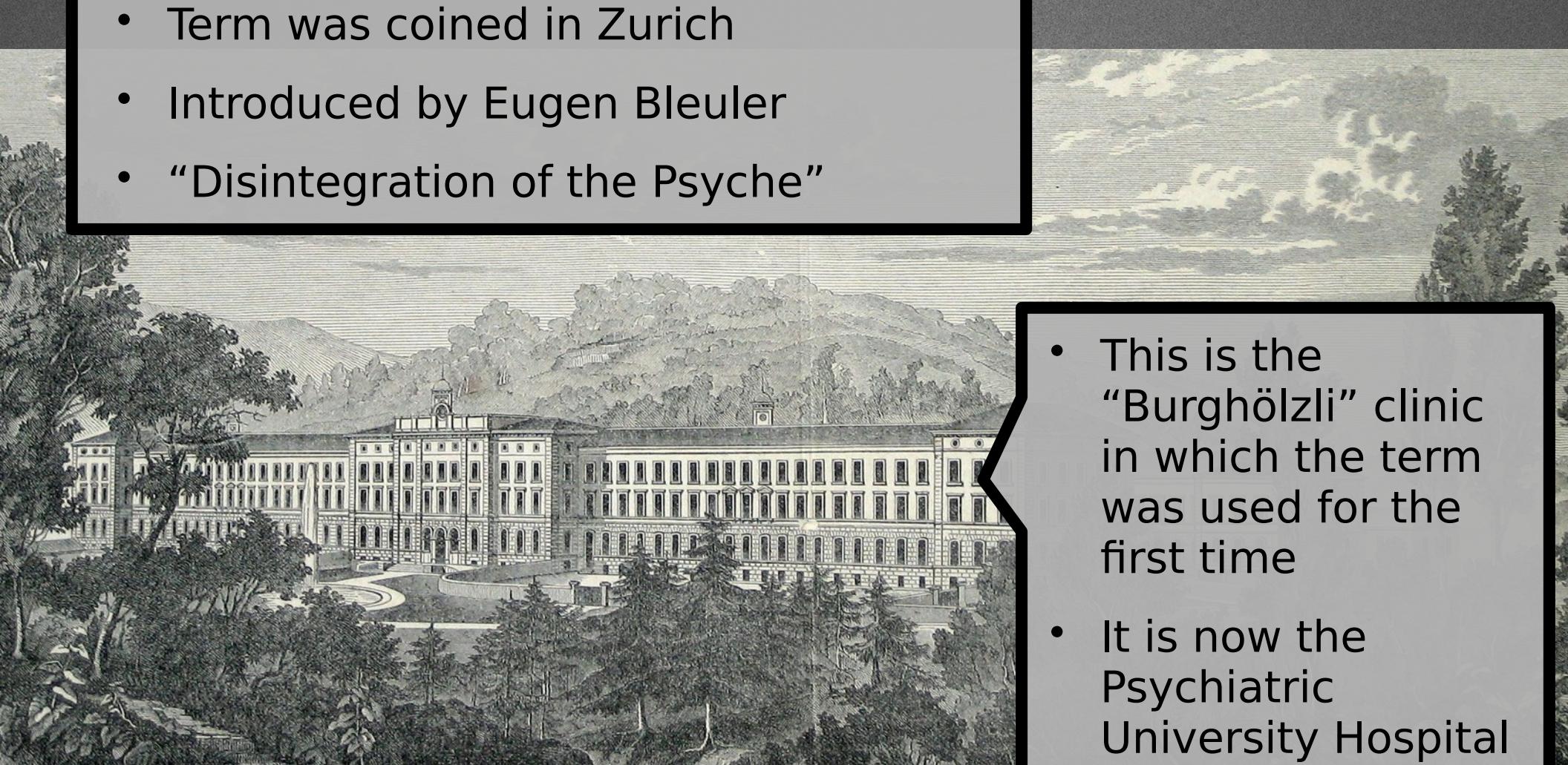
Jakob Siemerkus
University of Zurich & ETH Zurich

Only to be used by participants during the Computational Psychiatry Course 2020 (Translational Neuromodeling Unit Zurich), reproduction and other use and/or distribution to third parties are not allowed

Schizophrenia



- Term was coined in Zurich
- Introduced by Eugen Bleuler
- “Disintegration of the Psyche”



- This is the “Burghölzli” clinic in which the term was used for the first time
- It is now the Psychiatric University Hospital of Zurich

Schizophrenia

- One of the “major” psychiatric disorders
- 0.5% prevalence (Saha, 2005)
- Severe mental disorder
- Functional impairment
- Social dimension
- Many unsolved questions

Clinical Manifestation



Schizophrenia



Schizophrenia



- 37yo librarian
- Messy apartment
- Unable to talk
- Apathy
- Slowed down
- Lost her job months ago
- Diagnostic tests normal
- Starts talking (repeats the word “blue” or says sentences like “I’m blued in like blingo!”)
- Episode of schizophrenia
- Treatment
 - Antipsychotic 1 → no effect
 - Antipsychotic 2 → improvement, can dress herself, attends meetings → but side effect stiffness of muscles (EPMS)
 - Antipsychotic 3 → Clozapine is very effective, gains back many functions
- Discharged after 3 months to live with her family

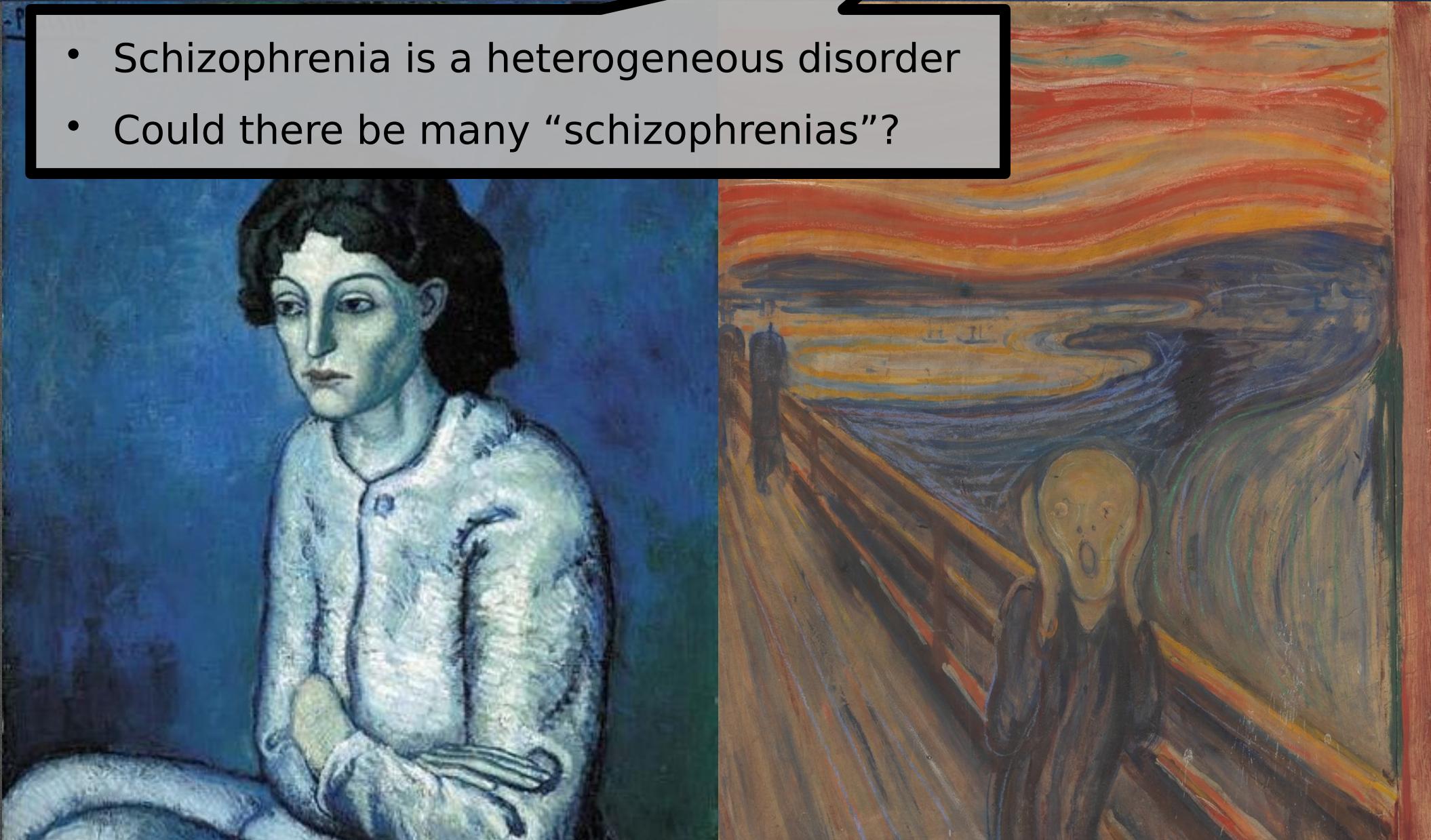
Schizophrenia

- 19yo student of physics
- Reports to the police about his neighbor:
 - Spying on him
 - Plotting to murder him
 - CIA/MP-relations
 - Hears N.'s voice
 - N. can read his mind
- Parents report that E. has had problems for about $\frac{1}{2}$ year, was unable to attend courses
- Episode of schizophrenia
- Treatment with antipsychotic
- Remission after only 2 weeks
- After stay at day care unit can be discharged
- Resumes his studies

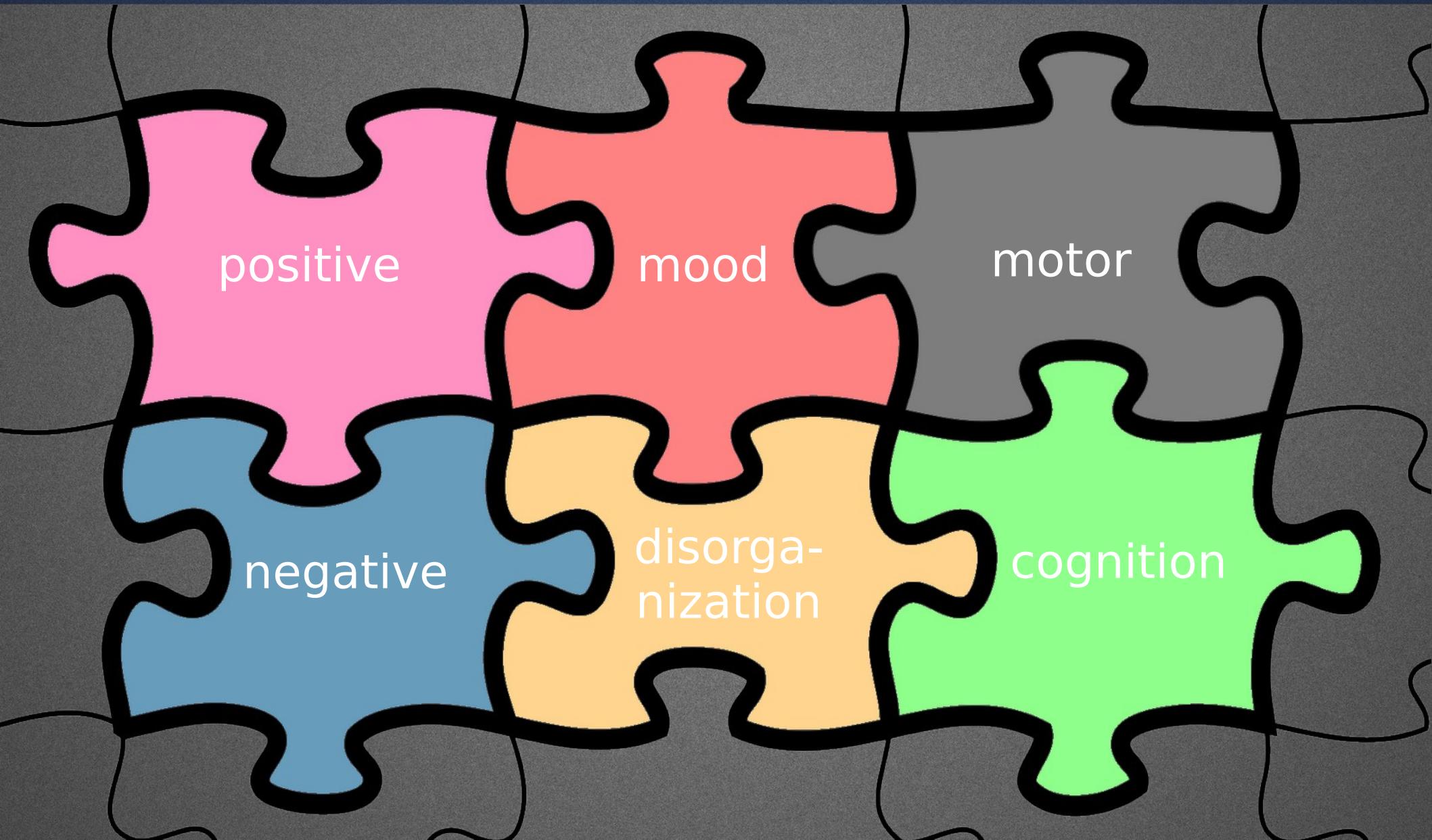


Schizophrenia(s?)

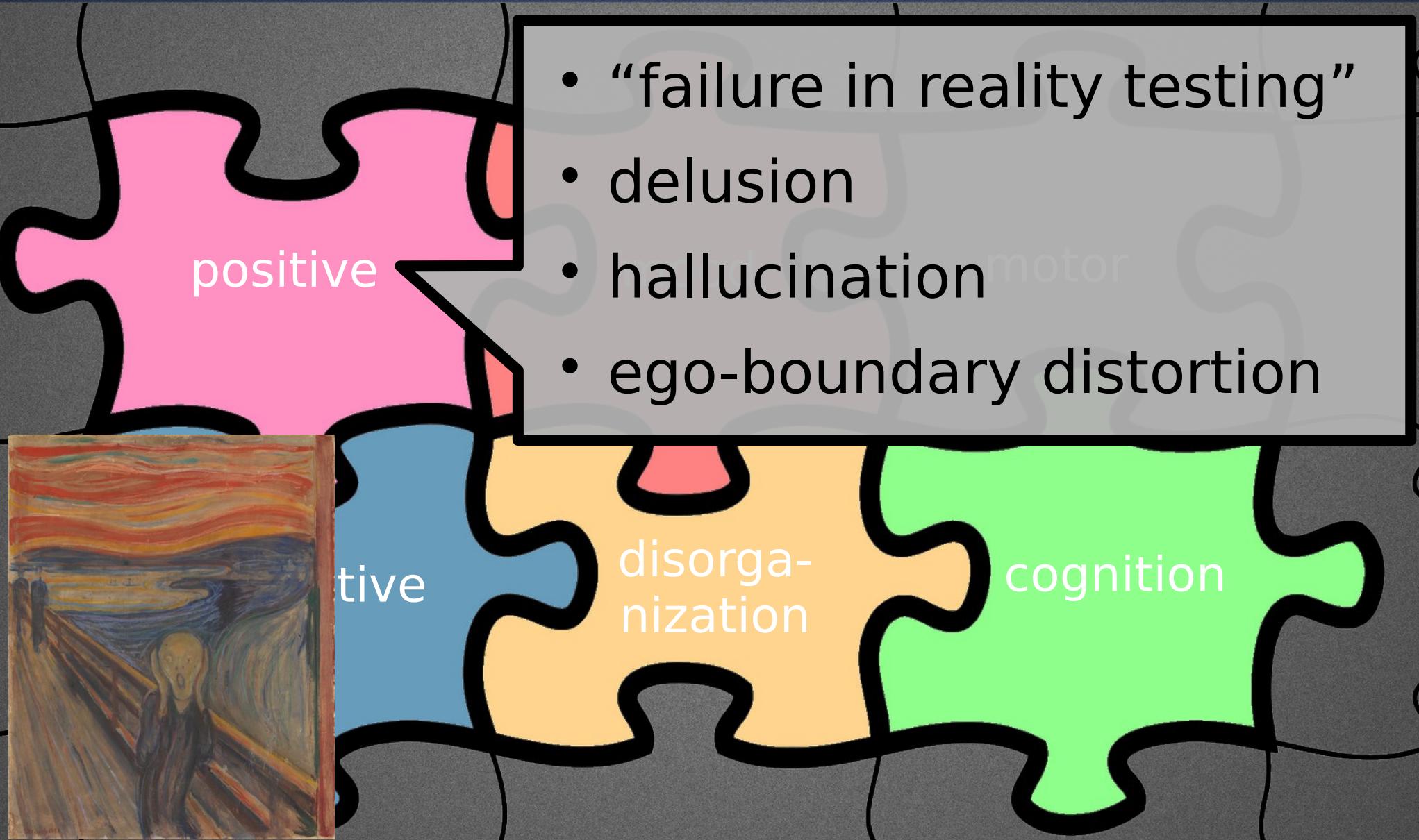
- Schizophrenia is a heterogeneous disorder
- Could there be many “schizophrenias”?



Main Symptom Categories

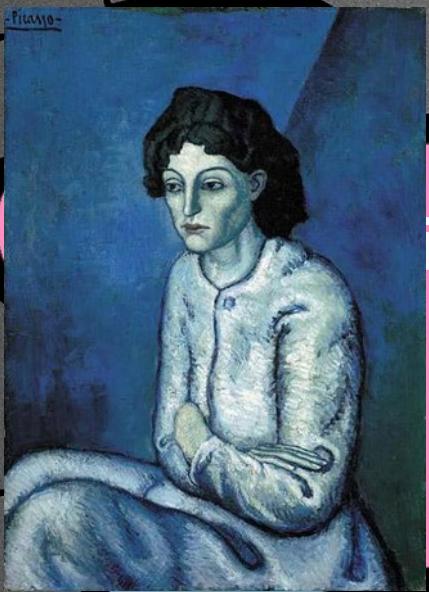


Main Symptom Categories



Main Symptom Categories

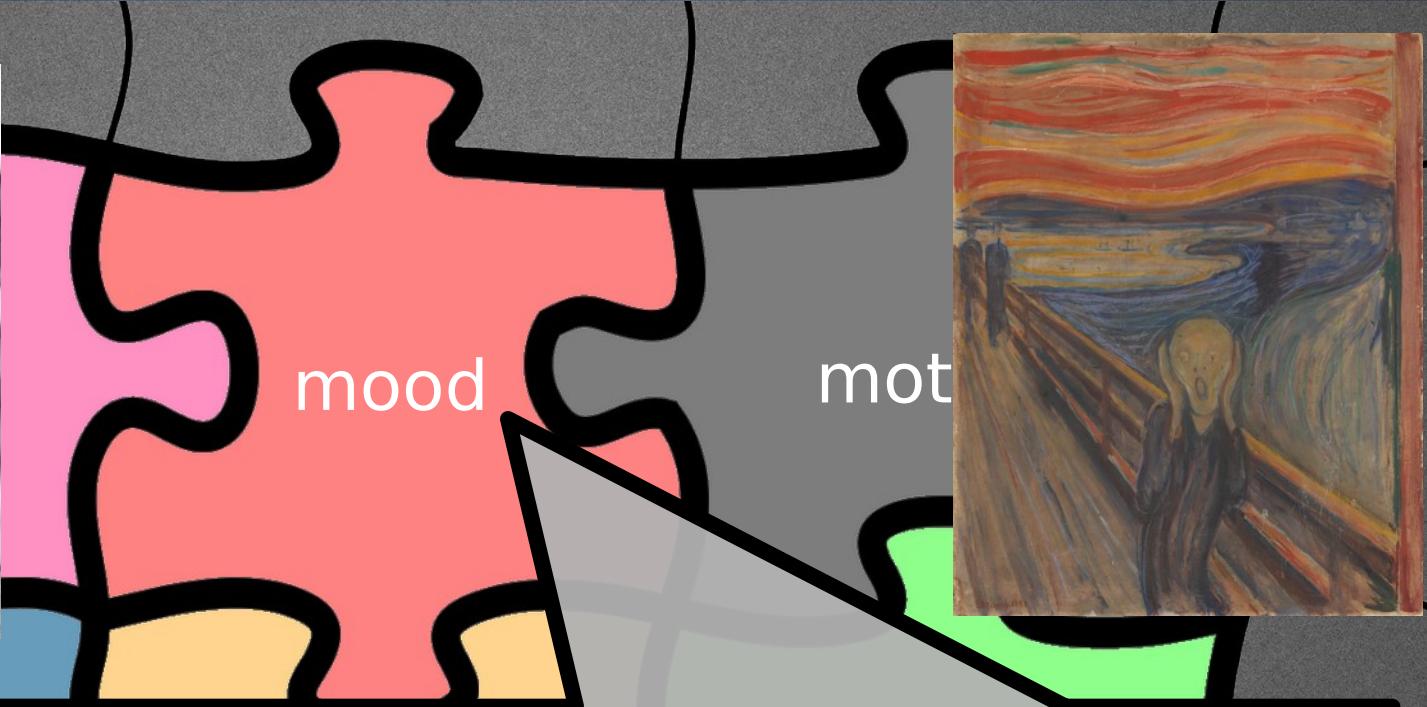
- loss of affective and driving functions
- impaired affective experience/expression
- loss of motivation & initiative
- reduced social drive
- slowed thinking



negative

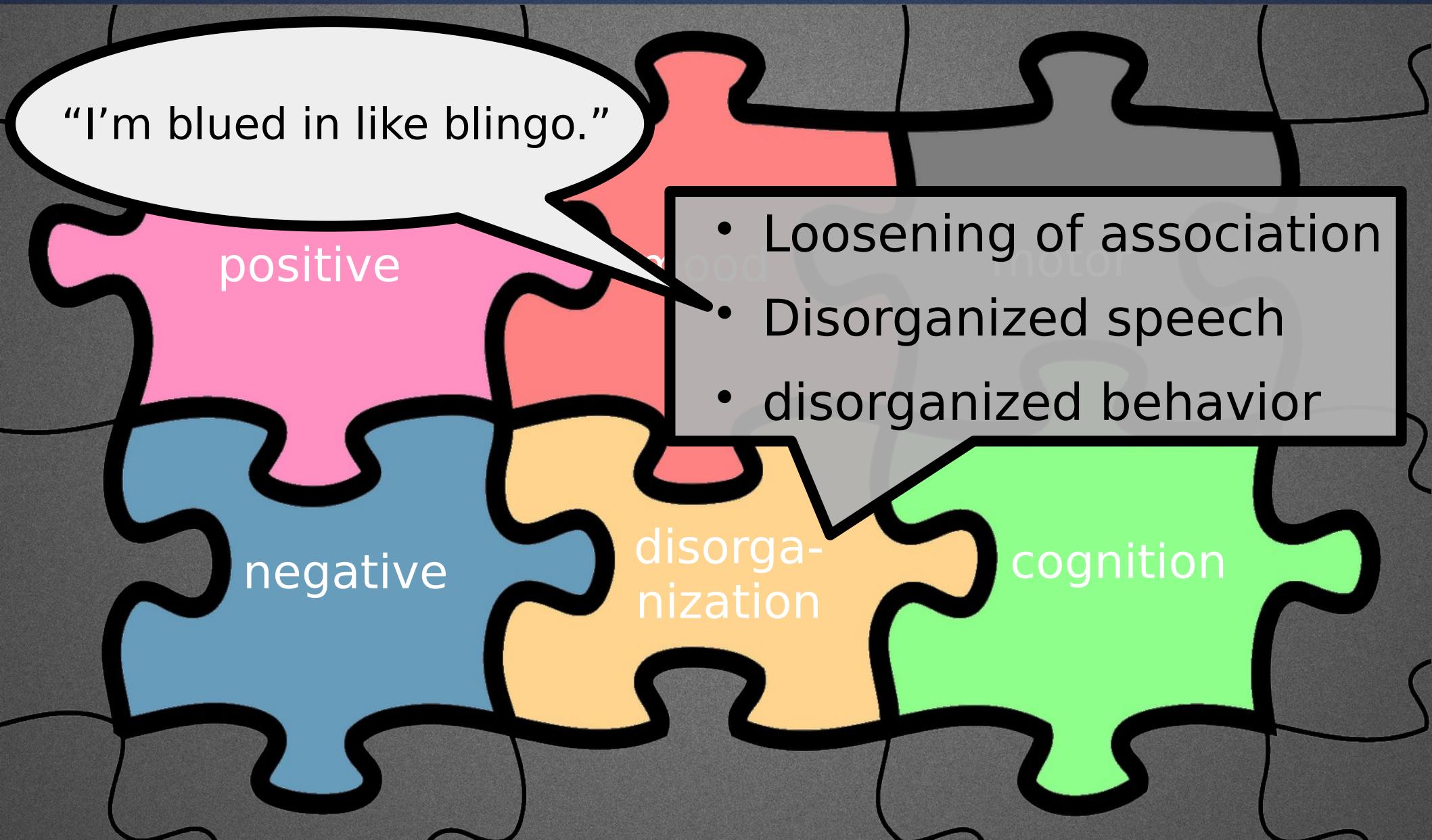
negative

Main Symptom Categories



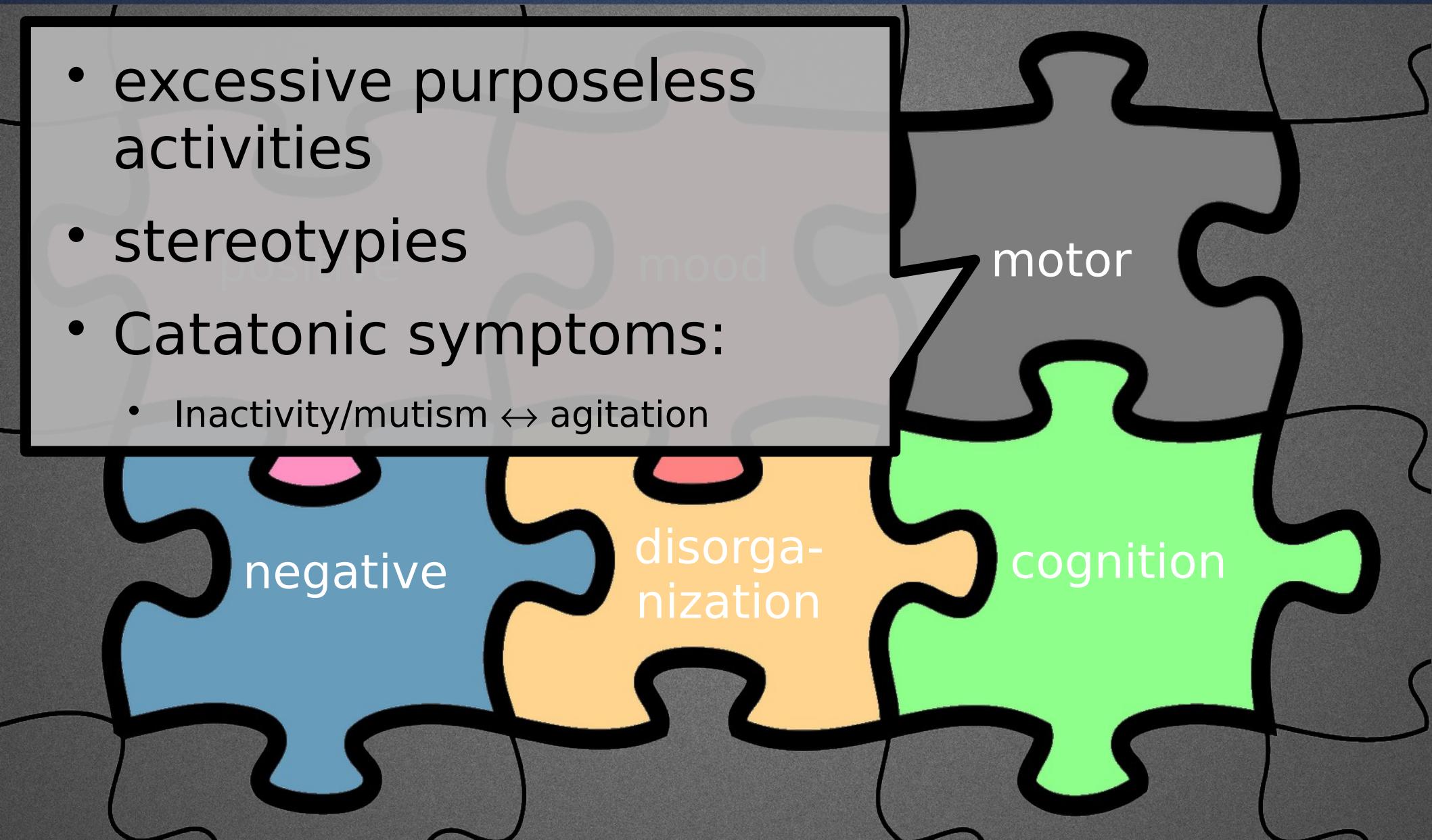
- overlap with negative symptoms
- anxiety, emotional arousal, and depression very frequent

Main Symptom Categories

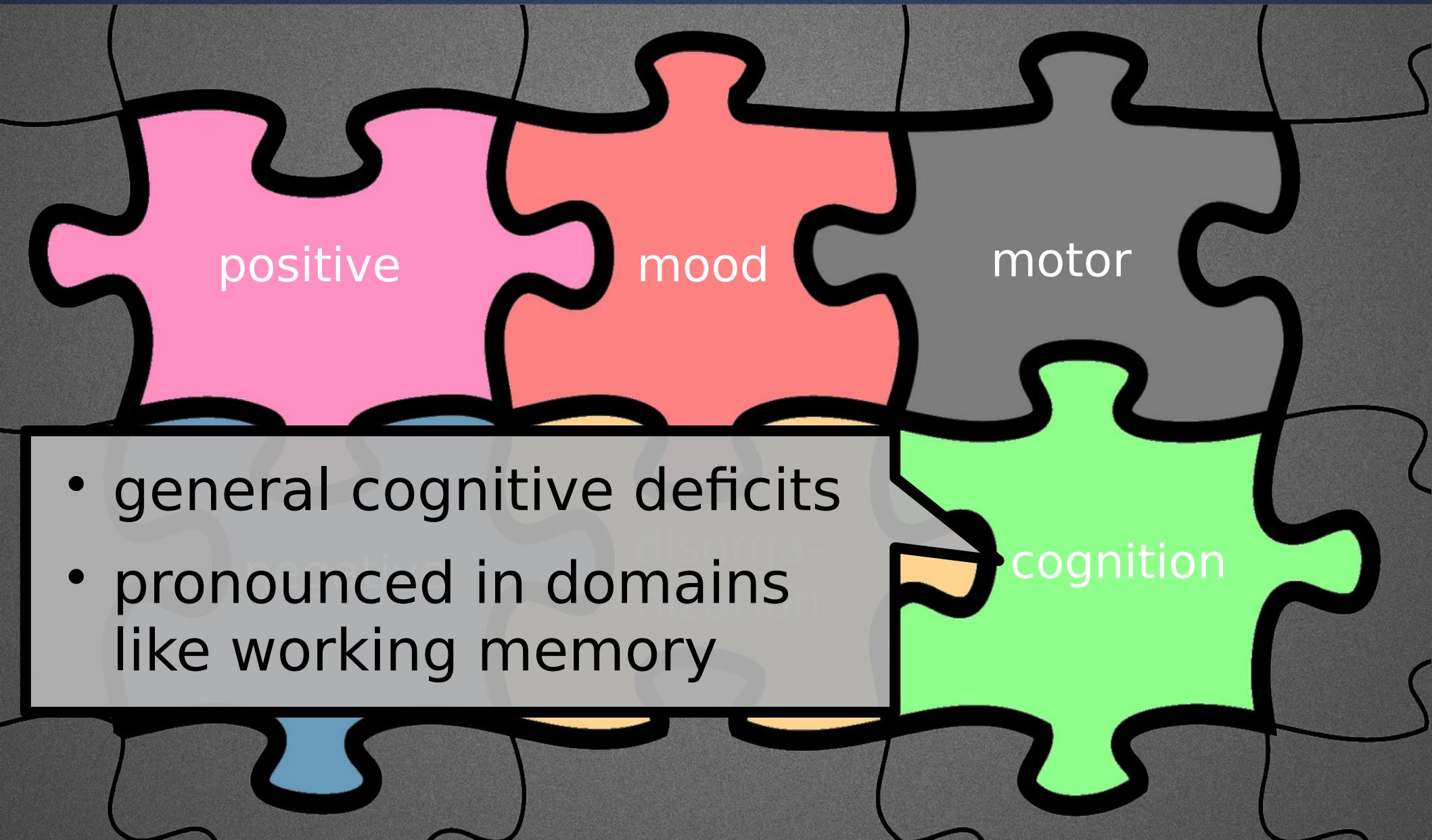


Main Symptom Categories

- excessive purposeless activities
- stereotypies
- Catatonic symptoms:
 - Inactivity/mutism ↔ agitation



Main Symptom Categories



Diagnostic Criteria

DSM 5

MAIN CRITERIA	<ul style="list-style-type: none">• ≥ 2 symptom (categories) present• AND ≥ 1 core symptom• no other cause
TIME	<ul style="list-style-type: none">• ≥ 1 month main criteria• ≥ 6 months symptoms/functional impairment
SYMPTOMS	<ul style="list-style-type: none">• (core) delusions• (core) hallucinations• (core) disorganized speech• negative symptoms (especially avolition, diminished emotional expression)• disorganized or catatonic behaviour

Diagnostic Criteria

DSM 5

MAIN CRITERIA

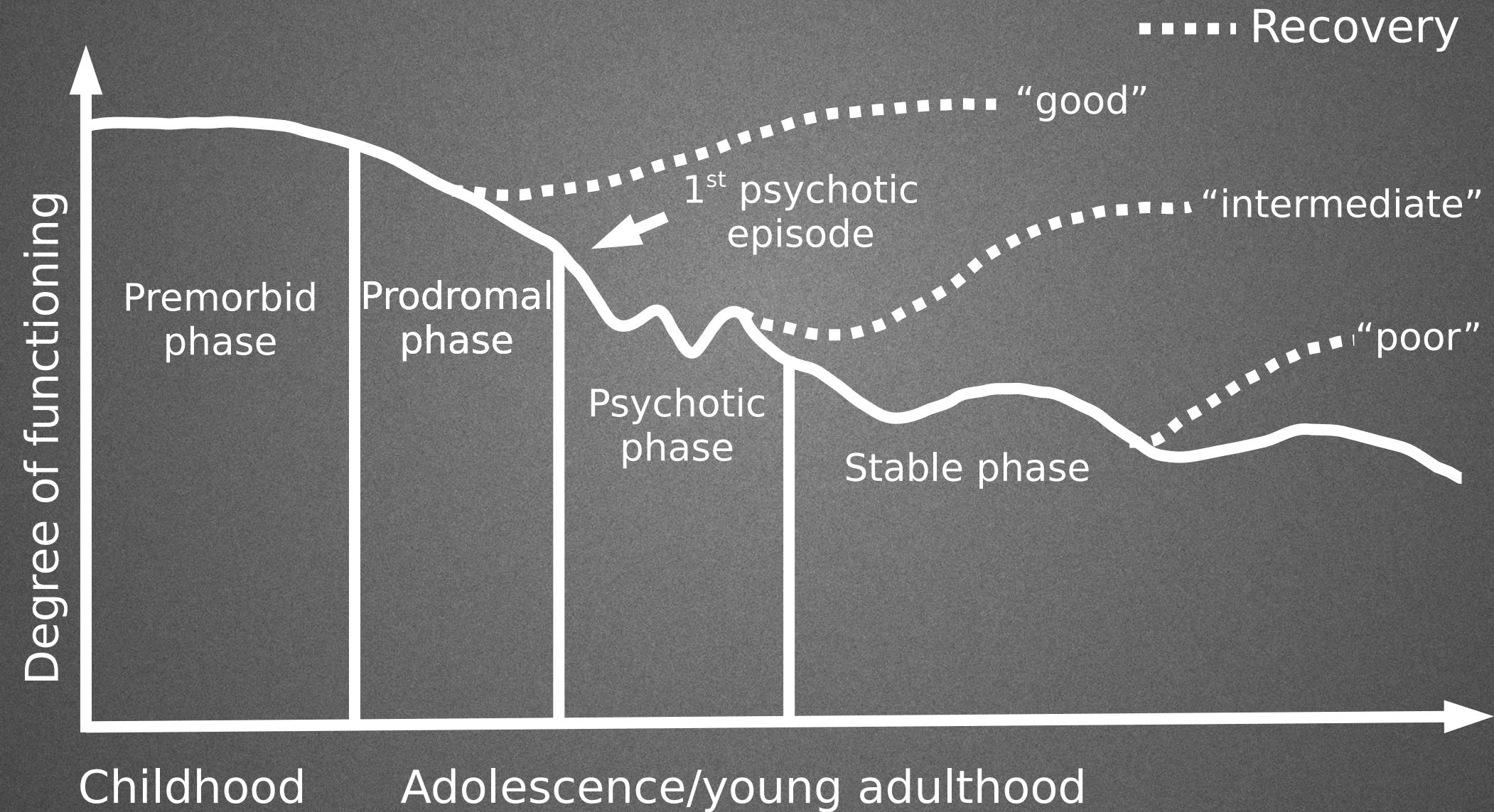
- ≥ 2 symptom (categories) present
- AND ≥ 1 core symptom
- no other cause

The screenshot shows the homepage of The Guardian website. At the top, there's a call to support the newspaper with buttons for 'Contribute' and 'Subscribe'. The navigation bar includes links for 'News', 'Opinion', 'Sport', 'Culture', 'Lifestyle', and 'More'. Below the navigation, a horizontal menu lists various news categories: 'Coronavirus', 'World', 'UK', 'Environment', 'Science', 'Global development', 'Football', 'Tech', 'Business', and 'Obituaries'. The main article visible is titled 'Covid-19 may cause brain complications in some, say doctors'. A yellow box next to the title indicates that the article is 'more than 2 months old'. Below the article, a sub-headline reads 'Stroke and psychosis found in small study of patients highlight need for research'. There are also links for 'Coronavirus - latest updates' and 'See all our coronavirus coverage'. The Guardian logo is prominently displayed on the right side of the header. The footer of the screenshot includes the text '(The Guardian, 2020)'.

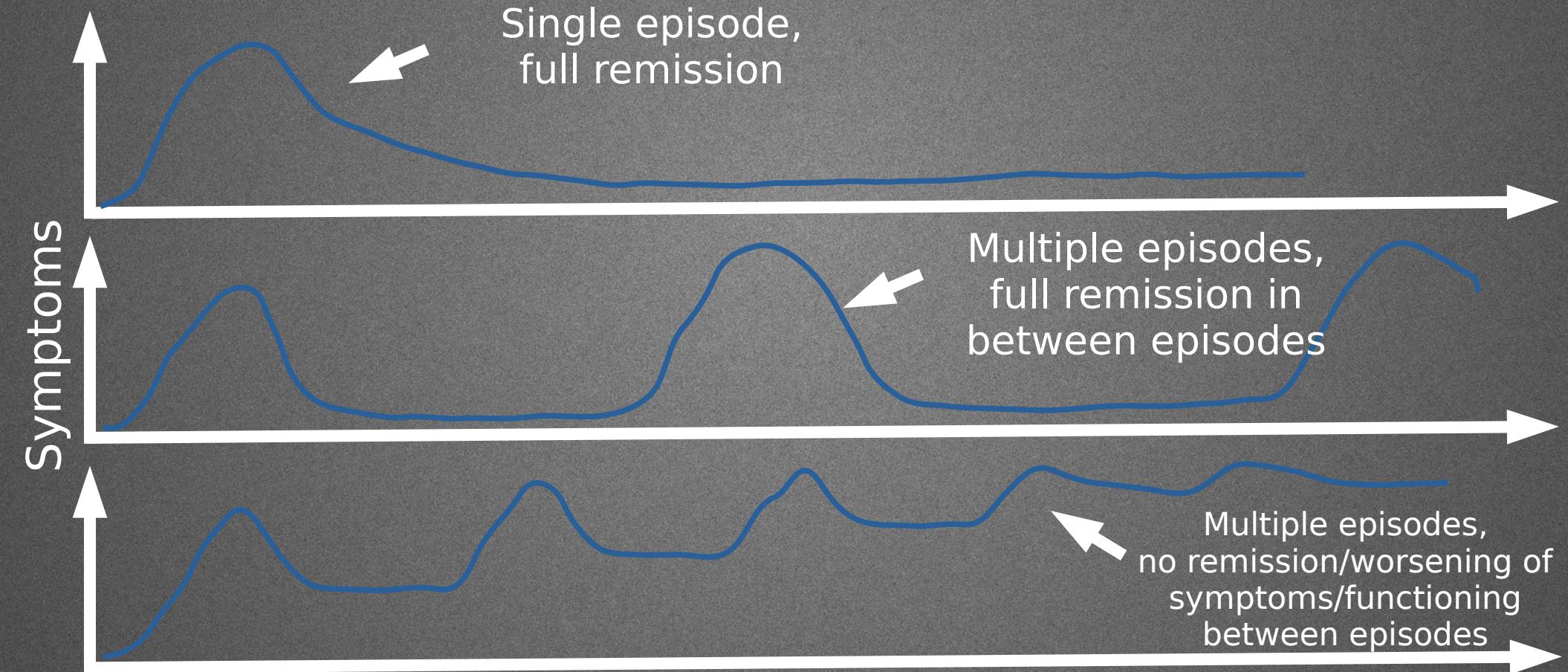


Trajectory Risk factors Outcome

Trajectory

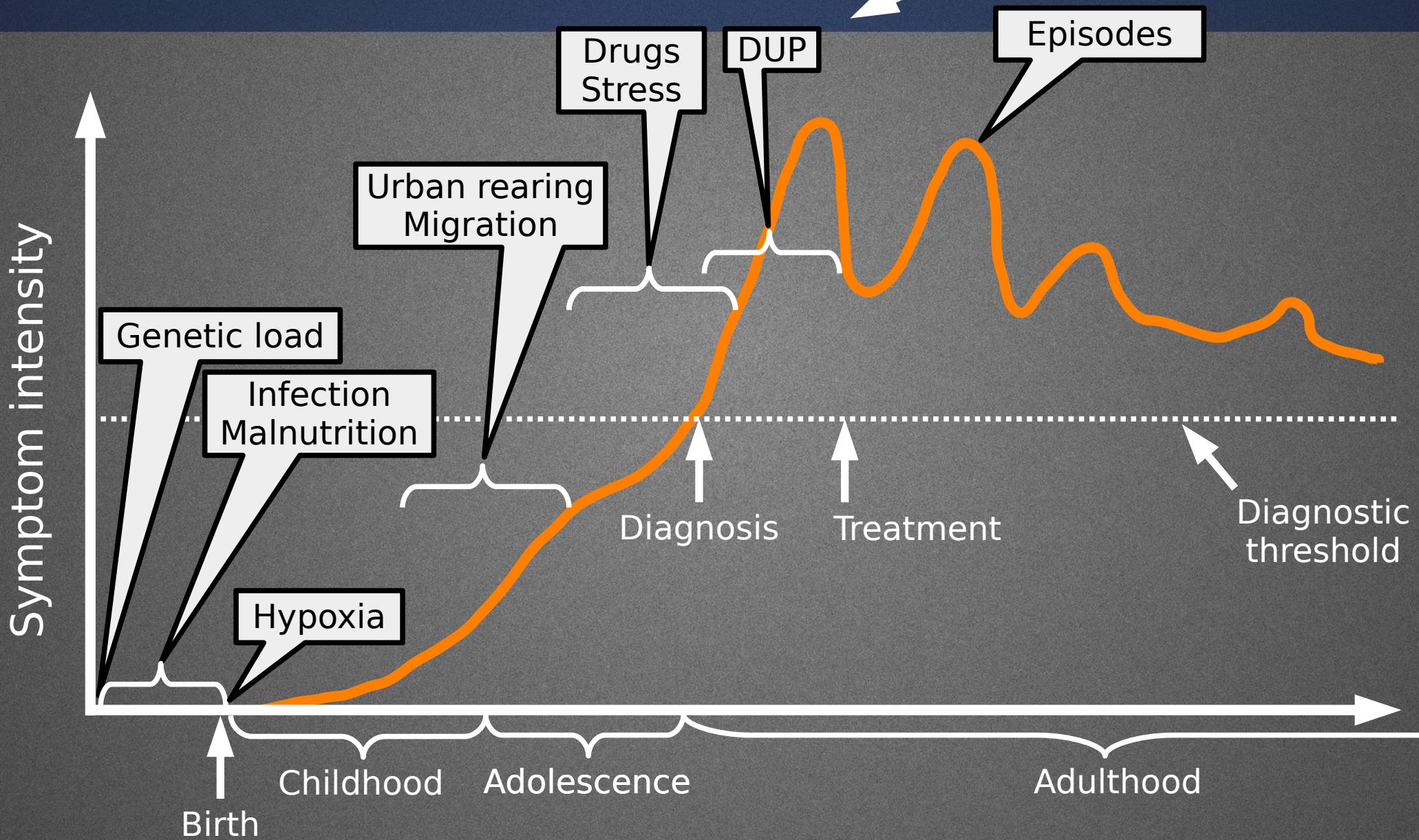


Trajectory



Risk Factors

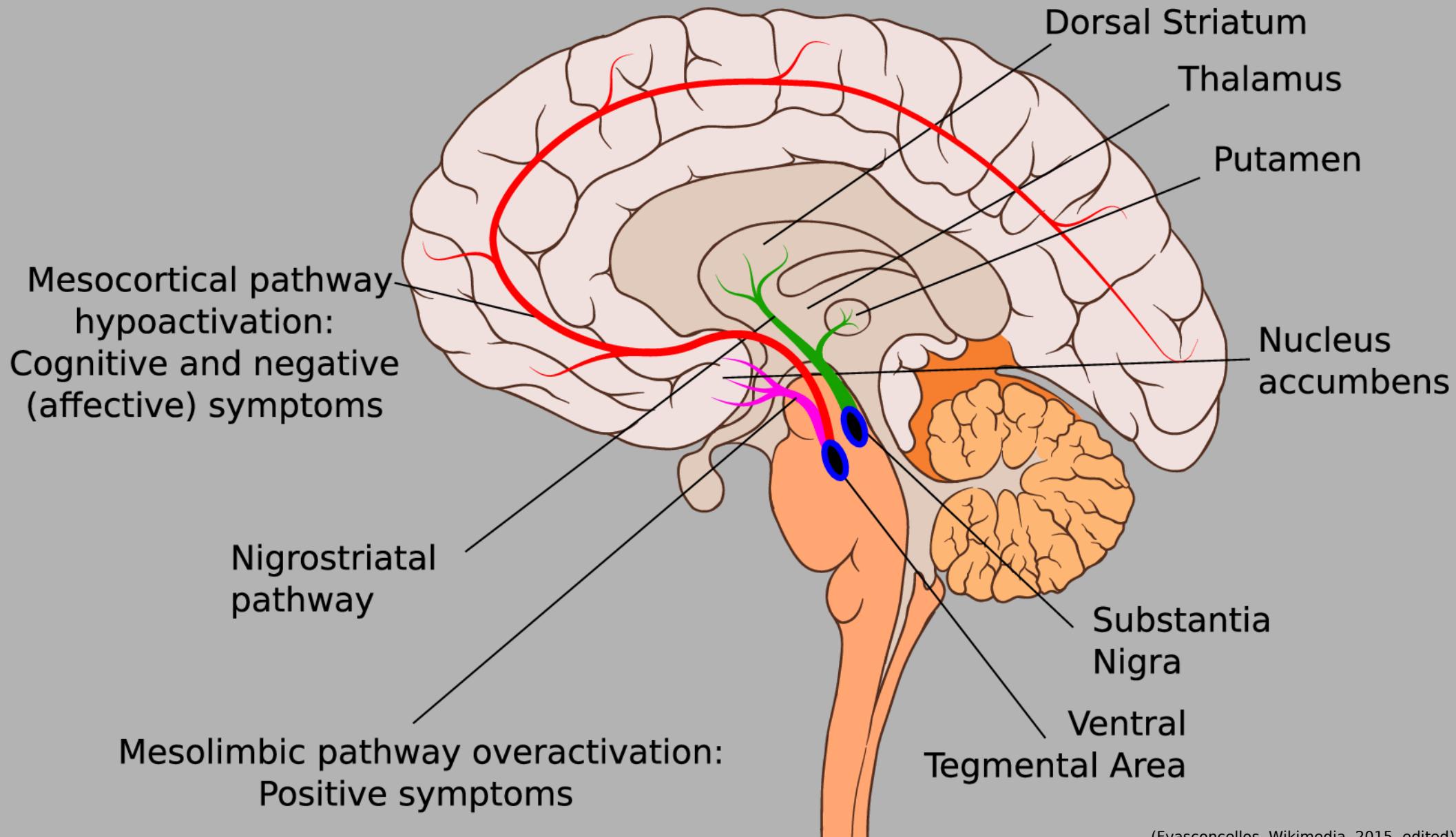
Duration of Untreated Psychosis
Closely related to “poor insight”
which means that somebody who
does not accept having a mental
disorder will reject treatment



Pathophysiology

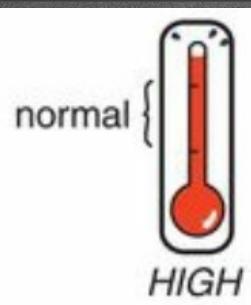
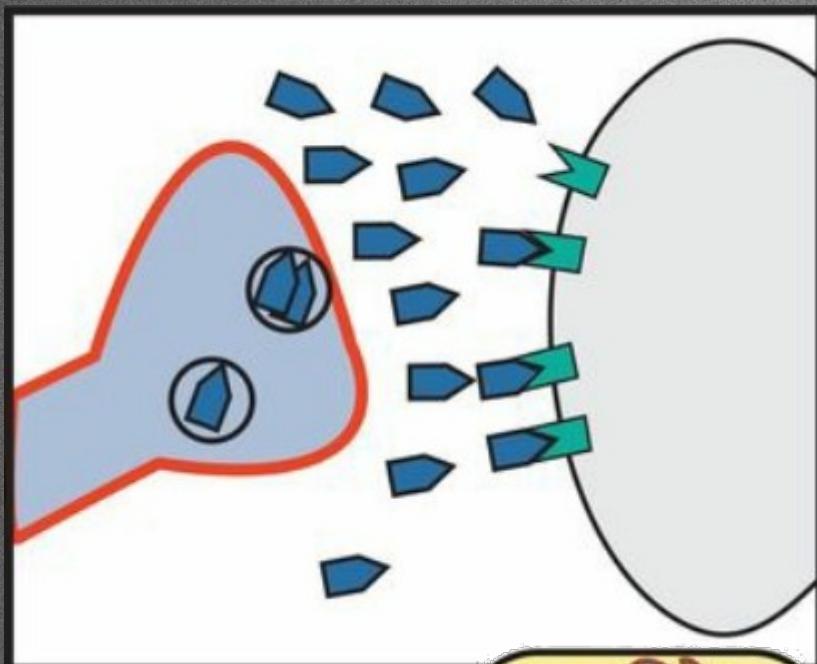


Dopamine Hypothesis



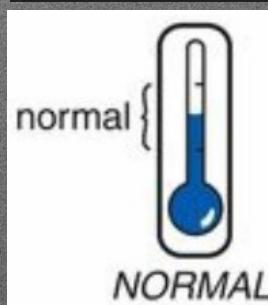
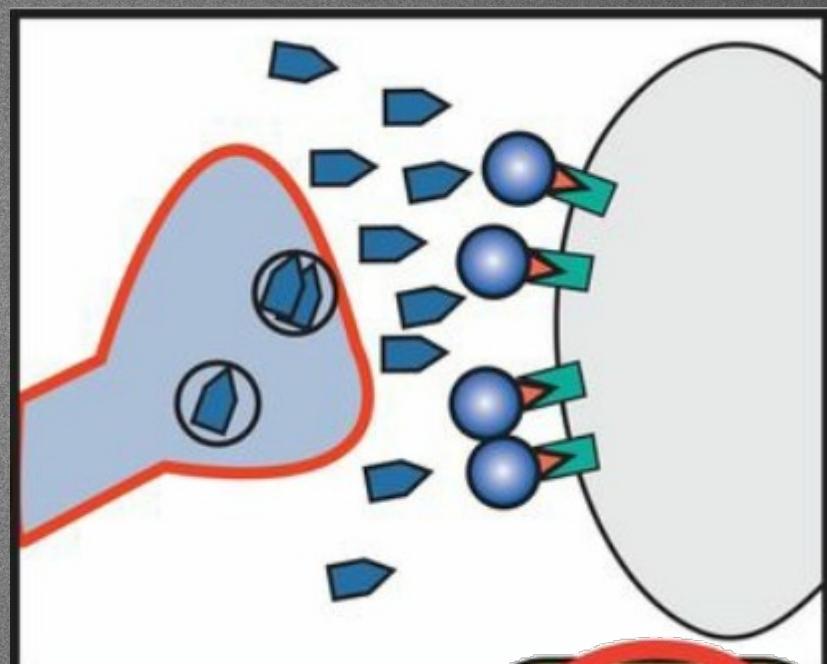
Antipsychotics

Mesolimbic Pathway
Untreated Schizophrenia



"hyperactive"
dopaminergic system

Mesolimbic Pathway
D2 Antagonist



"normalized"
dopaminergic system



Antipsychotics

Overall change in symptoms

SMD (95% CrI)

Clozapine -0.88 (-1.03 to -0.73)



Amisulpride -0.66 (-0.78 to -0.53)



Olanzapine -0.59 (-0.65 to -0.53)



Risperidone -0.56 (-0.63 to -0.50)



Paliperidone -0.50 (-0.60 to -0.39)



Zotepine -0.49 (-0.66 to -0.31)



Haloperidol -0.45 (-0.51 to -0.39)



Quetiapine -0.44 (-0.52 to -0.35)



Aripiprazole -0.43 (-0.52 to -0.34)



Sertindole -0.39 (-0.52 to -0.26)



Ziprasidone -0.39 (-0.49 to -0.30)



Chlorpromazine -0.38 (-0.54 to -0.23)



Asenapine -0.38 (-0.51 to -0.25)



Lurasidone -0.33 (-0.45 to -0.21)

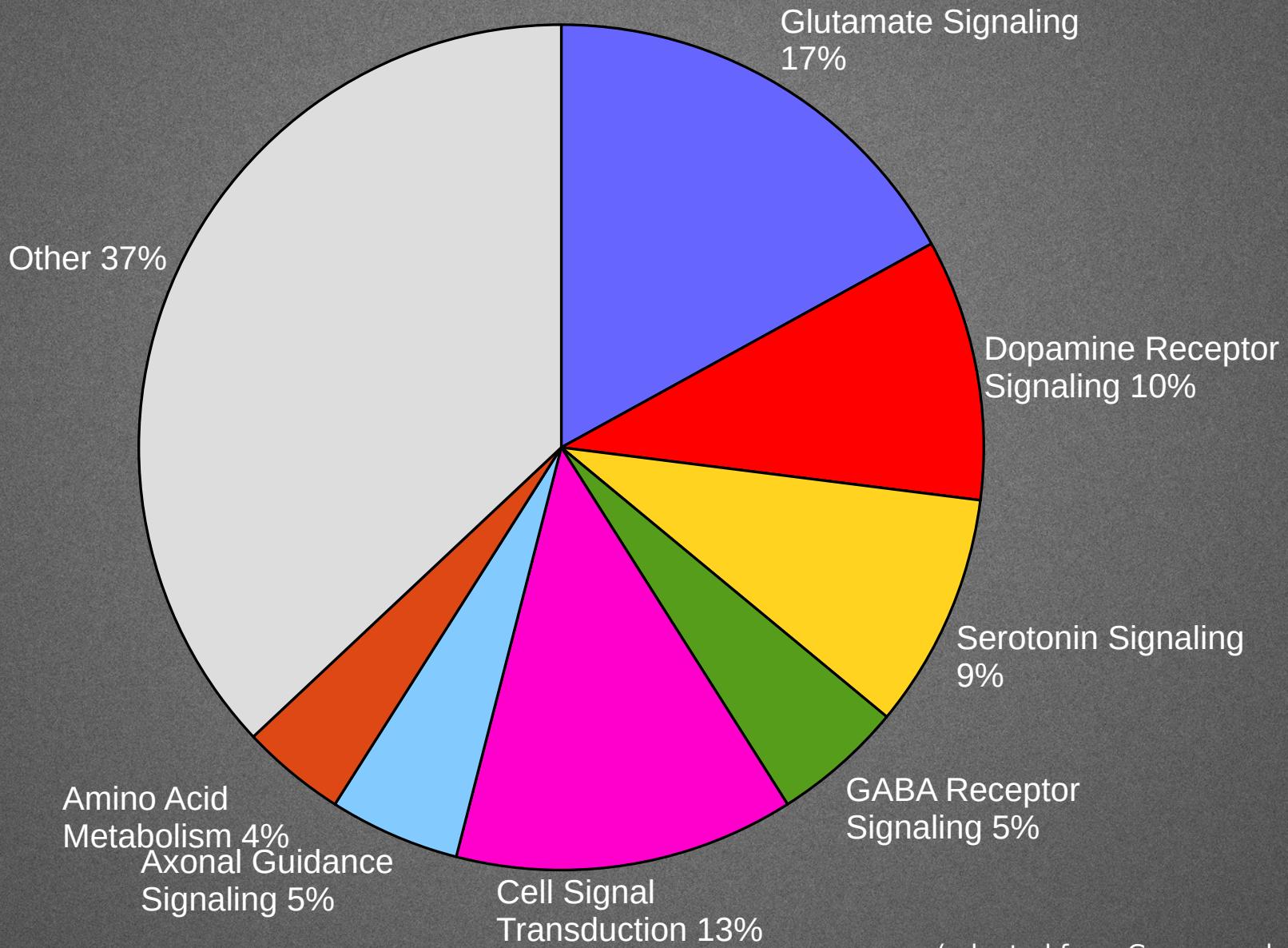


Iloperidone -0.33 (-0.43 to -0.22)



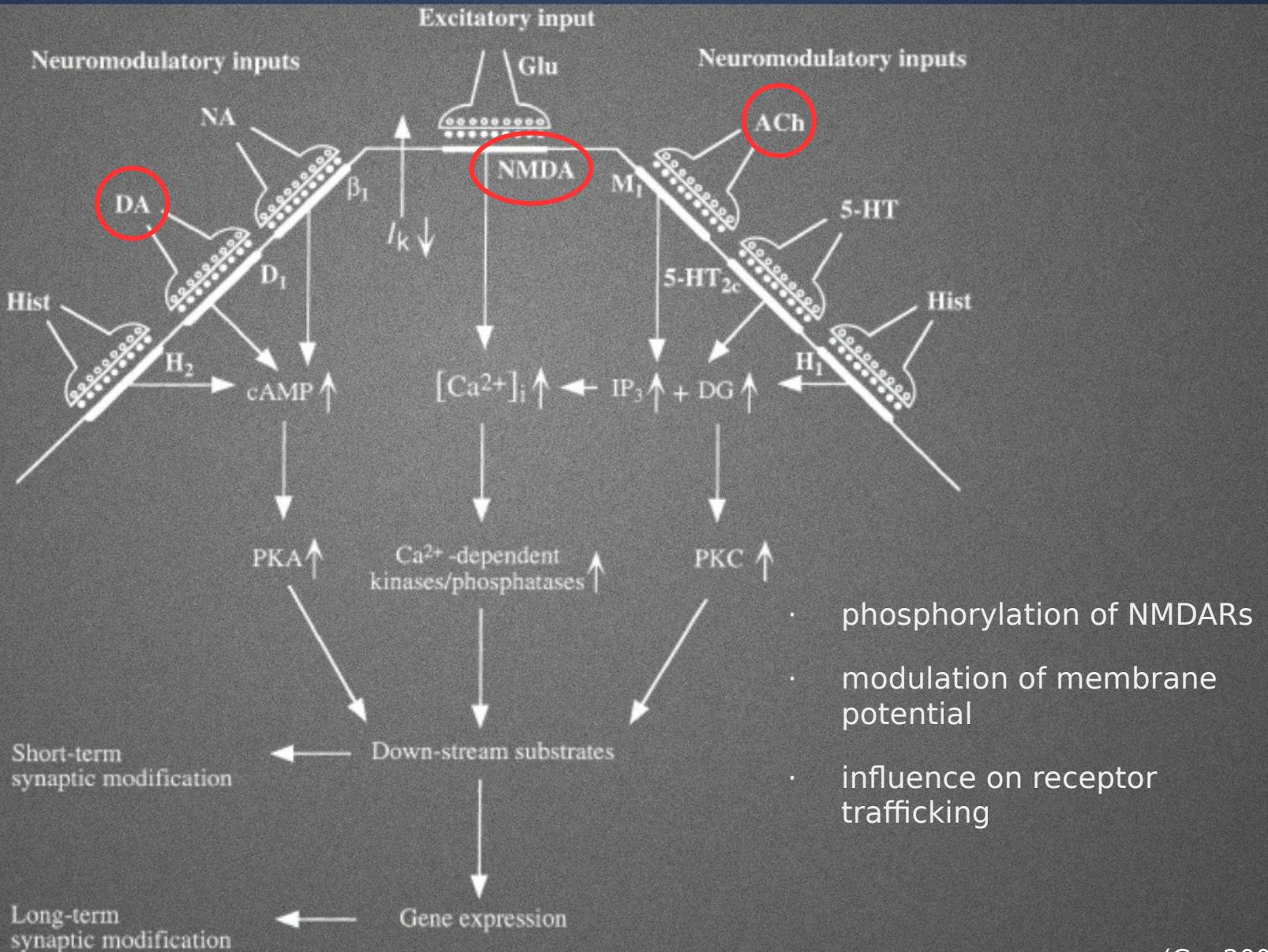
(adapted from Leucht et al., 2013)

Candidate Genes



(adapted from Greenwood et al., 2012)

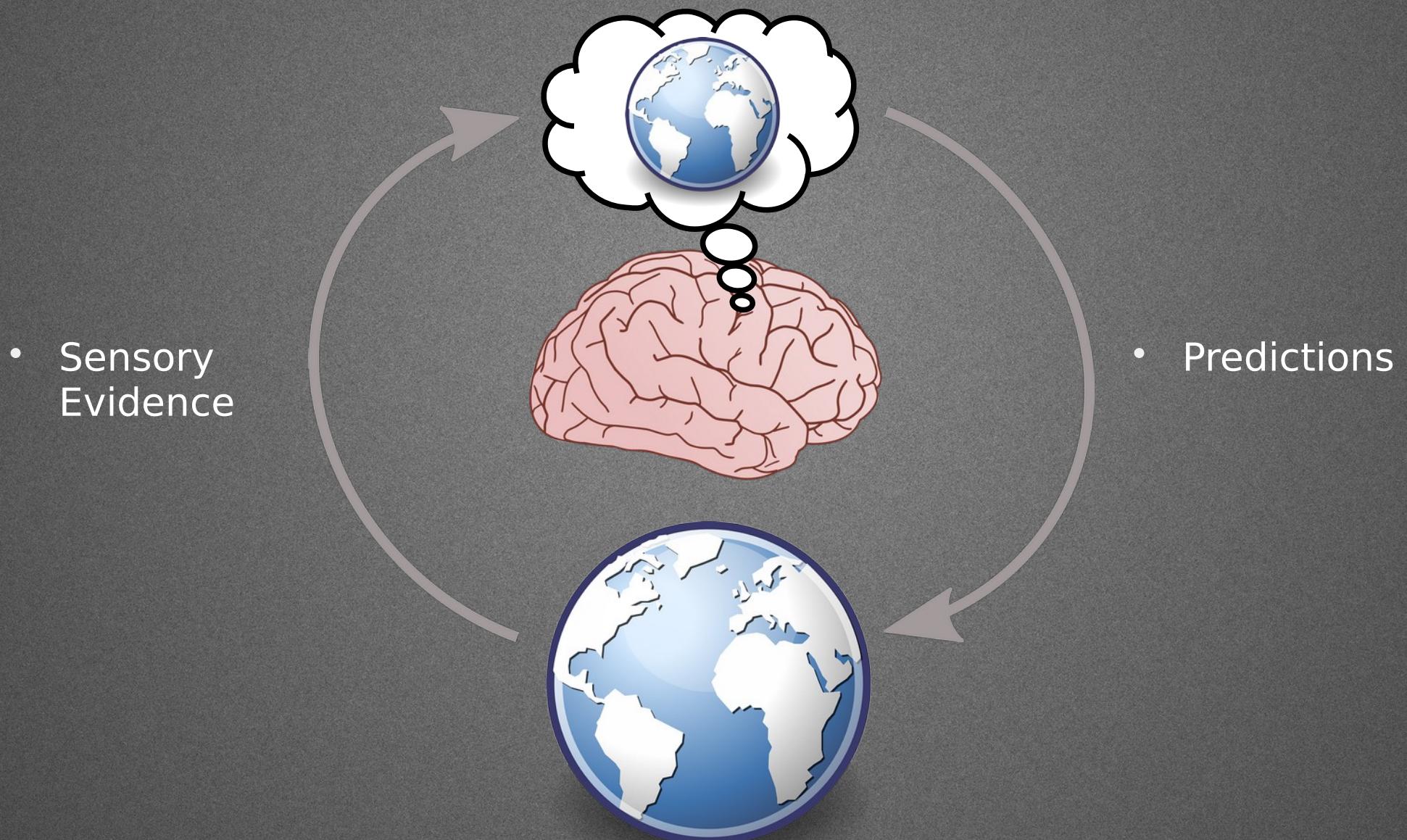
NMDAR × neuromodulator interactions



Dysconnection Hypothesis

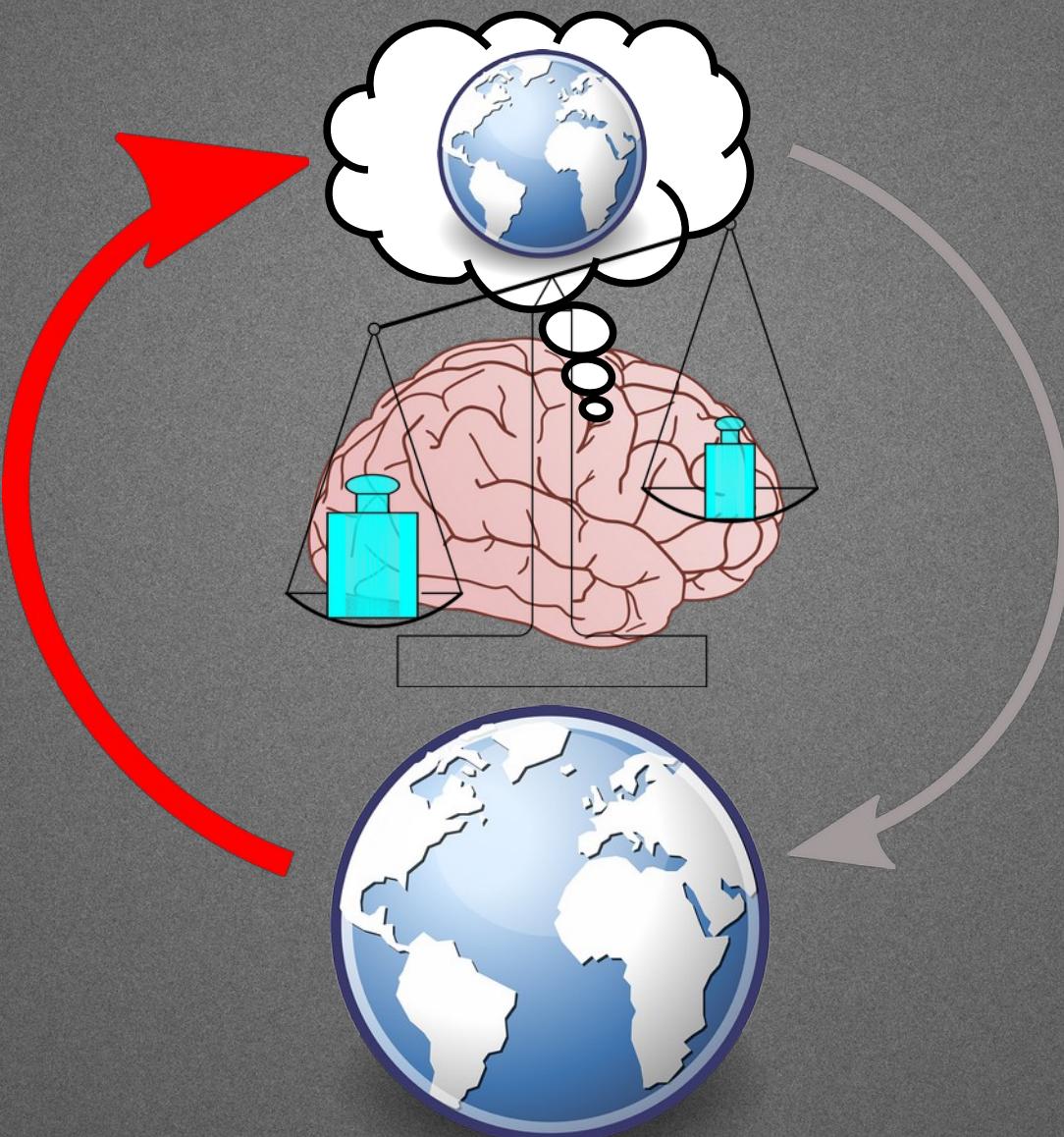
- Integrative computational perspective
 - Disturbed modulation of synaptic gain
 - “Dysbalance” in the integration of *sensory evidence* and *predictions*
- ...more of this later:
- Models of perception (F. Petzschner & L. Weber)
 - Models of Action Selection (P. Schwartenbeck, T. Parr & M. L. Pedersen)
 - From Prediction Errors to Computational Psychiatry (M. Garrido)
 - ...

Bayesian Brain



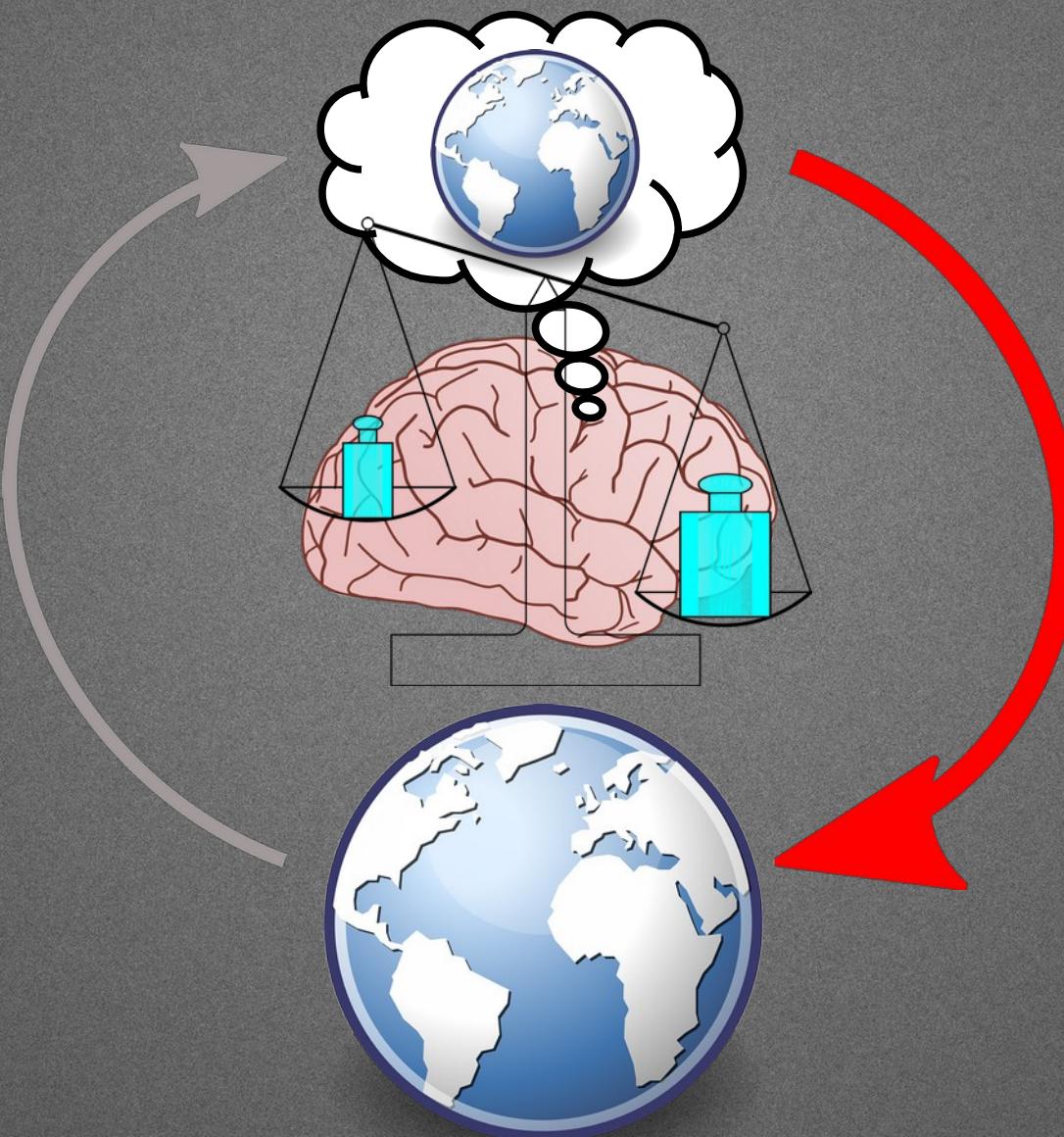
Bayesian Brain

- Sensory Evidence
- Predictions

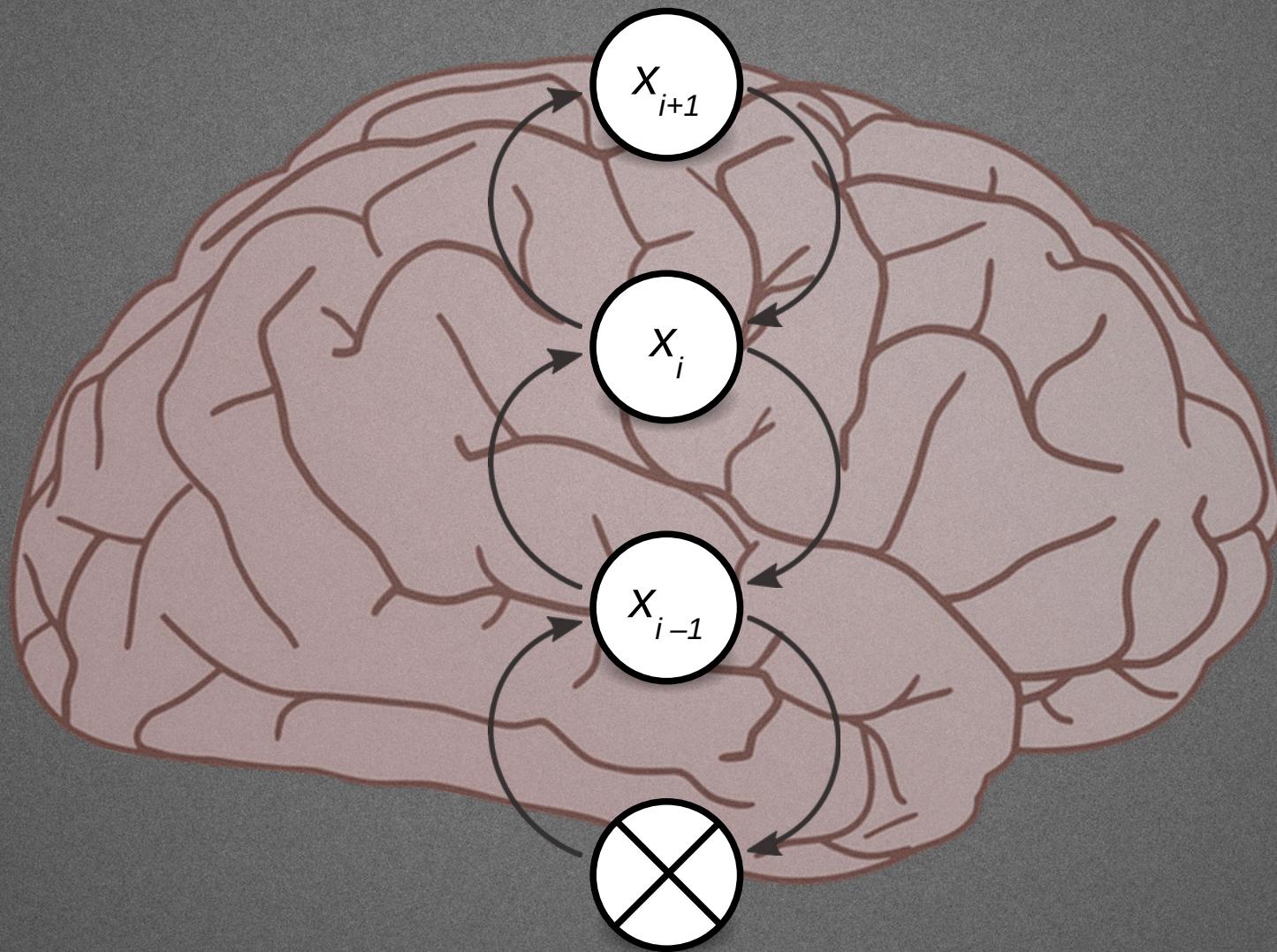


Bayesian Brain

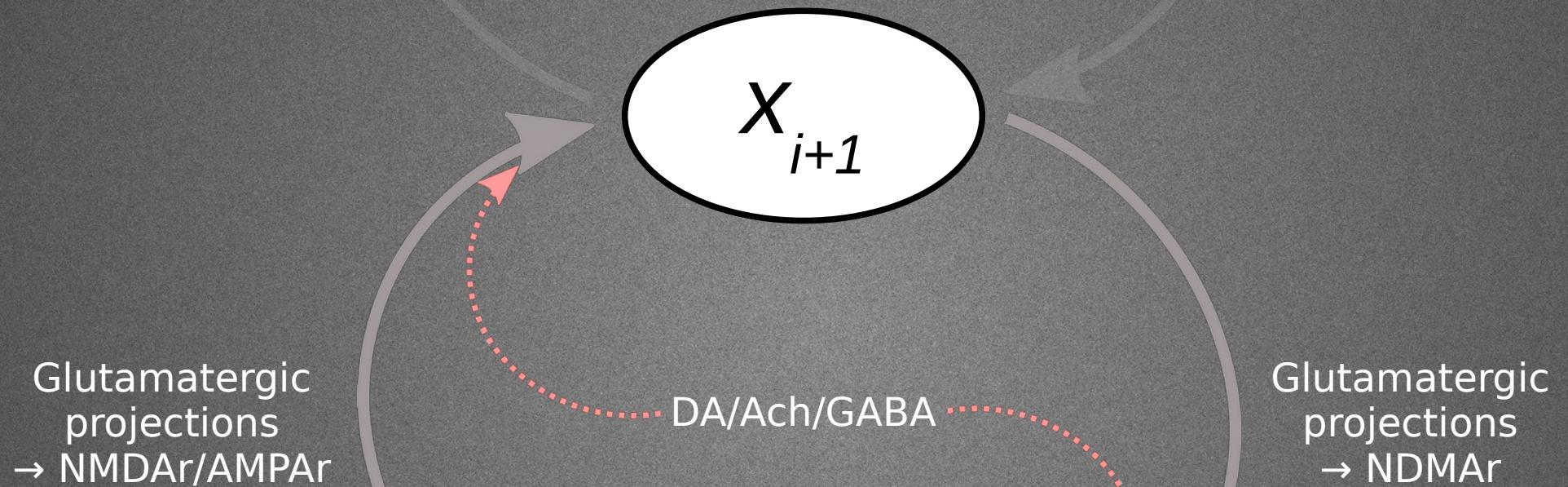
- Sensory Evidence
- Predictions



Predictive Coding



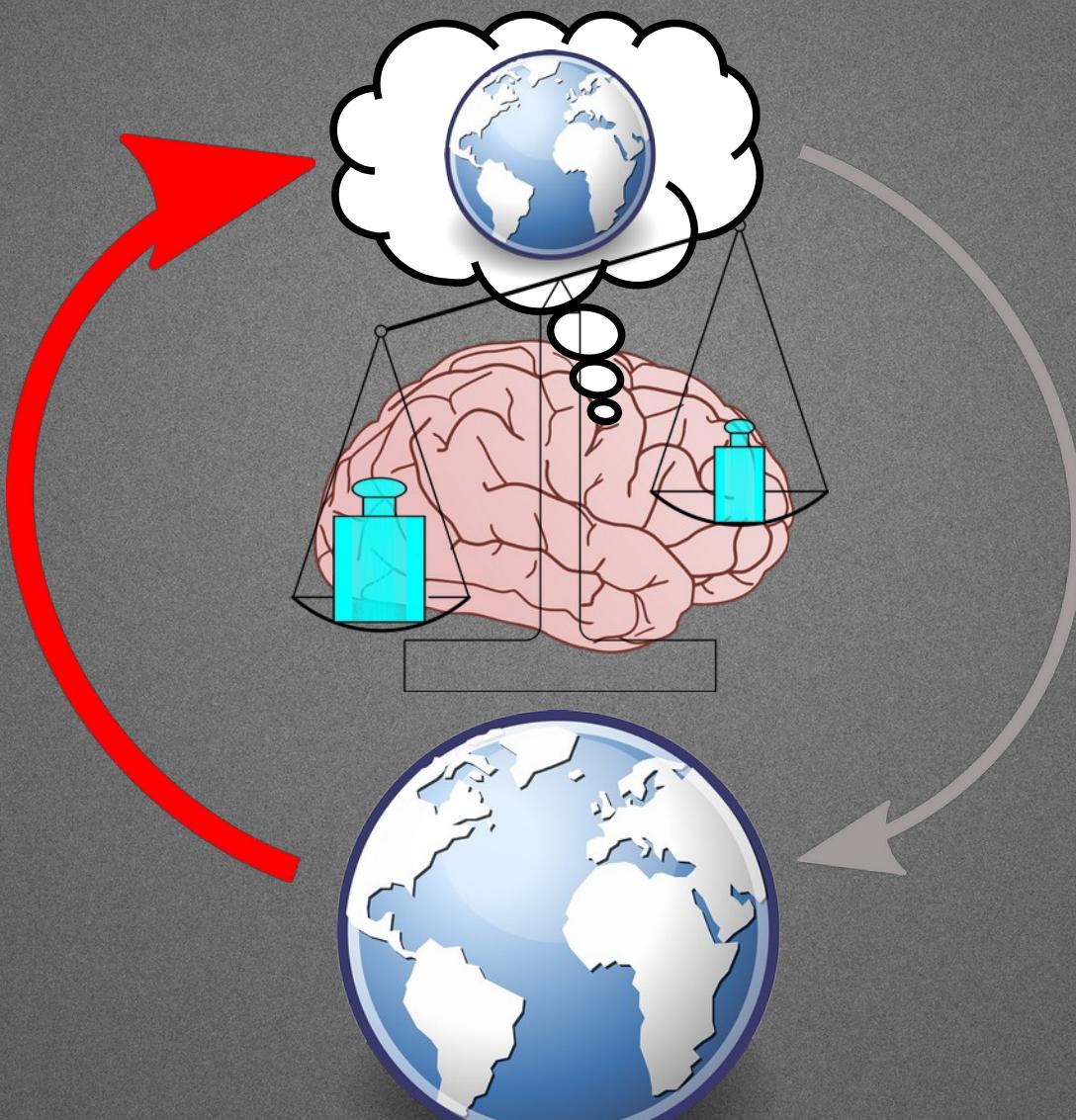
Dysconnectivity?



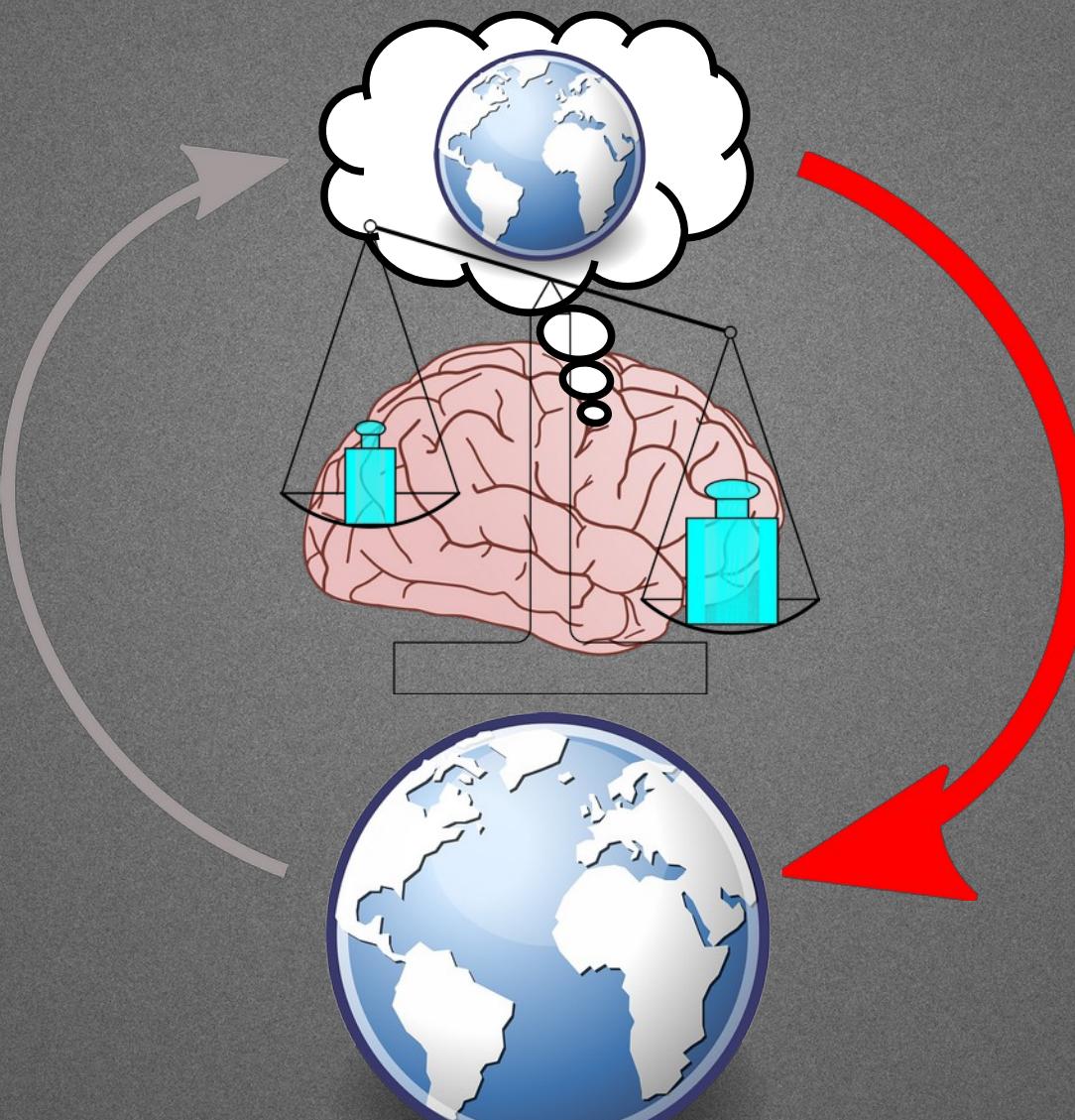
Bayesian Brain - Dysconnectivity

Trait phenomena

- ↓ susceptibility to illusions
- “Delusional mood”



Bayesian Brain - Dysconnectivity



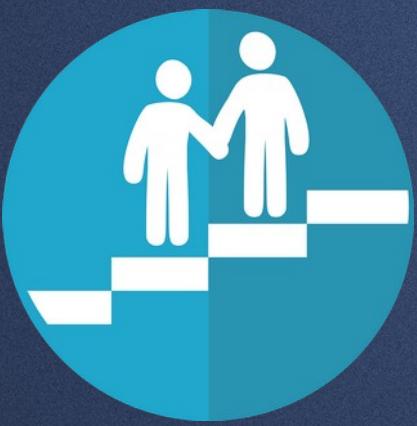
State phenomena

- Delusion
- Acoustic hallucinations

???

- Phentotypic expression
 - Continuum with affective disorders (Crow, 1986)
 - Failure of filter mechanisms (Hemsley and Zawada, 1976)
 - Internal monitoring deficiency (positive symptoms) & action initiation failure (negative symptoms) (Frith & Done, 1988)
 - Deficit vs. non-deficit SZ (Carpenter et al., 1988)
 - Aberrant salience syndrome (Kapur, 2003)
 - Dysconnection hypothesis (Stephan, 2009; Konrad & Winterer, 2008; dysmyelination: Segal et al., 2007)
 - Lateralization deficiency/language processing and distinction of thoughts and speech output (Crow, 2000)
- Pathophysiological
 - Abnormal transcallosal inter-hemispheric interaction → delusions of alien control (Nasralah, 1985)
 - Dysfunction of inhibitory circuits (reduced power in the gamma range bands) (Kwon, 1999)
 - Corollary discharge (Feinberg, 1978; Frith & Done, 1988)
 - Hyperdopaminergic models (Carlsson, 1977; Randrup & Munkvad, 1967, Snyder, 1976); prefrontal-limbic DA imbalance (Weinberger, 1987), phasic-tonic FA imbalance model (Grace, 1991); common pathway hypothesis (Seeman, 2010)
 - NMDAr-hypofunction (Olney & Farber, 1995)
 - Altered GABAergic transmission (altered neural synchrony/cognitive deficits; reductions in GABAergic neurons) (Benes & Berreta, 2001)
 - Cholinergic hypotheses (Tandon and Greden, 1989)
 - Inflammation – kynurenic acid as endogenous NMDAr antagonist (tryptophane metabolism)
- Pathogenesis
 - Early developmental models – disruptions intruterine/early postnatal (neuronal proliferation, migration, differentiation, elimination, neurogenesis) → impaired neuronal structure, abnormal brain maturation (Murray, 2002)
 - Late developmental models – deviations in later emerging processes such as synaptic/axonal pruning/neuronal apoptosis and/or myelination)
 - Neurodegeneration → atrophic processes
 - Acceleration of aging → cortico-limbic glutamatergic activity because of reduced inhibition by GABAergic interneurons → excitotoxicity
 - Disturbed excitatory/inhibitory balance as a
- Etiological
 - Polygenic/mutifactorial (Gottesman & Shields, 1967) → heritability, heterogeneity; copy number variations
 - Infectious diseases
 - Gene-environment interaction → two-hit-hypothesis (first genetic risk and early developmental alterations; then environmental factor) // epigenetic factors

Clinical Care



Clinical Care



National Schizophrenia & Psychosis Awareness Day
May 24th, 2018
www.earlypsychosisintervention.ca



Canadian Mental
Health Association
Mental health for all



Antipsychotics

- 50% respond to 1st line treatment
- Response ≠ remission, recovery or cure
- No prediction which of the antipsychotics is effective → “*trial & error*”
- Adherence
 - Poor insight – particular problem in SZ because of delusional beliefs about symptoms
 - Side effects

Treatment strategies

- **Building trust, therapeutic relationship & working alliance**
- Early treatment with antipsychotics
- Management and prevention of side-effects
- Activation & social support

Treatment strategies

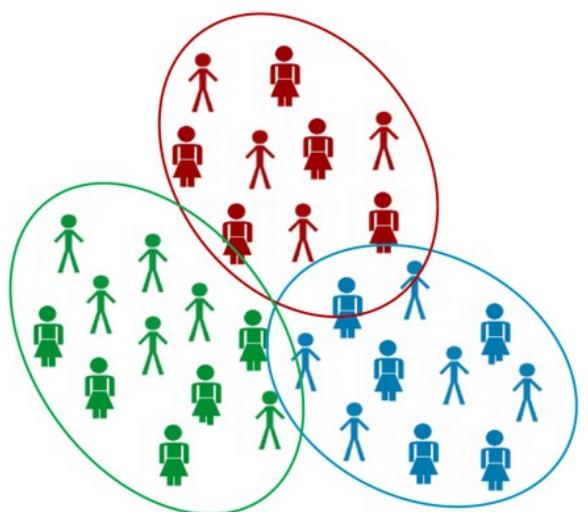
- Psychoeducation
- Low-threshold service
- Cognitive Behavioural Therapy
- Treatment resistance → Clozapine
- Antidepressant as co-medication

To summarize...

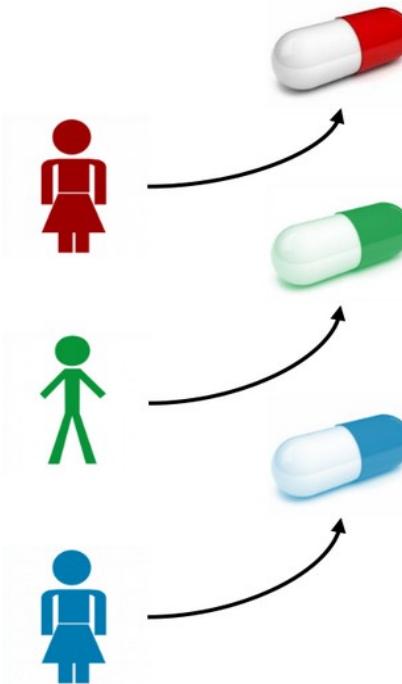
- SZ is a severe mental disorder
- Heterogeneous
- Functional impairment
- Antipsychotics are effective
- Pathophysiology?

To summarize...

- CP → different disease mechanisms



- disease mechanism A
- disease mechanism B
- disease mechanism C



(Stephan et al., 2015)

“Lost Years” by Bas Labruyère:

<https://vimeo.com/23611157>



Lost Years

vor 9 Jahre | Mehr



Bas Labruyère

PLUS + Folgen

▷ 7.721 ❤ 7 💼 3 💬 0

Mehr von Bas Labruyère

Nächstes Video automatisch abspielen



Lost Years

Bas Labruyère

Labruyère, B. (2011, May 11). Lost Years. <https://vimeo.com/23611157>

References

- Adams, R. A., Stephan, K. E., Brown, H. R., Frith, C. D., & Friston, K. J. (2013). The computational anatomy of psychosis. *Frontiers in Psychiatry*, 4, 47. <https://doi.org/10.3389/fpsyg.2013.00047>
- American Psychiatric Association. (2006). American Psychiatric Association Practice Guidelines for the treatment of psychiatric disorders: compendium 2006. Retrieved from https://books.google.ch/books?hl=de&lr=&id=zqI0AqtRSrYC&oi=fnd&pg=PR7&dq=PRACTICE+GUIDELINE+FOR+THE+Treatment+of+Patients+With++Schizophrenia++Second+Edition&ots=T9_5t9gBWf&sig=dNulu84Bacne15xIBcBlbO-aUvk
- American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5 (5 edition). Washington, D.C: American Psychiatric Publishing.
- Benkert, O., Hippius, H., & Anhelescu, I.-G. (2014). Kompendium der Psychiatrischen Pharmakotherapie (10., vollst. überarb. und aktualisierte Aufl). Springer.
- Bleuler, E. (1908). Die Prognose der Dementia praecox (Schizophreniegruppe). *Allgemeine Zeitschrift für Psychiatrie und Psychisch-Gerichtliche Medizin*, 65, 436-464.
- Corlett, P. R., Frith, C. D. & Fletcher, P. C. From drugs to deprivation: a Bayesian framework for understanding models of psychosis. *Psychopharmacology (Berl)* 206, 515-530 (2009).
- DGPPN, & Falkai, P. (Eds.). (2012). S3-Leitlinie Psychosoziale Therapien bei schweren psychischen Erkrankungen: S3-Praxisleitlinien in Psychiatrie und Psychotherapie. Springer-Verlag.
- Drake, R. J., Dunn, G., Tarrier, N., Bentall, R. P., Haddock, G., & Lewis, S. W. (2007). Insight as a predictor of the outcome of first-episode nonaffective psychosis in a prospective cohort study in England. *The Journal of Clinical Psychiatry*, 68(1), 81-86.
- Feldman, R. S., Jerrold S. Meyer, & Linda F. Quenzer. (1997). Principles of neuropsychopharmacology. Sunderland, Mass: Sinauer.
- Frith, C. D., & Friston, K. J. (2013). False Perceptions & False Beliefs: Understanding Schizophrenia. In A. Battro, S. Dehaene, & W. Singer (Eds.), *Neurosciences and the Human Person: New Perspectives on Human Activities*. Retrieved from <http://www.casinapioiv.va/content/dam/academia/pdf/sv121/sv121-frithc.pdf>
- Friston, K., Brown, H. R., Siemerkus, J., & Stephan, K. E. (2016). The dysconnection hypothesis (2016). *Schizophrenia Research*, 176(2-3), 83-94. <https://doi.org/10.1016/j.schres.2016.07.014>
- Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... Yung, A. (2013). The Psychosis High-Risk State: A Comprehensive State-of-the-Art Review. *JAMA Psychiatry*, 70(1), 107-120. <https://doi.org/10.1001/jamapsychiatry.2013.269>
- Greenwood, T. A., Light, G. A., Swerdlow, N. R., Radant, A. D., & Braff, D. L. (2012). Association Analysis of 94 Candidate Genes and Schizophrenia-Related Endophenotypes. *PLOS ONE*, 7(1), e29630. <https://doi.org/10.1371/journal.pone.0029630>
- Goldman, D., & Ducci, F. (2007). Deconstruction of Vulnerability to Complex Diseases: Enhanced Effect Sizes and Power of Intermediate Phenotypes [Research article]. <https://doi.org/10.1100/tsw.2007.210>
- Holzman, P. S. (2000). Eye movements and the search for the essence of schizophrenia. *Brain Research Reviews*, 31(2), 350-356. [https://doi.org/10.1016/S0165-0173\(99\)00051-X](https://doi.org/10.1016/S0165-0173(99)00051-X)
- Jaspers, K. (1973). Allgemeine Psychopathologie (9., unveränderte Auflage). Berlin, Heidelberg, New York: Springer.
- Jones, C., Hacker, D., Meaden, A., Cormac, I., Irving, C. B., Xia, J., ... Chen, J. (2018). Cognitive behavioural therapy plus standard care versus standard care plus other psychosocial treatments for people with schizophrenia. *Cochrane Database of Systematic Reviews*, (11). <https://doi.org/10.1002/14651858.CD008712.pub3>
- Kaiser, S., Berger, G., Conus, P., Kawohl, W., Müller, T. J., Schimmelmann, B. G., ... Seifritz, E. (2016). SGPP Behandlungsempfehlungen Schizophrenie - Version Februar 2016. Retrieved from http://www.psychiatrie.ch/sgpp/fachleute-und-kommissionen/behandlungsempfehlungen/index.php?elD=tx_securedownloads&u=0&g=0&t=1476207000&hash=b8badb079e7ebd98ce637fd851ff223a997c50&file=/fileadmin/SGPP/user_upload/Fachleute/Empfehlungen/d_Schizophrenia_Recommendations_final_Dez._2015_-_definitive_Fassung_-_Feb._2016.pdf
- Koethe, D., Gerth, C. W., Neatby, M. A., Haensel, A., Thies, M., Schneider, U., ... Leweke, F. M. (2006). Disturbances of visual information processing in early states of psychosis and experimental delta-9-tetrahydrocannabinol altered states of consciousness. *Schizophrenia Research*, 88(1-3), 142-150.
- Leucht, S., Busch, R., Kissling, W., & Kane, J. M. (2007). Early prediction of antipsychotic nonresponse among patients with schizophrenia. *The Journal of Clinical Psychiatry*, 68(3), 352-360.
- Leucht, S., Cipriani, A., Spinelli, L., Mavridis, D., Örey, D., Richter, F., ... Davis, J. M. (2013). Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *The Lancet*, 382(9896), 951-962. [https://doi.org/10.1016/S0140-6736\(13\)60733-3](https://doi.org/10.1016/S0140-6736(13)60733-3)
- Keshavan, M. S., Nasrallah, H. A., & Tandon, R. (2011). Schizophrenia, "Just the Facts" 6. Moving ahead with the schizophrenia concept: From the elephant to the mouse. *Schizophrenia Research*, 127(1), 3-13. <https://doi.org/10.1016/j.schres.2011.01.011>
- Keshavan, M. S., Tandon, R., Boutros, N. N., & Nasrallah, H. A. (2008). Schizophrenia, "just the facts": What we know in 2008: Part 3: Neurobiology. *Schizophrenia Research*, 106(2), 89-107. <https://doi.org/10.1016/j.schres.2008.07.020>
- Menezes, N. M., Arenovich, T., & Zipursky, R. B. (2006). A systematic review of longitudinal outcome studies of first-episode psychosis. *Psychological Medicine*, 36(10), 1349-1362. <https://doi.org/10.1017/S0033291706007951>

References

- Millan, M. J., Andrieux, A., Bartzokis, G., Cadenhead, K., Dazzan, P., Fusar-Poli, P., ... Weinberger, D. (2016). Altering the course of schizophrenia: progress and perspectives. *Nature Reviews Drug Discovery*, 15(7), 485-515. <https://doi.org/10.1038/nrd.2016.28>
- National Collaborating Centre for Mental Health (UK). (2014). *Psychosis and Schizophrenia in Adults: Treatment and Management*. Retrieved from <http://www.ncbi.nlm.nih.gov/books/NBK248060/>
- Perkins, D. O., Gu, H., Boteva, K., & Lieberman, J. A. (2005). Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *The American Journal of Psychiatry*, 162(10), 1785-1804. <https://doi.org/10.1176/appi.ajp.162.10.1785>
- Powers, A. R., Mathys, C., & Corlett, P. R. (2017). Pavlovian conditioning-induced hallucinations result from overweighting of perceptual priors. *Science*, 357(6351), 596-600. <https://doi.org/10.1126/science.aan3458>
- Saha, S., Chant, D., Welham, J., & McGrath, J. (2005). A Systematic Review of the Prevalence of Schizophrenia. *PLOS Medicine*, 2(5), e141. <https://doi.org/10.1371/journal.pmed.0020141>
- Saklad, S. R. (2018). Graphic representation of pharmacology: Development of an alternative model. *The Mental Health Clinician*, 7(5), 201-206. <https://doi.org/10.9740/mhc.2017.09.201>
- Schwartz, T. L., Sachdeva, S., & Stahl, S. M. (2012). Glutamate Neurocircuitry: Theoretical Underpinnings in Schizophrenia. *Frontiers in Pharmacology*, 3. <https://doi.org/10.3389/fphar.2012.00195>
- Sifafis, S., Tzachanis, D., Samara, M., & Papazisis, G. (2018). Antipsychotic Drugs: From Receptor-binding Profiles to Metabolic Side Effects. *Current Neuropharmacology*, 16(8), 1210-1223. <https://doi.org/10.2174/1570159X15666170630163616>
- Stephan, K. E., Diaconescu, A. O., & Iglesias, S. (2016). Bayesian inference, dysconnectivity and neuromodulation in schizophrenia. *Brain*, 139(7), 1874-1876. <https://doi.org/10.1093/brain/aww120>
- Stephan, K. E., Iglesias, S., Heinze, J., & Diaconescu, A. O. (2015). Translational Perspectives for Computational Neuroimaging. *Neuron*, 87(4), 716-732. <https://doi.org/10.1016/j.neuron.2015.07.008>
- Stephen M. Stahl. (2013). *Stahl's essential psychopharmacology: neuroscientific basis and practical application* (4th ed.). Cambridge: Cambridge University Press.
- Sterzer, P., Adams, R. A., Fletcher, P., Frith, C., Lawrie, S. M., Muckli, L., ... Corlett, P. R. (2018). The predictive coding account of psychosis. *Biological Psychiatry*. <https://doi.org/10.1016/j.biopsych.2018.05.015>
- Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008a). Schizophrenia, "Just the Facts": What we know in 2008: Part 1: Overview. *Schizophrenia Research*, 100(1), 4-19. <https://doi.org/10.1016/j.schres.2008.01.022>
- Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008b). Schizophrenia, "Just the Facts" What we know in 2008. 2. Epidemiology and etiology. *Schizophrenia Research*, 102(1), 1-18. <https://doi.org/10.1016/j.schres.2008.04.011>
- Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2009). Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophrenia Research*, 110(1), 1-23. <https://doi.org/10.1016/j.schres.2009.03.005>
- Tandon, R., Nasrallah, H. A., & Keshavan, M. S. (2010). Schizophrenia, "Just the Facts" 5. Treatment and prevention Past, present, and future. *Schizophrenia Research*, 122(1), 1-23. <https://doi.org/10.1016/j.schres.2010.05.025>
- Umbrecht, D., & Krilje, S. (2005). Mismatch negativity in schizophrenia: a meta-analysis. *Schizophrenia Research*, 76(1), 1-23. <https://doi.org/10.1016/j.schres.2004.12.002>
- van Os, J. (2009). A salience dysregulation syndrome. *The British Journal of Psychiatry*, 194(2), 101-103. <https://doi.org/10.1192/bjp.bp.108.054254>
- Tandon, R., Keshavan, M. S., & Nasrallah, H. A. (2008). Schizophrenia, "Just the Facts" What we know in 2008. 2. Epidemiology and etiology. *Schizophrenia Research*, 102(1), 1-18. <https://doi.org/10.1016/j.schres.2008.04.011>

References - Media

Labruyère, B. (2011, May 11). Lost Years. <https://vimeo.com/23611157>

Canada, S. (2018T06:29). Today is #NSPAD18! #Recovery is possible, and expected, with the right treatments. Effective treatment can include counselling, medication, meaningful activity, & support from loved ones --> <https://www.earlypsychosisintervention.ca/psychosis> #SupportSZ #CMHA100 #Schizophrenia #EndStigmapic.twitter.com/cTselJT9Yd [Tweet]. Retrieved August 23, 2019, from @schizophreniaca website: <https://twitter.com/schizophreniaca/status/999643428605526016>

Covid-19 may cause brain complications in some, say doctors. (2020, June 26). The Guardian. <http://www.theguardian.com/science/2020/jun/25/doctors-find-brain-issues-linked-to-covid-19-patients-study>

James, D. (2019). English: Two doses of intravenous ketamine, 50mg/ml and 10mg/ml. Retrieved from https://commons.wikimedia.org/wiki/File:Two_doses_of_iv_ketamine.jpg; edited

JanBaby. (n.d.). Free Image on Pixabay - Signpost, Road Signs, Sign, Post. Retrieved August 23, 2019, from <https://pixabay.com/illustrations/signpost-road-signs-sign-post-2030780/>

kaboldy. (2008). English: Kinematic sketches of mechanical scales. Retrieved from https://commons.wikimedia.org/wiki/File:Mechanical_scales2.svg; edited

mcmurtryjulie | Pixabay. (n.d.). Retrieved August 30, 2019, from <https://pixabay.com/users/mcmurtryjulie-2375405/>

Netherlands, S. van der W. from. (2010). In order to reach the highest mountains, you shouldn't be afraid of the deepest valleys. Retrieved from [https://commons.wikimedia.org/wiki/File:Depressed_\(4649749639\).jpg](https://commons.wikimedia.org/wiki/File:Depressed_(4649749639).jpg)

Munch, E. (1893). English: The Scream [Oil, tempora & pastel on cardboard]. National Gallery of Norway.

https://commons.wikimedia.org/wiki/File:Edvard_Munch,_1893,_The_Scream,_oil,_tempora_and_pastele_on_cardboard,_91_x_73_cm,_National_Gallery_of_Norway.jpg

Open-Clipart-Vectors. (n.d.). Free Image on Pixabay - Biology, Brain, Cortex, Holiday. Retrieved September 1, 2019, from <https://pixabay.com/vectors/biology-brain-cortex-holiday-1295897/>

OpenIcons. (n.d.). Free Image on Pixabay - World, Globe, Global, Earth. Retrieved September 1, 2019, from <https://pixabay.com/vectors/world-globe-global-earth-97864/>

Pablo Picasso, 1901-02, Femme aux Bras Croisés, Woman with Folded Arms (Madchenbildnis), oil on canvas, 81 × 58 cm (32 × 23 in).jpg. (2020). In Wikipedia.

[https://en.wikipedia.org/w/index.php?title=File:Pablo_Picasso,_1901-02,_Femme_aux_Bras_Crois%C3%A9s,_Woman_with_Folded_Arms_\(Madchenbildnis\),_oil_on_canvas,_81_%C3%97_58_cm_\(32_%C3%97_23_in\).jpg&oldid=974424175](https://en.wikipedia.org/w/index.php?title=File:Pablo_Picasso,_1901-02,_Femme_aux_Bras_Crois%C3%A9s,_Woman_with_Folded_Arms_(Madchenbildnis),_oil_on_canvas,_81_%C3%97_58_cm_(32_%C3%97_23_in).jpg&oldid=974424175)

Unknown. (1962). English: Advert from ca. 1962 for Thorazine (trade-name of chlorpromazine in the U.S.). An antipsychotic (neuroleptic, major tranquilizer, antischizophrenic, actaractic). In Europe it is known as Largactil. Retrieved from https://commons.wikimedia.org/wiki/File:Thorazine_advert.jpg

User:Fvasconcellos, U. P. J. L. (2015). English: The main dopaminergic pathways of the human brain: the mesocortical pathway, connecting the ventral tegmental area (VTA) with the frontal cortex; the mesolimbic pathway, connecting the VTA with the nucleus accumbens; the nigrostriatal pathway, connecting the substantia nigra with the dorsal striatum; and the tuberoinfundibular pathway, connecting the hypothalamus with the pituitary. Retrieved from https://commons.wikimedia.org/wiki/File:Dopaminergic_pathways.svg; edited

Questions?



THANK YOU!



Translational Neuromodeling Unit



Universität
Zürich



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

CONTACT:

siemerkus@biomed.ee.ethz.ch
translationalneuromodeling.org