

Mechanisms-Based Medicine

to redefine diseases / disorders /
syndrome definitions and descriptions

*Similar symptoms can have very different functional origins
while*

similar dysfunctions can produce different symptoms.

Psychiatric disorders case study

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The current situation

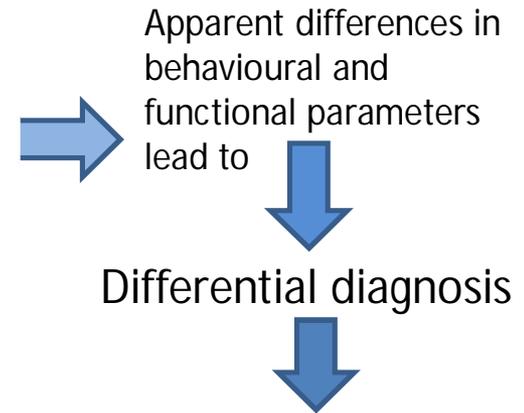
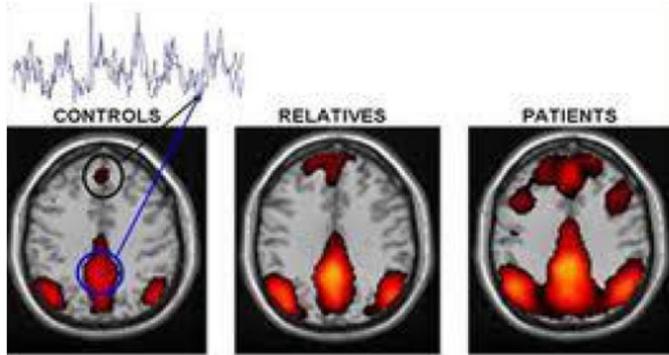
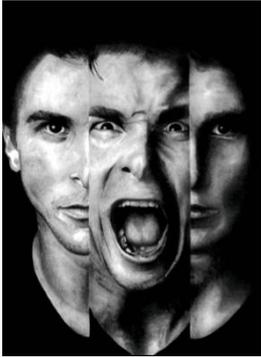


Table 3. Dosage Ranges for Antipsychotic Medications*

Agent	T _{1/2} (hr)	Suggested Dosage Range (mg/day)	Initial Dose (mg/day)
SSRIs/SNRIs			
Fluoxetine	24–72	20–40	5–10
Citalopram	35	20–40	5
Sertraline	24	100–200	12.5–25
Paroxetine	21	20–40	5–10
Escitalopram	27–32	10–20	5
Fluvoxamine	15	100–200	25
Venlafaxine	5–11	150–225	12.5
Benzodiazepines			
Alprazolam†‡	6–12	2–6	0.5–1
Lorazepam†	8–12	2–8	1.5–2
Clonazepam	18–50	1–4	0.25–0.5
Tricyclic antidepressants			
Imipramine‡	12–24	150–300	10
Clomipramine	11–20	50–150	10
Desipramine	28–36	100–200	10
MAOIs			
Phenelzine		45–60	15
Tranylcypromine		30–40	10

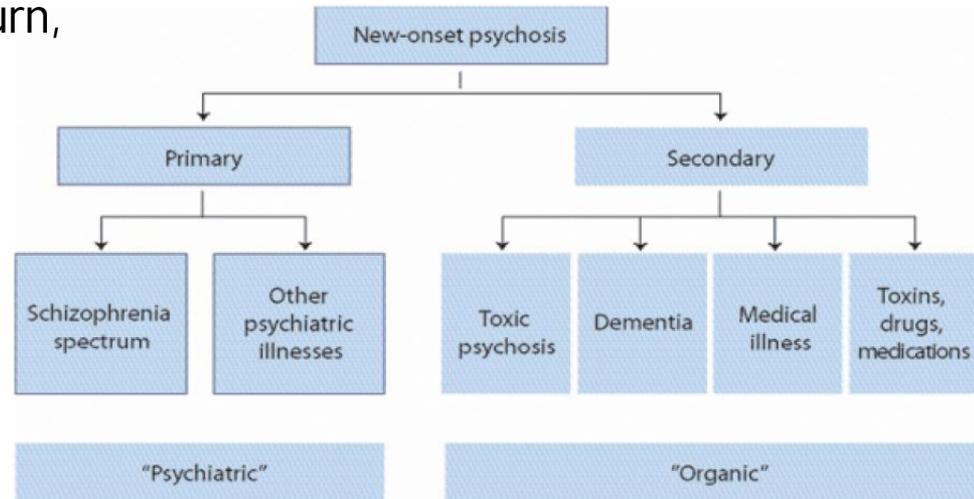
* Some patients will require higher doses than recommended range.
 † Multiple divided doses necessary.
 ‡ Plasma levels can guide treatment.

Which, in turn, leads to

Differential treatments

that are, all too often, unsatisfactory.

Differential diagnosis of new-onset psychosis



Searching under the street lamp because that is where there is light isn't necessarily the best idea...

Most clinical forms of psychiatric disorders share common genetic characteristics.



Smoller JW, Craddock N, Kendler K, Lee PH, Neale BM, Nurnberger JI, Ripke S, Santangelo S, Sullivan PF. Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *Lancet*. 381(9875):1371-9; 2013.

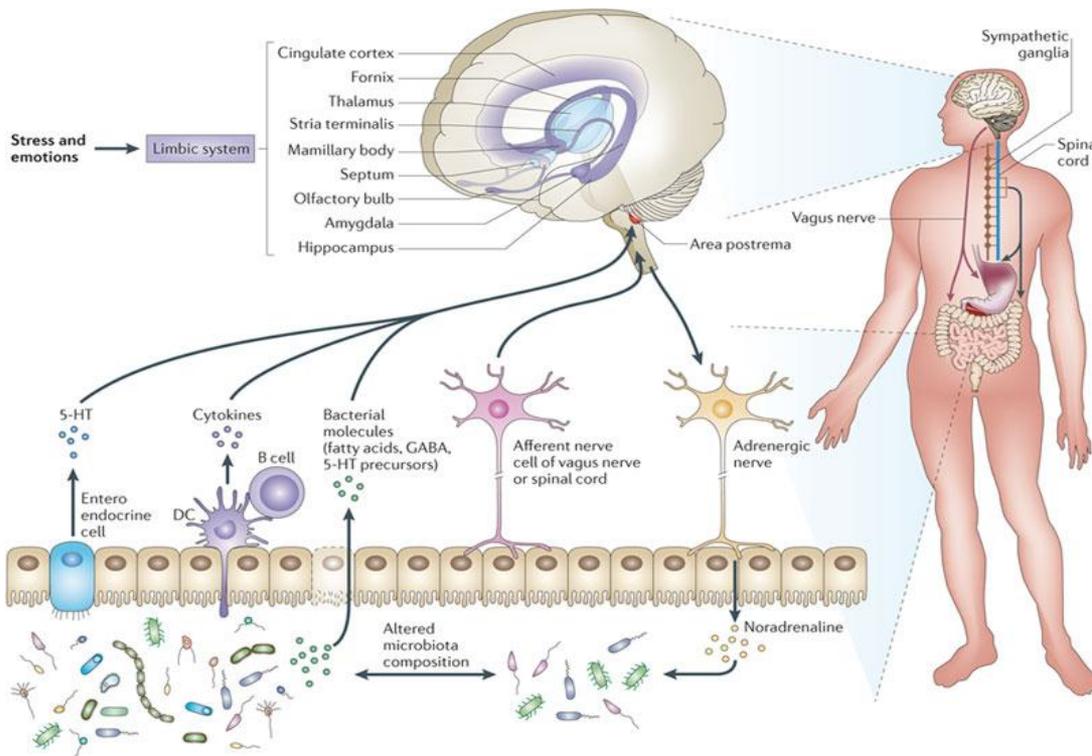


And

Cognitive functions, including behaviour, are deeply affected by somatic components and homeostasis.



Collins SM, Surette M, Bercik P. The interplay between the intestinal microbiota and the brain. *Nat Rev Microbiol*. 10(11):735-42; 2012.



Psychiatric disorders are not different from somatic diseases.

Similar symptoms can have very different functional origins while similar dysfunctions can produce different symptoms.

Medically unexplained symptoms are common across general/internal medicine and represent the most common diagnosis in some specialities.

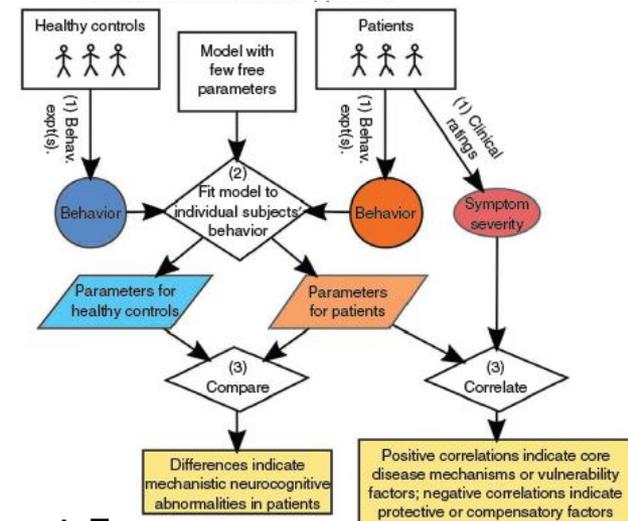
(Nimnuan C, Hotopf M, Wessely S. Medically unexplained symptoms: an epidemiological study in seven specialities. J Psychosom Res. 51(1):361-7; 2001).

From clinical and therapeutic standpoints the differential key resides with indirect regulatory mechanisms.



And thereby to personalised therapies.

This leads to treatment of the disorder itself (as opposed to its symptoms only).



This is what we aim to achieve within the next 5 years.

BMSystems is already applying this to other complex multifactor diseases / disorders