

The Tower of Babel in Psychiatry

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Abstract

Both accurate diagnosis and effective treatment of mental disorders remain an unfulfilled aim, but an accurate diagnosis is not required for optimal prescribing. Psychiatrists work as balancers among patients' requirements and misconceptions, while patients ask for actual and not stigmatized words in diagnosis and therapy language. We have to resolve the circle of misconceptions between patients, psychiatrists, other specialties, scientific institutions and journals, pharmaceutical companies, legal agencies, and media. What really needs to be changed is the way mental illness is seen by the public, and any such change will need the positive reaction of patients and carers. Isolation of psychiatry from the rest medical specialties has diminished value of diagnosis and treatment, reducing psychiatry to a nonspecific psychological support, which contributes to more increasing the stigma. In view of sosio-medical care, psychiatrists should return home to medicine, leaving non-medical interventions to non-medical practitioners. We need new neuroscientific models, such as the RDoC, having the potential to inform the development of a unified, dimensional, and biobehaviorally grounded psychiatric nosology. Renaming, redefining and reconceptualization processes, in this 'Tower of Babel' of mental health country, are long and challenging, but there is not serious difficulty other than our inner resistance to change.

Keywords

psychiatry, psychosis, schizophrenia, depression, antipsychotics, antidepressants, stigma, renaming

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'If names be not correct, language is not in accordance with the truth of things' (Confucius, the Analects)

The Tower of misconceptions

So far, both accurate diagnosis and definite and effective treatment of mental disorders remain an unfulfilled aim. In his Philosophical Remarks, L. Wittgenstein [1] commented that "the classifications made by philosophers and psychologists are as if one were to classify clouds by their shape". While the reliability of psychiatric diagnoses can be substantially improved by the use of explicit diagnostic criteria, their validity remains uncertain [2]. In most areas of medicine, prescribing is very closely aligned with drug labeling, as drugs usually have a known mode of action, in correspondence with the pathological condition for which changed. In psychiatry things are different. Selective serotonin reuptake inhibitors and other drugs initially developed for the treatment of depression are now generally also used as the main treatments for anxiety disorders. Nowadays, the biological basis of most mental disorders is poorly understood, the diagnostic criteria tend to shift, and diagnostic entities appear or disappear with relative ease. For this reason, the off-label prescribing of antipsychotics and antidepressants is very high [3-7]. Drugs such as quetiapine, initially developed for the treatment of psychotic symptoms, are now used in the treatment of depression, bipolar disorder, and, though off-label, for anxiety and other syndromes characterized by restlessness, anxiety, sleeping problems and agitation. [8]

A major weakness of *evidence-based medicine* is that it does not explain the large individual differences in the therapeutic response. For example, looking at the progression of depressed patients having received the same treatment, although many of them have a satisfactory outcome, others exhibit poor improvement, and some are getting worse [9]. The cause of these individual differences concerning the outcome remains largely unknown and the clinical characteristics have relatively low predictive value for patients to be improved. Scientists believe the answer come from the origin of the disease, i.e. it should be based on the knowledge of its cause [9]. But nowadays, in the era of *operationalized diagnosis* and *evidence-based medicine*, causes and treatment remain two separate areas of interest. Diagnosis is "proven" based on a group of symptoms, and the treatment is selected according to the diagnosis, while the potential causative effects and risk factors are not used in the choice of treatment. So, some perceptive clinicians may wonder "whether they have lost something along the way".

As a result of this diagnostic and treatment confusion, both therapists and patients live as in a virtual reality world. Not only the depressed have "depression", nor the psychotic a "psychosis". Also, "antidepressants" are prescribed not only for "depression", nor "antipsychotics" only for "psychosis". After so much research in the field of neuroscience, it seems that a firm diagnosis is not required in order to get the best possible treatment. Thus, psychiatrists work as balancers, between patient needs, guidelines, evidence-based surveys, meta-analyses, and everyday clinical requirements (Fig. 1).

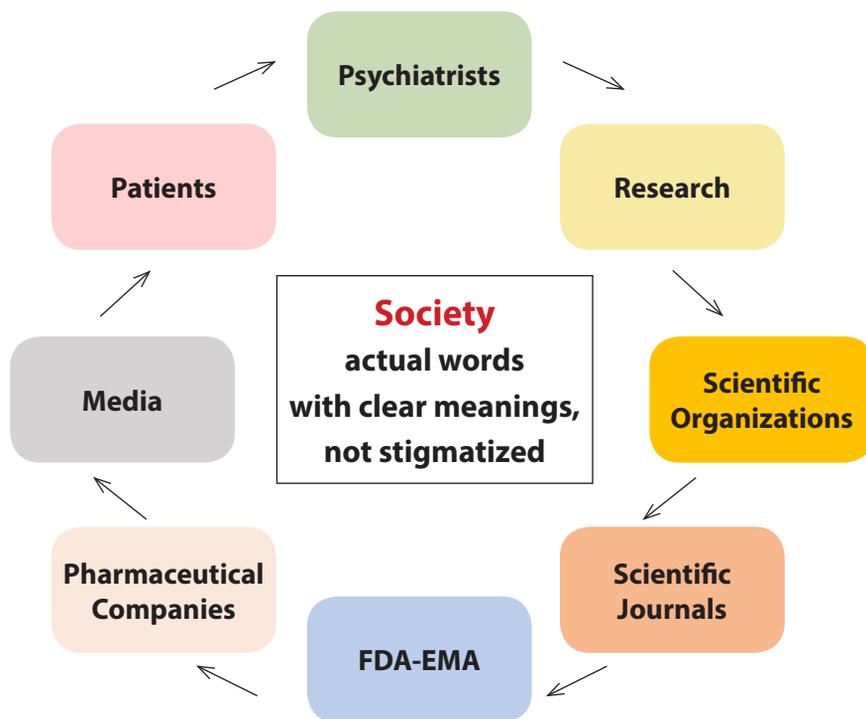


Figure 1. The 'Circle of Babel' in mental health area. Society needs real words with clear meanings, and not-stigmatized. We need actual words in the communication between patients, psychiatrists, other clinicians, scientific institutions and journals, pharmaceutical companies, legal agencies, and media. What really needs to be changed is the way that mental illness is seen by the public, while any such change will need to include assessments with patients and carers.

Repairing the Tower – Renaming things

According to Nancy Andreasen: [10] «Validity of psychiatric diagnosis has been sacrificed to achieve reliability. DSM diagnoses have given researchers a common nomenclature - but probably the wrong one. Although creating standardized diagnoses that would facilitate research was a major goal, DSM diagnoses are not useful for research because of their lack of validity». In the case of PTSD, as well as in many other mental disorders, the following paradox is observed: While according to the diagnostic criteria clinicians agree on diagnosis, which means there is a good *reliability*, it seems as if it is diagnosed something that more or less does not exist, which means *validity* (both context and face) is very low. PTSD in particular, is difficult to diagnose reliably due to the high degree of variety of symptoms. According to DSM IV criteria, an individual should have experienced 1 of the 5 *re-experiencing* symptoms, 3 of the 7 *avoidance* symptoms and 2 of the 5 *hyperarousal* symptoms. Thus, there are hundreds of different combinations of PTSD symptoms that could meet the diagnostic criteria, which makes it unlikely to come across two entirely identical PTSD cases. (Fig. 2).

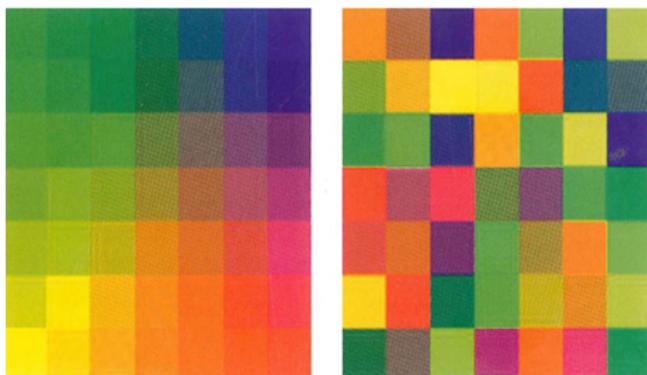


Figure 2. Visualization of two 'patients' with the same psychiatric diagnosis, eg. PTSD. While agree on diagnosis (good reliability), it is diagnosed something that more or less does not exist (very low context and face validity).

Hypotheses regarding the diagnostic entity of PTSD

- "PTSD is a diagnostic artifact", according to which if there is a significant problem of differential diagnosis, then it is a question of reliability concerning the construction of the criteria
- thus: PTSD does not exist as a diagnostic entity
- "PTSD leads to other disorders". For example, PTSD can lead to symptoms of anxiety and depression, the "self-healing" of which using psychoactive substances leads to substance abuse disorder
- thus: PTSD is identical with the *trauma*
- "Trauma leads to multiple disorders", (including PTSD), according to the *shared vulnerability model*, either in combination with pre-existing vulnerability or via direct effect
- thus: PTSD is encapsulated into the trauma

Epidemiological studies show that comorbidity in patients with PTSD is probably the rule rather than the exception, and this is the main reason for the extremely low diagnostic *validity*. The most common comorbidity of PTSD patients is that with major depression, followed by substance abuse disorder, and anxiety disorders. In addition, individuals suffering from any type of *trauma*, but do not meet the criteria for PTSD, may suffer far more from social or professional distress, compared to those who meet the criteria for PTSD [11].

In spite of the abundance of clinical observations and research data on the *continuum* of mental illness, the DSM 5 preferred to remain in the *categorical model* of mental illness classification, although there are some apparent "fallback" examples: On page 12, Introduction, DSM 5 entitled 'Dimensional Approach to Diagnosis', states that relevant evidences come from diverse sources, including studies of comorbidity, and the substantial need for not otherwise specified diagnoses, which represent the majority of diagnoses in areas such as eating disorders, personality disorders and autism spectrum disorders. In page 13, DSM states that despite the problem due to *categorical diagnoses*, the *DSM 5 Task Force* recognized it is premature scientifically to propose alternative definitions for most disorders, continuing that such reformulation of research goals should also keep central to the development of *dimensional approaches* that will likely supersede current categorical approaches in coming years.

Data indicating the 'continuum' of mental illness

- there is an inability to detect internally consistent and clearly distinct psychopathological clinical syndromes
- there are common predisposing genetic, neurobiological and neuropsychological factors were found in clinically overlapping categories of mental disorders
- there is a similar degree of efficacy of the same type of treatment was observed in patients with clinically overlapping or related diagnostic categories, e.g., efficacy of antipsychotic drugs in the treatment of psychotic symptoms regardless of their nosological context origins, such as schizophrenic disorders, mood disorders, dementia syndromes etc.

The DSM 5, implicitly but clearly, accepts the failure of the scientific community to deal with autism and proposes backtracking and reassessing the phenomenon of autism through the spectrum of autistic continuum (consolidation of autistic behavior, Asperger disorder and pervasive developmental disorder into autism spectrum disorder). It states that this change is designed to improve sensitivity and specificity of the criteria for *autism spectrum disorder*, and to identify more focused treatment.

It is also worth mentioning the room that DSM 5 dedicates (page 15) to some special patient groups. In the case of Gender Differences, it emphasizes that gender can influence

things in a variety of ways, including the different ways in which mental illness can be perceived by a woman. A similar attitude is observed (page 14) towards groups with cultural specificities (Cultural issues: (1) Cultural syndrome - recognizable by an outside observer, (2) Cultural idiom of distress - way of talking about suffering, (3) Cultural explanation - features of an explanatory model).

DSM 5 does not exactly follow the type of the Multi-axial System DSM IV (Nonaxial Documentation of Diagnosis), since Axis III is associated with Axis I and II (on the responsible medical condition), Axis IV uses ICD-9 CM conditions and old V codes, forming new Z codes in ICD-10 CM, and Axis V uses the WHO Disability Assessment Schedule.

Factors indicating the 'psychopathological spectrum'

- similar genetic factors and the familial nature of the disorder
- early environmental adversities
- similar characteristics of premorbid temperament and personality
- neuroanatomical and neurotransmitter substrate of the disorder
- psycho-physiological and neuro-psychological indicators
- common symptomatology
- comorbidity with other mental disorders
- similar clinical course
- similar indicated types of effective therapeutic interventions

DSM 5 seems to adhere to a similar fallback attitude concerning the cases of psychosis and schizophrenia, apparently due to the intractable diagnostic and therapeutic problems.

For this reason, it defines the diagnostic category "Schizophrenia spectrum and other related disorders", including: (1) Schizotypal disorder, (2) Delusional disorder, (3) Brief psychotic disorder, (4) Schizophreniform disorder, (5) Schizophrenia, (6) Schizoaffective disorder, (7) Substance/medication psychotic disorder, (8) Psychotic disorder due to another medical., (9) Catatonia - Associated with another mental disorder, Due to another medical condition, Unspecified catatonia, (10) Other specified schizophrenia spectrum and other psychotic disorders, (11) Unspecified schizophrenia spectrum and other psychotic disorders.

ICD-11 made a shift towards *dimensionality* concerned depressive episodes. In ICD-11, depressive episodes in depressive or bipolar disorders may be described in detail by using qualifiers indicating the presence of specific symptoms: the melancholic features qualifier, the anxiety symptoms qualifier; the panic attacks qualifiers, and the seasonal pattern qualifier. Additionally, depressive episodes can be described according to severity (mild, moderate, or severe) and remission status (in partial or in full remission). Also, for the 'Schizophrenia or Other Primary Psychotic Disorders' grouping in *ICD-11*, dimensional symptom specifiers and course specifiers were added. Symptom specifiers describe the current severity of symptoms in six domains: positive symptoms, negative symptoms, depressive symptoms, manic symptoms, psychomotor symptoms, and cognitive symptoms. The severity of each of these symptoms is rated on a 4-point scale ranging from "not present" to "present and severe." [12]. In ICD 11, the different personality disorders in ICD-10 were replaced with a single personality disorder diagnosis in ICD-11, which is characterized by problems in functioning of aspects of the self (eg, identity) and/or interpersonal dysfunction (eg, managing conflict in relationships). Fig. 3 shows a common conceptualization for the Personality Disorder criteria, between DSM 5, Five Factor Model, and ICD 11

Personality Disorder		
DSM-5 Section III	FFM	ICD-11
<ul style="list-style-type: none"> • negative affectivity, • detachment, • psychoticism, • antagonism, • disinhibition 	<ul style="list-style-type: none"> • neuroticism, • introversion, • openness, • antagonism, • Conscientiousness 	<ul style="list-style-type: none"> • Negative affectivity, • detachment, • dissociality, • disinhibition, • anankastia

Figure 3. A good practice paradigm. There is an almost identical conceptualization for Personality Disorder criteria, between DSM 5, Five Factor Model, and ICD 11

In another area, it is known that schizophrenia has its roots in the Greek terms 'schízein' (split) and 'phren' (mind). Due to its meaning of 'split mind' and its stigmatizing attributions, the discussion around changing the term of schizophrenia is ongoing [13]. Moreover, schizophrenia represents only the 30% poor outcome fraction of a much broader psychosis spectrum but receives all attention and forms the prism through which all psychosis is regarded [14]. The significance of renaming is to reduce the stigma associated with the term 'schizophrenia'.

The movement of 'renaming schizophrenia' originally started in Japan and other Asian countries has attracted international interest [15]. The movement towards renaming of schizophrenia in Japan started in 1993 upon receipt of a letter by The National Federation of Families with Mentally Ill in Japan addressed to the board of Japanese Society of Psychiatry of Neurology (JSPN), requesting to rename schizophrenia as the then-official term for the condition 'mind-splitting disease', was humiliating. A committee was established within JSPN to address the issue, public comments were collected, a new name ('disintegration disorder') was approved in 2002. There was a process of renaming in Korea, Taiwan, China, Hong Kong and Malaysia, where Chinese characters are used [15].

According to Guloksuz & van Os (2019) [16], a name change will reduce iatrogenic hopelessness, stigma and discrimination, although an extensive reconceptualisation is more challenging than a simple semantic revision. They extend the discussion on the reasons behind the death of the concept of 'schizophrenia' and the benefits of changing the name, proposing a spectrum approach with an umbrella *psychosis spectrum disorder* (PSD) category, similar to autism spectrum disorder. Following the trend in Asian countries, various different alternatives have been proposed by scholars, service patients and professional organisations across the world, each with a different emphasis and varying degrees of accompanying reconceptualization [14].

Some suggested names for 'schizophrenia'

After a person's name: Kraepelin–Bleuler disease, John Nash syndrome

Focused on failure in organization: Disorganised thinking disorder, Dysfunction perception syndrome

Focused on failure in integration: Disintegration disorder, Salience dysregulation syndrome

Focused on neurodevelopmental process: Neurodevelopmental psychosis, Social brain disorder

Others: Psychosis, Idiopathic psychosis, Endogenous psychosis, Psychosis spectrum disorder
dicated types of effective therapeutic interventions

Reconstructing the Tower – Redefining things

One in five people on this planet is in the vortex of a potential diagnostic and therapeutic fallacy, most regarding anxiety

and depression conditions, although research efforts trying to meet everyone's needs. The high co-morbidity of almost all mental disorders, with both mental and physical illnesses, coupled with the low to moderate therapeutic response of almost all diagnostic groups to pharmacotherapy and / or psychotherapy, indicate an ambiguity of diagnostic limits and accurate. For example, *major depression* is diagnosed with at least 5 out of 9 specific symptoms, one of which is necessarily the "depressed mood". The definition of this depressed mood and its assessment, both during the clinical examination and using the corresponding scales or questionnaires, is associated with "reduced" or "gloomy" mood, although not a few patients, or even unrecognized patients, suffer from "bad" or "negative" mood. "Dysthymic disorder", up to the previous diagnostic systems referred to a *mild chronic depressive condition*, but according to DSM 5 it is a *chronic condition of relapsing depression*. We can assume a sub-threshold emotional state can play the role of the central organizing parameter. These could be sub-threshold forms of depression, such as *atypical depression, characterological depression, neurotic depression, reactive depression, or anxious depression*. A basic organizing parameter in the development of depressive disorder may be some specific cognitive dysfunction based on an unknown yet organic damage. Also, some physical illness, such as an immunological illness, could play a key pathogenic role [17].

Is "depressive mood" the central parameter in "Depressive Disorder"?

- or a condition better suited to the term "dysthymia"?
- or the central parameter is "irritation" and "distress"?
- or "anxiety" and "anxiety distress"?
- many patients feel "reduced" or "gloomy" mood, while,
- many other suffer from "bad" or "negative" mood.
- there are also many sub-threshold forms of depression, such as a *typical depression, characterological depression, neurotic depression, reactive depression, and anxious depression*.
- is bipolar depression a state other than depression?
- is some "specific cognitive dysfunction", based on some yet unknown "brain failure" responsible?
- might an immunological illness be responsible?
- might it be a combination of the above, in a continuum of even an interaction?

In the same context, we may wonder how strong is the concept of "polarity", as the central organizing parameter in bipolar disorder. We all know that unequivocal episodes of depression or mania are in a rare occurrence. Mixed emotional states are probably the rule, and the inclusion of the "mixed" episode in DSM 5 is successful. We could suggest that phenomena such as "cyclicality" or "cognitive dysfunction", on the grounds of some yet unknown "organic base", or even a "psychotic process", are central organizing parameters in the development of the so-called "bipolar disorder". We may also think "liminality" as central organizing structure, given that borderline patients "feed" the diagnoses of the broad "bipolar spectrum". Finally,

it is worth highlighting autoimmune diseases, such as thyroidopathies, as a possible organizing parameter, knowing that a large proportion of “bipolar” patients experience different kinds of immunological and thyroid dysfunction.

Is “polarity” the central parameter in “Bipolar Disorder”?

- “unequivocal” depression and “unequivocal” mania are a rare occurrence
- mixed emotional states are probably the rule
- “cyclicity” may be more apparent than “polarity”
- is maybe some kind of “cognitive dysfunction” responsible, on the grounds of some currently unknown “brain damage”?
- might some specific and distinct “psychotic process” be responsible?
- maybe it is a part of a “single psychotic process”?
- might an inherent “liminality”, as the type observed in “borderline personality”, be responsible?
- might an immunological illness be responsible?
- may some kind of “specific thyroid dysfunction” be responsible?
- might it be some combination of the above, in a continuum of interaction?

The case of ‘anorexia nervosa’ is a typical paradigm of a worldwide misconception, having serious diagnostic and therapeutic consequences. For many decades ‘anorexia nervosa’, as indicate the label, is perceived as a disorder related to ‘lack of orexis’ (from the Greek ‘orexis’ for ‘appetite’ and ‘anorexia’ for the ‘loss of appetite’), having until now serious problems with therapy. We suggest that a specific type of ‘anankastic personality’ is the key factor of the so-named ‘anorexia nervosa’. Truth is that ‘anorectic’ individuals do not loss appetite; in fact, they just restrict feeding. They have an intense ‘sense of mastery / sense of control over her world’, which leads to an ‘over-control’ over of both her appetite and body. In this frame, patients develop a controlling behavior on eating, accompanying with weight loss, and body shape preoccupations. In Fig. 4 we demonstrate a hierarchical model, helping to understand the diagnosis of patients with the so named ‘anorexia nervosa’ disorder.

The taxonomy of mental health conditions gives a sense of order and a crude system for prescription, but it has little relevance to psychotropic drug action, since an accurate diagnosis is not required for optimal prescribing [18]. Neuroscientists suggested a *neuroscience-based nomenclature* (NbN) that takes more into account pharmacological indications and less the initial clinical observations. The reason for this effort is to reduce confusion about indications of psychiatric drugs and it is supported by the European College of Neuropsychopharmacology (ECNP), assisted by ACNP, CINP, AsCNP and IUPHARM.

The Neuroscience-based Nomenclature (NbN) renames more than 100 known psychotropic drugs by 1 of the 11 principle pharmacological domains that include terms such as serotonin dopamine, acetylcholine, and GABA. Also included in NbN are 9 familiar modes of action, such as agonist, an-

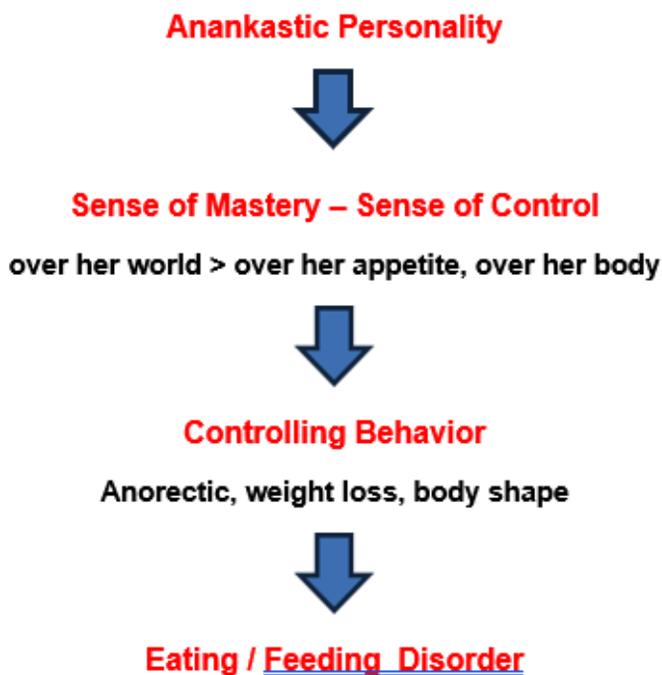


Figure 4. Is ‘anorexia’ the central pathogenic feature in the so-named ‘anorexia nervosa’ disorder? These individuals do not loss appetite; in fact they just restrict feeding. Here, we propose a hierarchical model helping to understand the diagnosis of patients with the so named ‘anorexia nervosa’. The patients suffer from a specific and severe form of an ‘anankastic personality disorder’, having the aberration of restrict feeding, and resulting in an ‘anankastic disorder of feeding’.

tagonist, reuptake inhibitor, and enzyme inhibitors. NbN has 4 additional dimensions or layers. The *first* layer enumerates the official indications as recognized by the regulatory agencies (ie, the FDA and other government organizations). The *second* layer states efficacy based on randomized controlled trials or substantial, evidence-based clinical data, as well as side effects (not the exhaustive list provided in manufacturers’ package inserts, but only the most common ones). The *third* layer is comprised of practical notes, highlighting potentially important drug interactions, metabolic issues, and specific warnings. The *fourth* section summarizes the neurobiological effects in laboratory animals and humans [19]. For Ghaemi [20], the Neuroscience-based Nomenclature approach is far too complex, pointing that the nomenclature should be biological and simple, and neutral as to clinical usage.

Different *guidelines for anxiety disorders* have been proposed by international scientific organizations like the Canadian Network for Mood and Anxiety Treatment (CANMAT) (2013), the International Society of Bipolar Disorder (2013), the National Institute of Clinical Excellence (NICE) (2014) and the World Federation of Societies of Biological Psychiatry (WFSBP) (2012). They suggested SSRIs or SNRIs, and on non-response, augmentation with benzodiazepines, quetiapine or aripiprazole, and for *obsessive compulsive disorder* SSRIs, and on non-response augmentation with risperidone.

Based on the *Guidelines for Depression*: (1) All antidepressants are superior when compared to the placebo, (2) No category of antidepressants has proven to be more effective than the others, (3) The newest antidepressants SSRIs-SNRIs are safer. All guidelines, regardless of where they originate, although starting with the aim of suggesting *evidence-based therapeutic models*, ultimately recommend adjusting the treatment according to the particularities of each case. On non-response to the drug treatment of a major depressive disorder case, which occurs in about 40% of the cases, they suggest (1) dose increase, (2) a change of the antidepressant from the same or another group, (3) a combination of two antidepressants from different groups (e.g., SSRI + mirtazapine), (4) augmentation such as lithium, quetiapine, aripiprazole or T3, (5) non-pharmaceutical interventions such as electroconvulsive therapy, phototherapy, sleep deprivation, physical exercise, St. John's wort, transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS).

"Depression" seems similar in its clinical characteristics and treatment responses in Bipolar Depression and Major Depressive Disorder. However, their characteristics differ, e.g., in family history, sex-distribution, onset-age, long term diagnostic stability, episode duration, recurrence rates, and treatment-responses [21]. Moreover, there is continued controversy about the value and risks of antidepressant drugs in bipolar depression, and lack of highly effective treatments encourages widespread drug-combinations and other off-label treatments. In a recent metanalysis, Baldessarini et al (2020) [22] found all available pharmacological treatments used for bipolar depression have limited efficacy, adding the risk adverse metabolic or neurological effects.

Finally, all guidelines *for Depression* end up in proposing essentially a *personalized drug administration*, tailored to the personal needs and characteristics of each case. In particular, they recommend taking into account: previous response, tolerance, family history of response, expected side effects, concomitant somatic diseases, possible interaction with other drugs, half-life, risk of overdose toxicity, treatment compliance, physician familiarization with the drug, drug product availability, price, and suicidality.

Guidelines for personalized pharmacological treatment in major depression

- previous response, tolerance, etc.
- family history of response
- expected side effects
- concomitant somatic diseases
- possible interaction with other drugs
- the drug half-life
- the risk of overdose toxicity
- treatment compliance
- the experience or familiarization of the physician with the drug
- drug product availability
- the price of the drug, and patient's other financial reasons
- suicidal ideation - suicidality?

The *guidelines for Bipolar Disorder* suggest the following: For *acute mania*, (1) initially olanzapine, quetiapine, risperidone, lithium or valproate are recommended, (2) secondarily haloperidol, aripiprazole, paliperidone and ECT, (3) excluding gabapentin, lamotrigine, topiramate and carbamazepine. For *bipolar depression*, it is recommended (1) initially lamotrigine, lithium, quetiapine, olanzapine, SSRIs or valproate are recommended, (2) secondarily venlafaxine, (3) excluding gabapentin, topiramate, aripiprazole and ziprasidone. For maintenance treatment, it is recommended: (1) lithium, olanzapine, quetiapine, valproate, (2) excluding monotherapy with gabapentin, topiramate, antidepressants and typical antipsychotics. Subsequently, as in the case of major depression, the guidelines suggest essentially instructions for personalized drug administration, depending on the specific needs of bipolar patients: mixed episodes, hypomania, rapid cycling, cyclothymia, comorbidity, psychoactive substances abuse, personality disorder, brain syndrome, metabolic diseases, pregnancy, diagnostic uncertainty.

Guidelines for personalized pharmacological treatment in bipolar disorder

- mixed episodes
- hypomania
- rapid-cycling
- cyclothymia
- comorbidity
- abuse of psychoactive substances
- personality disorder
- brain syndrome
- metabolic diseases
- pregnancy
- diagnostic uncertainty

When more scientific evidence will be gathering, we could be in a position to study psychiatric nosology in a dimensional framework, as a transdiagnostic biobehavioral system, according to the Research Domain Criteria (RDoC) or/and the Hierarchical Taxonomy of Psychopathology (HiTOP), which have the potential to inform the development of a unified, dimensional, and biobehaviorally-grounded psychiatric nosology [23]. The aim of RDoC is to provide a biologically informed framework for understanding mental disorders. The RDoC matrix distinguishes six domains of functioning (negative valence systems, positive valence systems, cognitive systems, social processes, arousal and regulatory systems, and sensorimotor systems) with various subconstructs and eight units of analysis: genes, molecules, cells, circuits, physiology, behavior, self-report, and paradigms. However, the RDoC matrix is too complex to guide diagnosis in clinical practice. [12]

How did we get here? How history reflects its consequences in present days? Is there a possibility to change the flow of history?

The term 'neurology' originated with English physician Thomas Willis following his study of brain anatomy in the 1660s. Subsequently in 1808, Johann Christian Reil, a German physician and philosopher, gave us the term 'psychiatrie' [24]. The split between medicine and psychiatry was lamented by Silas Weir Mitchell as early as 1894. This perpetuated the 'Cartesian dualism'. For many years, the brain basis of many psychiatric disorders has been called "functional" as if they had no organic roots because they defied neurological interpretation. This split became even more pronounced in the USA between 1935 and 1975, when psychoanalysis largely took over psychiatry. Gradually, psychiatry has become separated from the rest of the medical specialties.

According to Thibaut (2018) [25], "this isolation has seriously damaged psychiatry and caused important recruitment and funding problems, as well as diminished value of careful diagnosis, therefore reducing psychiatry to a nonspecific psychological support, which contributes to increasing the stigma". Limiting neurology to the study of the nervous system and psychiatry to the social brain or affect and its disorders is no longer sustainable. Psychiatrists should return home to medicine and leave non-medical interventions to non-medical practitioners [24].

Mental health issues are found across the world and in every population. According to the World Health Organization, around a third of the adult population worldwide suffers from a mental disorder such as depression, anxiety and psychosis. The WHO's report (2021) [26] states: "A fundamental shift within the mental health field is required, in order to end this current situation. This means rethinking policies, laws, systems, services and practices across the different sectors which negatively affect people with mental health conditions and psychosocial disabilities, ensuring that human rights underpin all actions in the field of mental health. In the mental health service context specifically, this means a move towards more balanced, person-centered, holistic, and recovery-oriented practices that consider people in the context of their whole lives, respecting their will and preferences in treatment, implementing alternatives to coercion, and promoting people's right to participation and community inclusion."

Treatments for depression and methods for preventing suicide are not evenly spread. There is clearly a gap between neuroscience development and mental health services. There exists a profound under-recognition of the suffering of mental health issues affecting millions of people across geographies. So, it is important to find treatments for mental health disorders that can be delivered in culturally diverse low and middle-income countries, where there are challenges of poverty, stigma and a lack of clinicians with specialist training in mental health. On the other hand, there is an over-treatment

and over-medicalization of mental health issues, often fueled by a pharmaceutical industry interested in the broadening of the boundaries of "illness", by pushing for more and wider diagnostic categories. [27]

Cosgrove et al (2023) [28], proposed that psychiatry, and the mental health field more generally, adopt a model of 'gentle medicine' with regard to both the diagnosis of and treatment for mental health conditions and focus greater attention on the upstream causes of distress. Moreover, the current psychiatric terminology can make it difficult for clinicians to explain to a patient suffering from anxiety why he or she should take an antidepressant drug ('but I am not depressed, I have anxiety'), or why the depressed patient should take an antipsychotic ('I am not schizophrenic'). Therefore, patients may be confused and also suffer additional stigma. [3]

For Kingdon et al (2013) [29], "a change in terminology could be expected to give a boost to destigmatization programmes and symbolize a change in the way of thinking about the condition. Any such change will need to include assessments with the key audiences – patients, carers and the general public". Indeed, changing names does not necessarily resolve the problem of stigma. Erasing words is not enough. The word police's focus on "just changing terms" misrepresents the depth and persistence of bias. The public is not an empty vessel waiting to replace its biases with affirming attitudes. Research has shown the worsening effects of *antistigma* programs based on a list of don'ts ("Don't talk about 'schizos,'" or "Don't say 'crazy'"). Protests to quash these terms rarely change behavior and sometimes lead to rebound effects [30]. It needs to be ensured that all members of society are treated respectfully and have equal rights. What really needs to be changed is the way that mental illness is seen by the public [13].

Concluding, in parallel with neuroscience priorities and huge development [31] [32], change can be productively introduced bottom-up at the level of individual clinical practice, health care organisations and country. A successful outcome presupposes societies that create communication with actual words, having real meanings and not stigmatized. As Guloksuz & van Os (2019) [16] have noted: "The road to change is long and challenging, but there is no obstacle other than our inner resistance to change".

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