Schizophrenia

Delusion or Reality

Why Diagnose?

- We would even argue that the sole reason as to why clinicians should undertake a diagnostic assessment is to develop a management plan for the patient. Otherwise the exercise becomes immoral, unethical, and unprofessional.
- (Mellsop & Kumar 2007)

Emil Kraepelin

- Born 1856
- 1878 Completed study of medicine at Wurzburg
- Worked in W. Wundt's Lab
- 1883 Published first edition of Compendium of Psychiatry
- 1917 Opened German Psychiatric Research Institute

Kraepelin's Big Idea

- "Judging from our experience in internal medicine ... similar disease processes will produce identical symptom pictures, identical pathological anatomy and identical etiology. "
- There are a discrete and discoverable number of psychiatric disorders, and each disorder has a typical symptom picture and is associated with a distinct brain pathology and etiology

Developing Classifications

- Kraepelin identified
- Catatonia
- Hebephrenia
- Dementia paranoides
- Developed the concept of Dementia Praecox as underlying disease
- Ultimately identified 10 subtypes
- All lead to irreversible deterioration in intellectual function

Eugen Bleuler

- Born 1857
- 1881 Completed study of medicine University of Zürich
- Published *Dementia Praecox or the Group of Schizophrenias*
- Did not accept dementia or praecox characterizations
- The core illness is separation of psychological function

Bleuler's four As

- Associations are loosened, thoughts are disconnected
- Ambivalence, holding conflicting emotions and attitudes
- Autism withdrawal from social world and preference for world of fantasy
- Affect is incongruent with circumstances

Schneider's First Rank Symptoms

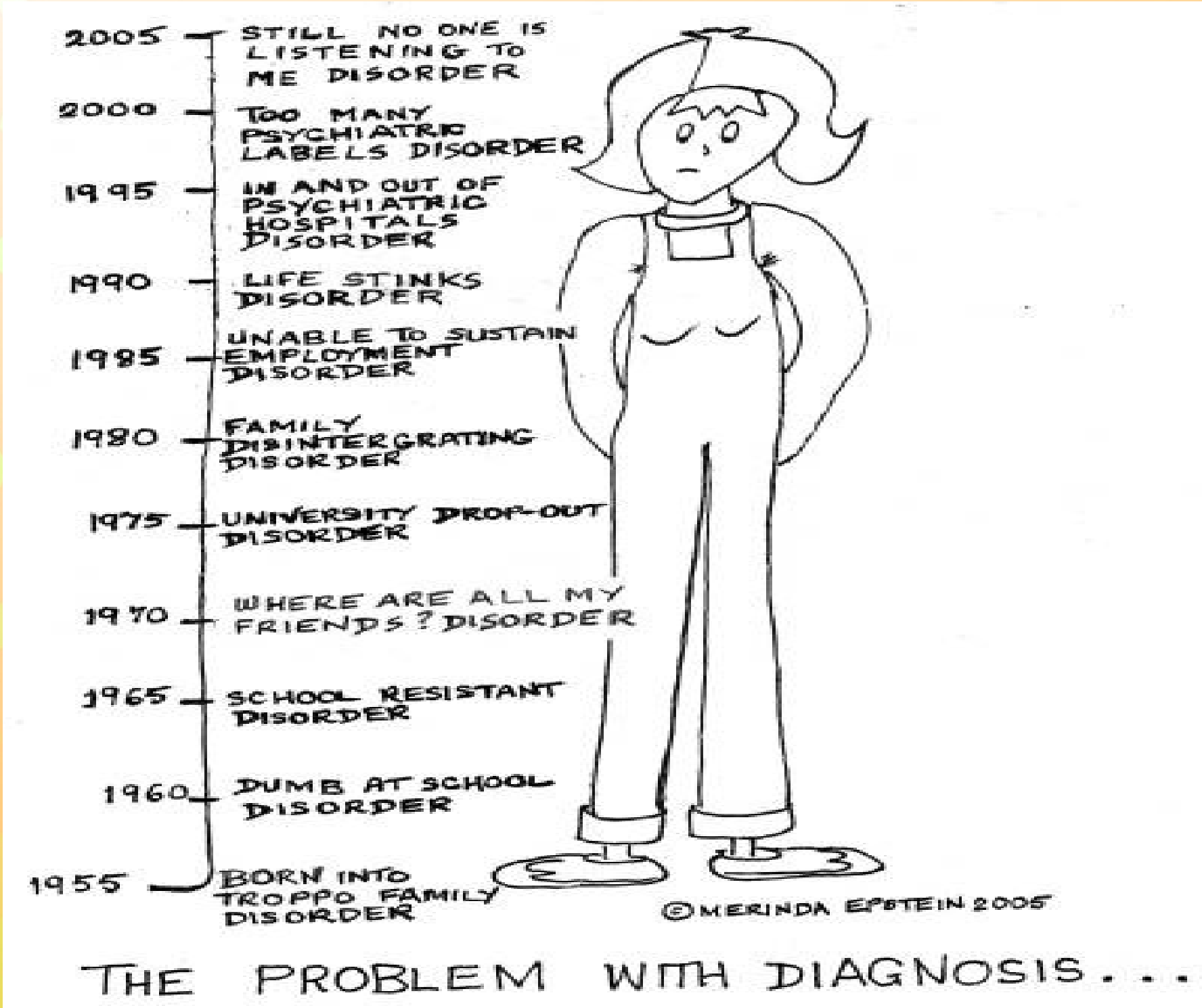
- Audible thoughts
- Voices heard arguing
- Voices heard commenting on ones actions
- Experience of influences playing on the body
- Thought withdrawal
- Thought insertion
- Thought broadcasting
- Delusional perception
- Feelings, impulses and volitional acts caused by others

Why "First Rank"

- An attempt to identify those characteristics that were particular to schizophrenia to aid in distinguishing it from more general problems in personality
- Attention is paid to the form of the symptom not the content
- Symptoms are not critically important features of schizophrenia but helpful in recognizing the disorder

The Reliability Problem

- In order to draw valid conclusions about any phenomenon we need to first be able to reliably identify it.
- In order to achieve reliable psychiatric diagnoses we must first reach consensus about the main features of each disorder
- Inconsistency in diagnosis is found in patients followed across psychiatrists and in the same patient with the same psychiatrist


2005
STILL NO ONE IS LISTENING TO ME DISORDER
2000
TOO MANY PSYCHIATRIC LABELS DISORDER
1995
IN AND OUT OF PSYCHIATRIC HOSPITALS DISORDER
1990
LIFE STINKS DISORDER
1985
UNABLE TO SUSTAIN EMPLOYMENT DISORDER
1980
FAMILY DISINTERGRATING DISORDER
1975
UNIVERSITY DROP-OUT DISORDER
1970
WHERE ARE ALL MY FRIENDS? DISORDER
1965
SCHOOL RESISTANT DISORDER
1960
DUMB AT SCHOOL DISORDER
1955
BORN INTO TROPPO FAMILY DISORDER
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THE PROBLEM WITH DIAGNOSIS...

Reliability

- There "appears to have been no essential change in diagnostic reliability over time" and that "there are no diagnostic categories for which reliability is uniformly high" and, unsurprisingly that reliability in "routine settings is even poorer" than that found in research settings.
  - (Spitzer and Fleiss 1974; 244)

On Being Sane in Insane Places

- In the classic Rosenhan et al study pseudo-patients presented with voices that said 'empty' or 'thud'
- All were diagnosed schizophrenic on the basis of this one symptom and discharged as “in remission”
- A follow up study warned doctors of pending pseudo-patients.
- This produced a 21% identification rate despite there being no pseudo-patients

Across the Pond

- Studies of British and American diagnosis of psychiatric disorders using structured interviews found Americans were much more likely to diagnose schizophrenia and British more likely to diagnose mania, depression or neurosis
- WHO study in Columbia, Czechoslovakia, China, Denmark, India, Nigeria, Soviet Union, UK and US found different local concepts of schizophrenia such as Soviet Schizophrenia

US-UK Diagnosis Project

- In the group of patients from one hospital in London, 85 were diagnosed with schizophrenia
- 163 would be schizophrenic by then current US standards
- 65 using ICD-8
- 55 using Schneider's first rank symptoms
- 28 Using RDC
- 19 Using DSM-III

UK Holland

Diagnosis	RDC		DSM-III-R		ICD-10	
Schizophreniform			N=20	2.8%		
Schizophrenia	N=268	38.0 %	N=371	52.6%	N=387	54.8%
Schizoaffective Manic	N=98	13.9%			N=41	5.8%
Schizoaffective Bipolar	N=129	18.3%	N=13	1.8%	N=23	3.3%
Schizoaffective Depressed	N=118	16.7%			N=40	5.7%
Major Depression	N=16	2.3%	N=71	10.1%	N=19	2.7%
Mania	N=18	2.6%	N=87	12.3%	N=61	8.6%
Bipolar Disorder	N=16	2.3%	N=66	9.4%	N=6	0.9%
Underspecified Psychosis	N=43	6.1%	N=68	9.6%	N=95	13.5%
Delusional Disorder			N=10	1.4%	N=18	2.6%
Not Classified					N=16	2.3%

Kappa

- The Kappa statistic is the measure of choice for looking at reliability of diagnostic classification. It compensates for base rate problem.
- Value ranges from 0 (chance level of agreement) to 1 (perfect agreement)

Kappa Results Multiple Studies

Diagnosis	Study 1	Study 2	Study 3	Study 4	Multi Study mean
Psychosis	0.73	0.62		0.56	0.55
Schizophrenia	0.77		0.42	0.68	0.57
Mood Disorder					0.41
Neurotic Depression			0.47		0.26
Psychotic Depression				0.19	0.24
Manic Depression				0.33	0.30
Personality Disorder			0.33	0.56	0.56

The Celestial Emporium of Benevolent Knowledge

All animals can be divided into the following classes

- Belonging to the Emperor
- Embalmed
- Trained
- Sucking pigs
- Mermaids
- Fabulous
- Stray dogs
- Etcetera
- Included in this classification
- With the vigorous movements of madmen
- Drawn with a fine camel hair brush
- Having just broken a large vase
- Looking from a distance like flies

Validity

- While reliability does not guarantee validity no diagnostic system can be valid without first being reliable
- None the less we can look at evidence for validity
- For a diagnostic system to work diagnoses must be jointly exhaustive and mutually exclusive

Five Criteria for Diagnostic Validity in Psychiatry

- A description of clear and consistent clinical features
- A uniform etiology or pathogenesis
- A uniform clinical course (prognosis)
- An increased prevalence in close relatives
- An investigatory marker of the disorder, such as a lab test

Dreapetomania

- We must never forget the contribution of Dr. Samuel Cartwright who in 1851 coined the term Dreapetomania to describe the disorder which involves an uncontrollable urge to run away observed in American Negro slaves.
- Cartwright S. (1851) New Orleans Medical and Surgical Journal

Comorbidity Problem

- DSM criteria typically include exclusion rules (Not better accounted for)
- In the ECA study of over 15,000 people 60% who met criteria for for one disorder (lifetime) met criteria for at least one additional diagnosis
- Average odds ratio of comorbidity= 2
- Odds ratio for depression & mania=36
- Odds ratio for schizophrenia & mania=46
- Odds ratio for schizophrenia & depression= 14

Discriminate Function

- Assign symptoms of one disorder negative scores and the second disorder positive scores
- Sum an individuals scores
- Multiple studies using variations of this type of discriminate function conclude that most patients average near zero
- There is no clear dividing line between schizophrenia and bipolar disorder but rather a continuum

Factor Analysis

- Studies of patients diagnosed schizophrenic produced 3 factors
- Positive symptoms (hallucinations & delusions)
- Negative symptoms (apathy, flatness, emotional withdrawal)
- Cognitive disorganization (thought disorder)
- Studies of other diagnostic groups (bipolar, psychotic depression) show similar factor structures

Disjunctive Diagnosis

- DSM-IV-TR requires 2 or more of 5 symptoms from criterion A.
- This leads to 15 ways two people could meet criteria and have no overlapping symptoms
- Only one criterion has to be met if delusions are bizarre or hallucinations are a running commentary or are two or more voices in conversation
- Kappa on bizarre ranges from 0.38-0.43

Outcomes

- The course and outcome of psychosis is so variable as to make prediction almost impossible.
- A 35 yr. study of patients diagnosed bipolar found 64% recovered completely and 22% remained seriously ill
- Outcomes are generally worse for those patients with more “schizophrenic” like symptoms

Non-specificity of Treatment Guidelines

- UK guidelines for treatment of schizophrenia include antipsychotics, antidepressants, benzodiazepines, mood stabilizers (lithium and anticonvulsants), family education, psychotherapy, CBT, and ECT
- The same treatments are included in the guidelines for depression and most are also included in guidelines for various anxiety disorders

Psychopharmacological Specificity

- Cade, (1949) described the calming effects of lithium on both manic and schizophrenic patients although the effect was greater in the former
- Johnstone, Crowe et al, (1988) double blind trial of lithium, pimozide or a combination
- Pimozide reduced hallucinations and delusions
- Lithium reduced elevated mood
- Drug response was not specific to diagnosis

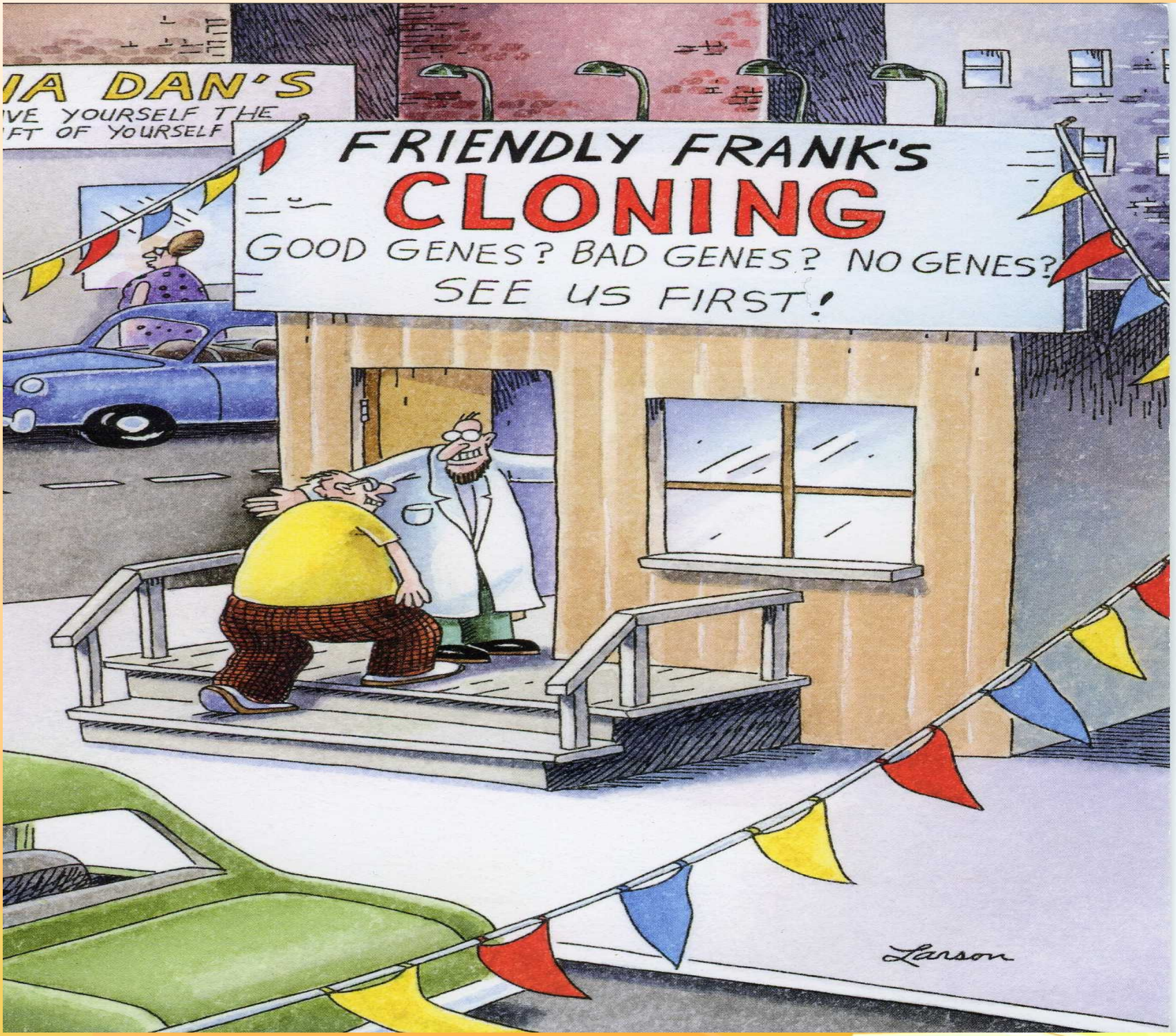
Psychopharmacological Puzzles

- The first successful trial of neuroleptics was conducted on patients with mania (Delay & Deniker, 1952)
- Atypical antipsychotics are now routinely used to treat mania
- Disconnect between dopamine receptor density changes and symptom changes

"If you're stumped, why not write an illegible prescription and hope the pharmacist comes up with something?"

Genetics

- Concordance rates of club foot in monozygotic twins are approximately 75% while those for congenital brain abnormalities are much lower
- Due to problems in reliability of diagnosis conclusions about concordance rates are questionable
- Calculation using probandwise vs. pairwise comparisons yield vastly different numbers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VE YOURSELF THE
FT OF YOURSELF
FRIENDLY FRANK'S
CLONING
GOOD GENES? BAD GENES? NO GENES?
SEE US FIRST!
Larson

E. F. Torrey's Estimate

- Concordance rate for monozygotic twins 28% and dizygotic twins 6% for schizophrenia
- Concordance rate for monozygotic twins 56% and dizygotic twins 14% for bipolar disorder
- These results suggest greater genetic influence in bipolar and that nearly ¾ of people with the genes never develop schizophrenia

Failure to Find Association

- Sanders et al (2008) conducted genetic association study with 14 schizophrenia candidate genes in 1870 subjects with schizophrenia or schizoaffective diagnosis and 2002 controls
- Neither experiment-wide nor gene-wide statistical significance was found in primary or secondary analysis
- It is unlikely these genes account for substantial portion of risk for schizophrenia

Discontinuity Hypothesis

- It has been traditionally argued that people with psychosis are qualitatively different from “normals”
- Specifically positive psychotic symptoms are categorical and their existence indicates pathology

Hallucinations

- In a sample of 375 college students, 39% reported hearing their thoughts out loud (a Schneiderian first rank symptom)
- In a 19th century interview study of 14,000 people 8% of men and 12% of women reported at least on vivid hallucinatory experience
- In the same sample 5% reported conversations with their hallucinations
- ECA study found 11-13% reported hallucinations

Delusions

- DSM-IV defines delusions as: A false belief based on incorrect inference about external reality and firmly sustained in spite of what almost everyone else believes and in spite of what usually constitutes in incontrovertible and obvious proof or evidence to the contrary
- [it] is not ordinarily accepted by other members of a persons culture or subculture

The problem

- Definitions of 'incorrect inference', 'external reality' and 'incontrovertible proof' are not given
- A delusion in one culture may not be one in another culture
- Delusions are sometimes regarded not as beliefs but 'empty speech acts' (Berrios, 1991)

Firmly Held Beliefs

- “When faced with a choice between changing one's mind and proving there is no need to do so, almost everyone gets busy on the proof”
  - John Kenneth Galbraith
- “Even paranoids have enemies”
  - Golda Meir to Henry Kissinger after being accused of being paranoid about Arabs
- The man with the elephant in his ear

Common beliefs

		Sex				Age			
All Adults	All Adults	Male	Female	18-12	25-29	30-39	40-49	50-64	65 & over
		%	%	%	%	%	%	%	%
God	90	86	93	84	82	91	90	91	95
Survival of Soul after death	84	78	89	85	88	81	86	82	84
Miracles	84	77	90	86	85	82	85	83	82
Heaven	82	75	89	83	71	83	84	80	85
Resurrection of Christ	80	73	86	76	68	81	82	81	84
The Virgin birth of Jesus	77	70	83	76	60	79	80	78	80
Hell	69	65	73	74	63	69	72	66	68
The Devil	68	64	73	68	62	72	72	68	62
Ghosts	51	45	58	58	65	55	57	48	27
Astrology	31	25	36	37	43	37	23	32	17
Reincarnation	27	23	30	30	40	30	25	26	14

Dimensions and Outcome

- Outcome has been used as an indication of validity of psychiatric diagnosis
- Symptom dimensions have been closely associated with development, socio-demographic background, clinical history, as well as outcome and treatment provided
- In a study of 5 possible dimensions in 156 first episode patients and 1571 chronic patients dimensions proved to be better predictors of outcome than categorical diagnosis

The Future

- DSM-V may include a move toward dimensional diagnosis
- Dimensional models seem to be a better fit with data from genetic studies
- Dimensional diagnosis lends itself to more quantitative study of outcome and specifics of treatment response
- Dimensional models avoid the discontinuity hypothesis