History of Psychopharmacology

Ira D Glick, MD

Stanford University School of Medicine

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Disclosures

Dr Glick has had equity in Johnson & Johnson, has been on Advisory Boards, Speakers Bureaus, and has done Investigator-initiated studies for industry.

He has had NIMH funding over most of his career.

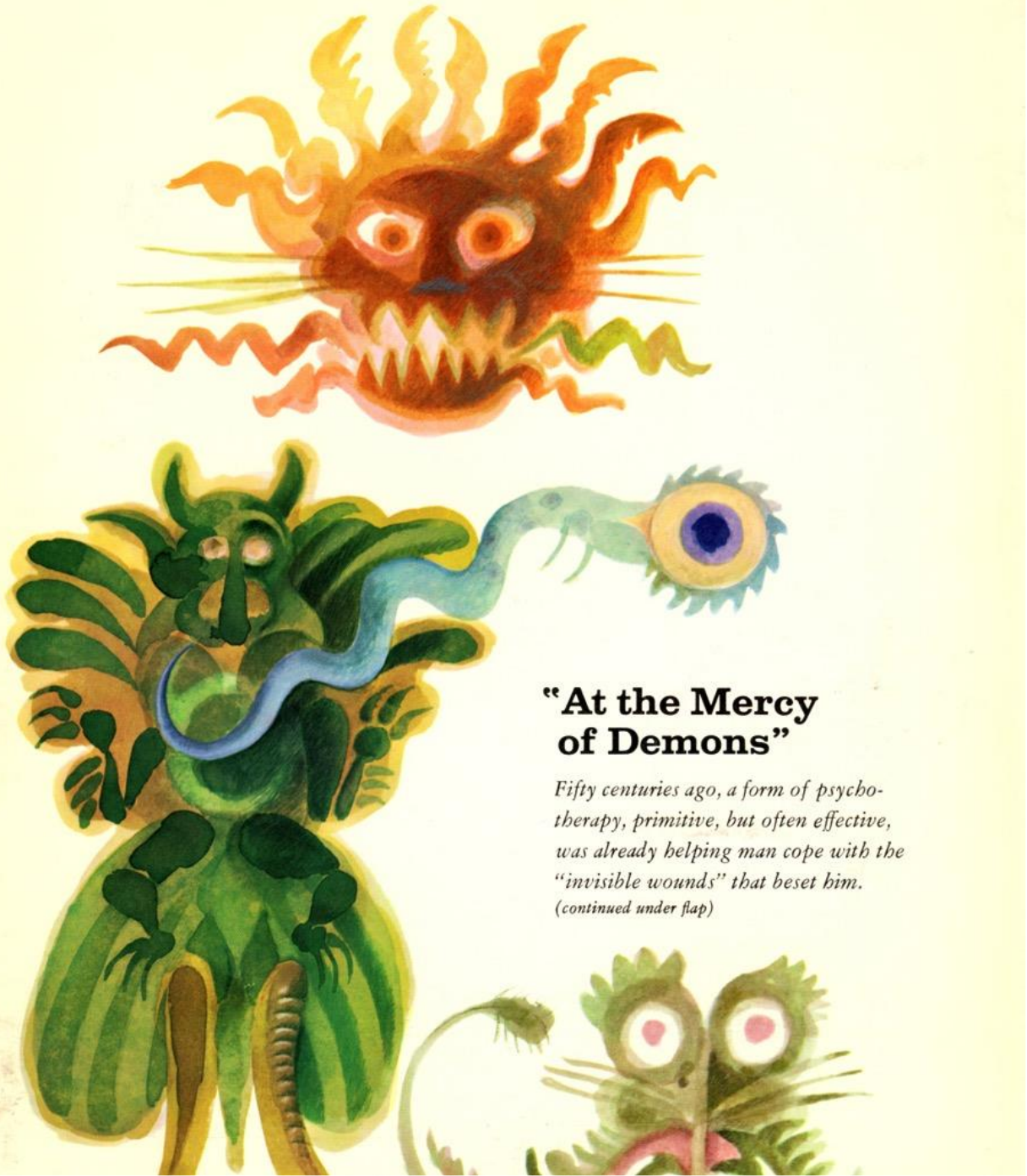
Outline

- Introduction
- History of Treatment of the “Mentally Ill”
- History of Development/Advances in Clinical Medicine
- History of Psychopharmacology
- Summary and Conclusion

Evolution of Mankind

History of Treatment of the "Mentally Ill"

- Prehistoric-caveman times
- Egyptian
- Greek/Roman
- Middle Eastern
- Dark Ages
- Renaissance
- 20th Century



"At the Mercy of Demons"

Fifty centuries ago, a form of psychotherapy, primitive, but often effective, was already helping man cope with the "invisible wounds" that beset him.

(continued under flap)

20th Century

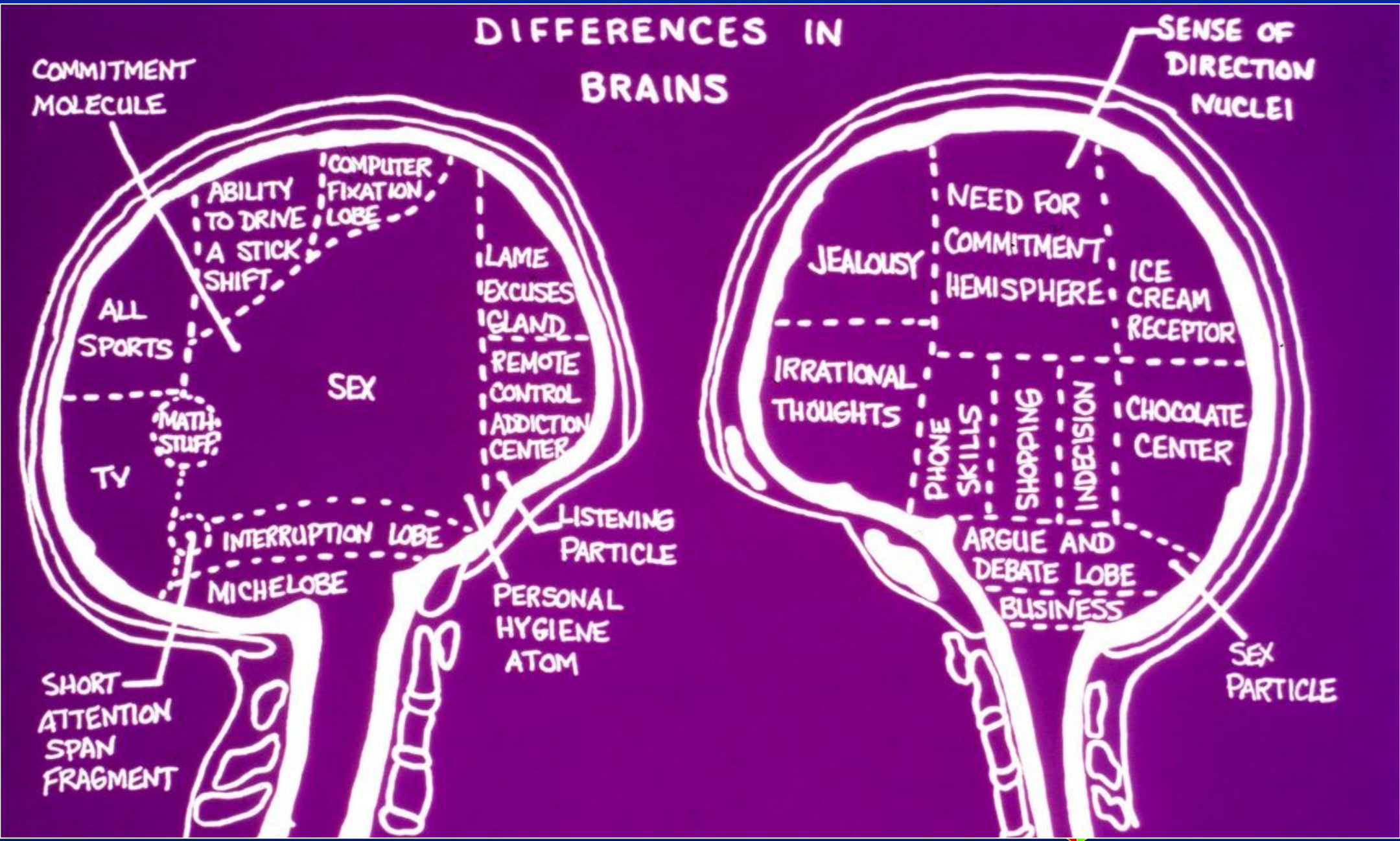
- Freud and the Psychoanalytic Model to understand human behavior and psychopathology- cocaine……
- "You can read my mind"

A Short History of the Field of Clinical Medicine: Medical Developments of Past 1000 Years

- Elucidation of human anatomy & physiology
- Discovery of cells & their sub-structures
- Elucidation of chemistry of life
- Application of statistics of medicine
- Development of anesthesia: includes opium
- Discovery of relational microbes to disease

Medical Developments (cont'd)

- Elucidation of inheritance and genetics
- Knowledge of the Immune System
- Development of body imaging: stages
- Discovery of antimicrobial agents
- Development of molecular pharmacotherapy


DIFFERENCES IN BRAINS
COMMITMENT MOLECULE
ABILITY TO DRIVE A STICK SHIFT
COMPUTER FIXATION LOBE
LAME EXCUSES GLAND
ALL SPORTS
SEX
REMOTE CONTROL ADDICTION CENTER
MATH STUFF
TV
INTERRUPTION LOBE
LISTENING PARTICLE
MICHELOBE
PERSONAL HYGIENE ATOM
SHORT ATTENTION SPAN FRAGMENT
SENSE OF DIRECTION NUCLEI
NEED FOR COMMITMENT HEMISPHERE
JEALOUSY
ICE CREAM RECEPTOR
IRRATIONAL THOUGHTS
PHONE SKILLS
SHOPPING
INDECISION
CHOCOLATE CENTER
ARGUE AND DEBATE LOBE
BUSINESS
SEX PARTICLE

History of Psychopharmacology: Macro and Micro Hx of Neuropsychopharmacology

- Neuro-psycho-pharmacology
- Psychotropic drugs
- Neuro-pharmacology
- Clinical methodology
- Psychopharmacology – Donald Klein contributions and mentorees/colleagues

Neuro-Psycho-Pharmacology: Birth of Psychopharmacology, Late 1950s

- Study of relationship of neuronal and mental events associated with CNS drugs
- Change of model from psychoanalytic to biologic triggered by:
  - Therapeutic effectiveness of psychotropic drugs
  - Technology for tracking brain molecule Δ's to M of A

Neuro-Psycho-Pharmacology (cont'd)

- 1960s – CINP and ACNP: Aim was for basic and clinical scientists to connect for education and research
- BUT FIELDS DIVERGED! – breakdown in communication

Psychotropic Drugs

- P' pharm starts → in late 1800s:
  - Agitation – morphine and hyocine
  - Calming/sleep – chloral hydrate
  - Anxiety – K bromide
- 1900s = changed hospital milieu and dx treated:
  - Meds – barbs, amphet, and vitamins (nic acid and thiamine),
  - Diphenyl hydramine associated with other drugs that ↓ pellagra, syphilis, epilepsy, Korsakoff, and amnesia.

Psychotropic Drugs (cont'd)

- 1950s – Li (MDI), CPZ (S), MPB (Anxiety) and IMI (Dep) ⇨ to end of century

- By the end of 20th century: 28 APs plus 13 anti-depressants,10 anti-anxiety, and 3 mood stabilizers
- As well as using APs for bipolar disorder and anti depressants for anxiety disorders

Neuro/Pharmacology

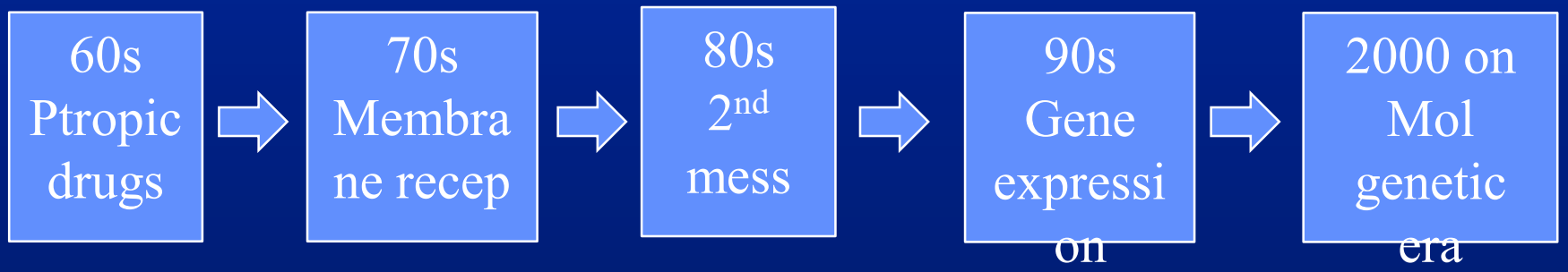
- Results from:
  - Behave Pharm = drugs as prototypes
  - Neuro Pharm = M of A in brain
  - Aim: ↑ effectiveness and ↓ S E
- Resulted from: neurotransmitters and transmission in CNS

Neuro/Pharmacology, con't

- 1950s: anti-SER of CPZ
- 1960s: S DA-receptor blockade
  - Dep: IMI has NOREP and SER and Anti-Chol effects
- Neuronal networks MA from pre-syn vesicles → glut and GABA

Neuro/Pharmacology, con't

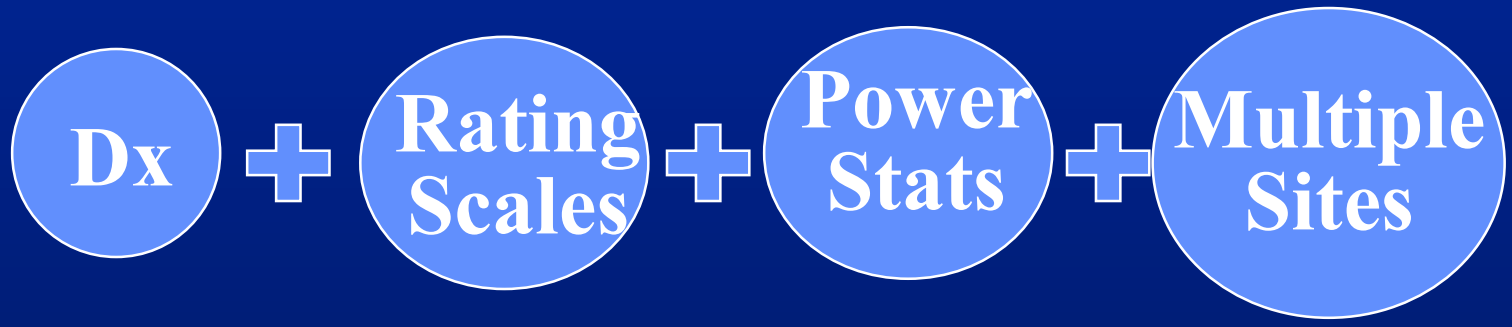
First 50 years:



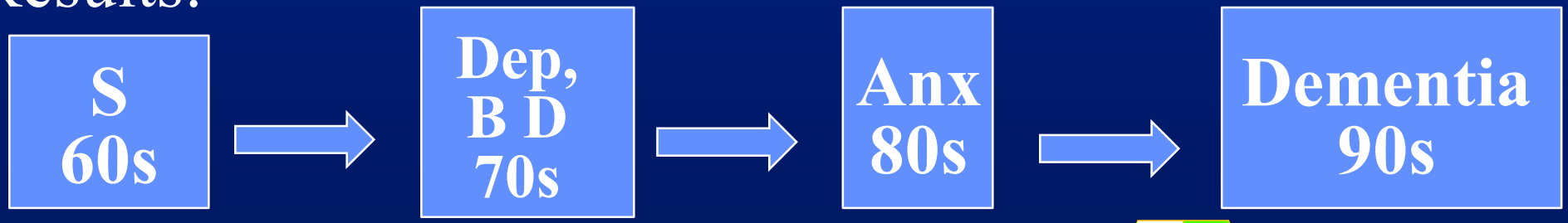
Primary targets of meds encoded by CNS genes

Clinical Methodology

- RCT – used to demonstrate efficacy for pharmacological heterogeneity within psych dx
- Model:



- Results:
-



Clinical Methodology (cont'd)

- Focus shifted to:
  - Rating scales ⇨ mental pathology + behavioral anomalies and decreased social function
  - Pharmacologic dissection and ⇧ MAOs – Atyp Depression and IMI for Panic Disorder

Psychopharmacology

- ≡ from neurotransmitters ⇨mol-genetic era, roots in the 1840s with hashish, ⇨proteins and genes are different as patients respond differently to same drug (dementia vs melancholic dep vs regression)
- ⇧ scope: (Mes, LSD ~ S) and psychotherapeutic drugs (early 1900s) and therapeutics (1980s)

Psychopharmacology (cont'd)

- 1930s ⇨ amphetamines for narcolepsy and hyperkinetic kids
- 1970s – testing of neuropsychopharm Ho – supportive of
  - DA Ho for S
  - SER Ho for Dep
  - Physostigmine ⇧ memory in normals ⇨ AChol for Alz dis

SUMMARY: Molecular genetic research ⇨ new treatments for psychiatric disorders with DSM guides > RDOCS

Don Klein's Scientific Contributions to Psychopharmacology: Father of Modern P'pharm

- Initiated program of research into schizophrenia, found early Rx crucial

- Mood disorders:
  - Depression > single syndrome
  - Each syndrome had differential treatments
  - Differentiated depression vs demoralization, re treatment

Don Klein's Scientific Contributions to Psychopharmacology (cont'd)

- Anxiety disorders
  - Discovered panic disorder
  - His methodology linked Sx with drug, i.e. CPZ/IMI/Pl
  - Differentiated actual anxiety vs anticipatory anxiety
  - Pathophysiology disturbed suffocation alarm, Rx prevents agoraphobia – it is the only psychiatric disorder we can induce (CO_2)

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Don Klein's Scientific Contribution to Psychopharmacology (cont'd)

- Child Psych:
  - Separation Anxiety Disorder
  - Simulants for hyperactive children
  - Focus on childhood psychopathology

- Text: Diagnosis and Drug Treatment of Psychiatric Disorders in Adults and Children (with John Davis)

Hillside Kleins and Fink Tree

Glick Psychopharmacology

- Psychiatric effects of oral contraceptives
- Efficacy of hospital psychiatry
- Efficacy of psychopharmacology medications
- Model psychopharmacology curriculum
- Psychopharmacology treatment of athletes
- Efficacy of combining medication with individual psychotherapy and/or family psychotherapy

Should Antipsychotic Medications for Schizophrenia Be Given for a Lifetime

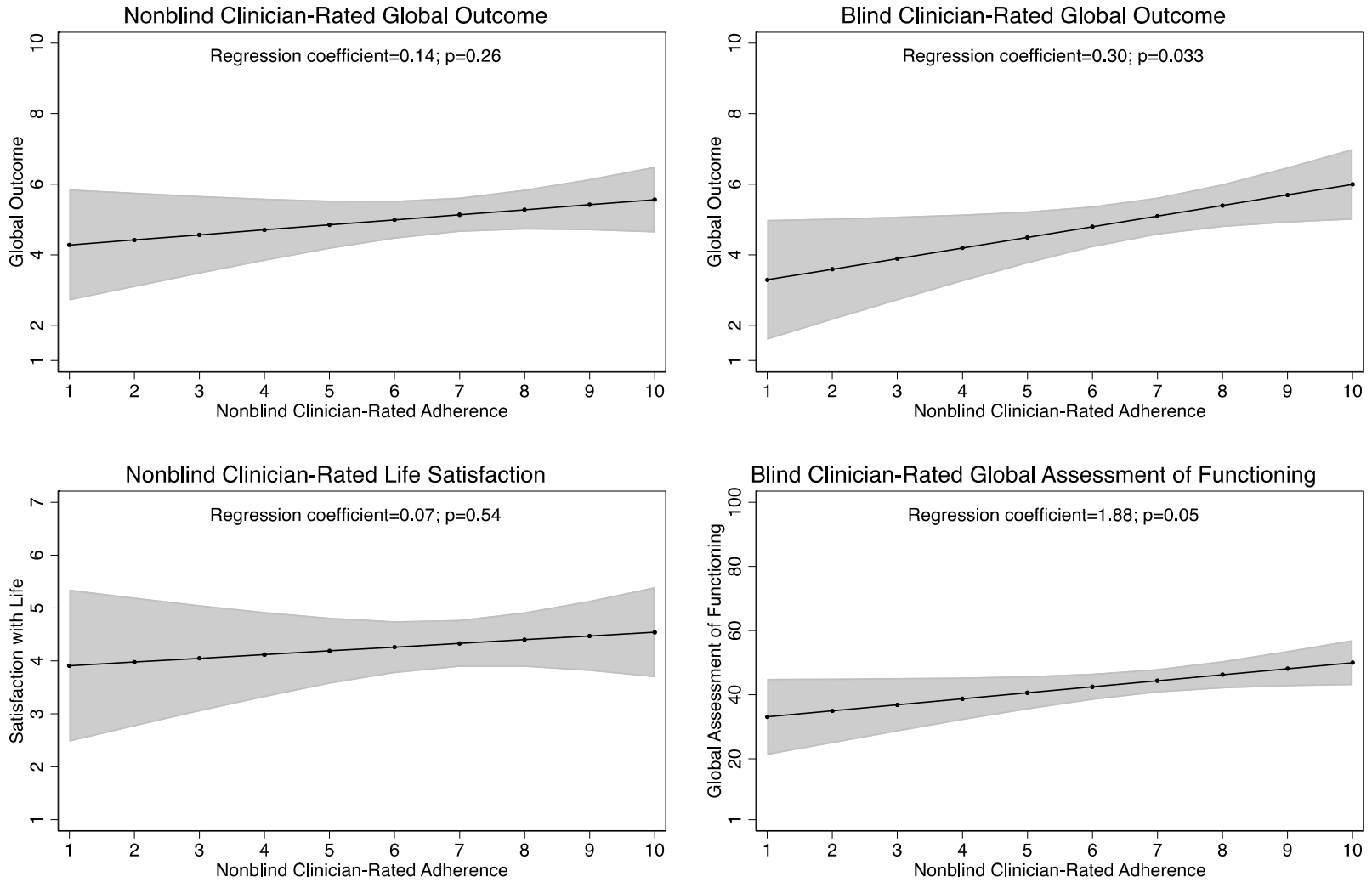
- Glick I D, Davis J M , Zamora D et al: Should Antipsychotic Medications for Schizophrenia Be Given for a Lifetime? A Naturalistic Long-Term Follow-up Study, J Clin. Psychopharm, 2017,37:125-130
- Glick I D, Zamora D, Kamis, D , Davis J: Should Antipsychotic Medications for Schizophrenia Be Given for a Lifetime?: Replication of a Naturalistic, Long-Term, Follow-Up Study of Antipsychotic Treatment" CNS Spectrums, 2019, 24: 557-563.
- Glick ID, ZamoraD D, Davis J etal: Are patients with schozpphrenia better off with lifetime antipsyhotic medication: Replication of a naturalistic long-term follow-up study of antipsychotic treatments. Clinical psychopharmacology (in press)

Study Questions

- Antipsychotic adherence?
- Global life outcome?
- Life satisfaction?

Outcome Data

Figure 1 - Associations Between Medication Adherence and Life Outcomes (n=34) *



* Models are adjusted for family support, substance use disorder, age, marital status, race, and number of years in treatment.

Results

The data suggests, not proves:

- the better the adherence to antipsychotic medication, the better the lifetime outcome and satisfaction
- the worse the adherence associated with disastrous outcomes

Psychopharmacology: Current Status

- Psychiatric disorders are like medical diseases
- They have multiple etiologies – but most have a strong genetic etiology
- As such, psychopharmacology medicines help to varying degrees
- And may need to be treated over a lifetime

Psychopharmacology: Current Status

- Psychiatry in midst paradigm shift
- Etiology: interaction between genetics, environmental factors, and development/regulation neural circuitry
- Clinical practice: little informed by above, practice-gap
- Treatment: neuroscience faculty have to teach

History of Psychopharmacology: Summary and Conclusion

- I have reviewed:
  - History of treatment of mentally ill
  - History of developments in medicine
  - History of modern psychopharmacology
  - Klein contributions

Where are we now in history?

Hillside Tree

Columbia

Klein	Panic Disorder
Quitkin	Atypical Depression
Leibowitz	Social Anxiety DO
Leiberman	Schizophrenia
Posner	Suicidality

Kleber/Levin	Substance Use Disorders

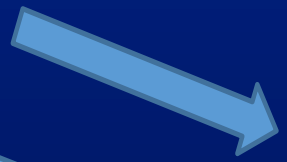
Leiberman	Schizophrenia
Leiberman	Schizophrenia
Leiberman	Schizophrenia

LIJ Hillside

Donald Klein MD

Fred Quitkin
Ira Glick MD
Burt Angrist MD

Cornell/Stanford	Schizophrenia
Glick	Family studies in Psychopharm



LIJ/Hillsdie	Schizophrenia
Kane	Movement Disorders
Leiberman	

NYU/NY Harbor VA

Angrist	Schizophrenia
Rotrosen	Substance Use Disorders
Wolkin	Movement Disorders
Adler	ADHD

Summary and Conclusion (cont'd)

Message: Psychiatry takes its central place in modern medicine – i.e. psychiatric disorders are like medical diseases and treatments are as effective as medical diseases

Use the "lessons learned" from the past to understand and develop new treatments for patients we serve

Acknowledgement and (Lifetime) Thanks

- My patients
- My students
- My mentors: Kleins, Epstein, Michels, Schatzberg
- My colleagues
- ACNP and ASCP – Parthenon
- My Co researchers
- My family
- Others too numerous to mention