NEUROPSYCHOPHARMACOLOGY

1961-2011: 50 Years of Progress

1960s

Protein phosphorylation as a biological regulatory mechanism,

late 1950s-early 1960s

Peptide hormone production in the brain, mid 1950s-early 1960s

1 Hamilton Rating **Scale for Depression,** 1960

Involvement of serotonin and norepinephrine in the actions of antidepressants, 1960-1966

2 Mechanisms for storage, release and inactivation of biogenic amine transmitters, early 1960's

Benzodiazepines for the treatment of anxiety, 1960-63

L-DOPA for the treatment of Parkinson's disease, 1962-1968

Stimulants for the treatment of ADHD, 1963

Histofluorescense for visualization and mapping of brain monoamines, 1963

Dopamine receptor antagonism in the actions of antipsychotic drugs, 1963

SPECT Instrumentation, 1963-1964

Methadone treatment for opiate addictions,

Clinical Trial Ethics -Declaration of Helsinki, 1964

Drug discrimination to assess subjective effects of drugs in

animals, 1964

disorders, 1965

ICD-8 with expanded chapter on mental

Federal Laboratory Welfare Act that regulates the treatment of animals in research, 1966

LTP, 1966

Imipramine for treatment of panic

disorders, 1967

DSM-II, 1968

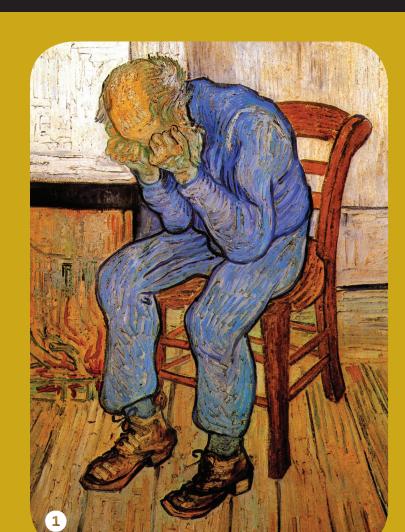
Descriptor of stages of EEG sleep and their measurement, 1968

3 Immunohistochemistry to label specific neuronal subpopulations in brain, 1969.

Selective neurotoxins to lesion catecholamine or serotonin neurons in

brain, 1968-1973

Family, adoption and twin studies showing impact of heredity on psychiatric illnesses including alcoholism and drug abuse,



Neurotransmitters Synaptic vesicle Neurotransmitter re-uptake pump Voltagegated Ca⁺



1970s

Presynaptic autoreceptors, early 1970s

Role of synaptic and molecular plasticity in learning and memory, in psychotropic drug action and in disease pathophysiology,

1970

Opioid receptors as targets of opiate drugs, 1971

Research Diagnostic Criteria, 1972

PET Instrumentation, 1972-1975

> MRI Instrumentation, 1973-1979

4 2-deoxyglucose autoradiography to image functional changes in brain

activity, 1974

G-proteins and their role in signal transduction, mid

IRBs, 1974

Sanger method for sequencing DNA, 1975

Single ion channel function (patch clamp), mid-late 1970s

5 Endorphins and **enkephalins, 1975-1976**

6 GABA-A receptors

as the target for

benzodiazepines,

1975-1978

1970s-early 1980s

Radioligand binding methodology, early

Acetylcholinesterase inhibitors for the treatment of

1970s

1978

1978

Schedule for Affective Disorders and Schizophrenia (SADS),

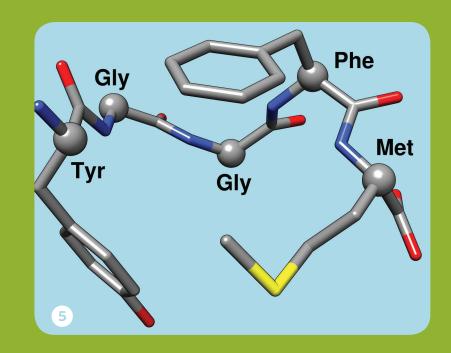
Alzheimer's Disease.

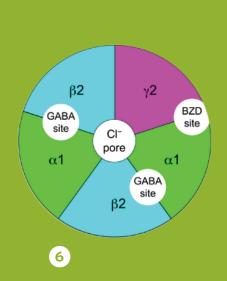
PET Human Glucose Metabolism, 1978-1979

National Alliance for the Mentally III (NAMI), 1979

Synaptic vesicleassociated proteins and their involvement in transmitter release, late 1970s-early 1980s







1980s

"Linkage" methodology for genetic diseases,

1980

Buprenorphine for opi-

ate addiction, 1980

Structural MRI for brain,

1980

PTSD as a diagnostic **entity, 1980**

DSM-III, 1980

PET Human Cerebral Blood Flow, 1980 -1983 **NARSAD, 1981**

Microdialysis methodology, 1982

Discovery that

involves alterations in

Cloning and

5-HT2A receptors as a target for behavioral effects of major

schizophrenia cytoarchitecture, 1982

characterization of the nicotinic acetylcholine receptor, 1983

hallucinogens, 1983

7 PET for Human Dopamine (D2/D3) receptors, 1983

PCR, 1983

8 In situ hybridization histochemistry to visualize gene expression in brain, 1983

Nicotine patch for treatment of nicotine addiction, 1985

Naltrexone for treatment for opioid dependence, 1985

1993

WHO ICD-10 Diagnostic

Anticonvulsants

for manic mood

stabilization, 1994

Brain reward circuits

drug cues, 1994

Cloning and

characterization of neurotransmitter **G-protein coupled** receptors, 1986

Cloning and characterization of gamma-aminobutyric acid (GABA) and glycine ionotropic receptors, 1987

SSRI (fluoxetine) for the treatment of MDD, 1987

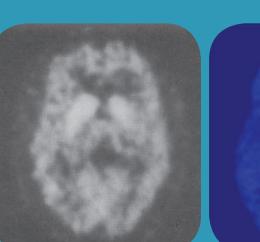
Dopamine transporters as targets for behavioral effects of cocaine, 1987 **DSM-IIIR**, 1987

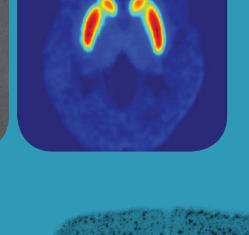
Knockout mice, 1989

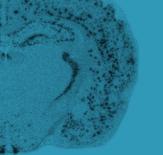
5-HT2A receptors as a target for behavioral effects of atypical antipsychotic drugs, 1989

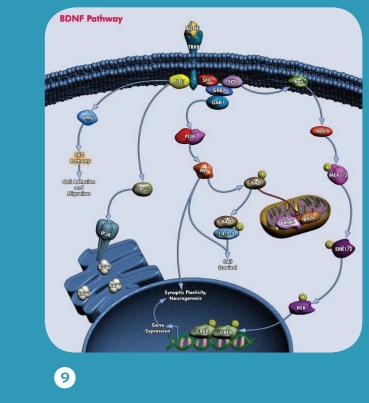
9 BDNF and the neurotrophin family, 1988-1990

RNA interference, gene silencing by double-stranded RNA, late 1980slate 1990s









1990s

10 Antidepressants for preventing recurrences of MDD, 1990

11 Cannabinoid receptors as targets for marijuana, 1990 and endocannabinoids, 1992

High throughput sequencing of DNA, 1990

Cloning and characterization of plasma membrane and vesicular transporters, 1990-1992

Viral vector-mediated gene transfer, 1991

Naltrexone for alcohol addiction, 1992

Functional MRI for brain,

Endogenous

cannabinoids, 1992

1992

Neuropharmacology of

cognitive circuitry, 1992

Development of first line atypical antipsychotics based on 5-HT2A/D2 receptor antagonism, 1992-1999

Huntington's Disease DSM-IV, 1994 gene and the role of

trinucleotide repeats in First neurocircuitry disease pathology, model of schizophrenia based on post-mortem studies, 1995

Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research, 1993 1998

12 Re-discovery of neurogenesis occurring in adult mammalian (including human) brain, reflexively activated in addicted individuals by

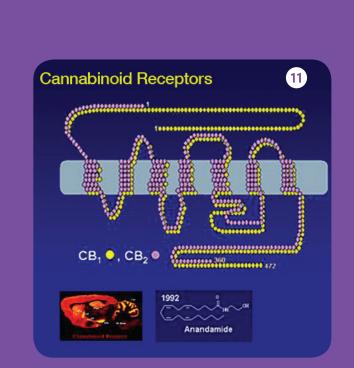
Imaging studies showing impact of functional

alleles on behaviors,

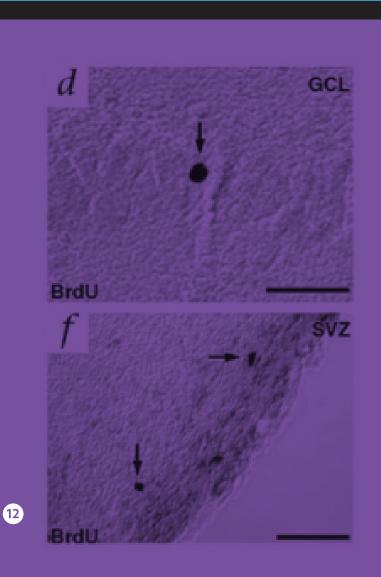
1998 Large-scale analysis of large protein complexes

(proteomics), late 1990s Clozapine as a uniquely efficacious antipsychotic drug for treatment Response, Remission, Recovery, resistant schizophrenia, Relapse, Recurrence

Recovery Syndrome **Acute Continuation Maintenance Treatment Phases**



ISHH of Neuropeptide Y



2000s

ACNP-final2.indd 1

Crystal structure of rhodopsin, 2000

13 Draft sequence of the human genome, 2000

NMDA receptor antagonists as rapidly acting antidepressants, 2000

3D structure of an acetylcholine binding protein revealing the ligand binding domain of the nAChR, 2001

Extended release stimulant medications for ADHD, 2000- 2002

Roles for glia in synaptic structure and function, 2001

Clozapine as a uniquely efficacious antipsychotic drug for suicidal patients, 2002

Optogenetic tools to study brain circuitry in behaving animals, early-mid 2000s

Deep brain stimulation for Parkinson's Disease (2002) and OCD (2009)

Varenicline for nicotine addiction, 2006

Crystal structure of the Leucine transporter, 2007

14 Crystal structure of the beta-2 adrenergic receptor, 2007



