

BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
John H. Krystal, M.D.	Robert L. McNeil, Jr. Professor and Deputy Chairman for Research, Dept. Psychiatry Yale University School of Medicine

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Chicago, Chicago, IL	B.A.	1976-1980	Behavioral Sciences
Yale University, New Haven, CT	M.D.	1980-1984	Medicine
Dept. Psychiatry, Yale University	Residency	1984-1988	Psychiatry
Diplomate in Psychiatry (ABPN)		1991	

A. Positions and Honors.**Positions and Employment**

1988-1993	Assistant Professor, Department of Psychiatry, Yale Medical School (YMS)
1991--	VA Alcohol Research Center, Director (co-Director 2009-)
1993-1996	Deputy Chief for Research and Academic Affairs, Psychiatry Service, WHVAMC
1993-1998	Associate Professor of Psychiatry, YMS
1996-2000	Director, Division of Cognitive and Clinical Neuroscience, Dept. Psychiatry, YMS
1998-2000	Professor of Psychiatry, YMS
2000--	National Center PTSD, Director, Clinical Neuroscience Division
2000-2003	Albert E. Kent Professor and Deputy Chairman for Research, Dept. Psychiatry, YMS
2003--	Robert L. McNeil, Jr. Professor of Translational Research & Deputy Chairman, Psychiatry
2009--	Chairman, Psychiatry, YMS, & Chief of Psychiatry, Yale New Haven Hospital

Professional Activities: 1993 NIAAA Center Review Committee; 1994-1998 NIAAA ALCP-1/AA3 Review Committee; 1996-1997 NIH Director's Working Group on New Investigators; 1997 Institute of Medicine, National Academy of Sciences, Committee on Halcion; 1997 Co-Director, VA/DOD Program on Stress and Gulf War Illnesses; 2000-2007 NIMH Board of Scientific Counselors (Chairman 2004-2007); 2000-2003-VA Medical Research Advisory Group; 2003- NARSAD Scientific Council; 2004-2005 Chairman, VA New Freedom Commission Research Subcommittee; 2005-2009 Board of Directors, Research Society on Alcoholism, 2006-2009 Council, American College of Neuropsychopharmacology, 2008 NIMH Blue Ribbon Panel on Intramural Research; 2008- Department of Defense Health Board, Psychological Health External Advisory Committee; 2008-2012 National Institutes of Health, National Advisory Council on Alcohol Abuse and Alcoholism (NIAAA);

Editorial Boards 1999-2006 Managing Editor, Psychopharmacology; 2006- Editor, Biological Psychiatry. Several editorial board positions.

Honors 1980 Phi Beta Kappa; 1989 Danieli Award, Society for Traumatic Stress Studies; 1993, 1998 Alden Lecturer, Duke University; 1999 Senior Scientist Award, Biennial Winter Conference on Schizophrenia Research; 2000 Distinguished Scientist Award, NARSAD; 2001 Joel Elkes International Award – American College of Neuropsychopharmacology (ACNP); 2003 Han Jörg Weitbrecht Scientific Award, Bayer; 2005 APA APIRE/Kempf Award for Psychobiology Research; 2005- Thompson-ISI “Most Highly Cited Researcher” (top 0.5% in citations); 2007 Distinguished Lecturer APA, 2007 President's Plenary Lecture ACNP, 2008-Director General's Neuroscience (Psychiatry, Neurology) Review Committee, Hadassah Medical Organization, Jerusalem, Israel; 2008-External Review Committee, Maryland Psychiatric Research Center, University of Maryland; 2008-NIH Director's Pioneer Award Review Committee, 2008- Department of Defense, Health

Board-Psychological Health Subcommittee, 2009 – NIAAA National Alcohol Advisory Council, 2009 Anna Monika Prize for Depression Research

B. Selected peer-reviewed publications (selected from 250+ peer-reviewed publications)

1. Redmond DE Jr, Krystal JH: Multiple mechanisms of withdrawal from opioid drugs. *Ann Rev Neurosci*, 1984;7:443-78
2. Rasmussen K, Beitner D, Krystal J, Aghajanian G, Nestler E: Opiate withdrawal and the rat locus coeruleus: Behavioral, electrophysiological and biochemical correlates. *J. Neurosci*, 1990;10:2308-2317
3. Krystal JH, Karper LP, Seibyl JP, Freeman GK, Delaney R, Bremner JD, Heninger GR, Bowers MB Jr, Charney DS: Subanesthetic effects of the NMDA antagonist, ketamine, in humans: psychotomimetic, perceptual, cognitive, and neuroendocrine effects. *Arch Gen Psychiatry* 1994;51:199-214
4. McCarthy G, Puce A, Constable RT, Krystal JH, Gore JC, Goldman-Rakic P. Activation of human prefrontal cortex during spatial and object working memory tasks measure by functional MRI. *Cerebral Cortex* 1996;6:600-611
5. Laruelle M, Abi-Dargham A, van Dyck CH, Gil R, D'Souza CD, Erdos J, McCance E, Rosenblatt W, Fingado C, Zoghbi SS, Baldwin RM, Seibyl JP, Krystal JH, Charney DS, Innis RB. SPECT imaging of amphetamine-induced dopamine release in drug free schizophrenic patients. *Proc Nat Acad Sci USA* 1996;93:9235-9240.
6. Krystal, JH, Cramer, JA, Krol, WF, Kirk, GF, Rosenheck, RA, Naltrexone in the treatment of alcohol dependence *New England J. Med* 2001; 345:1734-1739
7. Kaufman J, Yang B-Z, Douglas-Palumberi H, Houshyar S, Lipschitz D, Krystal JH, Gelernter J. Social supports and serotonin transporter gene moderate depression in maltreated children. *Proc Natl Acad Sci USA* 2004;101(49):17316-17321
8. Petrakis IP, Limoncelli D, Gueorguieva R, Boutros NN, Trevisan L, Gelernter J, Krystal JH. Altered NMDA glutamate receptor antagonist response in individuals with a familial vulnerability to alcoholism. *Am J Psychiatry* 2004(10):1776-1782
9. Krystal JH, Abi-Saab W, Perry E, D'Souza DC, Liu N, Gueorguieva R, McDougall L, Hunsberger T, Belger A, Levine L, Breier A. Preliminary evidence of attenuation of the disruptive effects of the NMDA glutamate receptor antagonist, ketamine, on working memory by pretreatment with the group II metabotropic glutamate receptor (mGluR) agonist, LY354740, in healthy human subjects. *Psychopharmacology* 2005;179(1):303-9
10. Staley JK, Gottschalk PC, Petrakis I, Zoghbi S, Verhoeff NP, Seibyl JP, Van Dyck C, Innis RB, Krystal JH. Cortical GABA-A receptors and the recovery from alcohol dependence: relationship to clinical features of alcohol dependence and cigarette smoking. *Arch Gen Psychiatry* 2005;62:877-888.
11. Krystal JH, Perry EB Jr, Belger A, Madonick SH, Abi-Dargham A, Cooper T, Casselo K, MacDougall L, Abi-Saab W, D'Souza DC. Comparative and interactive human psychopharmacologic effects of ketamine and amphetamine: implications for glutamatergic and dopaminergic model psychoses and cognitive function. *Arch Gen Psychiatry* 2005 62: 985-995.
12. Mason GF, Petrakis IL, de Graaf RA, Appel M, Gueorguieva R, Ruff E, Coric V, Epperson CN, Rothman DL, Krystal JH. Cortical GABA levels and the recovery from alcohol dependence: relationship to neurotoxicity and cigarette smoking. *Biological Psychiatry* 2006; 59: 85-93.
13. Krystal JH, Staley J, Mason G, Petrakis IL, Kaufman J, Harris RA, Gelernter J, Lappalainen J. Gamma-aminobutyric acid type A receptors and alcoholism: intoxication, dependence, vulnerability, and treatment. *Arch Gen Psychiatry*. 2006;63(9):957-68
14. Czermak C, Staley J, Kasserman S, Young, Henry, Seibyl J, Southwick S, Krystal JH, Neumeister A. $\alpha 4 \beta 2$ Nicotinic acetylcholine receptor availability in posttraumatic stress disorder. *Int J Neuropsychopharmacology* 2008;11(3):419-24 PMID18190729
15. Sanacora G, Zarate CA Jr, Krystal JH, Manji HK. Targeting the glutamatergic system to develop novel, improved therapeutics for mood disorders. *Nature: Drug Discovery* 2008;7(5):426-37 PMC2715836
16. Driesen NR, Leung HC, Calhoun VD, Constable RT, Gueorguieva R, Hoffman R, Skudlarski P, Goldman-Rakic PS, Krystal JH. Impairment of working memory maintenance and response in schizophrenia: functional magnetic resonance imaging evidence. *Biological Psychiatry* 2008;64(12):1026-34 PMID2650279

C. Research Support.**Ongoing Research Support**

Krystal (Role: Director) 06/04/2006-5/31/2011

NIAAA 2P50- AA012870-09 Center for the Translational Neuroscience of Alcoholism (CTNA-2)

This renewal application will study mechanisms through which disturbances in glutamate and dopamine neurotransmission within cortico-limbic circuitry contribute to the vulnerability to persistent heavy drinking and alcohol dependence. Building on these insights, it will explore a novel approach to the pharmacotherapy of alcohol dependence that emerges directly from mechanistic CTNA research.

2R01AA011321-06A2 (Krystal) 9/30/2007-8/31/2012

NIAAA Cortical GABA Function in Alcoholism

This competitive renewal application will study Single Photon Emission Tomography (SPECT)

[123] iomazenil binding to assess GABA receptor function and proton Magnetic Resonance Spectroscopy (MRS) to assess GABA concentration in smoking and nonsmoking alcoholics.

1 R01 AA017173-01 (O'Malley/Gueorguieva, PI: Krystal-Co-Investigator) 4/15/2008-3/31/2011

NIAAA Trajectories of Drinking and Compliance in the COMBINE Study

This study will assess patterns of change over time in drinking and compliance in the COMBINE study using the trajectory-based approach.

R01MH081132 (Tolin, PI: Krystal-Yale Site PI) 4/01/2008-03/31/2013

NIH/NIMH Exposure, D-Cycloserine Enhancement, and Genetic Modulators in Panic Disorder

The aims of this multi-site, double-blind, randomized controlled trial are (1) to compare the relative benefit of augmenting exposure-based cognitive-behavioral therapy with d-cycloserine as compared to placebo for patients with panic disorder, and (2) to study variability at specific gene sites as a predictor of treatment response.

1R21DA024228A-01A1 (PI: Krystal) 07/01/2008-06/30/2010

NIH/NIDA Interactive Impact of Cocaine and Schizophrenia on Prefrontal Function

This project probes hypotheses about the nature of PFC dopaminergic dysfunction in two dopamine-related disorders, schizophrenia and cocaine dependence.

R14 MH083436 (Woods, PI: Krystal) 07/01/2008-06/30/2010

NIH/NIMH Huperzine for Cognitive and Functional Impairment in Schizophrenia

This study is a placebo controlled trial of huperzine as adjunct treatment in schizophrenia.

R01 AA016834-01A2 (PI: Petrakis- Krystal – Co-Investigator effort begins 9/2009) 08/01/2008-06/30/2013

NIH/NIAAA Mecamylamine for the Treatment of Alcohol Dependence

This study proposes that acute antagonism of the nicotinic receptor, using mecamylamine will be effective in reducing ethanol consumption in alcohol dependent individuals and that there is a moderating effect of smoking on this effect, in that non-smokers will benefit the most from this medication. By exploring the relationship between smoking and response to mecamylamine on ethanol consumption, this proposal will serve to provide insight into the underlying neurobiology of the interaction between alcohol and nicotine dependence.

VA Krystal (Role: PI) 10/01/2006-9/30/2010

DEPARTMENT OF VETERANS AFFAIRS VA Alcoholism Research Center.

This grant supports pilot alcoholism research studies and research training at the VA Connecticut Healthcare

VA Krystal (Role: PI – Clinical Neurosciences Division) 10/01/2009-9/30/2010

DEPARTMENT OF VETERANS AFFAIRS National Center for PTSD

(renewable yearly)

This center provides support for five Core Laboratories, to study brain function and other neurobiological changes that underlie the symptoms of PTSD.

VA Krystal/Rosenheck (PI) 09/01/2006-12/31/2009
 DEPARTMENT OF VETERANS AFFAIRS CSP#504 Risperidone Treatment for Military Service Related
 Chronic Post-Traumatic Stress Disorder. This grant will evaluate the efficacy and durability of risperidone in
 the treatment of veterans with military service related to chronic post-traumatic stress disorder (PTSD) at 20
 VAMC hospitals.

VA Rosenheck/Krystal (Co-PI) 07/01/2006-12/31/2009
 DEPARTMENT OF VETERANS AFFAIRS CSP#555 Long-Acting Injectable Risperidone in the
 Treatment of Schizophrenia. This study will evaluate the relative effectiveness of oral and the only currently
 FDA-approved long-acting injectable antipsychotic medication for the treatment of chronically symptomatic
 patients with schizophrenia in 20 VA Medical Centers.

Completed Research Support (within the past three years)

K05-AA-014906-05 Krystal (Role: PI) 7/15/2004-6/30/2009
 NIAAA Amino Acid Neurotransmitter Dysregulation in Alcoholism
 This award supported Dr. Krystal's projects to further characterize alteration in amino acid neurotransmission
 associated with alcohol dependence and to unite psychopharmacologic and neuroimaging techniques with
 molecular genetic (candidate gene) and molecular neuroscientific (mRNA expression) arrays.

P50 MH068789-05 (McCormack, PI Program Project: Krystal) 12/1/05-11/30/09
 NIMH CONTE Center: Calcium Signaling and Prefrontal Deficits in Schizophrenia
 The aim of the translational/clinical section is to use agents that improve working memory in animals and to
 study their action in humans using functional magnetic resonance imaging and working memory paradigms.

I-P50 AA-12870-05 Krystal (Role: Director) 6/1/2001-5/31/2006
 NIAAA P50 Center for the Translational Neuroscience of Alcoholism (CTNA-1).
 This award supported projects and core resources devoted to translating basic neuroscience advances into
 clinical insights related to alcoholism.

NARSAD – 2006 Distinguished Investigator Award Krystal (Role: PI) 5/1/2006-4/30/2007
 NARSAD GABRA2 Contribution to NMDA Receptor Deficient-related Prefrontal Dysfunction
 This study explored the implication of GABRA2 and NMDA receptors in cognitive deficits relevant to
 schizophrenia, characterizes the interplay of GABA and glutamate in regulating normal PFC function and
 provided a human laboratory-based paradigm for testing the efficacy of putative therapeutic agents targeting
 GABRA2.

R21-AA014543-01A1 Krystal (Role: PI) 9/24/2004-8/31/2008
 NIAAA Novel Glutamatergic Detoxification Strategies
 This pilot study compared the effectiveness of the lamotrigine and memantine to standard treatment of acute
 alcohol withdrawal and abstinence initiation in alcohol dependent patients, and the effect of these drugs on
 NMDA neurotransmission.

VA Krystal (Role: Co-Director) 01/01/2000-9/30/2006
 DEPARTMENT OF VETERANS AFFAIRS VA Schizophrenia Center
 This center provided support for three Core Laboratories, each with a pilot project, related to schizophrenia.