FEDERALLY-FUNDED RELAPSE PRODUCING EXPERIMENTS in PSYCHIATRY:
DRUG WASHOUT / CHEMICAL PROVOCATION
A PARTIAL BIBLIOGRAPHY (Jan 2000)
By VERA HASSNER SHARAV

National Institute of Mental Health:


Daniel DG; Weinberger DR; Jones DW; Zigun JR; Coppola R; Handel S; Bigelow LB; Goldberg TE; Berman KF; Kleinman JE: “The effect of amphetamine on regional cerebral blood flow during cognitive activation in schizophrenia,” Journal of Neuroscience, 1991, 11: 1907-1917

Goldberg TE; Bigelow LB; Weinberger DR; Daniel DG; Kleinman JE: “Cognitive and behavioral effects of the coadministration of dextroamphetamine and haloperidol in schizophrenia,” American Journal of Psychiatry 1991 Jan; 148 (1): 78-84


Schulz SC; Cornelius J; Schulz PM; Soloff PH: “The amphetamine challenge test in patients with borderline disorder,” American Journal Psychiatry, 1988 Jul; 145 (7): 809-14

Brookhaven National Laboratories:
Gatley SJ; Volkow ND; Gifford AN; Ding YS; Logan J; Wang GJ, “Model for estimating dopamine transporter occupancy and subsequent increases in synaptic dopamine using positron emission tomography and carbon-11-labeled cocaine,” Biochemical Pharmacology, 1997, 53: 43-52 NIH-GRANT-NUMBER: DA 06278DANIDA. DA09490DANIDA.

Schlyer DJ; Volkow ND; Fowler JS; Wolf AP; Shiu CY; Dewey SL; Bendriem B; Logan J; Raulli R; Hitzemann R; et al “Regional distribution and kinetics of haloperidol binding in human brain: a PET study with [18F] haloperidol,” Synapse 1992, 11: 10-9

Volkow ND; Wang GJ; Fowler JS; Logan J; Gatley SJ; Hitzemann R; Chen AD; Dewey SL; Pappas N: “Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects,” Nature 1997 Apr 24; 386 (6627): 830-3


Volkow ND; Wang GJ; Gatley SJ; Fowler JS; Ding YS; Logan J; Hitzemann R; Angrist B; Lieberman J : “Temporal relationships between the pharmacokinetics of methylphenidate in the human brain and its behavioral and cardiovascular effects.” published in Psychopharmacology (Berl) 1996 Jan; 123 (1): 26-33 NIH-GRANT-NUMBER: 1R01-DA09490-01DANIDA.

Volkow ND; Wang GJ; Fowler JS; Gatley SJ; Ding YS; Logan J; Dewey SL; Hitzemann R; Lieberman J: “Relationship between psychostimulant-induced "high" and dopamine transporter occupancy.” in Proc of the Nat’l Acad of Science, 1996, 93: 10388-92 NIH-GRANT-NUMBER: 09490-01.

Volkow ND; Wang GJ; Fowler JS; Logan J; Hitzemann R; Gatley SJ; MacGregor RR; Wolf AP: “Cocaine uptake is decreased in the brain of detoxified cocaine abusers,” in Neuropsychopharmacology 1996 Mar; 14 (3): 159-68 NIH-GRANT-NUMBER: 5RO1-DA06891DANIDA. NS15638NSNINDS.


Volkow ND; Ding YS; Fowler JS; Wang GJ; Logan J; Gatley JS; Dewey S; Ashby C; Liebermann J; Hitzemann R; et al: “Is methylphenidate like cocaine? Studies on their pharmacokinetics and distribution in the human brain.” CITE: Arch Gen Psychiatry 1995 Jun; 52 (6): 456-63


Yousef KA; Volkow ND; Schlyer DJ; Fowler JS; Wolf AP; Wang GJ; Smith MR; Brodie JD;

Wang GJ; Volkow ND; Fowler JS; Logan J; Abumrad NN; Hitzemann RJ; Pappas NS; Pascani K “Dopamine D2 receptor availability in opiate-dependent subjects before and after naloxone-precipitated withdrawal.” Neuropsychopharmacology 1997, 16: 174-82  NIH-GRANT-NUMBER: 5RO1-DA06891DANIDA. 1RO1 AA09481-01AANIAAA.

Department of Psychiatry, University of Illinois at Chicago:


Sharma RP; Shapiro LE; Kamath SK; Soll EA; Watanabe MD; Davis JM : “Acute dietary tryptophan depletion: effects on schizophrenic positive and negative symptoms,” Neuropsychobiology 1997, 35: 5-10  NIH-GRANT-NUMBER: MH48888MHNIMH.

Sharma RP; Dowd SM; Davis JM; Janicak PG : “Age of illness onset and schizophrenic symptomatology during an inpatient washout period,” Schizophrenia Research, 1996, 20: 295-300
 NIH-GRANT-NUMBER: MH 48888MHNIMH.


Sharma RP; Faull K; Javaid JI; Davis JM : “Cerebrospinal fluid levels of phenylacetic acid in mental illness: behavioral associations and response to neuroleptic treatment.” Acta Psychiatry Scandinavia 1995, 91: 293-8  NIH-GRANT-NUMBER: MH-48888MHNIMH. MH-30854MHNIMH.

Sharma RP; Javaid JI; Faull K; Davis JM; Janicak PG : “ CSF and plasma MHPG, and CSF MHPG index: pretreatment levels in diagnostic groups and response to somatic treatments.” Psychiatry Research, 1994, 51: 51-60


Pandey SC; Sharma RP; Janicak PG; Marks RC; Davis JM; Pandey GN: “Platelet serotonin-2 receptors in schizophrenia: effects of illness and neuroleptic treatment” Psychiatry
Pandey GN; Sharma RP; Janicak PG; Davis JM: “Monoamine oxidase and cortisol response in depression and schizophrenia.” Psychiatry Research 1992 Oct; 44 (1): 1-8


Sharma RP, Javaid JI, Pandey GN, Easton M, Davis JM: “Pharmacological effects of methylphenidate on plasma homovanillic acid and growth hormone,” Psychiatry Research, 1990, 32: 9-17

University of Cincinnati College of Medicine:

Duke University Medical Center


Harvard University Medical School, Charlestown, Massachusetts

Hillside Hospital, Long Island Jewish Medical Center:


Lieberman JA; Kane JM; Sarantakos S; Gadaleta D; Woerner M; Alvir J; Ramos-Lorenzi J “Prediction of relapse in schizophrenia.” *Archives of General Psychiatry*, 1987, 44: 597-603

NIH-GRANT-NUMBER: MH-3880MHNIMH. MH-00537MHNIMH.

Lieberman JA, Kane JM, Alvir J: “Provocative tests with psychostimulant drugs in schizophrenia,” *Psychopharmacology*, 1987, 91: 415-433

Lieberman JA; Alvir JM; Woerner M; Degroof G; Bilder RM; Ashtari M; Bogerts B; Mayerhoff DI; Geisler SH; Loebel A; et al: “Prospective study of psychobiology in first-episode schizophrenia at Hillside Hospital,” *Schizophrenia Bulletin*, 1992, 18: 351-7

NIH-GRANT-NUMBER: MH-41646MHNIMH. MH-00537MHNIMH. MH-41960MHNIMH.


Lieberman JA; Jody D; Alvir JM; Ashtari M; Levy DL; Bogerts B; Degroof G; Mayerhoff DI; Cooper T “Brain morphology, dopamine, and eye-tracking abnormalities in first-episode schizophrenia. Prevalence and clinical correlates.” *Archives of General Psychiatry*, 1993, 50: 357-68 NIH-GRANT-NUMBER: MH-41646MHNIMH. MH-00537MHNIMH. MH-41960MHNIMH.


Maryland Psychiatric Research Center:
Buchanan RW; Kirkpatrick B; Summerfelt A; Hanlon TE; Levine J; Carpenter WT Jr: “Clinical


Mount Sinai School of Medicine / Bronx Veterans Affairs Medical Center:


Harvey PD; Davidson M; Powchik P; Schmeidler J; McQueeney R; Kaminsky R; Davis KL: “Time course and clinical predictors of treatment response in schizophrenia,” *Schizophrenia Research*, 1991, 5: 161-6


Khan RS; Amin F; Powchik P; Knott P; Goldstein M; Apter S; Kerman B; Jaff S; Davidson M: “Increments in plasma homovanillic acid concentrations after neuroleptic discontinuation are associated with worsening of schizophrenic symptoms,” *Prog Neuropsychopharmacology Biological Psychiatry* 1990; 14 (6): 879-84


Siegel BV Jr; Trestman RL; O'Flaithbheartaigh S; Mitropoulou V; Amin F; Kirrane R; Silverman J; Schmeidler J; Keefe RS; Siever LJ: "D-amphetamine challenge effects on Wisconsin Card Sort Test. Performance in schizotypal personality disorder. *Schizophrenia Research* 1996 May; 20 (1-2): 29-32

**NYS Psychiatric Institute, College of Physicians and Surgeons, Columbia University:**

Papp LA; Martinez JM; Klein DF; Coplan JD; Norman RG; Cole R; de Jesus MJ; Ross D; Goetz R; Gorman JM: “Respiratory psychophysiology of panic disorder: three respiratory challenges in 98 subjects,” *American Journal of Psychiatry*, 1997 Nov; 154: 1557-65


NYU Medical Center/ Manhattan Veterans Affairs Medical Center:
Angrist B; Peselow E; Rubinstein M; Wolkin A; Rotrosen J: “Amphetamine response and relapse risk after depot neuroleptic discontinuation.” *Psychopharmacology* (Berl) 1985, 85: 277-83 NIH-GRANT-NUMBER: MH 35976MHNIMH.


Pittsburgh Veterans Affairs Medical Center:


Malas KL; van Kammen DP; de Fraites EA; Brown GM; Gold PW : “Reduced growth hormone response to apomorphine in schizophrenic patients with poor premorbid social functioning.” *Journal of Neural Transmitters* 1987, 69: 319-24


Nofzinger EA; van Kammen DP; Gilbertson MW; Gurklis JA; Peters JL: “Electroencephalographic sleep in clinically stable schizophrenic patients: two-weeks versus six-weeks neuroleptic-free,” *Biological Psychiatry*, 1993, 33: 829-35 NIH-GRANT: R01MH44-841MHNIMH. MH16804MHNIMH.


van Kammen DP; Docherty JP; Marder SR; Bunney WE Jr: “Acute amphetamine response predicts antidepressant and antipsychotic responses to lithium carbonate in schizophrenic patients,” Psychiatry Research, 1981, 4 (3): 313-325

van Kammen DP; Docherty JP; Marder SR; Schulz SC; Dalton L; Bunney WE Jr: “Antipsychotic effects of pimozide in schizophrenia. Treatment response prediction with acute dextroamphetamine response,” Archives of General Psychiatry, 1982a, 39 (3): 261-266

van Kammen DP; Bunney WE Jr; Docherty JP; Marder SR; Ebert MH; Rosenblatt JE; Rayner JN: “d-Amphetamine-induced heterogeneous changes in psychotic behavior in schizophrenia,” American Journal of Psychiatry, 1982b, 139 (8): 991-997


van Kammen DP, Docherty JP, Marder SR, Rosenblatt JE, Bunney WE: “Lithium attenuates the activation-euphoria but not the psychosis induced by d-amphetamine in schizophrenia,” Psychopharmacology, (Berl), 1985a, 87: 111-115

van Kammen DP; van Kammen WB; Mann LS; Seppala T; Linnoila M: “Dopamine metabolism in the cerebrospinal fluid of drug-free schizophrenic patients with and without cortical atrophy,” Archives of General Psychiatry, 1986, 43: 978-83


van Kammen DP; Peters J; Yao J; van Kammen WB; Neylan T; Shaw D; Linnoila M: “Norepinephrine in acute exacerbations of chronic schizophrenia. Negative symptoms revisited,” Archives of General Psychiatry 1990a, 47: 161-8


van Kammen DP; Peters J; Yao J; Neylan T; Beuger M; Pontius E; O'Connell DT “CSF chromogranin A-like immunoreactivity in schizophrenia. Assessment of clinical and biochemical relationships,” Schizophrenia Research, 1991, 6: 31-9


van Kammen et al., ”Behavioral vs. biochemical prediction of clinical stability following haloperidol withdrawal in schizophrenia,” *Archives of General Psychiatry*, 1995, 52:673-678


**Washington University, St. Louis**

Newcomer JW, Farber NB, Jevtovic-Todorovic V, Selke G, Melson AK, Hershey T, Craft S, Olney JW: “Ketamine-induced NMDA receptor hypofunction as a model of memory impairment and psychosis,” Neuropsychopharmacology 1999 Feb;20(2):106-18

**Yale University School of Medicine/ West Haven Veterans Affairs Medical Center**


Glazer WM, Charney DS, Heninger GR: “Noradrenergic function in schizophrenia,” Arch Gen Psychiatry 1987 Oct;44(10):898-904


Krystal JH, Karper LP, Seibyl JP, Freeman GK, Delaney R, Bremner JD, Heninger GR, Bowers


Fenfluramine “challenge” experiments
NYS Psychiatric Institute, Columbia University:


Pine DS, Wasserman GA, Coplan J, Fried JA, Huang YY, Kassir S, Greenhill L, Shaffer D, Parsons B: “Platelet Serotonin 2A (5-HT2A) receptor characteristics and parenting
NIMH GRANT: MH-16432; MH-43878

**CUNY Queens College, Mount Sinai School of Medicine:**
Halperin JM, Newcorn JH, Schwartz ST, Sharma V, Siever LJ, Koda VH, Gabriel S: “Age-related changes in the association between serotonergic function and aggression in boys with ADHD,” *Biological Psychiatry*, 1997, 41:682-689 NIMH :1 RO1 MH-46448; NIH-NCRR 5NO1 RR0071

NIMH grant: 1 RO1 MH-46448; NIH-NCRR: 5 MO1 RR0071


In 1999, in the wake of public criticism about experiments such as those listed above, Dr. William Carpenter, director of Maryland Psychiatric Research Center (MPRC), a leading defender of provocation experiments in psychiatry, examined data from ketamine experiments conducted at MPRC, at NIMH, and Yale University. He reported that “56 subjects participated in approximately 62 placebo and 150 ketamine infusions.” He further reported that 12 of the Yale patients,

“experienced more difficulty than was observed in the MPRC and NIMH studies…Worsening of general clinical condition and of psychosis was more profound in several cases including [ ] two where the procedure was terminated early…The greater difficulty in the Yale experience may be due to the inclusion of more acutely ill patients.” See, Carpenter, WT. “The schizophrenia ketamine challenge study debate,” *Biological Psychiatry*, 1999, 46: 1081-1091.