

**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:**

Breier A, Su TP, Saunders R, Carson RE, Kolachana BS, de Bartolomeis A, Weinberger DR, Weisenfeld N, Malhotra AK, Eckelman WC, and Pickar D: "Schizophrenia is associated with elevated amphetamine-induced synaptic dopamine concentrations: evidence from a novel positron emission tomography method," *Proceedings National Academy of Science*, 1997, 94:2569-74

Breier A, Malhotra AK, Pinals DA, Weisenfeld NI, Pickar D: "Association of ketamine-induced psychosis with focal activation of the prefrontal cortex in healthy volunteers," *American Journal of Psychiatry*, 1997, 154: 805-811

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

Malhotra AK, Pinals DA, Adler CM, Elman I, Clifton A, Pickar D, Breier A: "Ketamine-induced exacerbation of psychotic symptoms and cognitive impairment in neuroleptic-free schizophrenics," *Neuropsychopharmacology* 1997 Sep;17(3):141-50

Malhotra, AK, Pinals DA, Adler CM, Elman I, Clifton A, Pickar D, Breier, A: "Ketamine-Induced Exacerbation of Psychotic Symptoms and Cognitive Impairment in Neuroleptic-Free Schizophrenics," *Neuropsychopharmacology*, 1997a, 17: 141-150

Malhotra, A.K, Adler, C. M., Kennison, S.D., Elman, I, Pickar, D, Breier, A: "Clozapine blunts N-Methyl-d-Aspartate antagonist-induced psychosis: a study with Ketamine," *Biological Psychiatry*, 1997b, 42: 664-668

Prien RF, Cole JO, Belkin NF: "Relapse in chronic schizophrenics following abrupt withdrawal of tranquilizing medication," *British Journal of Psychiatry*, 1969, 115: 679-686

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; Shiue 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; Fowler JS; Logan J; Angrist B; Hitzemann R; Lieberman J; Pappas N, "Effects of methylphenidate on regional brain glucose metabolism in humans: relationship to dopamine D2 receptors," published in *American Journal of Psychiatry* 1997 Jan; 154 (1): 50-5. NIH-GRANT-NUMBER: DA-06891DANIDA.
- 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: 5R01-DA06891DANIDA. NS15638NSNINDS.
- Volkow ND; Fowler JS; Hitzemann R; Wang GJ: "Neurochemical mechanisms underlying responses to psychostimulants." in *NIDA Research Monograph* 1996; 159: 322-48 NIH-GRANT-NUMBER: DA06891DANIDA.
- 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
- Volkow ND; Wang GJ; Fowler JS; Logan J; Schlyer D; Hitzemann R; Lieberman J; Angrist B; Pappas N; MacGregor R; et al "Imaging endogenous dopamine competition with [11C]raclopride in the human brain," *Synapse* 1994 Apr; 16 (4): 255-62 NIH-GRANT-NUMBER: NIDA 5R01-DA06891DANIDA. NINDS NS15638NSNINDS.
- Yousef KA; Volkow ND; Schlyer DJ; Fowler JS; Wolf AP; Wang GJ; Smith MR; Brodie JD;

Warner D; "Haloperidol blocks the uptake of [18F]N-methylspiroperidol by extrastriatal dopamine receptors in schizophrenic patients." in Synapse 1995 Jan; 19 (1): 14-7 NIH-GRANT-NUMBER: NS-15638NSNINDS.

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, Singh V, Janicak PG, Javaid JI, Pandey GN: "The prolactin response to fenfluramine in schizophrenia is associated with negative symptoms," Schizophr Res 1999 Aug 23;39(1):85-9

Sharma RP; Janicak PG; Bissette G; Nemeroff CB: TITL: CSF neurotensin concentrations and antipsychotic treatment in schizophrenia and schizoaffective disorder, *American Journal of Psychiatry* 1997, 154: 1019-21 NIH-GRANT-NUMBER: MH-48888MHNIMH;. MH-39415MHNIMH.

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; Bissette G; Janicak PG; Davis JM; Nemeroff CB: "Elevation of CSF somatostatin concentrations in mania." *American Journal of Psychiatry* 1995, 152: 1807-9  
NIH-GRANT-NUMBER: MH-48888MHNIMH. MH-42088MHNIMH. MH-39415MHNIMH.

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 GN; Pandey SC; Dwivedi Y; Sharma RP; Janicak PG; Davis JM: "Platelet serotonin-2A receptors: a potential biological marker for suicidal behavior." *Am J Psychiatry* 1995 Jun; 152 (6): 850-5  
NIH-GRANT-NUMBER: MH-36169MHNIMH.

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*

*Research*, 1993 48: 57-68 NIH-GRANT-NUMBER: RO1-MH36169MHNIMH.  
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, Jainacak, PG, Davis, JM, "Behavioral and biochemical effects of methylphenidate in schizophrenic and nonschizophrenic patients," *Biological Psychiatry*, 1991, 30:459-66

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:**

Strakowski SM, Sax KW, Setters MJ, Stanton SP, Keck Jr. PE: "Lack of enhanced response to repeated d-amphetamine challenge in first-episode psychosis: implications for a sensitization model of psychosis in humans," *Biological Psychiatry*, 1997, 42: 749-755 NIH Public Service GRANT: MO1RR08084

#### **Duke University Medical Center**

Mathew RJ, Wilson WH: "Changes in cerebral blood flow and mental state after amphetamine challenge in schizophrenic patients," *Neuropsychobiology*, 1989, 21:117-123  
NIH-GRANT-NUMBER: MH42114MHNIMH.

Mathew RJ, Wilson WH: "Cerebral blood flow responses to inhaled carbon dioxide in schizophrenia," *Acta Psychiatry Scandinavia*, 1990, 81: 497-506

#### **Harvard University Medical School, Charlestown, Massachusetts**

Tsai G, van Kammen DP, Chen S, Kelley ME, Grier A, Coyle JT "Glutamatergic neurotransmission involves structural and clinical deficits of schizophrenia," *Biol Psychiatry* 1998 Oct 15;44(8):667-74

#### **Hillside Hospital, Long Island Jewish Medical Center:**

Jody, D, Lieberman, JA, Geisler, S, Szymanski, S, Alvir, JM, "Behavioral response to methylphenidate and treatment outcome in first episode schizophrenia," *Psychopharmacol Bull*, 1990, 26:224-30

Koreen, AR, Lieberman, JA, Alvir, J, Chakos, M, "The behavioral effect of m-chlorophenylpiperazine (mCPP) and methylphenidate in first episode schizophrenia and normal controls," *Neuropsychopharmacology*, 1997, 16:61-8  
NIH-GRANT-NUMBER: MH-41646MHNIMH. MH-41960MHNIMH. MH-00537MHNIMH.

Levy, DL, Smith, M, Robinson, D, Jody, D, Lerner, G, Alvir, J, Geisler, SH, Szymanski, SR, Gonzalez, A, Mayerhoff, DI, et al, "Methylphenidate increases thought disorder in recent onset schizophrenics, but not in normal controls," *Biological Psychiatry*, 1993, 34:507-14

- Lieberman JA, Kane JM, Gadaleta D, et al: "Methylphenidate challenge as predictor of relapse in schizophrenia," *American Journal of Psychiatry*, 1984, 141: 633-638
- 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; Degreef 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: "Prediction of outcome in first-episode schizophrenia," *Journal of Clinical Psychiatry*, 1993, 54 Suppl: 13-17 NIH-GRANT-NUMBER: MH-3880MHNIMH. MH-00537MHNIMH.
- Lieberman JA; Jody D; Alvir JM; Ashtari M; Levy DL; Bogerts B; Degreef 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: MH41646MHNIMH. MH00537MHNIMH. MH41960MHNIMH.
- Lieberman JA, Alvir J, Geisler S, Ramos-Lorenzi J, Woerner M, Novacenko H, Cooper T, Kane JM: "Methylphenidate response, psychopathology and tardive dyskinesia as predictors of relapse in schizophrenia," *Neuropsychopharmacology*, 1994, 11:107-18 NIH-GRANT-NUMBER: MH38880MHNIMH. MH00537MHNIMH.
- Perovich, RM, Lieberman JA, Fleischhacker WW, Alvir J: "The behavioral toxicity of bromocriptine in patients with psychiatric illness," *J Clinical Psychopharmacology*, 1989, 9: 417-22 NIH-GRANT-NUMBER: MH-00537MHNIMH. MH-41960MHNIMH.
- Robinson, D, Mayerhoff, D, Alvir, J, Cooper, T, Lieberman, J, "Mood responses of remitted schizophrenics to methylphenidate infusion," *Psychopharmacology (Berl)*, 1991, 105:247-52
- Szymanski S; Lieberman JA; Alvir JM; Mayerhoff D; Loebel A; Geisler S; Chakos M; Koreen A; Jody D; Kane J: "Gender differences in onset of illness, treatment response, course, and biologic indexes in first-episode schizophrenic patients," *American Journal of Psychiatry*, 1995, 152 : 698-703 NIH-GRANT: MH-41646MHNIMH. MH-41960MHNIMH. MH-00537MHNIMH.

**Maryland Psychiatric Research Center:**

Buchanan RW; Kirkpatrick B; Summerfelt A; Hanlon TE; Levine J; Carpenter WT Jr: "Clinical

predictors of relapse following neuroleptic withdrawal." CITE: Biol Psychiatry 1992 Jul 1; 32 (1): 72-8 NIH-GRANT-NUMBER: MH35996MHNIMH. MH40279MHNIMH.

Dixon L, Thaker G, Conley R, Ross D, Cascella N, Tamminga C: "Changes in psychopathology and dyskinesia after neuroleptic withdrawal in a double-blind design," *Schizophrenia Research*, 1993, 10: 267-271 NIMH 4R 37MH 37073-09MHNIMH. NIMH 5R01 MH42234-02MHNIMH

Kirpatrick B, Carpenter WT, K, Buchanan RW, Breier A, Tamminga CA: "Plasma prolactin as a predictor of relapse in drug-free schizophrenic outpatients," *Biological Psychiatry*, 1992, 32: 1049-54 NIH-GRANT #: MH-40279MHNIMH. MH-35996MHNIMH

Kirpatrick B, Buchanan RW, Maeda K, Carpenter WT Jr, Jauch D, Tamminga CA: "Effect of neuroleptic withdrawal on plasma prolactin: a possible marker receptor adaptation," *Biological Psychiatry*, 1989 NIH-GRANT #: MH35996MHNIMH. MH40279MHNIMH

Lahti, AC, Koffel, B, LaPorte, D, Tamminga, CA, "Subanesthetic doses of ketamine stimulate psychosis in schizophrenia," *Neuropsychopharmacology*, 1995, 13: 9-19 NIMH-40279MHNIMH

Tamminga CA, Gotts MD, Thaker GK, Alphs LD, Foster NL: " Dopamine agonist treatment of schizophrenia with N-propylnorapomorphine " *Archives of General Psychiatry*, 1986 NIH-GRANT #: MH37073-02MHNIMH

Tamminga CA, Thaker GK, Buchanan R, Kirkpatrick B, Alphs LD, Chase TN, Carpenter WT: " Limbic system abnormalities identified in schizophrenia using positron emission tomography with fluorodeoxyglucose and neocortical alterations with deficit syndrome," *Archives of General Psychiatry*, 1992, 49: 522-530

Tamminga, CA, Holcomb HH, Gao, X.-M & Lahti, AC, "Glutamate pharmacology and the treatment of schizophrenia: current status and future directions," *International Clinical Psychopharmacology*, 10 Suppl.3:29-37, 1995

Thaker GK, Wagman AM, Kirpatrick B, Tamminga CA: "Alterations in sleep polygraphy after neuroleptic withdrawal: a putative supersensitive dopaminergic mechanism," *Biological Psychiatry*, 1989, NIH-GRANT #: R3 MH40641-01MHNIMH. R1 MH3703-01A1MHNIMH. MH35996MHNIMH

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

Davidson, M, Keefe, RSE, Mohs, RC et al., "L-dopa challenge and relapse in schizophrenia," *American Journal of Psychiatry*, 1987, 144: 934-938

Davidson M, Kahn RS, Powchik P, Wame P, Losonczy MF, Kaminsky R, Apter S, Jaff S, Davis KL: "Changes in plasma homovanillic acid concentrations in schizophrenic patients following neuroleptic discontinuation," *Archives of General Psychiatry*, 1991, 48: 73-76

Harvey PD, Putnam KM, Davidson, M, Kahn RS, Powchick P, McQueeney R, Keefe RS, Davis KL: "Brief neuroleptic discontinuation and clinical symptoms in Kraepelinian and non-Kraepelinian chronic schizophrenic patients," *Psychiatry Research*, 1991, 38: 285-292

NIH-GRANT-NUMBER: MH-37922MHNIMH.

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

Iqbal N, Asnis GM, Wetzler S, Kahn RS, Kay SR, van Praag HM: "The MCPP challenge test in schizophrenia: hormonal and behavioral responses," *Biological Psych*, 1991, 30: 770-778

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

Kahn RS, Siever LJ, Gabriel S, Amin F, Stern RG, DuMont K, Apter S, Davidson M: "Serotonin function in schizophrenia: effects of meta-chlorophenylpiperazine in schizophrenic patients and healthy subjects," *Psychiatry Research*, 1992, 43: 1-12 NIH-GRANT-NUMBER: R01 MH-46957-01MHNIMH.

Kahn RS, Siever L, Davidson M, Greenwald C, Moore C: "Haloperidol and clozapine treatment and their effect on M-chlorophenylpiperazine-mediated responses in schizophrenia: implications for the mechanism of action of clozapine," *Psychopharmacology (Berl)* 1993a, 112 (1 Supp.): S90-4

Kahn RS, Davidson M, Siever LJ, Sevy S, Davis KL: "Clozapine treatment and its effect on neuroendocrine responses induced by the serotonin agonist, m-chlorophenylpiperazine," *Biological Psychiatry*, 1994, 35: 909-912

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 NIH-GRANT-NUMBER: MH42827-02MHNIMH.

**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 NIH-GRANT-NUMBER: MH-41778MHNIMH. MH-30906MHNIMH. MH-00858MHNIMH.

Gorman JM, Fyer, MR, Liebowitz, MR, Klein, DF, "Pharmacologic provocation of panic attacks," In: Melzer, HY, Ed., *Psychopharmacology: The Third Generation of Progress*. NY: Raven Press, 1996, pp. 985-993

Liebowitz, MR, Fryer, AJ, Gorman, JM et al, "Lactate provocation of panic attacks: I. Clinical and behavioral findings," *Archives of General Psychiatry*, 1984, 41:764-770

**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.

Sanfilipo M, Wolkin A, Angrist B, van Kammen DP, Duncan E, Wieland S, Cooper TB: "Amphetamine and negative symptoms of schizophrenia," *Psychopharmacology* (Berl), 1996, 123:211-214

Wolkin A, Angrist B, Wolf AP: "Effects of amphetamine on local cerebral metabolism in normal and schizophrenic subjects as determined by positron emission tomography," *Psychopharmacology*, 1987, 92: 241-246

Wolkin A, Sanfilipo M, Angrist B, Duncan E, Wieland S, Wolf AP, Rodie JD, Cooper TB, Laska E Rotrosen JP: "Acute d-amphetamine challenge in schizophrenia: effects on cerebral glucose utilization and clinical symptomatology," *Biological Psychiatry*, 1994; 36: 317-325 NIH-GRANT: NS-15638NSNINDS.

**Pittsburgh Veterans Affairs Medical Center:**

Beuger M, van Kammen DP, Kelley ME, Yao J: "Dopamine turnover in schizophrenia before and after haloperidol withdrawal. CSF, plasma, and urine studies," *Neuropsychopharmacology*, 1996, 15: 75-86 NIH-GRANT-NUMBER: RO1MH44-841MHNIMH.

Forman SD, Bissette G, Yao J, Nemeroff CB, van Kammen DP: "Cerebrospinal fluid corticotropin-releasing factor increases following haloperidol withdrawal in chronic schizophrenia," *Schizophrenia Research*, 1994, 12: 43-51 NIMH MH-44841MHNIMH. NIMH MH-42088; NIMHMH-39415MHNIMH.

KeKelley ME, Gilbertson M, Mouton A, van Kammen DP: "Deterioration in premorbid functioning in schizophrenia: a developmental model of negative symptoms in drug-free patients," *American Journal of Psychiatry*, 1992, 149: 1543-1548

Malas KL; van Kammen DP; de Fraités 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

Neylan TC, van Kammen DP, Kelley ME, Peters JL: "Sleep in schizophrenic patients on and off haloperidol therapy. Clinically stable vs relapsed patients," *Archives of General Psychiatry*, 1992, 49: 643-649

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: RO1MH44-841MHNIMH. MH16804MHNIMH.

- Peters J; Van Kammen DP; Gelernter J; Yao J; Shaw D: "Neuropeptide Y-like immunoreactivity in schizophrenia. Relationships with clinical measures," *Schizophrenia Research*, 1990, 3: 287-94
- Steinhauer, SR, van Kammen DP, Colbert K, Peters JL, Zubin J: "Pupillary constriction during haloperidol treatment as a predictor of relapse following drug withdrawal in schizophrenic patients," *Psychiatry Research*, 1992, 43: 287-298 NIH-GRANT-NUMBER: MH-43615MHNIMH.
- 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, Bunney WE: "Prediction of early relapse after pimozide discontinuation by response to d-amphetamine during pimozide treatment," *Biological Psychiatry*, 1982, 17; 233-342
- 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, van Kammen WB, et al: "CSF norepinephrine in schizophrenia is elevated prior to relapse after haloperidol withdrawal," *Biological Psychiatry*, 1989, 26: 176-188
- 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, McAdam D, Mouton A, Breeding W: "Prediction of relapse following neuroleptic withdrawal: the role of noradrenaline," *Clinical Neuropharmacology*, 1990b, 13: 436-437
- van Kammen DP; Peters J; Yao J; Neylan T; Beuger M; Pontius E; O'Connor DT "CSF chromogranin A-like immunoreactivity in schizophrenia. Assessment of clinical and biochemical relationships," *Schizophrenia Research*, 1991, 6: 31-9
- van Kammen DP, Guidotti A, Kelley ME, Gurklis J, Guarneri P, Gilbertson MW, Yao JK, Peters J, Costa E: "CSF diazepam-binding inhibitor and schizophrenia: clinical and biochemical

- relationships," *Biological Psychiatry*, 1993, 34: 515-522 NIH-GRANT-NUMBER: MH R0144-841MHNIMH.
- van Kammen DP, Kelley ME, Gilbertson MW, Gurklis J, O'Connor DT: "CSF dopamine beta-hydroxylase in schizophrenia: associations with premorbid functioning and brain computerized tomography scan measures," *American Journal of Psychiatry*, 1994 151: 372-278 NIMH MH-44841MHNIMH
- van Kammen DP, Agren H, Yao JK, O'Connor DT, Gurklis J, Peters JL: "Noradrenergic activity and prediction of psychotic relapse following haloperidol withdrawal in schizophrenia," *American Journal of Psychiatry*, 1994, 51: 379-384
- van Kammen et al., "Behavioral vs. biochemical prediction of clinical stability following haloperidol withdrawal in schizophrenia," *Archives of General Psychiatry*, 1995, 52:673-678
- van Kammen DP, Kelley ME, Gurklis JA, Gibertson MW, Yao JK, Condray R, Peters JL: "Predicting duration of clinical stability following haloperidol withdrawal in schizophrenic patients," *Neuropsychopharmacology*, 1996, 14; 275-283  
NIH-GRANT-NUMBER: RO1MH44-841MHNIMH.
- van Kammen DP, Poltorak M, Kelley ME, Yao JK, Gurklis JA, Peters JL, Hemperly JJ, Wright RD, Freed WJ: "Further studies of elevated cerebrospinal fluid neuronal cell adhesion molecule in schizophrenia," *Biol Psychiatry* 1998 May 1;43(9):680-6
- Yao JK, van Kammen DP: "Red blood cell membrane dynamics in schizophrenia. I. Membrane fluidity," *Schizophrenia Research*, 1994, 11: 209-216  
NIH-GRANT-NUMBER: MH43742MHNIMH. MH44841MHNIMH.
- Yao JK; van Kammen DP; Moss HB; Sokulski DE: "Decreased serotonergic responsivity in platelets of drug-free patients with schizophrenia," *Psychiatry Research*, 1996, 63: 123-32 NIH-GRANT-NUMBER: MH-43742MHNIMH. MH-44841MHNIMH. P50-DA 05605DANIDA.
- Yao JK; van Kammen DP; Gurklis JA: "Abnormal incorporation of arachidonic acid into platelets of drug-free patients with schizophrenia," *Psychiatry Research*, 1996, 60: 11-21  
NIH-GRANT-NUMBER: MH-43742MHNIMH. MH-44841MHNIMH.

#### **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**

- Bremner JD, Innis RB, Ng CK, Staib LH, Salomon RM, Bronen RA, Duncan J, Southwick SM, Krystal JH, Rich D, Zubal G, Dey H, Soufer R, Charney DS : "Positron emission tomography measurement of cerebral metabolic correlates of yohimbine administration in combat-related posttraumatic stress disorder," *Arch Gen Psychiatry* 1997; 54::246-54

- Bremner JD, Licinio J, Darnell A, Krystal JH, Owens MJ, Southwick SM, Nemeroff CB, Charney DS: "Elevated CSF corticotropin-releasing factor concentrations in posttraumatic stress disorder," *Am J Psychiatry* 1997 May;154(5):624-9
- Bremner JD, Innis RB, Salomon RM, Staib LH, Ng CK, Miller HL, Bronen RA, Krystal JH, Duncan J, Rich D, Price LH, Malison R, Dey H, Soufer R, Charney DS: "Positron emission tomography measurement of cerebral metabolic correlates of tryptophan depletion-induced depressive relapse," *Arch Gen Psychiatry* 1997 Apr;54(4):364-74
- Charney DS, Woods SW, Krystal JH, Nagy LM, Heninger GR: "Noradrenergic neuronal dysregulation in panic disorder: the effects of intravenous yohimbine and clonidine in panic disorder patients," *Acta Psychiatr Scand* 1992 Oct;86(4):273-82
- Charney DS, Woods SW, Goodman WK, Heninger GR: "Neurobiological mechanisms of panic anxiety: biochemical and behavioral correlates of yohimbine-induced panic attacks," *Am J Psychiatry* 1987 Aug;144(8):1030-6
- Delgado, PL, Charney, DS, Price, LH, Aghjanian, GK, Landis, H, Heninger, GR, "Serotonin function and the mechanism of antidepressant action: Reversal of antidepressant induced remission by rapid depletion of plasma tryptophan," *Archives of General Psychiatry*, 1990, 47:411-418
- Delgado, PL, Price, LH, Miller, HL, et al "Rapid serotonin depletion as a provocative challenge test for patients with major depression: Relevance to antidepressant action and the neurobiology of depression," *Psychopharmacology Bulletin*, 1991, 27:321-330
- Glazer WM, Charney DS, Heninger GR: "Noradrenergic function in schizophrenia," *Arch Gen Psychiatry* 1987 Oct;44(10):898-904
- Grillon C, Morgan CA 3rd, Davis M, Southwick SM: "Effects of experimental context and explicit threat cues on acoustic startle in Vietnam veterans with posttraumatic stress disorder," *Biol Psychiatry* 1998 Nov 15;44(10):1027-36
- Kosten TR, Wahby V, Giller E Jr, Mason J: "The dexamethasone suppression test and thyrotropin-releasing hormone stimulation test in posttraumatic stress disorder," *Biol Psychiatry* 1990 Oct 15;28(8):657-64
- Krystal JH, D'Souza DC, Karper LP, Bennett A, Abi-Dargham A, Abi-Saab D, Cassello K, Bowers MB Jr, Vegso S, Heninger GR, Charney DS: "Interactive effects of subanesthetic ketamine and haloperidol in healthy humans," *Psychopharmacology (Berl)* 1999 Jul;145(2):193-204
- Krystal JH, Petrakis IL, Webb E, Cooney NL, Karper LP, Namanworth S, Stetson P, Trevisan LA, Charney DS: "Dose-related ethanol-like effects of the NMDA antagonist, ketamine, in recently detoxified alcoholic," *Arch Gen Psychiatry* 1998 Apr;55(4):354-60
- Krystal JH, Karper LP, Seibyl JP, Freeman GK, Delaney R, Bremner JD, Heninger GR, Bowers

MB, Charney DS: "Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans," *Archives of General Psychiatry*, 1994, 51: 199-214 Federal Funding: Dept. of VA, Schizophrenia Biological Research Center, West Haven and NIMH: MH- 30929

Krystal JH, Seibyl JP, Price LH, Woods SW, Heninger GR, Aghajanian GK, Charney DS: "m-Chlorophenylpiperazine effects in neuroleptic-free schizophrenic patients. Evidence implicating serotonergic systems in the positive symptoms of schizophrenia," *Archives of General Psychiatry*, 1993, 50: 624-35

Laruelle, M et al., "Single photon emission computerized tomography imaging of amphetamine-induced dopamine release in drug-free schizophrenic subjects," *Proceedings National Academy of Science*, 1996, 93:9235-9240 GRANT: M01RR00125; MH-54192

Morgan CA 3rd, Grillon C, Southwick SM, Nagy LM, Davis M, Krystal JH, Charney DS: "Yohimbine facilitated acoustic startle in combat veterans with post-traumatic stress disorder," *Psychopharmacology (Berl)* 1995 Feb;117(4):466-71

Randall PK, Bremner JD, Krystal JH, Nagy LM, Heninger GR, Nicolaou AL, Charney DS: "Effects of the benzodiazepine antagonist flumazenil in PTSD," *Biol Psychiatry* 1995 Sep 1;38(5):319-24

Rasmusson AM, Southwick SM, Hauger RL, Charney DS: " Plasma neuropeptide Y (NPY) increases in humans in response to the alpha 2 antagonist yohimbine," *Neuropsychopharmacology* 1998 Jul;19(1):95-8

Southwick SM, Krystal JH, Bremner JD, Morgan CA 3rd, Nicolaou AL, Nagy LM, Johnson DR, Heninger GR, Charney DS: "Noradrenergic and serotonergic function in posttraumatic stress disorder," *Arch Gen Psychiatry* 1997 Aug;54(8):749-58

Woods SW, Charney DS, Delgado PL, Heninger GR: "The effect of long-term imipramine treatment on carbon dioxide-induced anxiety in panic disorder patients," *J Clin Psychiatry* 1990 Dec;51(12):505-7

Yehuda R, Southwick SM, Krystal JH, Bremner D, Charney DS, Mason JW: "Enhanced suppression of cortisol following dexamethasone administration in posttraumatic stress disorder," *Am J Psychiatry* 1993 Jan;150(1):83-6

**Fenfluramine "challenge" experiments  
NYS Psychiatric Institute, Columbia University:**

Pine DS, Coplan JD, Wasserman GA, Miller LS, Fried JE, Davies M, Cooper TB, Greenhill L, Shaffer D, Parsons B: "Neuroendocrine response to fenfluramine challenge in boys," *Archives of General Psychiatry*, 1997, 54: 839-846 NIMH GRANT: MH-16432; MH-43878; MH-01391; MH01039

Pine DS, Wasserman GA, Coplan J, Fried JA, Huang YY, Kassir S, Greenhill L, Shaffer D, Parsons B: "Platelet Serotonin 2A (5-HT<sub>2A</sub>) receptor characteristics and parenting

factors for boys at risk for delinquency: a preliminary report," *American Journal of Psychiatry*, 1996, 153: 538-544  
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

Halperin JM, Newcorn JH, Kpstein I, McKay K, Schwartz ST, Siever LJ, Sharma V: "Serotonin, aggression, and parental psychopathology in children with Attention-Deficit Hyperactivity Disorder," *Journal of the American Academy of Child & Adolescent Psychiatry*, 1997, 36: 1391-1398  
NIMH grant: 1 RO1 MH-46448; NIH-NCRR: 5 MO1 RR0071

Koda VH, Halperin JM, Newcorn JH, Schwartz ST, McKay KE: "Gender differences in the prolactin response to fenfluramine challenge in children with disruptive behavior disorders," *Ann N Y Acad Sci* 1996 Sep 20;794:369-71

Donovan AM, Halperin JM, Newcorn JH, Sharma V: "Thermal response to serotonergic challenge and aggression in attention deficit hyperactivity disorder children," *Child Adolesc Psychopharmacol* 1999;9(2):85-91

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.