

# ***Association of FKBP5, COMT and CHRNA5 Polymorphisms with PTSD among patients at Risk for PTSD***

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- There are no conflicts of interest associated with his research.

# **PTSD Diagnosis in 1994 – DSM-IV**

- A1. Exposure to traumatic event
- A2. Experienced fear, helplessness, horror
- B. Re-experiences traumatic event
- C. Avoid stimuli associated with event
- D. Experiences hyper-arousal symptoms
- E. Duration of symptoms > 1 month
- F. Symptom cause distress or impairment

# Prevalence of Traumatic Event Exposure

- Lifetime experience of qualifying traumatic event in U.S.: 60-90% <sup>1,2,3,4</sup>
- Lifetime prevalence of crime/aggravated assault: 36% <sup>2</sup>
- Prevalence of combat experience <5%<sup>4</sup>

1. Norris, FH. 1992. J Consult Clin Psychol, 60:409-418
2. Resnick, H. 1993. J Consult Clin Psychol, 61:984-991
3. Breslau, N. 1998. Arch Gen Psychiatry, 55:626-632
4. Kessler, R. 1995. Arch Gen Psychiatry, 52:1048-1060

# Prevalence of PTSD

- General population prevalence of PTSD in U.S.: 7.8-9.2% <sup>1,3</sup>
- Women twice as likely as men to have lifetime PTSD <sup>1</sup>
- Risk of PTSD after sexual/aggravated assault: 20-60% <sup>1,2,3</sup>
- Risk of PTSD after combat 10-15%<sup>4</sup>

1. Kessler, R. 1995. Arch Gen Psychiatry, 52:1048-1060
2. Resnick, H. 1993. J Consult Clin Psychol, 61:984-991
3. Breslau, N. 1998. Arch Gen Psychiatry, 55:626-632
4. Boscarino, J. 2006. *Ann Epidemiol*, 16: 248-58.

# Risk Factors for PTSD

- History of childhood trauma<sup>1</sup>
- Female gender<sup>2</sup>
- Recent stressful life events<sup>3</sup>
- Non-right handedness<sup>4</sup>
- Personality disorders, (e.g., ASP)<sup>5</sup>
- Low self-esteem<sup>3</sup>
- History of depression before trauma<sup>3</sup>

1. Kessler, R. 1995. Arch Gen Psychiatry, 52:1048-1060

2. Resnick, H. 1993. J Consult Clin Psychol, 61:984-991

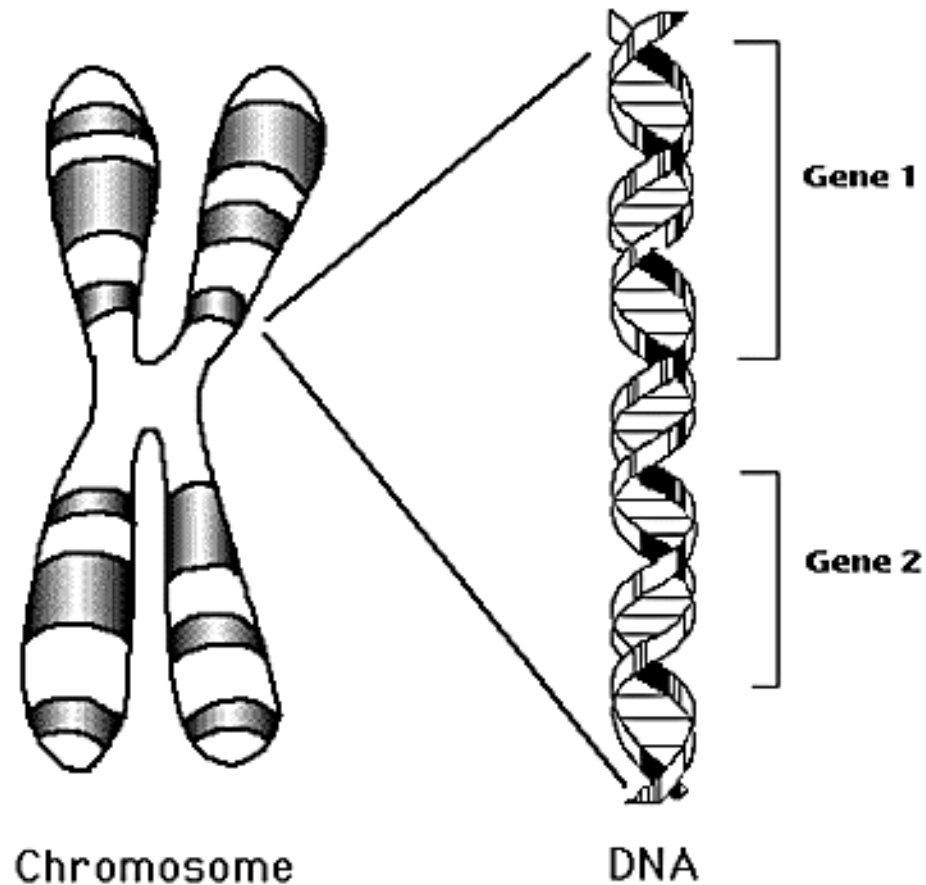
3. Boscarino, J. 2009. Soc Psychiatry Psychiatr Epidemiol. 44: 887-898

4. Boscarino, J. 2007. Psychosom Med, 69: 365-369

5. Sadock, B. Synopsis in Psychiatry, 10<sup>th</sup> Ed., 2007

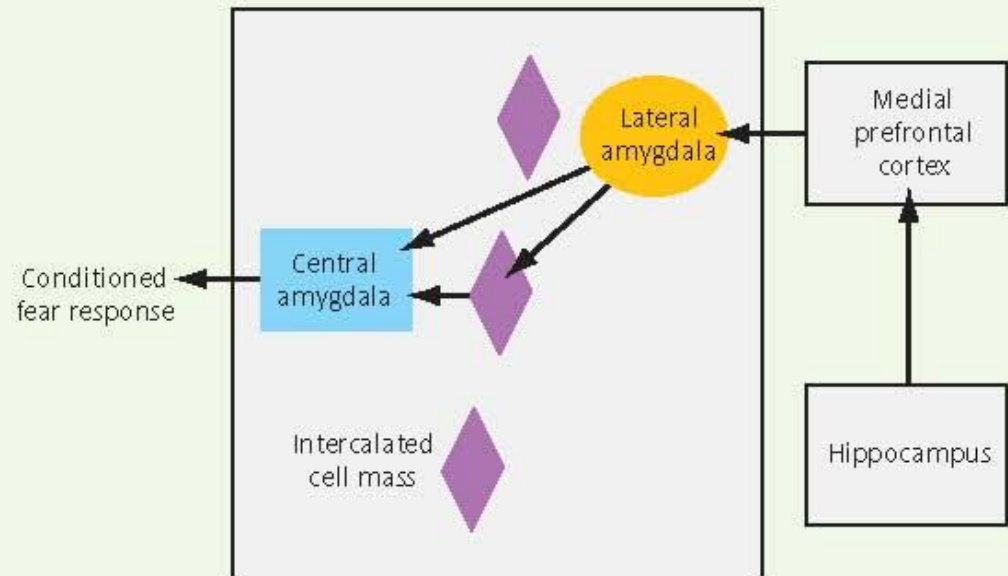
# Genetics of PTSD

Search for Genetics of PTSD



**Genes**

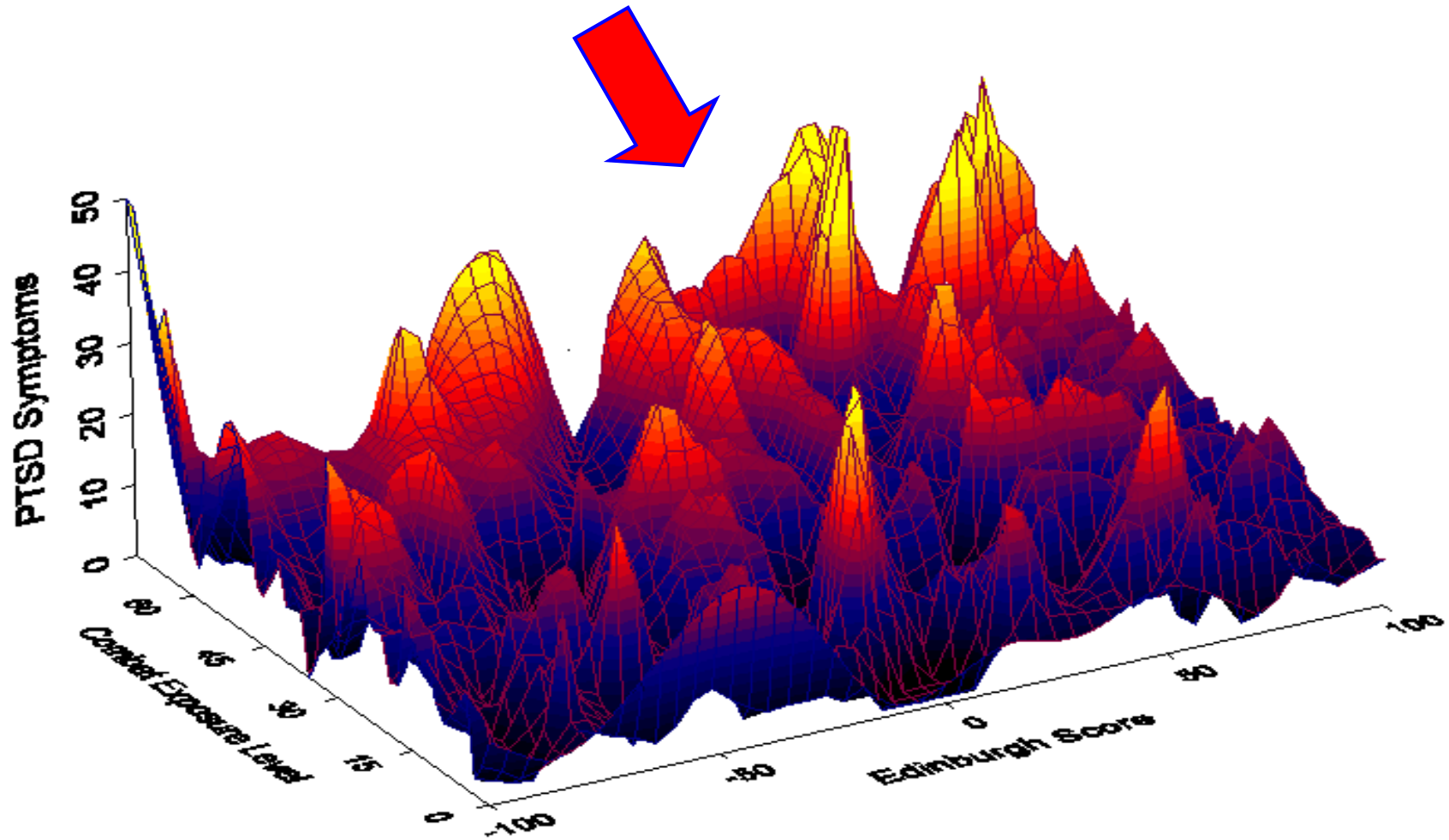
# The Anatomy of Fear Extinction



The fear extinction model has its origins in the classical conditioning that Ivan Petrovich Pavlov (left) first developed in dogs. Specific molecular events within the lateral amygdala facilitate extinction of fear learning (the conditioned fear response) hypothetically by stimulating inhibitory intercalated cell mass activity on the central amygdala. Regions within the prefrontal cortex (ventral and medial aspects) have an inhibitory influence on fear learning in the lateral and central amygdala, an influence modulated by hippocampal input to the ventral/medial prefrontal cortex. Circuit drawing modified from Sotres-Bayon F, Bush DEA, LeDoux JE: Emotional perseveration: an update on prefrontal-amygdala interactions in fear extinction. *Learn Mem* 2004; 11:525–535.

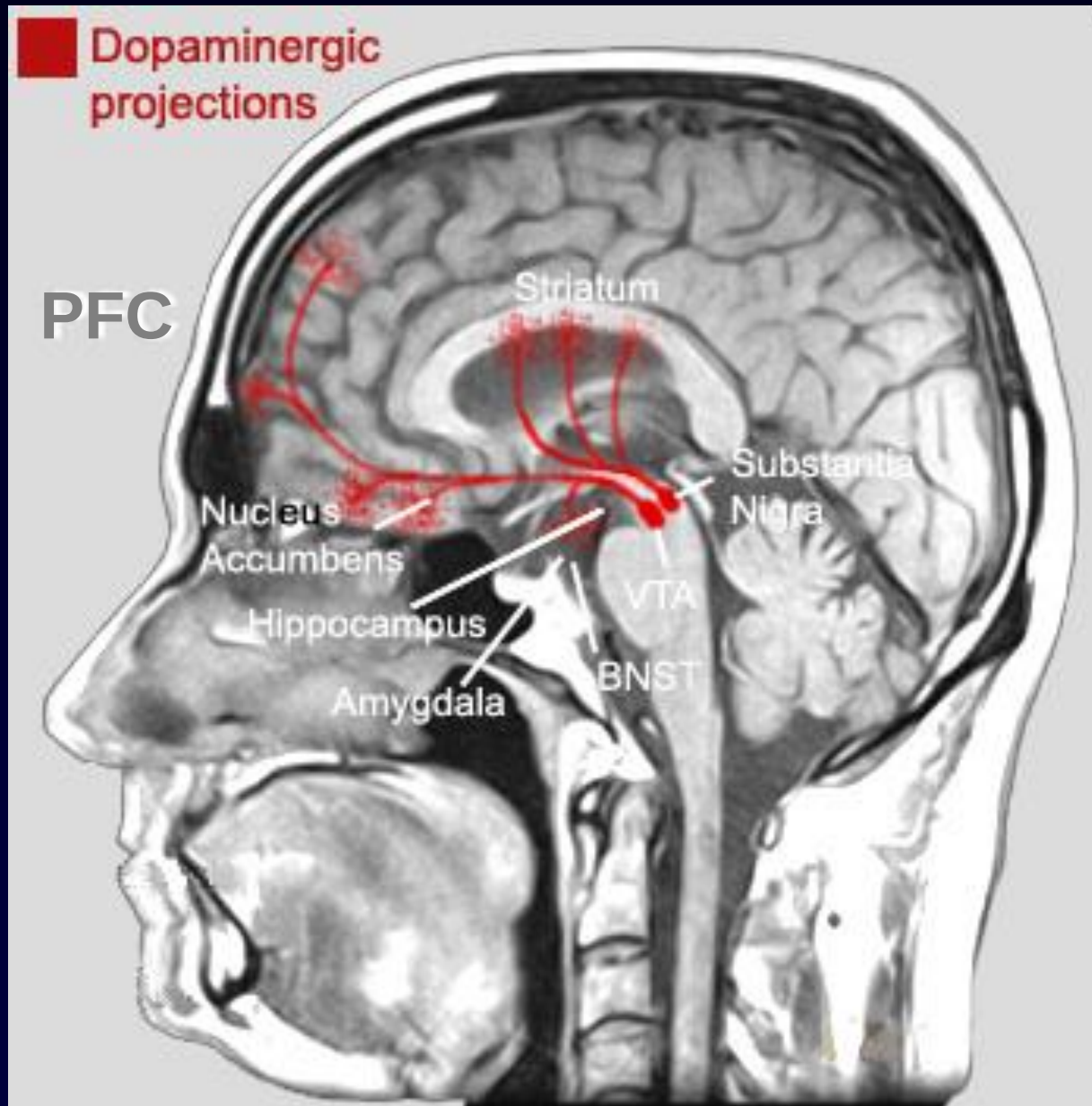


# PTSD Symptoms by Combat Exposure by Handedness



Boscarino & Hoffman, *Psychosomatic Medicine*, 2007

# PTSD and the Brain



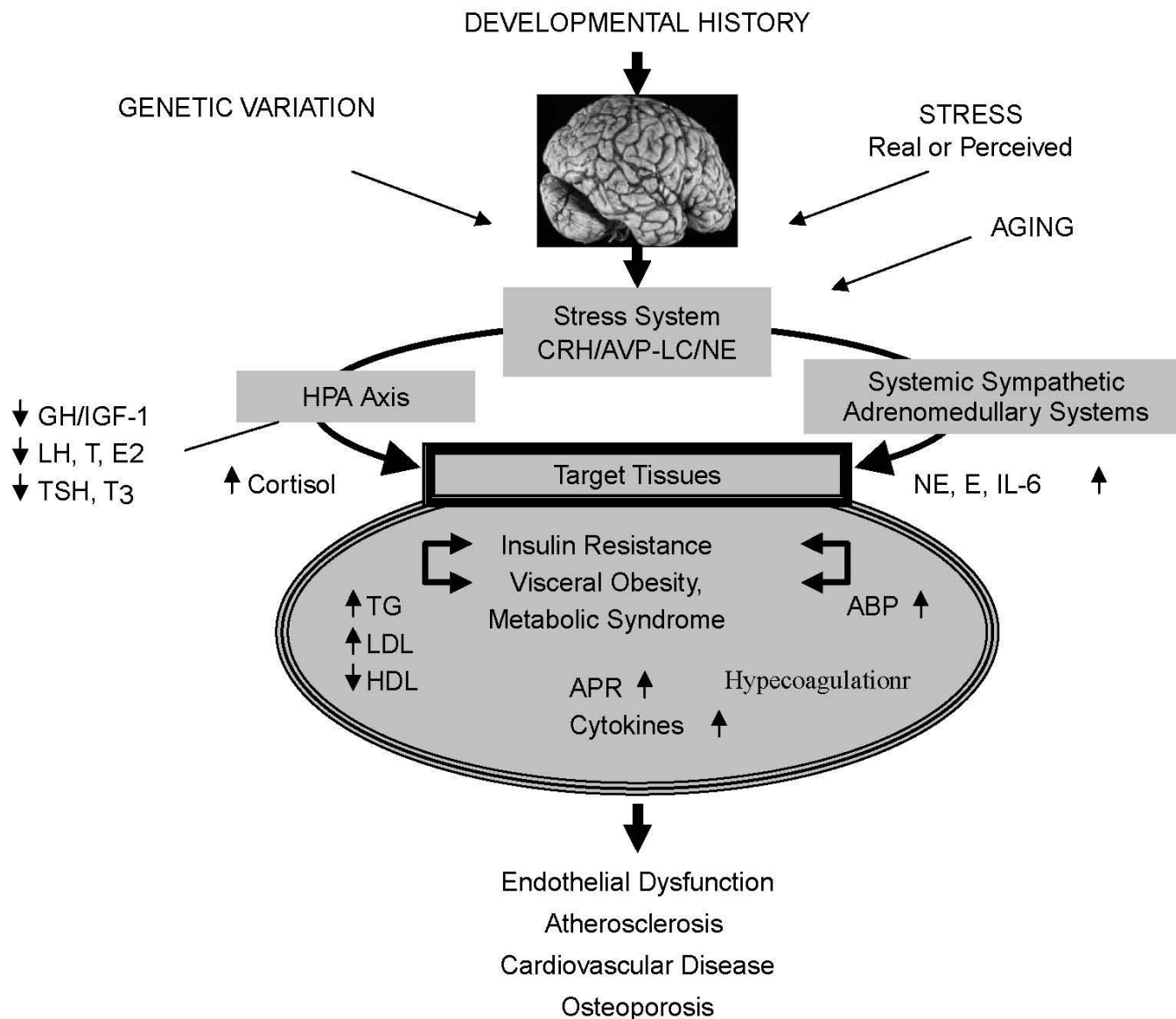


Figure 2. Endogenous/exogenous inputs to the stress system and their effects on the metabolic and cardiovascular systems and bone. ABP, arterial blood pressure; APR, acute phase reactants; AVP, arginine vasopressin; CRH, corticotropin-releasing hormone; E, epinephrine; E2, estradiol; GH, growth hormone; HDL, high-density lipoprotein; HPA axis, hypothalamic–pituitary–adrenal axis; IGF-1, insulin-like growth factor-1; IL-6, interleukin-6; LC, locus caeruleus; LDL, low-density lipoprotein; LH, luteinizing hormone; NE, norepinephrine; T, testosterone; T3, triiodothyronine; TG, triglyceride; TSH, thyroid-stimulating hormone.

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**Forthcoming: Psychiatry Research, 2011**

# Method

- Cross-sectional, candidate-gene study among Geisinger Clinic's outpatients
- Electronic Health Record (EHR) data were reviewed for patients prescribed pain meds. Patients selected for a phone interview if they had 4+ prescription orders for pain in the prior 12 months
- Cases were identified based on the *Diagnostic and Statistical Manual of Mental Disorder, Version IV* (DSM-IV) criteria

## Method (cont'd)

- A modified Composite International Diagnostic Interview (CIDI) was used to obtain data on mental health status by telephone.
- Data were gathered on detailed drug, psychological, and environmental exposures.
- Data were also collected on exposure to psychological trauma and post-traumatic stress disorder (PTSD)
- Altogether, 705 patients completed the CIDI; 505 of these patients (72%) provided DNA for genotyping and completed the NEO Five-Factor Personality Inventory.

# Sample design for pain study

2459 adult long-term opiate users

- 9 primary care & 3 specialty clinics
- $\geq 4$  prescriptions
- not cancer-related
- July 2006 – June 2007

86 not contacted (study quota met)

2373 attempted contact (mail/phone)

983 not reachable or not qualified

- Institutionalized (nursing home, correctional facility, mental institution, etc.)
- Incapable of answering questions
- Language barrier
- Denied taking medication
- Deceased
- Disconnected phone
- Busy signal/answering machine
- Business/wrong number

1390 surveyed (8/07 – 11/08)

685 Not interested/declined study

705 consented and completed questionnaire

505 genotyped

# Collection of DNA

- Following the phone survey, patients were mailed buccal swab kits
- Patients provided a sample of their DNA (cheek cells) and returned by mail to Geisinger Clinic
- Altogether, 505 patients provided usable DNA of the 705 interviewed (72%)



# Candidate Genes/SNPs Studied

| SNP Marker | Gene   | SNP Marker | Gene   | SNP Marker | Gene   |
|------------|--------|------------|--------|------------|--------|
| rs2283265  | DRD2   | rs279859   | GABRA2 | rs6265     | BDNF   |
| rs2734838  | DRD2   | rs17537141 | GABRA2 | rs929623   | BDNF   |
| rs11246226 | DRD4   | rs279830   | GABRA2 | rs9785023  | NPY    |
| rs3758653  | DRD4   | rs4646316  | COMT   | rs540825   | OPRM1  |
| rs11080122 | SLC6A4 | rs4680     | COMT   | rs1799971  | OPRM1  |
| rs140701   | SLC6A4 | rs9296157  | FKBP5  | rs6923231  | OPRM1  |
| rs6280     | DRD3   | rs9470080  | FKBP5  | rs6495308  | CHRNA3 |
| rs1800828  | DRD3   | rs9296158  | FKBP5  | rs660652   | CHRNA3 |
| rs324030   | DRD3   | rs4867796  | DRD1   | rs1051730  | CHRNA3 |
| rs5906957  | MAOA   | rs251937   | DRD1   | rs16969968 | CHRNA5 |
| rs2072743  | MAOA   |            |        | rs12443170 | CHRNA3 |

# DSM-IV Drug Dependence by Significant Predictors

| Study Predictors                     | Total Sample Percent (N) | Lifetime Drug Dependence Percent (N) | No Lifetime Drug Dependence Percent (N) |
|--------------------------------------|--------------------------|--------------------------------------|-----------------------------------------|
| <b>Lifetime Opioid Drug Abuse</b>    |                          |                                      |                                         |
| % Yes                                | 12.3 (88)                | <u>31.8</u> (79)                     | 1.9 (9)***                              |
| % No                                 | 87.7 (617)               | 68.3 (172)                           | 98.1 (445)                              |
| <b>Severity Opioid Dependence</b>    |                          |                                      |                                         |
| % High                               | 15.1 (108)               | <u>30.4</u> (77)                     | 6.8 (31)***                             |
| % Not High                           | 84.9 (597)               | 69.6 (174)                           | 93.2 (423)                              |
| <b>Lifetime Alcohol Dependence</b>   |                          |                                      |                                         |
| % Yes                                | 9.7 (68)                 | <u>14.3</u> (36)                     | 7.1 (32)**                              |
| % No                                 | 90.3 (637)               | 85.7 (215)                           | 92.9 (442)                              |
| <b>Lifetime Tobacco Dependence</b>   |                          |                                      |                                         |
| % Yes                                | 36.3 (251)               | <u>41.8</u> (103)                    | 33.4 (148)***                           |
| % No                                 | 63.7 (454)               | 58.2 (148)                           | 66.6 (306)                              |
| <b>Lifetime Posttraumatic Stress</b> |                          |                                      |                                         |
| % Yes                                | 13.2 (97)                | <u>21.3</u> (55)                     | 8.7 (42)***                             |
| % No                                 | 86.9 (608)               | 78.7 (196)                           | 91.3 (412)                              |

\*\* p<0.01

\*\*\* p<0.001

Boscarino et al. Addiction vol. 105; 2010.

# DSM-IV Drug Dependence by Significant Predictors

| Study Predictors                       | Total Sample<br>Percent (N) | Lifetime<br>Drug Dependence<br>Percent (N) | No Lifetime Drug<br>Dependence<br>Percent (N) |
|----------------------------------------|-----------------------------|--------------------------------------------|-----------------------------------------------|
| <b>History Childhood Neglect</b>       |                             |                                            |                                               |
| % High                                 | 24.6 (178)                  | <u>33.0</u> (84)                           | 20.1 (94)**                                   |
| % Not High                             | 75.4 (527)                  | 67.0 (167)                                 | 79.9 (360)                                    |
| <b>History Exposure to Trauma</b>      |                             |                                            |                                               |
| % High                                 | 22.5 (161)                  | <u>31.8</u> (80)                           | 17.5 (81)***                                  |
| % Not High                             | 77.5 (544)                  | 68.2 (171)                                 | 82.5 (373)                                    |
| <b>History Illicit Drug Use</b>        |                             |                                            |                                               |
| % Yes                                  | 38.1 (273)                  | <u>50.3</u> (127)                          | 31.5 (146)***                                 |
| % No                                   | 61.9 (432)                  | 49.7 (124)                                 | 68.5 (308)                                    |
| <b>History Substance Treatment</b>     |                             |                                            |                                               |
| % Yes                                  | 21.8 (153)                  | <u>36.4</u> (90)                           | 13.9 (63)***                                  |
| % No                                   | 78.2 (552)                  | 63.6 (161)                                 | 86.1 (391)                                    |
| <b>History Anti-Social Personality</b> |                             |                                            |                                               |
| % Yes                                  | 23.3 (167)                  | <u>32.7</u> (83)                           | 18.3 (84)***                                  |
| % No                                   | 76.7 (538)                  | 67.3 (168)                                 | 81.7 (370)                                    |
| (N =)                                  | (705)                       | (251)                                      | (454)                                         |

\*\* p<0.01

\*\*\* p<0.001

Boscarino et al. Addiction vol. 105; 2010.

# Candidate Genes for PTSD

- HPA stress axis system
  - FKBP5
  - CRH-R1
- Locus coeruleus/noradrenergic systems
  - COMT
  - NPY
- Limbic-frontal brain/mesolimbic system
  - CHRNA5
  - DRD2
- Opioid system
  - OPRM1

# Statistical methods (SNP Level)

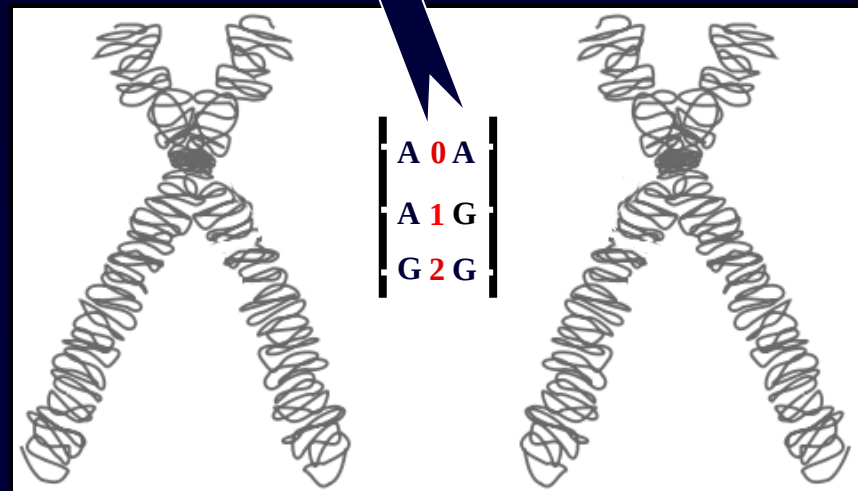
- Linear models (additive genetic)

- continuous:  $E(Y) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_n G_A$

- dichotomous:  $\log(p/1-p) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_n G_A$

- adjustments:

| DEM                             | Confounders                                                                                |
|---------------------------------|--------------------------------------------------------------------------------------------|
| age<br>gender<br>income<br>etc. | income<br>education status<br>trauma exposure<br>childhood neglect<br>neuroticism,<br>etc. |



## Table 1: Covariates in Genetic Model by PTSD

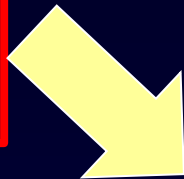
| Study Variables   |                 | Total      | No PTSD    | PTSD*     |                |         |
|-------------------|-----------------|------------|------------|-----------|----------------|---------|
|                   |                 | % (n)      | % (n)      | % (n)     | OR 95% C.I.    | P-value |
| Age:              | 18-39           | 10.3 (52)  | 9.1 (39)   | 17.6 (13) | 5.52 2.06-14.8 | 0.001   |
|                   | 40-64           | 65.2 (328) | 63.9 (274) | 73.0 (54) | 3.27 1.44-7.39 | 0.005   |
|                   | 65+ (ref)       | 24.5 (123) | 27.0 (116) | 9.5 (7)   | --             | --      |
| Gender:           | Male (ref)      | 30.2 (152) | 31.9 (137) | 20.3 (15) | --             | --      |
|                   | Female          | 69.8 (351) | 68.1 (292) | 79.7 (59) | 1.85 1.01-3.37 | 0.037   |
| Income:           | >\$30,000 (ref) | 57.5 (289) | 59.7 (256) | 44.6 (33) | --             | --      |
|                   | <\$30,000       | 42.5 (214) | 40.3 (173) | 55.4 (41) | 1.84 1.12-3.02 | 0.016   |
| Married:          | No (ref)        | 38.2 (192) | 35.9 (154) | 51.4 (38) | --             | --      |
|                   | Yes             | 61.8 (311) | 64.1 (275) | 48.6 (36) | 0.53 0.32-0.87 | 0.013   |
| High trauma:      | No (ref)        | 78.5 (395) | 82.1 (352) | 58.1 (43) | --             | --      |
|                   | Yes             | 21.5 (108) | 17.9 (77)  | 41.9 (31) | 3.30 1.95-5.56 | < 0.001 |
| High adversity:   | No (ref)        | 73.2 (368) | 77.2 (331) | 50.0 (37) | --             | --      |
|                   | Yes             | 26.8 (135) | 22.8 (98)  | 50.0 (37) | 3.38 2.03-5.62 | < 0.001 |
| High neuroticism: | No (ref)        | 78.3 (394) | 82.3 (353) | 55.4 (41) | --             | --      |
|                   | Yes             | 21.7 (109) | 17.7 (76)  | 44.6 (33) | 3.74 2.22-6.30 | < 0.001 |

\*The lifetime prevalence of PTSD among pain patients was 14.7% (95% CI = 11.7-18.1%).

# Exploratory Genetic Results

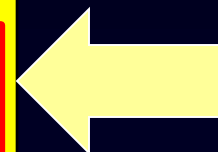
| Phenotype/Gene (SNP) Marker<br>(N = 503; Call Rate ~ 95%) | Crude Results |           |           | Adjusted Results* |           |           |
|-----------------------------------------------------------|---------------|-----------|-----------|-------------------|-----------|-----------|
|                                                           | OR            | 95% C.I.  | (p)       | OR                | 95% C.I.  | (p)       |
| <b>Lifetime Opioid Dependence (n=176)</b>                 |               |           |           |                   |           |           |
| DRD3-280-Additive                                         | 1.54          | 1.15-2.05 | (0.003)   | 1.42              | 1.05-1.91 | (0.021)   |
| DRD3-828-Additive                                         | 1.57          | 1.15-2.13 | (0.005)   | 1.53              | 1.11-2.12 | (0.010)   |
| DRD3-828-Dominant                                         | 0.34          | 0.14-0.83 | (0.018)   | 0.36              | 0.14-0.92 | (0.032)   |
| <b>Lifetime PTSD (n=73)</b>                               |               |           |           |                   |           |           |
| FKBP5-080-Dominant (R)                                    | 2.77          | 1.43-5.40 | (0.003)   | 2.83              | 1.41-5.69 | (0.003)   |
| COMT-680-Additive                                         | 1.57          | 1.10-2.24 | (0.014)   | 1.57              | 1.08-2.88 | (0.018)   |
| CHRNA3-730-Additive                                       | 1.38          | 0.98-1.94 | (0.064)   | 1.47              | 1.03-2.10 | (0.034)   |
| CRH-402-Additive                                          | 1.49          | 1.01-2.2  | (0.046)   | 1.33              | 0.89-2.01 | (0.167)   |
| <b>Lifetime Abuse - Any Drug (n=44)</b>                   |               |           |           |                   |           |           |
| CHRNA3-652-Dominant                                       | 0.45          | 0.24-0.84 | (0.013)   | 0.42              | 0.21-0.81 | (0.010)   |
| <b>Lifetime Poly-Drug Dependence (n=114)</b>              |               |           |           |                   |           |           |
| CHRNA3-170-Additive (2)                                   | 1.40          | 0.97-2.04 | (0.071)   | 1.56              | 1.07-2.30 | (0.023)   |
| <b>Lifetime Cigarette Dependence (n=180)</b>              |               |           |           |                   |           |           |
| CHRNA3-652-Additive (2)                                   | 1.70          | 1.28-2.25 | (0.00021) | 1.70              | 1.27-2.27 | (0.00031) |
| CHRNA3-308-Additive (2)                                   | 1.39          | 1.04-1.86 | (0.026)   | 1.43              | 1.06-1.93 | (0.021)   |
| <b>Amphetamine Use – Ever (n = 79)</b>                    |               |           |           |                   |           |           |
| DRD2-838-Dominant (1)                                     | 0.61          | 0.37-0.99 | (0.047)   | 0.61              | 0.37-0.99 | (0.049)   |

\*Adjusted for age, gender, education, income, whites only



# Exploratory Genetic Results (con't)

| Phenotype/Gene (SNP) Marker<br>(N = 503; Call Rate 90-95%) | Adjusted Results* |           |            | Adjusted Results**    |            |                |
|------------------------------------------------------------|-------------------|-----------|------------|-----------------------|------------|----------------|
|                                                            | OR                | 95% C.I.  | (p)        | OR                    | 95% C.I.   | (p)            |
| <b>Lifetime PTSD (n=73)</b>                                |                   |           |            |                       |            |                |
| FKBP5 + COMT + CHRNA5 (0-4)                                | 1.60              | 1.25-2.06 | (0.000210) | 1.70                  | 1.27-2.24  | (0.000185)     |
| FKBP5 + COMT + CHRNA5 + CRH (0-6)                          | 1.60              | 1.24-2.07 | (0.000313) | 1.53                  | 1.99-1.96  | (0.000903)     |
| 1. FKBP5 + COMT + CHRNA3 (0-4)                             | —                 | —         | —          | 1.71                  | 1.29-2.26  | (0.000190)     |
| <b>Interaction:</b> high trauma x neuroticism              | —                 | —         | —          | <b>5.70</b>           | 2.05-15.81 | (0.003)        |
| 2. FKBP5 + COMT + CHRNA3 (0-4)                             | —                 | —         | —          | 1.78                  | 1.34-2.67  | (0.000065)     |
| <b>Interaction:</b> high neglect x neuroticism             | —                 | —         | —          | <b>6.04</b>           | 2.58-14.15 | (0.002)        |
| 3. FKBP5 + COMT + CHRNA3 + CRH (0-6)                       | —                 | —         | —          | 1.51                  | 1.18-1.95  | (0.002)        |
| <b>Interaction:</b> high trauma x neuroticism              | —                 | —         | —          | <b>6.46</b>           | 2.09-19.91 | (0.004)        |
| 4. FKBP5 + COMT + CHRNA3 + CRH (0-6)                       | —                 | —         | —          | 1.56                  | 1.22-2.01  | (0.000503)     |
| <b>Interaction:</b> high neglect x neuroticism             | —                 | —         | —          | <b>6.24</b>           | 2.55-15.27 | (0.0142)       |
| 5. FKBP5 + COMT + CHRNA3 (0-4)                             | —                 | —         | —          | 2.70                  | 1.43-5.11  | (0.002)        |
| <b>Interaction: FKBP5COMTCHRNA x CRH</b>                   | —                 | —         | —          | <b>(See Figure 2)</b> |            | <b>(0.049)</b> |



\*Logistic regressions adj. for age, gender, education, income, whites only

\*\*Logistic regressions adj. for age, gender, education, income, lifetime trauma, childhood neglect, neuroticism , whites only

**FKBP5** = FK Binding Protein 5; **COMT** = catechol-O-methyltransferase; **CHARNA3** = cholinergic receptor, nicotinic, alpha polypeptide 3; **CRN-R1** = corticotropin releasing hormone receptor 1



### Table 2: Individual SNP and Cumulative Risk Allele Model

| Genetic markers                           | Unadjusted Results |         | Adjusted Results† |         | Adjusted Results†† |          |
|-------------------------------------------|--------------------|---------|-------------------|---------|--------------------|----------|
| Individual SNPs                           | OR 95% C.I.        | P-value | OR 95% C.I.       | P-value | OR 95% C.I.        | P-value  |
| CHRNA5 rs16969968[A]                      | 1.37 0.97-1.91     | 0.072   | 1.46 1.02-2.08    | 0.037   | 1.50 1.03-2.19     | 0.034    |
| FKBP5 rs9470080[T]*                       | 2.77 1.43-5.40     | 0.003   | 2.94 1.46-5.94    | 0.003   | 2.57 1.23-5.38     | 0.012    |
| COMT rs4680[G]                            | 1.57 1.10-2.24     | 0.014   | 1.55 1.06-2.26    | 0.023   | 1.68 1.13-2.51     | 0.010    |
|                                           |                    |         |                   |         |                    |          |
| Cumulative Risk-allele ( <i>model 1</i> ) | OR 95% C.I.        | P-value | OR 95% C.I.       | P-value | OR 95% C.I.        | P-value  |
| rs16969968 + rs9470080 + rs4680)          | 1.52 1.19-1.93     | 0.001   | 1.55 1.20-2.00    | 0.001   | 1.65 1.25-2.16     | 0.000426 |

†Adjusted for demographic variables, including age, gender, income, education, and marital status.

††Adjusted for demographic variables plus: lifetime history of trauma exposure, history of childhood adversity, and neuroticism.

# Table 3: Association between Risk Alleles and PTSD

| Genetic marker      |           |     | Total      | No PTSD    | PTSD      |
|---------------------|-----------|-----|------------|------------|-----------|
| Genotype (value)    |           |     | % (n)      | % (n)      | % (n)     |
| CHRNA5 (rs16969968) | GG        | (0) | 46.4 (228) | 48.1 (201) | 37.0 (27) |
|                     | AG        | (1) | 38.9 (191) | 38.0 (159) | 43.8 (32) |
|                     | AA        | (2) | 14.7 (72)  | 13.9 (58)  | 19.2 (14) |
|                     |           |     |            |            |           |
| FKBP5 (rs9470080)   | CC+CT     | (0) | 89.2 (421) | 91.0 (366) | 78.6 (55) |
|                     | TT        | (1) | 10.8 (51)  | 9.0 (36)   | 21.4 (15) |
|                     |           |     |            |            |           |
| COMT (rs4680)       | GG        | (0) | 25.8 (128) | 27.4 (116) | 16.4 (12) |
|                     | AG        | (1) | 49.6 (246) | 49.6 (210) | 49.3 (36) |
|                     | AA        | (2) | 24.6 (122) | 22.9 (97)  | 34.2 (25) |
|                     |           |     |            |            |           |
| Risk-Allele Count   | 0 Alleles | (0) | 11.2 (52)  | 12.8 (51)  | 1.4 (1)   |
|                     | 1 Alleles | (1) | 30.9 (144) | 31.0 (123) | 30.4 (21) |
|                     | 2 Alleles | (2) | 32.4 (151) | 33.8 (134) | 24.6 (17) |
|                     | 3 Alleles | (3) | 19.5 (91)  | 17.4 (69)  | 31.9 (22) |
|                     | 4+Alleles | (4) | 6.0 (28)   | 5.0 (20)   | 11.6 (8)  |

# SNP Marker Specifications

| Marker specifications (NCBI build 37.1) |        |                              |                       |                       |
|-----------------------------------------|--------|------------------------------|-----------------------|-----------------------|
| SNP                                     | Gene   | Chromosome<br>(map location) | MAF<br>(minor/common) | Functional annotation |
| rs16969968                              | CHRNA5 | 15 (78882925)                | 35% (A/G)             | Missense (D↔N)        |
| rs9470080                               | FKBP5  | 6 (35646435)                 | 33% (T/C)             | Intron                |
| rs4680                                  | COMT   | 22 (19951271)                | 49.5% (G/A)           | Missense (V↔M)        |
| MAF: minor allele frequency             |        |                              |                       |                       |

# Genetic Predictors of PTSD: Best Model (N= 502)

| Predictor  | Odds Ratio | Lower 95% CI | Upper 95% CI | P-value |
|------------|------------|--------------|--------------|---------|
| FK+CM+CH5* | 1.65       | 1.25         | 2.16         | .000426 |

\*FK = FK Binding Protein 5 (FKBP5); CM = catechol-O-methyltransferase (COMT); CH5 = cholinergic receptor, nicotinic, alpha polypeptide 5 (CHARNA5)

FK+CM+CH5 = 0-4 at-risk alleles (continuous variable)

# World Trade Center Disaster Study



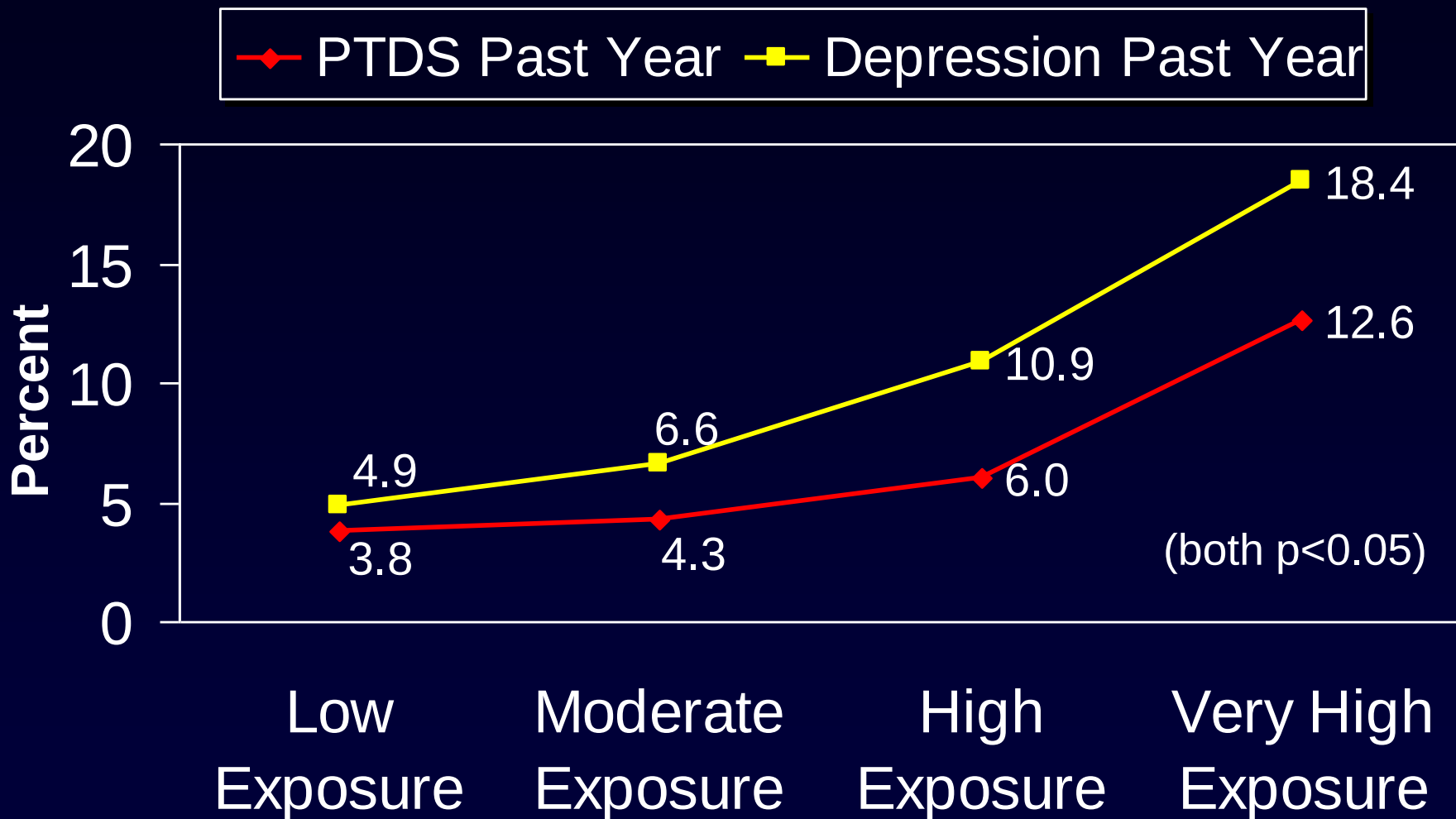
NBC News

# **WTCD Study Contributors**

(Impact of Mental Health Services in NY after WTC Disaster - R01 MH66403)

- Joseph Boscarino, PhD, MPH – Study PI
- Richard Adams, PhD
- Charles Figley, PhD
- Sandro Galea, MD, DrPH
- Heidi Resnick, PhD
- Edna Foa, PhD
- Joel Gold, MD
- Michael Bucuvalas, PhD
- David Vlahov, PhD

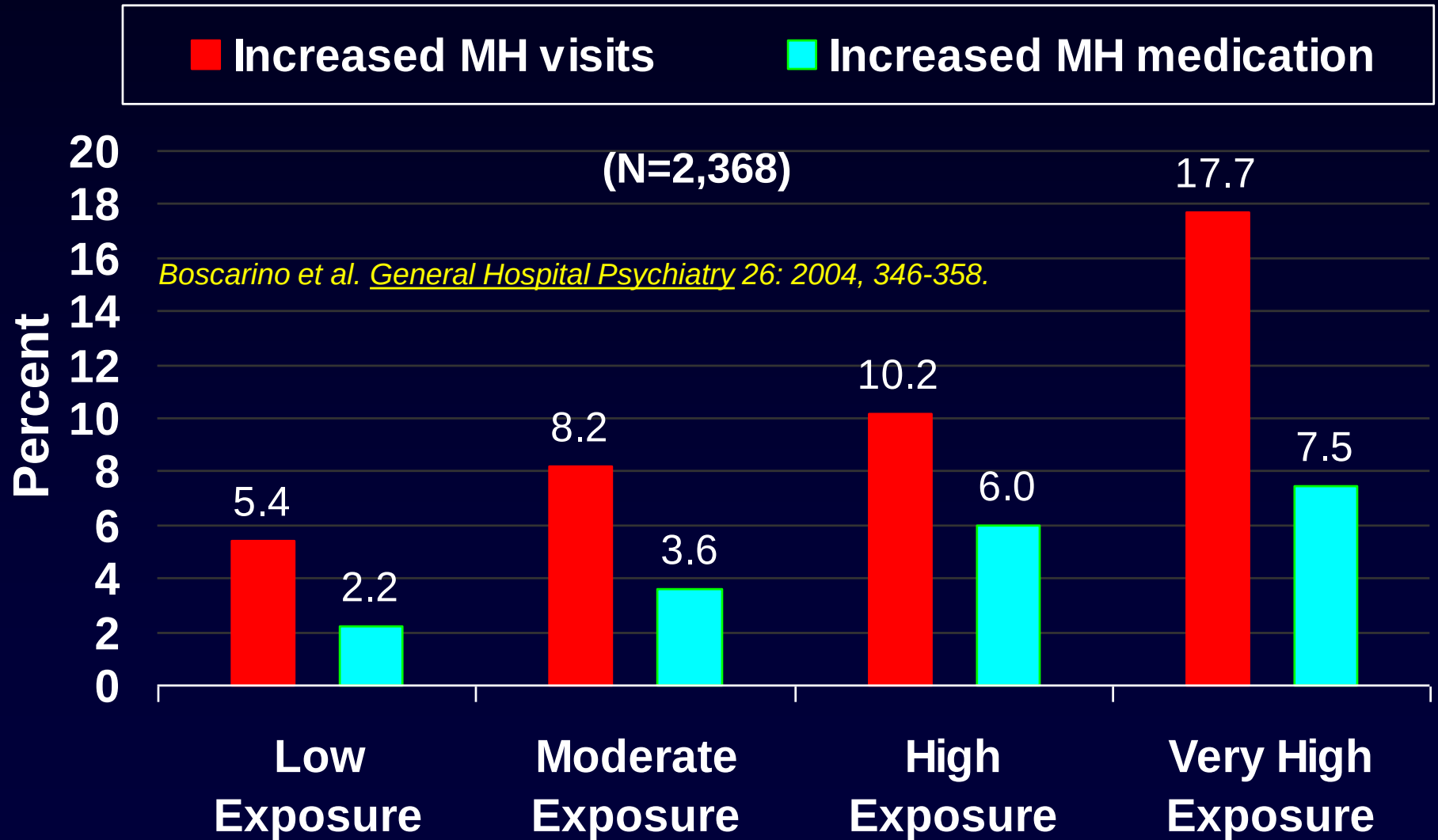
# Prevalence of PTSD and depression by Exposure to WTC disaster - wave 1 (N=2,368)



*Boscarino et al. Mental Health Service Use 1-Year after the World Trade Center Disaster. General Hospital Psychiatry 26: 2004, 346-358.*

# Exposure to WTC disaster and mental health visits/medication use – W1

(all comparisons significant at  $p < .05$ ,  $\chi^2$  test)





# ***Developing PTSD Risk Assessment Tools Using the World Trade Center Study***

**(NIMH # R21-MH-086317)**

- ❑ The objective of this application is to differentiate trauma survivors who recover from PTSD from those who develop enduring symptoms.**
- ❑ To meet this objective, we are using a dataset originally developed by the WTCD Study.**
- ❑ These data were collected during a NIMH-funded study, “Impact of Mental Health Treatment in NY after WTC Disaster” (MH-66403).**
- ❑ This study collected detailed medical, mental status, trauma, demographic, psychosocial, and exposure data spanning both the pre-WTCD and post-WTCD periods.**

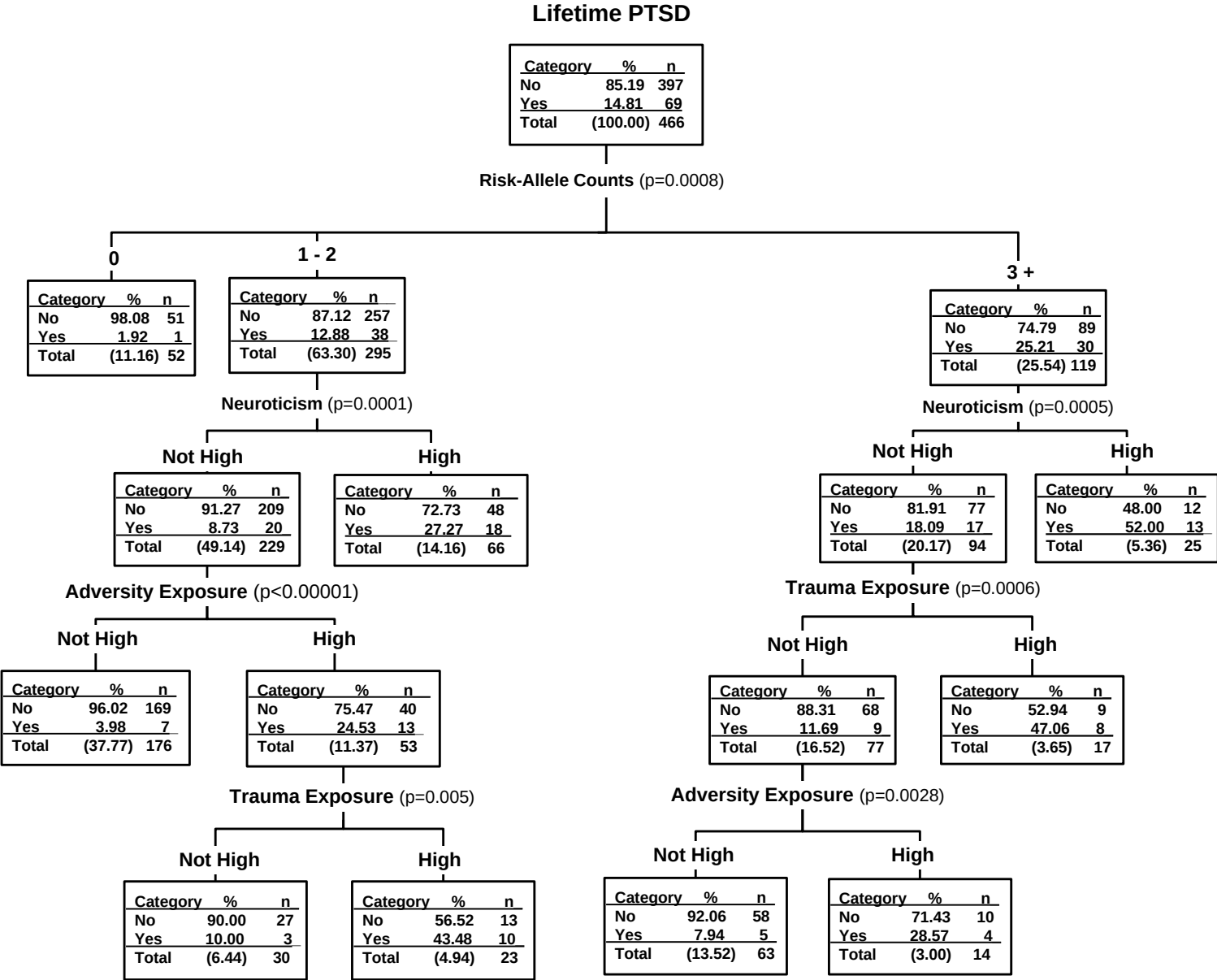
# Genetic vs. Psychosocial Predictors of PTSD (N= 502)

| Predictor                    | Odds Ratio | Lower 95% CI | Upper 95% CI | P-value                  |
|------------------------------|------------|--------------|--------------|--------------------------|
| FK+CM+CH5*                   | 1.65       | 1.25         | 2.16         | .000426                  |
| WTCD PTSD Prediction Model** | 34.26      | 15.90        | 73.82        | .00000000000000000000184 |

\*FK = FK Binding Protein 5 (FKBP5); CM = catechol-O-methyltransferase (COMT); CH5 = cholinergic receptor, nicotinic, alpha polypeptide 5 (CHARNA5)

**\*\*Positive PTSD screener, sleep problems, depression symptoms, trauma history, age, gender, ethnicity, etc.**

**Figure 1. Regression-tree results showing interactions between risk-allele counts, neuroticism, trauma exposure & childhood adversity**  
(all p-values shown Bonferroni adjusted hierarchically for multiple comparisons)



**Figure 2. Percent prevalence of PTSD, trauma, adversity and neuroticism by risk-allele counts\***

