The Story of MAOA: “The Warrior Gene”
“The Warrior Gene”? 

- MAOA breaks down adrenaline, dopamine, serotonin 
- In mice: territoriality, predatory behavior
X-Linked Borderline Mental Retardation with Prominent Behavioral Disturbance: Phenotype, Genetic Localization, and Evidence for Disturbed Monoamine Metabolism


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Summary
We have identified a large Dutch kindred with a new form of X-linked nondysmorphic mild mental retardation. All affected males in this family show very characteristic abnormal behavior, in particular aggressive and sometimes violent behavior. Other types of impulsive behavior include arson, attempted rape, and exhibitionism. Attempted suicide has been reported in a single case. The locus for this disorder could be assigned to the Xp11-21 interval between DXS7 and DXS77 by linkage analysis using markers spanning the X chromosome. A maximal multipoint lod score of 3.69 was obtained at the monoamine oxidase type A (MAOA) locus in Xp11.23-11.4. Results of 24-h urine analysis in three affected males indicated a marked disturbance of monoamine metabolism. These data are compatible with a primary defect in the structural gene for MAOA and/or monoamine oxidase type B (MAOB). Normal platelet MAOB activity suggests that the unusual behavior pattern in this family may be caused by isolated MAOA deficiency.
Figure 1 Pedigree of family with borderline mental retardation with prominent behavioral disturbance. Only individuals known to be at genetic risk are shown. Blackened squares denote affected males. Clinically evaluated individuals are indicated by a horizontal line above the symbol.
• “In one instance, an affected male was convicted of the rape of his sister... Fights occurred with other inmates... While working in the fields, he stabbed one of the wardens in the chest with a pitchfork...”
• “Another affected male tried to run over his boss with a car... after having been told that his work was not up to par.”
• “At least two affected males in this family are known arsonists. This latter behavior appears linked to stressful circumstances, such as the death of a relative.”
• Estimated average IQ of affected males = 85
“The Warrior Gene”? 

• MAOA breaks down adrenaline, dopamine, serotonin 
• In mice: territoriality, predatory behavior 
• In humans, commonly studied repeat variant: 
  – Low activity allele = 30 – 50% of men 
  – No main effect.
Caspi et al. (2002) Science
N = 442

Composite index of antisocial behavior (z scores)

-0.5  0   0.25  0.5  0.75  1

None        Probable       Severe

Low MAOA activity, n = 163
High MAOA activity, n = 279
Caspi et al. (2002) *Science*

**A**

Conduct disorder (%)

- Low MAOA activity
  - No maltreatment: 108
  - Probable maltreatment: 42
  - Severe maltreatment: 13

- High MAOA activity
  - No maltreatment: 180
  - Probable maltreatment: 79
  - Severe maltreatment: 20

**B**

Convicted for violent offense (%)

- Low MAOA activity
  - No maltreatment: 42
  - Probable maltreatment: 79
  - Severe maltreatment: 20

- High MAOA activity
  - No maltreatment: 108
  - Probable maltreatment: 42
  - Severe maltreatment: 13

**C**

Disposition toward violence (z scores)

- Low MAOA activity
  - No maltreatment: 108
  - Probable maltreatment: 42
  - Severe maltreatment: 13

- High MAOA activity
  - No maltreatment: 180
  - Probable maltreatment: 79
  - Severe maltreatment: 20

**D**

Antisocial personality disorder symptoms (z scores)

- Low MAOA activity
  - No maltreatment: 107
  - Probable maltreatment: 39
  - Severe maltreatment: 12

- High MAOA activity
  - No maltreatment: 171
  - Probable maltreatment: 74
  - Severe maltreatment: 18
In Ramseur, North Carolina, a reincarnation of a modernist dog-trot house. The original was designed by Stephen Atkinson more than a decade ago and became a darling of design magazines. This one was built by Terrie Moffitt and Avshalom Caspi, psychology professors at Duke University, who saw the house on the cover of a book, and wrote to Mr. Atkinson. He made a bargain with them: they could have the plans free, but if they made substantial changes, he would charge them.

Tony Cenicola/The New York Times
Explorer: Born To Rage Preview: Does Henry Rollins Have The Warrior Gene?

Possible 'Happiness Gene' Is Strictly for the Ladies

Lindy West
8/30/12 6:40pm · Filed to: SCIENCE

Later this month, the “warrior gene” will guide us through...
Sometimes it replicates...

N = 841 25 year old, mostly European ancestry, mixed males & females
Also tested with no effect: alcohol, tobacco, marijuana, harsh discipline

Derringer et al. 2010
But not in larger samples*

Byrd & Manuck (2014)

Criticism: selected statistical method doesn’t account for “main effect” in test of interaction.

“relative p-values” approach is NOT the same as more widely accepted practice of meta-analysis of effect size
Haberstick et al. (2014) MAOA genotype, childhood maltreatment, and their interaction in the etiology of adult antisocial behavior
“When the police arrived at Bradley Waldroup's trailer home in the mountains of Tennessee, they found a war zone. There was blood on the walls, blood on the carpet, blood on the truck outside, even blood on the Bible that Waldroup had been reading before all hell broke loose.”

“Assistant District Attorney Drew Robinson says that on Oct. 16, 2006, Waldroup was waiting for his estranged wife to arrive with their four kids for the weekend. He had been drinking, and when his wife said she was leaving with her friend, Leslie Bradshaw, they began to fight. Soon, Waldroup had shot Bradshaw eight times and sliced her head open with a sharp object. When Waldroup was finished with her, he chased after his wife, Penny, with a machete, chopping off her finger and cutting her over and over.”

NPR, Can Your Genes Make You Murder?, 1 July 2010
• Waldroup had history of abuse + MAOA “risk” allele
  – "His genetic makeup, combined with his history of child abuse, together created a vulnerability that he would be a violent adult.”
    • William Bernet, psychiatrist, Vanderbilt University
  – "This was somebody who was intoxicated and mad and was gonna hurt somebody. And it had little to nothing to do with his genetic makeup.”
    • Terry Holmes, psychiatrist, Moccasin Bend Mental Health Institute
• Convicted, sentence reduced from death penalty to 32 years

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  – Low activity allele = 30 – 50% of men
  – No main effect* and no consistent interaction*

• Being male
  – Testosterone?
  – Y chromosome?