The MAOA gene predicts happiness in women

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ABSTRACT

Psychologists, quality of life and well-being researchers have grown increasingly interested in understanding the factors that are associated with human happiness. Although twin studies estimate that genetic factors account for 35–50% of the variance in human happiness, knowledge of specific genes is limited. However, recent advances in molecular genetics can now provide a window into neurobiological markers of human happiness. This investigation examines association between happiness and monoamine oxidase A (MAOA) genotype. Data were drawn from a longitudinal study of a population-based cohort, followed for three decades. In women, low expression of MAOA (MAOA-L) was related significantly to greater happiness (0.261 SD increase with one L-allele, 0.522 SD with two L-alleles, P=0.002) after adjusting for the potential effects of age, gender, race, education, household income, marital status, employment status, mental disorder, physical health, relationship quality, religiosity, abuse history, recent negative life events and self-esteem use in linear regression models. In contrast, no such association was found in men. This new finding may help explain the gender difference on happiness and provide a link between MAOA and human happiness.

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1. Introduction

Psychologists, quality of life and well-being researchers have grown increasingly interested in understanding the factors that are associated with human happiness, perhaps one of the few uniformly embraced priorities (Huppert, 2010; Reichhardt, 2006). Researchers typically use multi-item scales to measure happiness, either on a general level or by asking people how happy they are in specific situations (Myers, 1992). Happiness depends on many factors, including genes, personality, age, income, health, social relationships, and religiosity (Easterlin, 2003; Myers and Diener, 1995). Certainly, happiness may decline with negative experiences or problems, but even serious problems often result in gradual recuperation. Gender also may play a role, in that women tend to be happier than men (Aldous and Ganey, 1999; Alesina et al, 2004; Myers and Diener, 1995) despite having substantially higher rates of mood and anxiety disorders.

Although twin studies estimate that genetic factors account for 35–50% of the variance in human happiness (Bartels et al, 2010; Weiss et al, 2008), knowledge of specific genes is limited. However, recent advances in molecular genetics can now provide a window into neurobiological markers of human happiness. De Neve (2011) reported an association between 5-HTTLPR and life satisfaction. Saphire-Bernstein et al, (2011) found a link between self-esteem and oxytocin receptor gene (OXTR). Monoamine oxidase A (MAOA) may be a particularly relevant candidate gene for modulating happiness because of its involvement in mood regulation (Rivera et al, 2008). MAOA is a catabolic enzyme of serotonin, noradrenaline, and dopamine neurotransmitters (Hariri et al, 2005). MAOA, located on the x chromosome, possesses a variable number of tandem repeats polymorphism (MAOA-uVNTR), resulting in genotypes with low-activity (MAOA-L) and high-activity (MAOA-H) alleles (Sabol et al, 1998). The MAOA-L allele is a risk factor for stress-related negative consequences such as alcoholism (Tikkanen et al, 2010), aggressiveness (McDermott et al, 2009), and antisocial problems (Caspi et al, 2002). Nonetheless, to date, no direct association between MAOA genotype and happiness has been reported.

2. Materials and methods

2.1. Participants

The Children in the Community (CIC) sample is a general population cohort based on households randomly sampled in 1975 when
they lived in 100 rural, suburban, urban, and central city block groups
cross-stratified by mean income and ethnic composition in two up-
state New York counties. Racial distribution (91% Caucasian, 8%
African-American) and socioeconomic status (21% with family in-
come below the poverty line, 25% with upper middle class education-
al and income) of the sample was represented the region that was
selected in 1975 for its similarity in composition to the entire USA.
It is one of the few studies in the world that has conducted systemat-
ic, interview-based assessments of psychopathology over 30 years
beginning in late childhood in randomly ascertained individuals. Ad-
ditional information regarding study methods is available on the
study website (www.nyspi.org/childcom), which provides informa-
tion on the 7 assessments of this cohort, their parents and offspring,
and the nearly 240 publications based on these data. Data for this
study were drawn from the 345 Caucasian subjects include 193
women and 152 men who were assessed for MAOA genotype in
2010 at mean age of 38 and happiness in 2004 at mean age of 33.

2.2. Measures

2.2.1. Happiness measure

Happiness was assessed with the 4-item Subjective Happiness Scale
(Lyubomirsky, 2001; Lyubomirsky and Lepper, 1999). Two items ask re-
pondents to characterize themselves using both absolute ratings and
ratings relative to peers, whereas the other two items offer brief de-
scriptions of happy and unhappy individuals and ask respondents the
extent to which each characterization describes them. Responses to
the four items then are combined and averaged to provide a single con-
tinuous composite score, ranging from 1 to 7. Many studies (Duckworth
et al, 2005; McCullough et al, 2002) have employed this happiness mea-
sure over more than a decade, supporting its validity and utility. At
mean age 33, happiness scores ranged from 2.25 to 7.0, mean = 5.37
(median = 5.50) and SD = 0.97. Internal consistency was 0.82.

2.2.2. MAOA gene analysis

Genomic DNA was prepared from saliva samples using Oragene-DNA
kits (DNA Genotek, Ottawa, Ontario, Canada). There were no significant
demographic differences between those individuals who provided, or
did not provide, saliva samples. The MAOA-LPR genotyping was modified
from the method of Ducci and colleagues (Ducci et al, 2006). The MAOA
gene promoter VNTR polymorphism was amplified from 10 ng genomic
DNA using the primer sequences: Forward 5'–(CCG ACC CGT CTC CAG
AAA CAT G)-3' and Reverse-5' (GTT CCG GTA GGC AGT GTC)-3'.
Since GC content is high in the VNTR region, Invitrogen's PlatinumTaq
and PCR X Enhancer System kits (Invitrogen, Carlsbad, CA) were used
for amplification, with 5 μM of each primer and 25 mM dNTPs in a total
reaction volume of 15 μL. Amplifications were performed on a Perkin-
Elmer 9700 thermocycler (Applied Biosystems, Foster City, CA) with
1 cycle at 96 °C for 10 min followed by 35 cycles of 94 °C for 15 s,
55 °C for 15 s, 72 °C for 30 s, and a final 3 min extension at 72 °C. The
fluorescent dye 6-FAM labeled the forward primer; amplicons were visu-
alyzed with GeneScan-500 LIZ Size Standard (Applied Biosystems,
Foster City, CA) and analyzed on an ABI 3730 capillary sequencer. Allele sizes
(allele 2–183 bp; 3–213 bp; allele 3.5–232 bp; allele 4–244 bp; allele
5–272 bp) were determined using GeneMapper v4.0 (Applied Bio-
systems, Foster City, CA). Genotyping accuracy was determined empiri-
cally by duplicate genotyping of 25% of the samples selected randomly.
The error rate was <0.005, and the completion rate was >0.95. Geno-
types were available for 193 women and 152 men. The allele frequencies
of 2, 3, 3.5, 4 or 5 copies of the 30-bp repeated sequence were as follows:
2 (0.012 in female; 0.006 in male), 3 (0.364 in female; 0.331 in male), 3.5
(0.014 in female; 0.12 in male), 4 (0.607 in female; 0.632 in male) and
5 (0.002 in female; 0.018 in male) copies. Enzyme expression is known
to be 2–10 times higher for the 3.5 and 4 repeats than for the 3 repeat
(Sabol et al, 1998). Therefore the 3.5-repeat and 4 repeat alleles were
classified as high activity (H) whereas the 3 repeat alleles were classified
as low activity (L). The 2 and 5 repeat alleles were excluded because their
activity levels are not yet clear. Since MAOA is an X-linked gene women
can be classified as having high (H), intermediate or low (L) MAOA activ-
ity but men can only be classified by having high or low activity. The ge-
notype frequencies for females were: LL: 16.6%, LH: 42.4%, HH: 41.0%; for
males they were: L: 33.1% and H: 66.9%. The genotype frequencies were
in Hardy–Weinberg equilibrium.

2.2.3. Covariates

Covariates include age, gender, race, education, household in-
come, marital status, employment status, mental disorder, recent
negative life events (Chen et al, 2006, 2009), physical health, relation-
ship quality, religiosity, abuse history and self-esteem. Physical health
was measured by overall health, incapacitation due to illness/injury,
and energy level (8 items, reliability = 0.76) (Chen et al, 2004, 2009).
Relationship quality with partner or closest confidante was measured
by 9 items (reliability = 0.90) (Chen et al, 2004, 2006). Re-
ligiosity includes 2 items: to do what God wants me to do, and attend-
ance at religious service (reliability = 0.66) (Chen et al, 2004). Abuse
data were obtained by official records and self-report (Chen et al,
2001). Self-esteem was measured at mean age of 22 by four items
(reliability = 0.69) (Berenson et al, 2005).

2.2.4. Data analysis

Happiness scores are expressed as mean and standard deviation
(SD). We use the standardized happiness score (Z-score) to facilitate
understanding of effect sizes (full sample mean = 0, SD = 1). Data are
analyzed with linear regression analyses to estimate the main effect
for MAOA-L allele on happiness after adjusting for age, gender, race,
education, household income, marital status, employment status,
mental disorder, physical health, relationship quality, religiosity
and abuse history on happiness, negative life events and self-esteem.

3. Results

Among the 345 subjects, 33 (9.6%), 132 (38.3%) and 180 (52.2%)
subjects have two MAOA-L alleles, one MAOA-L allele and no
MAOA-L allele, respectively. Subjects with two, one and no MAOA-L
alleles have a mean happiness score of 5.83 (SD = 0.75), 5.40 (SD =
1.03) and 5.27 (SD = 0.95), respectively (F = 4.69, P = 0.01). After
adjusting for the potential effects of age, gender, race, education,
household income, marital status, employment status, mental disor-
der, physical health, relationship quality, religiosity, abuse history,
recent negative life events and self-esteem in the linear regression
model, there was a 0.174 difference in mean happiness score
(Z-score) (see Table 1). Comparing to having no MAOA-L allele, hav-
ing one MAOA-L allele increased the happiness score by 0.174 SD and
having two MAOA-L alleles increased it by 0.348 SD.

Among the 152 men, 52 (34.2%) and 100 (65.8%) men have one
MAOA-L allele and no MAOA-L allele, respectively. Men with one
and no MAOA-L alleles have a mean happiness score of 5.23 (SD =
1.05) and 5.24 (SD = 0.94), respectively (t = 0.10, P = 0.92). After
adjusting for the potential effects of age, gender, race, education,
household income, marital status, employment status, mental disor-
der, physical health, relationship quality, religiosity, abuse history,
recent negative life events and self-esteem in the linear regression
model, there was no statistical significant association between happi-
ness score and MAOA-L allele (see Table 2).

Among the 193 women, 33 (17.1%), 80 (41.5%) and 80 (41.5%)
women have two MAOA-L alleles, one MAOA-L allele and no
MAOA-L allele, respectively. Women with two, one and no MAOA-L
alleles have a mean happiness score of 5.83 (SD = 0.75), 5.50 (SD =
1.00) and 5.30 (SD = 0.97), respectively (F = 3.67, P = 0.03). After
adjusting for the potential effects of age, gender, race, education,
household income, marital status, employment status, mental disor-
der, physical health, relationship quality, religiosity, abuse history,
women may be more sensitive to positive aspects of the environment (Rivera et al., 2008; Schulze et al., 2000; Yu et al., 2005) and decreased overall response to antidepressant treatment (Domshke et al., 2008). Studies also showed that MAOA-H genotype has been related to increased risk for panic disorder in female patients (Deckert et al., 1999; Domshke et al., in press). Poorer quality of life is strongly associated with having major depression disorder and panic disorder (Guan et al., 2011).

Our findings also show that, among men, MAOA-L carriers are not significantly happier than non-carriers. MAOA has an androgen responsive element in the MAOA promoter (Ou et al., 2006). The higher level of testosterone in men could compensate for the MAOA-L allele effect seen in women. Sjoberg et al. (2008) reported a significant interaction effect between testosterone and MAOA on antisocial behavior in a male clinical sample such that among MAOA-L-MAOA-H) individuals, high testosterone level was associated with antisocial problems, which may explain in part the decreased likelihood of a positive outcome in MAOA-L men in our sample.

Future directions might encompass an increasing focus by researchers on genotypes implicated in psychological well-being in contrast to the current emphasis on psychopathology. Certainly, it could be argued that how well-being is enhanced deserves at least as much attention as how disorders arise; however, such knowledge remains limited. There is no single ‘happiness’ gene and likely to be a set of genes whose expression influences subjective well-being. Future work should attempt to identify other genes that are associated with human happiness. Our study shows a significant main effect of MAOA-L on happiness for women based on a relatively small sample size. It is important that this research be closely replicated in a large sample in the future.

5. Conclusion

In this study, we found that there was a 0.172 difference in mean happiness score between subjects with one MAOA-L allele and subjects with no MAOA-L allele after adjusting for the potential effects of age, gender, race, education, household income, marital status, employment status, mental disorder, physical health, relationship quality, religiosity, abuse history, recent negative life events and self-esteem. In women, low expression of MAOA (MAOA-L) was related to happiness. Our finding may help explain the gender difference on happiness and provide a link between MAOA and human happiness.

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