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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.

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, noradrenalin, 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

Abbreviations: MAOA, mono-amine-oxidase type A; 5-HTT, serotonin transporter; OXTR, oxytocin receptor; CIC, children in the community study; SD, standard deviation.

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they lived in 100 rural, suburban, urban, and central city block groups cross-stratified by mean income and ethnic composition in two upstate New York counties. Racial distribution (91% Caucasian, 8% African-American) and socioeconomic status (21% with family income below the poverty line, 25% with upper middle class educational 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 systematic, interview-based assessments of psychopathology over 30 years beginning in late childhood in randomly ascertained individuals. Additional information regarding study methods is available on the study website (www.nyspi.org/childcom), which provides information 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 respondents to characterize themselves using both absolute ratings and ratings relative to peers, whereas the other two items offer brief descriptions 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 continuous composite score, ranging from 1 to 7. Many studies (Duckworth et al, 2005; McCullough et al, 2002) have employed this happiness measure 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 rxx = 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′-(CCC AGG CTG CTC CAG AAA CAT G)-3′ and Reverse-5′(GTT CGG GAC CTG GGC AGT TGT G)-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 visualized 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 Biosystems, Foster City, CA). Genotyping accuracy was determined empirically by duplicate genotyping of 25% of the samples selected randomly. The error rate was <0.005, and the completion rate was >0.95. Genotypes 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 activity but men can only be classified by having high or low activity. The genotype 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 income, marital status, employment status, mental disorder, recent negative life events (Chen et al, 2006, 2009), physical health, relationship 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). Religiosity includes 2 items: to do what God wants me to do, and attendance at religious service (reliability = 0.66) (Chen et al, 2004). Abuse data were obtained by official records and self-report (Cohen 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, abuse history, recent 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 disorder, 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, having 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 disorder, 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 happiness 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 disorder, physical health, relationship quality, religiosity, abuse history,

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Table 1
Happiness as predicted by MAOA genotype for the total sample (N = 362) at mean age 33 after controlling for covariates [a].

	Estimate	Standard error	P value
MAO-L allele	0.174	0.072	0.016
Gender	0.241	0.100	0.016
Marital status	0.187	0.095	0.050
Employ status	0.344	0.138	0.013
Education	0.045	0.105	0.666
Mental disorder	−0.749	0.125	<0.001
Age	0.001	0.017	0.966
Income	0.001	0.045	0.974
Religiosity	0.067	0.047	0.152
Relationship quality	0.250	0.046	0.002
Physical health	0.152	0.049	<0.001
Abuse history	−0.033	0.134	0.804
Negative life event	−0.053	0.990	0.593
Self-esteem	0.062	0.026	0.016

MAOA-L allele was coded: 0 = no MAOA-L allele, 1 = one MAOA-L allele, 2 = two MAOA-L alleles.
Gender was coded: 1 = female, 0 = male; Marital status was coded 1 = married, 0 = unmarried; employ status was coded 1 = employed, 0 = unemployed; education was coded 1 > high school, 0 = high school or less; mental disorder was coded 1 = with mental disorder, 0 = without any mental disorder; abuse was coded 1 = with abuse history, 0 = without abuse history. Negative life event was coded 1 = with any recent negative life events, 0 = without negative life event.
[a] Standardized scores (Z-score) were used for all continuous variables (happiness, age, income, religiosity, relationship quality, physical health and self-esteem).

recent negative life events and self-esteem in the linear regression model, there was a 0.261 difference (P = 0.002) in mean happiness score (Z-score) (see Table 2). Comparing to having no MAOA-L allele, having one MAOA-L allele increased the happiness score by 0.261 SD and having two MAOA-L alleles increased it by 0.522 SD.

4. Discussion

Study findings suggest that the low expression allele of the monoamine oxidase (MAOA-L) gene predicts higher self-reported happiness in women. These findings appear to contradict a literature that supports stronger negative outcomes such as increased risk for antisocial behavior following childhood maltreatment among individuals with a MAOA-L allele (Caspi et al, 2002; Kim-Cohen et al, 2006). However, in the Dunedin sample of adult males, this MAOA polymorphism did not mitigate effects of stress on increased risk for depression, suggesting that in adults, MAOA activity moderates the impact of stress specifically towards an antisocial outcome (Caspi et al, 2003). Higher monoamine levels may relate to happiness, even though MAOA-L allele is a risk for alcoholism and antisocial behavior.

MAOA-H has been associated with greater 5HT1A receptor availability in women, but not in men (Mickey et al, 2008), with the MAOA-H gene predicting a substantial 42–74% of the variance in receptor availability in women, depending on the brain region. Kinnally et al (2009) reported that perceptions of better parental care offset negative effects of childhood abuse and other traumatic events among women carriers of the low activity MAOA allele but not among women without MAOA-L, suggesting that MAOA-L women may be more sensitive to positive aspects of the environment and thus less susceptible to stressors or, perhaps, more resilient.

Table 2
Happiness as predicted by MAOA genotype by gender after controlling for covariates [a].

	Estimate	Standard error	P value
Male (N = 152)	−0.021	0.142	0.880
Female (N = 193)	0.261	0.085	0.002

[a] Standardized score was used for happiness measure. MAOA-L allele was coded: 0 = no MAOA-L allele, 1 = one MAOA-L allele, 2 = two MAOA-L alleles. Covariates were controlled as the same as in Table 1.

The MAOA-H genotype has been related to increased risk for depression (Rivera et al, 2008; Schulze et al, 2000; Yu et al, 2005) and decreased overall response to antidepressant treatment (Domschke et al, 2008). Studies also found that MAOA-H genotype has been related to increase risk for panic disorder in female patients (Deckert et al, 1999; Domschke 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 (but not 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 significantly to greater happiness (0.261 SD increase with one L-allele, 0.522 SD with two L-alleles, P = 0.002). 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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