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, 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, 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

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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 up-state 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 r_{xx} = 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, 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, 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, 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, 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, education, household income, marital status, employment status, mental disorder, physical health, relationship quality, religiosity, abuse history, recent negative