Available online at www.sciencedirect.com
SCIENCE DIRECT®
ELSEVIER
Personality and Individual Differences 37 (2004) 621–626
PERSONALITY AND INDIVIDUAL DIFFERENCES
www.elsevier.com/locate/paid

Are there sex differences in the association between the 5HTT gene and neuroticism? A meta-analysis

M.R. Munafò [a,*], T.G. Clark [b], J. Flint [c]

[a] *Cancer Research UK GPRG, Department of Clinical Pharmacology, University of Oxford, Oxford OX2 6HE, UK*
[b] *Cancer Research UK Centre for Statistics in Medicine, University of Oxford, Oxford OX3 7LF, UK*
[c] *Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford OX3 7BN, UK*

Received 2 June 2003; received in revised form 7 September 2003; accepted 29 September 2003
Available online 19 November 2003

Abstract

An association between polymorphism in the serotonin transporter gene linked promoter region (5HTT-LPR) and the human personality trait of neuroticism has been reported. One potentially important factor moderating the genetic effect of this polymorphism on neuroticism is sex.

We sought to address the question of whether sex moderates the association between the 5HTT-LPR polymorphism and anxiety-related personality traits in humans by means of meta-analytic techniques.

Transformed personality trait scores were entered into a 2×3 ANOVA with sex (male, female) and genotype (ss, sl, ll) as between-subject factors. This indicated a main effect of sex ($p = 0.04$) and genotype ($p = 0.01$) on personality. The interaction was not significant ($p = 0.65$).

The results of this meta-analysis do not offer any support for a moderating effect of sex on the association of the short allele of the 5HTT gene with neuroticism.

Keywords: Personality; Genetics; Serotonin transporter; Neuroticism; Sex differences

1. Introduction

A recent meta-analysis of genetic association studies and human personality reported a significant association between polymorphism in the promoter region of the serotonin transporter gene (5HTT-LPR) and the personality trait neuroticism (Munafò et al., 2003). One potentially

* Corresponding author. Tel.: +44-1865-224807; fax: +44-1865-224989.
E-mail address: marcus.munafo@clinpharm.ox.ac.uk (M.R. Munafò).

0191-8869/$ - see front matter
doi:10.1016/j.paid.2003.09.031

important factor that may moderate the genetic effect of the 5HTT-LPR on neuroticism is sex. Higher mean neuroticism scores have been consistently reported in women, but, with one exception (Viken, Rose, Kaprio, & Koskenvuo, 1994), studies report no difference in heritability between males and females. Three studies find evidence of sex-specific genetic factors (Eaves, Heath, Neale, Hewitt, & Martin, 1998; Fanous, Gardner, Prescott, Cancro, & Kendler, 2002; Martin et al., 2000), though one did not (Lake, Eaves, Maes, Heath, & Martin, 2000). It is not known whether individual loci show sex-specific effects, although this has been suggested (Fullerton et al., 2003; Du, Bakish, & Hrdina, 2000).

We sought to address the question of whether sex moderates the association between the 5HTT-LPR polymorphism and anxiety-related personality traits in humans by contacting the authors of eligible association studies to request the release of data grouped separately for men and women.

2. Methods

Studies reporting data on the association between the 5HTT-LPR polymorphism and neuroticism cited in a recent meta-analysis of genetic association studies of human personality (Munafò et al., 2003) were included.

To model the potential effects of sex and genotype on personality scores, we transformed the scores to a logarithmic Z-score (log[score/standard error]). These scores followed a Normal distribution. A 2×3 ANOVA with sex (male, female) and genotype (ss, sl, ll) was then performed. Within this framework we were able to assess any main effects of, or interaction effects between, sex and genotype on personality score by performing an F-test.

3. Results

Seventy-nine studies contributed to the original meta-analysis (Munafò et al., 2003) on which this analysis is based. Of these, a total of 22 studies were eligible for inclusion in the present analysis. Only one study reported data separately for men and women (Du et al., 2000), while one study (Lesch et al., 1996) consisted of ''primarily'' male participants and one study (Nakamura et al., 1997) consisted entirely of female participants. For the remaining studies the authors were contacted directly and requested to release their data grouped by sex and genotype as mean personality trait score and standard deviation. This resulted in the release of data in the case of 8 studies, so that a total of $k = 11$ studies contributed to the meta-analysis, representing 50% of the eligible studies, consisting of $N = 2723$ participants, representing 44% of participants in eligible studies. In two cases the data released was not published in the original report (Comings et al., 1999; Cruz et al., 1995). The characteristics of included studies are described in Table 1.

A 2×3 ANOVA with sex (male, female) and genotype (ss, sl, ll) indicated a significant main effect of sex ($F[1,41] = 4.319$, $p = 0.04$), with females showing higher mean personality scores, and a significant main effect of genotype ($F[2,41] = 4.935$, $p = 0.01$), with the highest mean personality scores being in the sl genotype group. There was no significant sex$\times$genotype interaction ($F[2,41] = 0.435$, $p = 0.65$).