Loneliness in adolescence: gene × environment interactions involving the serotonin transporter gene

Eeske van Roekel,1 Ron H.J. Scholte,1 Maaike Verhagen,1 Luc Goossens,2 and Rutger C.M.E. Engels1

1Behavioural Science Institute, Radboud University Nijmegen, The Netherlands; 2Center for Developmental Psychology, Catholic University Leuven, Belgium

Background: Loneliness is assumed to peak in early adolescence and to decrease throughout middle and late adolescence, but longitudinal confirmation of this tendency is lacking. Behavioral genetic studies with twin designs have found a significant genetic component for loneliness in children and adults, but no molecular genetic studies have been conducted to reveal the functional polymorphisms involved. Methods: Associations among the serotonin transporter gene (5-HTTLPR), sex, parental support, and loneliness were examined in a longitudinal study spanning five annual waves (N = 306). Results: Using latent growth curve modeling (LGCM), loneliness was found to be highest in early adolescence and slowly declined throughout adolescence. The 5-HTTLPR genotype was related to the development of loneliness, in that short allele carriers remained stable in loneliness over time, whereas adolescents with the long-long genotype decreased in loneliness. Interactions were found between maternal support and 5-HTTLPR genotype, showing that adolescents who perceived little support from their mothers and carried a short allele were at increased risk for developing loneliness. Conclusions: Our study is the first to chart adolescent loneliness longitudinally and to examine the genetic underpinnings of loneliness. Our results contribute to a further understanding of the environmental and genetic basis of loneliness. Replication of our results is needed in both population-based and clinical samples. Keywords: Loneliness, serotonin transporter, 5-HTTLPR, parental support, gene–environment interaction, adolescence.

Loneliness is defined as the negative emotional response to the discrepancy between the actual and desired quantity and quality of one's social network (Perlman & Peplau, 1981). Because loneliness is related to various mental and physical health problems such as anxiety, schizophrenia, depression, sleep disturbance, poorer immune functioning, and cardiovascular disease (Heinrich & Gullone, 2006), it is important to examine both its developmental course and its antecedents. The present study is the first to chart changes in loneliness in adolescence and examined the roles of both genes and perceived parental support as predictors of loneliness during this phase of life.

The developmental course of loneliness in adolescence

Loneliness can be experienced from early childhood on, but is found to peak during early adolescence (Heinrich & Gullone, 2006). A possible explanation for this increase in loneliness can be that early adolescence is a turbulent period in which peers become increasingly important, the self is mainly defined in terms of one’s social relationships (Parkhurst & Hopmeyer, 1999), and young people make the transition from primary school to secondary school, which leads to temporary disruption of the social network. Because attachment and identity issues are gradually resolved during adolescence and new friendships are formed in secondary school, one may expect that loneliness declines slowly throughout middle and late adolescence. Cross-sectional studies using age cohorts indeed suggest a decline in loneliness from early to late adolescence (e.g., Marcoen & Goossens, 1993). Although such cross-sectional studies provide valuable information about the developmental trends in levels of loneliness, longitudinal data are necessary to examine intra-individual changes in loneliness.

Genes and loneliness

Behavioral genetic studies using twin designs have found a significant genetic component for loneliness in children and adults, with estimates ranging between 48% and 55% (Boomsma, Willemsen, Dolan, Hawkley, & Cacioppo, 2005; McGuire & Clifford, 2000). No molecular-genetic studies have been conducted to find polymorphisms involved in loneliness. In the present study, we examined the relations between loneliness in adolescence and 5-HTTLPR, a functional polymorphism in the promoter region of the serotonin transporter gene (5-HT). The 5-HTTLPR genotype is a variable repeat sequence in the promoter region of the gene, which...
encodes two allelic variants: a short allele and a long allele. Carrying the short allele of the 5-HTTLPR genotype may be a susceptibility factor, which can lead to mental problems if and when negative environmental conditions apply (the ‘double hit’ hypothesis, Murphy et al., 2008). Up to now, no studies have examined the relation between loneliness and the 5-HTTLPR genotype. In previous research, however, this polymorphism has been linked to depressive symptoms, which are highly correlated with loneliness (Weeks, Michela, Peplau, & Bragg, 1980), and to shyness, which is a precursor for loneliness (Fox et al., 2005).

5-HTTLPR genotype in depression

Direct effects of the 5-HTTLPR genotype have been found rather rarely in adult samples, with short alleles being more prevalent in depressive patients (Hauser et al., 2003; Hoefgen et al., 2005), and with the short-short genotype being significantly related to depressive outcomes (Cervilla et al., 2006; Kaufman et al., 2004). However, significant gene × environment interactions, in which the 5-HTTLPR genotype interacts with negative environmental factors, such as life stress, and predicted depression in adults, have been obtained somewhat more consistently (for review, see Munafò, Durrant, Lewis, & Flint, 2009).

The study of Eley et al. (2004) found a significant direct effect of the 5-HTTLPR genotype on depression in adolescence for girls only, whereas the Sjöberg et al. (2006) study found no such effects for either gender. Both studies found significant gene × environment interactions with adverse life events and conflicts in the family and psychosocial risks, respectively, as negative environmental conditions, in girls only. In both cases, female short allele carriers were at greater risk for depression in stressful environments.

Presumed biological mechanisms

In recent years, an increasing number of studies have tried to disentangle the biological mechanisms underlying the relation between the 5-HTTLPR genotype and depression. These studies showed that carrying the short allele was a risk factor for problems with negative affect regulation. The first line of studies examining the biological mechanism investigated the role of the 5-HTTLPR genotype in neural activation in response to emotional stimuli (e.g., fearful and angry faces). Results indicated that short allele carriers displayed stronger amygdala activation in response to fearful stimuli, compared to long allele carriers (Heinz et al., 2004; Pezawas et al., 2005). This overactivation of the amygdala may reflect oversensitivity to threat-related signals.

The second line of research in this area revealed reduced connectivity (or reduced functional coupling) in carriers of the short allele between the amygdala and the perigenual anterior cingulate cortex (pACC) (Pezawas et al., 2005). Because the coupling between these two brain structures is conceptualized as the feedback circuit involved in the extinction of negative affect, a loss of functional integration between these areas can lead to less inhibitory regulation of the amygdala. In addition, short allele carriers also showed greater connectivity between the amygdala and the ventromedial prefrontal cortex (vmPFC) (Heinz et al., 2004). The latter type of increased functional coupling does not necessarily indicate a greater risk for psychopathology, but rather suggests a compensatory effort of the vmPFC to regulate the overactivated amygdala.

The same underlying biological mechanism may play a role in the development of loneliness as well. Because loneliness is defined as the negative emotional response to the discrepancy between one’s actual and desired social relationships, one may expect that the 5-HTTLPR genotype is also relevant in loneliness.

Environmental factors

Environmental effects, such as negative life events (Paykel, 2003), negative parenting, and maltreatment (Alloy, Abramson, Smith, Gibb, & Neeren, 2006), have a direct influence on depression and related problems. High perceived parental support, one particular aspect of effective parenting, is related to lower levels of loneliness (Franziò & Davis, 1985). Perceived support from primary caregivers (mostly mothers) has also been found to interact with the 5-HTTLPR genotype in predicting behavioral inhibition and depression in children (Fox et al., 2005; Kaufman et al., 2004). In short, one may expect that perceived parental support is related to loneliness, and that it interacts with the 5-HTTLPR genotype in predicting loneliness.

The present study

The aim of the present study was to test the relation between the 5-HTTLPR genotype and the onset and development of loneliness, using a longitudinal five-wave design. Subsequently, we examined whether perceived parental support is related to the onset and development of loneliness and whether the 5-HTTLPR genotype interacts with parental support in predicting loneliness. We hypothesized that loneliness will be highest in early adolescence, and will slowly decrease throughout adolescence. We expected the short allele of the 5-HTTLPR genotype and low levels of maternal and paternal support to be related to higher onset and slower decrease of loneliness. Furthermore, we expected the 5-HTTLPR genotype to interact with parental support in predicting loneliness, such that short allele carriers who receive low levels of parental support demonstrate the highest levels of loneliness.
Method

Participants and procedure

Data for the present study were derived from the longitudinal Dutch survey study 'Family and Health', which examines different family processes in relation to various health behaviors in adolescence (Harakeh, Scholte, de Vries, & Engels, 2005). Addresses of families with at least two children, aged 13–16 years, were derived from registers of 22 municipalities. The families were sent a letter in which they were invited to participate. Of the responding 885 families who fulfilled the criteria: parents were married or living together, all family members were biologically related to each other, and participating siblings were neither twins nor mentally or physically disabled, 428 families were selected to obtain an equal distribution of sibling dyads (boy–boy, girl–girl, boy–girl), and an equal division of educational levels.

Only the data of the youngest adolescent in each family were used, because these adolescents were entering adolescence at T1, thus allowing us to examine changes in loneliness at the start of adolescence. At the first wave, the mean age of these adolescents was 13.4 (SD = .50), 53.3% were girls. The age ranges at the successive waves were 12–14 years (T1), 13–15 years (T2), 14–16 years (T3), 15–17 years (T4), and 16–18 years (T5). At any given point in time throughout the study, the age range (youngest – oldest participant) was 1 year and 9 months.

One-third of the adolescents attended lower education, one-third intermediate general education, and one-third the highest level of secondary school. The number of drop-outs in subsequent waves was low, with 4% drop-outs (excluding drop-outs who did not (drop-outs; T; p = .033). The items tapped several aspects of emotional support (e.g., ‘This person shows me that he/she loves me’) and instrumental support (e.g., ‘This person explains or shows how I can make or do something’). The participants rated each item on a 5-point Likert scale (1 = very untrue, 5 = very true) and the mean scores were computed for each parent separately. Total scores, therefore, ranged between 1 and 5. Cronbach’s alpha was .77 for maternal support, and .80 for paternal support.

5-HTTLPR genotyping. Genotyping of the 5-HTTLPR polymorphism in the SLC6A4 (5-HTT, SERT) gene was performed by simple sequence length analysis. PCR was on 50 ng genomic DNA using 10 pmol of forward primer (5’-GGCGGTGCGCTCTGAAACGTG-3’) and 10 pmol reverse primer (5’-GAGGACGCTGGCAACACAC-3’). 25 mM dNTPs, 5 U Taq DNA polymerase (Invitrogen, Breda, The Netherlands) in a PCR buffer containing 0.3 M Tris-HCl (pH 8.5), 75 mM ammoniumsulfate and 7.5 mM MgCl2. The cycling conditions for the polymerase chain reaction started with 5 min at 92°C, followed by 35 cycles of 1 min at 92°C, 1 min at the optimized annealing temperature (57.5°C), and 1 min 72°C, then followed by an extra 5 min 72°C. PCR products were analyzed on a 2% agarose gel. The amplification yielded distinct bands at 484 bp (short ‘s’ allele) and 528 bp (long ‘l’ allele).

To investigate the random genotyping error rate, the lab included 5 duplicate DNA samples per 96-well plate, which were 100% consistent. In addition, 4 blanks were included in each plate, which were required to be negative. By running PEDCHECK (O’Connell & Weeks, 1998) for single point Mendelian inconsistencies on the markers, we identified one family with potential pedigree errors. This family was removed from the analysis. Hardy–Weinberg equilibrium (HWE) proportions were estimated from parental genotype information using the Markov–Chain Monte-Carlo approximation of the exact test implemented in the GENEPOP package V 3.3 (Raymond & Rousset, 1995). No deviations from HWE were detected (p = .96). To maximize the power of the analyses, 5HTTLPR genotype was dummy-coded into 1 (short-short and short-long) and 2 (long-long).

Statistical analyses

We used latent growth curve modeling (LGCM) in Mplus (Muthén & Muthén, 1998–2007) to estimate both the
initial level of loneliness at baseline (intercept) and the rate of change in loneliness from baseline across time (slope; Duncan, Duncan, & Strycker, 2006). As individual growth is estimated for each adolescent separately, LGCM is an excellent approach to take individual variations in the development of loneliness into account and to determine which predictors are associated with differential developments. Parameters in the models were estimated by applying the maximum likelihood estimator with robust standard errors (MLR), as required when dependent variables have non-normal distributions. In the first step, the basic model without the predictors was tested. In the second step, the relation between the 5-HTTLPR polymorphism and onset and development of loneliness was examined. In the third step, the relation between sex and loneliness was examined and the interaction between sex and the 5-HTTLPR polymorphism was included in the model. All variables were centered before computing the interaction terms, to avoid multicollinearity. Finally, the relations between perceived support from fathers and mothers and loneliness were examined separately, and the interactions between perceived support and the 5-HTTLPR polymorphism (for fathers and mothers separately) were added to the model. Model fit was assessed by the following global fit indices: $\chi^2$, CFI (with a cut-off value of .95) and RMSEA (with a cut-off value of .06) (Hu & Bentler, 1999).

Results
Descriptive statistics

Of the 306 participants, 55 (18%) were homozygous for the short allele, 147 (48%) carried the heterozygous genotype, and 104 (34%) were homozygous for the long allele. The average level of loneliness at baseline (T1) was 18.85 (SD = 6.66). The mean levels of the five repeated measures of loneliness are illustrated in Figure 1. The level of loneliness marginally decreased over time (Wilks’ $\Lambda = .97$, $F[4, 286] = 2.36$, $p = .053$). The average scores for support were 4.11 (SD = .41) for perceived maternal support and 3.92 (SD = .47) for perceived paternal support. To check whether the levels of maternal support significantly differed from the levels of paternal support, we conducted a paired samples $t$-test, which showed that the levels of maternal support were significantly higher than the levels of paternal support, $t(302) = 8.36$, $p < .001$.

Correlations between 5-HTTLPR genotype, sex, support received from mother and father, and loneliness are depicted in Table 1. These findings showed that 5-HTTLPR genotype and sex were not significantly related to loneliness. Support from both mother and father were negatively related to loneliness at most time points.

Table 1 Correlations between model variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 5-HTTLPR $^a$</td>
<td>-</td>
<td>.03</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<tr>
<td>2. Sex $^b$</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
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<tr>
<td>3. Support (mother)</td>
<td>.01</td>
<td>.09</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>4. Support (father)</td>
<td>.05</td>
<td>.11*</td>
<td>.60**</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>5. Loneliness (T1)</td>
<td>.02</td>
<td>-.08</td>
<td>-.18**</td>
<td>-.21**</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>6. Loneliness (T2)</td>
<td>.02</td>
<td>.06</td>
<td>-.07</td>
<td>-.15**</td>
<td>.55**</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>7. Loneliness (T3)</td>
<td>-.00</td>
<td>-.04</td>
<td>-.19**</td>
<td>-.19**</td>
<td>.51**</td>
<td>.62**</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>8. Loneliness (T4)</td>
<td>-.04</td>
<td>-.06</td>
<td>-.18**</td>
<td>-.08</td>
<td>.42**</td>
<td>.47**</td>
<td>.53**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9. Loneliness (T5)</td>
<td>-.11</td>
<td>.10</td>
<td>-.15**</td>
<td>-.03</td>
<td>.48**</td>
<td>.38**</td>
<td>.47**</td>
<td>.70**</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ 1 = short-short, short-long; 2 = long-long.

$^b$ 1 = boy; 2 = girl.

*p < .05. **p < .01.

Model findings

First, the basic model without predictors was tested. The intercept and slope were significant ($\beta_0 = 18.933$, $p < .001$; $\beta_1 = -.334$, $p < .010$), which indicated that participants on average scored 18.93 on the loneliness scale at baseline, and the level of loneliness decreased over time ($\chi^2 [df = 10, n = 304] = 345.75$, CFI = .92, and RMSEA = .095).

Second, we included the 5-HTTLPR genotype as a predictor in the model ($\chi^2 [df = 13, n = 304] = 40.58$, CFI = .93, and RMSEA = .084). The relation between the 5-HTTLPR genotype and the intercept was not significant ($\beta = .057$, SE = .068 $p = .402$). The 5-HTTLPR genotype was significantly related to the slope ($\beta = -.169$, SE = .082 $p = .041$).
between the 5-HTTLPR genotype and the slope of loneliness is illustrated in Figure 2.

As can be seen in Figure 2, carriers of the long-long genotype decreased in loneliness over time, while the levels of loneliness in participants carrying at least one short allele remained relatively stable over time.

Third, the relation between sex and the level of loneliness was examined. Sex was included as a predictor, along with the 5-HTTLPR genotype. The 5-HTTLPR genotype was still negatively related to the slope, whereas sex was positively related to the slope ($\beta = .201$, SE = .080 $p = .012$), indicating that the level of loneliness in girls generally remained stable over time, while the level of loneliness in boys slightly decreased. In addition, the interaction term between sex and the 5-HTTLPR genotype was included as a predictor in the model. This model fitted the data relatively well ($\chi^2 [df = 19, n = 304] = 52.03$, CFI = .93, and RMSEA = .076), but the interaction term was neither related to intercept nor slope.

In the fourth model, the associations between support from father and mother and loneliness were examined. First, both support from father and the 5-HTTLPR genotype were included as predictors in the model. Paternal support was negatively related to the intercept ($\beta = -.269$, $p = .000$) and positively to the slope ($\beta = .215$, $p = .041$), whereas the 5-HTTLPR genotype was significantly related to neither the intercept nor the slope ($p = .500$ and .051, respectively). This model showed a relatively good fit ($\chi^2 [df = 16, n = 304] = 44.47$, CFI = .93, and RMSEA = .077). The interaction term between support from father and the 5-HTTLPR genotype was included in the model. This interaction was not significantly related to either the intercept or the slope (respectively $\beta = -.051$, $p = .807$; $\beta = -.061$, $p = .830$) ($\chi^2 [df = 19, n = 304] = 46.05$, CFI = .94, and RMSEA = .068). Furthermore, maternal support and the 5-HTTLPR genotype were included in the model ($\chi^2 [df = 16, n = 304] = 49.08$, CFI = .92, and RMSEA = .082). Support from mother was negatively related to the intercept ($\beta = -.196$, $p = .003$), but not to the slope. The 5-HTTLPR genotype was not significant in predicting the intercept in the basic model, but predicted the slope of loneliness ($\beta = -.169$, $p = .040$). Subsequently, the interaction term between support from mother and the 5-HTTLPR genotype was included in the model, which is illustrated in Figure 3. This interaction was positively related to the intercept of loneliness ($\beta = .564$, $p = .003$), indicating that short allele carriers who received high social support from their mothers had lower levels of loneliness at baseline than short allele carriers who received low support. For the long-long genotype, no significant relation existed between support and the intercept of loneliness ($\chi^2 [df = 19, n = 304] = 54.23$, CFI = .92, and RMSEA = .078).

**Discussion**

The aim of the present study was to examine the effect of 5-HTTLPR genotype, sex, parental support, and their interactions on the onset and development of loneliness in adolescence. Our longitudinal results, the first to appear in the published literature across such a relatively long period, showed that the levels of loneliness were highest in early adolescence and slowly decreased throughout adolescence. This is in accordance with our expectations and an earlier cohort study (Marcoen & Goossens, 1993).

We did not find any effects of 5-HTTLPR genotypes on baseline levels of loneliness. These results were in line with cross-sectional research on the relations between 5-HTTLPR genotype and depression, in which direct effects of the 5-HTTLPR genotype were rarely found (for a review, see Munafo et al., 2009). A prominent finding of our study, however, was the genetic underpinning of changes in loneliness in the
teenage years: the 5-HTTLPR genotype was related to the development of loneliness, with short allele carriers remaining stable in loneliness over time, whereas adolescents with the long-long genotype showed a decrease in loneliness. Our results can be interpreted in different ways. First, both loneliness and depressive symptoms reflect a high degree of negative affectivity (i.e., a high tendency to develop negative feelings). Short allele carriers have been found to be at risk for developing problems with negative emotion regulation (e.g., Pezawas et al., 2005), that are also implied in the development of loneliness or, as our results indicated, to being unable to reduce feelings of loneliness. Second, loneliness is a precursor (Qualter, Brown, Munn, & Rotenberg, in press) or even a proxy for depressive symptoms. Future research on the underlying mechanism is in order.

Additionally, a main effect of sex on the development of loneliness was found, with girls being stable in loneliness over time, and with boys decreasing. Because the origins of these differences remain unclear, sex differences in loneliness should be examined in greater detail in future studies. The interaction between 5-HTTLPR genotype and sex was not significant, which implies that sex does not have a moderating role in the relation of 5-HTTLPR genotype and loneliness. This finding contrasts with the results of an earlier cross-sectional study on depression in adolescence, in which a direct effect of 5-HTTLPR genotype was found exclusively for girls (Eley et al., 2004).

Perceived parental support was found to be pivotal in the onset and the development of loneliness. In line with our expectations, perceived support from both father and mother were negatively related to the baseline level of loneliness, indicating that high levels of perceived parental support can be seen as a protective factor against loneliness. Support received from mother was not related to the development of loneliness over time, whereas support from father was positively related to the slope of loneliness, which implies that high levels of paternal support lead to an increase in loneliness. A possible explanation is that fathers might react to the emotional problems of their child at baseline by providing more support, which has been found in a previous study (Eisenberg, Fabes, & Murphy, 1996). A possible reason why we did not find this association in mothers is that, in our sample, mothers scored significantly higher on support than fathers. The gene–environment interaction between paternal support and 5-HTTLPR genotype was not significant, whereas the interaction between maternal support and 5-HTTLPR genotype was significantly related to the intercept of loneliness. These results show that adolescents who received little support from their mother and carried a short allele were at increased risk for developing loneliness and that they might benefit more from higher levels of maternal support. This is in line with results from a study by Fox et al. (2005), who found that the 5-HTTLPR genotype interacts with maternal support in predicting children's behavioral inhibition and shyness.

Although no studies yet have examined the role of 5-HTTLPR genotype in loneliness, studies on depression showed that this genotype often interacted with parental behavior, such as support, in predicting depression in children and adolescents (Kaufman et al., 2004; Sjöberg et al., 2006). These results are also in line with the presumed underlying mechanism in depression, in which short allele carriers have problems with regulation of negative emotions. Carrying a short allele can put one at risk, but the problematic behavior may only come to the fore when another risk factor, such as low maternal support, is present.

Since loneliness is a complex phenotype, it is likely that multiple environmental and biological factors influence its onset and developmental course. Regarding the environment, environmental assets and stressors other than perceived parental support may exert their effects on adolescent loneliness as well. For example, stressful life events have been found to be important in loneliness (Segrin, 1999) and to interact with the 5-HTTLPR genotype in predicting depression (Caspi et al., 2003). Concerning genetic vulnerabilities, additional polymorphisms involved in the serotonin pathway may also play a role in loneliness. Polymorphisms related to the enzymes tryptophan hydroxylase 1 and 2, which are involved in serotonin synthesis, have been related to depression (Gizatullin, Zaboli, Jönsson, Asberg, & Leopardi, 2006) and are involved in the basic emotion regulation circuit (Brown et al., 2005). In future studies with large longitudinal samples, it is important that multiple environmental and genetic influences on loneliness will be examined. Finally, it is important to recognize that environmental factors have direct effects, and in addition show moderate heritability and specific associations with genes. Studies on depression revealed that exposure to negative life events is partly genetically determined (Paykel, 2003) and that key features of negative parenting, such as low parental support, are also partly genetically determined. Such additional effects of environmental factors on loneliness should be considered in future research.

Limitations

A number of limitations have to be mentioned. First, like any findings on gene × environment interactions in non-clinical samples, our results are primarily hypothesis-generating or exploratory. The next step is to establish clinical relevance of the gene × environment interaction obtained within a clinical population, which includes the estimation of the strength of the interaction (Dempfle et al., 2008). Second, population stratification (Marchini, Cardon, Phillips, & Donnelly, 2004) might have occurred,
although this is not very likely because the number of adolescents not born in the Netherlands was very low (1.2%), and the number of adolescents not born in a European country was even lower (.2%). Further, the 5-HTTLPR genotype frequencies were in line with the frequencies usually found in Caucasian samples (Hariri & Holmes, 2006), which minimizes the chance that population stratification occurred. Third, support from parents was reported by the adolescents, which may not be a precise measure of the actual behavior. However, the way adolescents perceived the support given may be more important than the actual support provided by parents (Steinberg, Lamborn, Dornbusch, & Darling, 1992).

### Conclusion

Our study is the first to explore adolescent loneliness longitudinally and to examine the genetic underpinnings of loneliness. Our results contribute to a further understanding of the environmental and genetic bases of loneliness. Our main finding was that the 5-HTTLPR genotype was related to the development of loneliness, and interacted with maternal support in predicting the level of loneliness at baseline. We would like to emphasize that replication of our results is needed in both population-based and clinical samples with sufficient sample size, before any recommendations for interventions can be made.

### Key points

- Previous studies on loneliness have shown that loneliness has a substantial genetic component and that it decreases throughout adolescence. However, no longitudinal or molecular-genetic studies have been conducted to examine this in more detail.

- Key points of this study are: (1) Loneliness peaks in early adolescence and slowly decreases throughout adolescence; (2) Girls remain relatively stable in loneliness over time, whereas loneliness in boys decreases; (3) The 5-HTTLPR genotype is related to the slope of loneliness, in which short allele carriers remained stable in loneliness over time, while adolescents with the long-long genotype decreased in loneliness; (4) Parental support was positively related to the onset of loneliness, and an interaction was found between maternal support and 5-HTTLPR genotype, in which adolescents who receive little support from their mother and carry a short allele were at increased risk for developing loneliness.

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