The +1444C>T polymorphism in the CRP gene: a study on personality traits and suicidal behaviour
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\textbf{Objectives} Numerous studies have shown associations between an on-going depression and elevated serum levels of the acute-phase reactant C-reactive protein (CRP). Also, in suicidal behaviour, a proinflammatory state has been suggested to be of importance for the pathophysiology. There is a genetic susceptibility to suicidal behaviour, but studies with respect to genes related to inflammation are sparse. We have previously reported an association between a polymorphism located in the CRP gene, +1444C>T (rs1130864), and the personality trait impulsiveness in women assessed using the Karolinska Scales of Personality. The present study aims to replicate these results in suicide attempters and examine whether the polymorphism is associated with suicidal behaviour.

\textbf{Materials and methods} The +1444C>T polymorphism was genotyped in suicide attempters from two cohorts (a total of 106 patients) and healthy controls (n=517).

\textbf{Results} We could replicate our previous finding, as the +1444T allele was associated with higher scores in the Karolinska Scales of Personality factor extraversion and its subscale impulsiveness in one of the patient cohorts. Furthermore, the +1444T allele was significantly more common among suicide attempters compared with the +1444C allele.

\textbf{Introduction} Numerous studies suggest that inflammation may be of specific importance for suicidal behaviour and we have previously observed increased levels of soluble interleukin-2 (IL-2) receptor in plasma (Nassberger and Träskman-Bendz, 1993) as well as increased levels of IL-6 in cerebrospinal fluid (CSF) of suicide attempters (Lindqvist \textit{et al.}, 2009). Moreover, postmortem examination of brains from suicide victims showed an increased expression of cytokines in the orbitofrontal cortex (Tonelli \textit{et al.}, 2008) and evidence of microgliosis (Steiner \textit{et al.}, 2008). In the latter study, microgliosis was present in suicide victims with schizophrenia and depression and not in patients from the same diagnostic groups who died from other causes. Also, suicide attempters show a different plasma cytokine profile compared with depressed, nonsuicidal patients (Janelidze \textit{et al.}, 2011). Studies reporting associations between suicidality and asthma (Kuo \textit{et al.}, 2010) as well as allergy are also noteworthy (Messias \textit{et al.}, 2010).

With respect to suicidality, twin studies have shown that suicidal behaviour is partly attributable to genetic factors. Research on genetic variations in immune-related genes and suicide is hitherto sparse. We therefore chose to examine a candidate gene, C-reactive protein (CRP), for this purpose.

\textbf{Conclusion} The present results lend further support to the relevance of inflammation for suicidal behaviour. The association between the polymorphism and personality trait impulsiveness reinforces our hypothesis of the importance of immune-related genes also for normal mental functions such as personality traits. Given the fact that impulsiveness is a well-known risk factor for suicidal behaviour, we further hypothesize that the polymorphism studied may in part explain this relationship. \textit{Psychiatr Genet} 23:70–76 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Keywords: +1444C>T, C-reactive protein, impulsiveness, inflammation, rs1130864, suicidal behaviour

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Received 27 August 2012 Accepted 27 October 2012

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of a single nucleotide polymorphism (SNP) (rs1130864, +1444C>T), located in the 3’ untranslated region of the CRP gene, on the immunohistochemical staining of CRP in the hippocampal area (Kok et al., 2011). These data indicate that CRP is important for mental functions.

Polymorphisms in the CRP gene have been reported to moderate a positive correlation between depressive symptoms and the protein (Halder et al., 2010). The SNP +1444C>T has not only been associated with serum levels of the protein (Jones et al., 2009; Marioni et al., 2010) but also with personality traits including impulsiveness in women (Suchankova et al., 2009), which is of potential interest for further investigations as impulsivity is an important risk factor for suicidal behaviour (Braquehais et al., 2009).

The aim of the present study was to examine the +1444C>T SNP in suicide attempters (n = 106) and healthy controls (n = 517). We also analysed the influence of the SNP on personality traits in patients who had been assessed by Karolinska Scales of Personality (KSP) (n = 41). We hypothesized that the T allele in the SNP studied would be associated with impulsiveness and that the same allele would be more prevalent among patients than controls.

**Materials and methods**

**Patients**

The suicide attempters participating in the present study were from two cohorts. Suicidal cohort 1 (n = 42, 21 women and 21 men; mean age±SD of 51.0±10.1) was a 10-year follow-up study of suicide attempters who were recruited between 1986 and 1992 (index period). The recruitment of individuals in suicidal cohort 2 took place between 2005 and 2008, and involved 64 suicide attempters (38 women and 26 men; mean age±SD of 38.1±14.0), which are included in a recently published paper (Janczidze et al., 2011). None of the bipolar patients were manic at the time of recruitment; all except two were diagnosed with depression. The study participants in both suicidal cohorts were diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III-R and DSM-IV, respectively). For suicidal cohort 1, the diagnoses were made by two psychiatrists after a consensus discussion, whereas for suicidal cohort 2, diagnoses were made using the Structured Clinical Interview for DSM-IV Axis I Disorders (First, 1997). The primary axis I diagnosis and suicide attempt methods are reported in Table 1. Suicide attempters in both cohorts were admitted to the medical intensive care unit of the Lund University Hospital. Within a few days, they were referred to a psychiatric ward of the Lund University Hospital, where they underwent a general physical and psychiatric examination.

The studies were carried out at the Lund Suicide Research Centre at the Department of Psychiatry of Lund University Hospital. Suicidal cohort 1 was approved by the Lund University Medical Ethics Committee and suicidal cohort 2 was approved by the Lund Ethical Review Board. All patients provided informed consent to participate in the research programme.

The control participants were from two population-based cohorts that included 270 women and 247 men, respectively. All women born on uneven days in the year 1956 and living in Gothenburg, Sweden, constituted the primary cohort (n = 1137); this population-based group had originally been recruited for a study of obesity, anthropometrics and cardiovascular risk factors (Rosmond and Björntorp, 1998). At the age of 42 years, the women (80% of the original cohort) reported self-measurements of body weight, height and circumference ratio over the waist and hips (WHR). WHR was then used for a selection of 450 women in total with low, median or high WHR. Of these women, 270 (60%) volunteered to provide blood samples for genotyping. All participating women provided their informed consent and the study protocol was approved by the ethical committee at the University of Gothenburg. The male population was recruited from among all men born during the first 6 months in 1944 and living in Gothenburg, Sweden (n = 1302), and were identified using the population registry (Rosmond et al., 1996). A total of 450 men were selected for further investigation in line with the procedure described above. Overall, 275 men volunteered to participate in the study. However, 28 of these men could not be genotyped because of lack of blood samples. At the time of investigation, the men were 51 years old. All participating individuals provided their informed consent.

**Table 1** Primary axis I diagnosis and suicide attempt methods of suicide attempters in two cohorts

<table>
<thead>
<tr>
<th>Primary axis I diagnosis [%]</th>
<th>Suicide attempters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort 1 (n=42)</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>14 (33.3)</td>
</tr>
<tr>
<td>Dysthmic disorder</td>
<td>9 (21.4)</td>
</tr>
<tr>
<td>Depressive disorder NOS</td>
<td>3 (7.1)</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>0</td>
</tr>
<tr>
<td>Adjustment disorder</td>
<td>8 (19.0)</td>
</tr>
<tr>
<td>Alcohol abuse or dependence</td>
<td>4 (9.5)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>0</td>
</tr>
<tr>
<td>Psychosis</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>0</td>
</tr>
<tr>
<td>Obsessive–compulsive disorder</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Pathological gambling</td>
<td>0</td>
</tr>
</tbody>
</table>

**Suicide attempt method [%]**

<table>
<thead>
<tr>
<th>Suicide attempt method [%]</th>
<th>Suicide attempters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cohort 1 (n=42)</td>
</tr>
<tr>
<td>Intoxication</td>
<td>39 (92.9)</td>
</tr>
<tr>
<td>Hanging</td>
<td>0</td>
</tr>
<tr>
<td>Drowning</td>
<td>0</td>
</tr>
<tr>
<td>Car accident</td>
<td>0</td>
</tr>
<tr>
<td>Wrist cutting</td>
<td>3 (7.1)</td>
</tr>
<tr>
<td>Suffocation</td>
<td>0</td>
</tr>
</tbody>
</table>

NOS, not otherwise specified.

*Diagnosis missing for four of the patients; record of suicide attempt method missing for one patient.*
Genotyping
Human genomic DNA was extracted from blood samples using the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany). For suicidal cohort 2, blood samples for seven individuals were unavailable and they could not be included in the genotyping study. The genotyping of DNA samples from patients was performed at KBiosciences (Hoddesdon, UK). The procedure used to genotype the control cohorts has been reported previously (Suchankova et al., 2009). The primer pair that was used for the PCR was 5'-biotin-CTG GTC TGG GAG CTC GTT AAC TA-3'/5'-GGC CTT CCT TCT TCT CAG CTC TT-3'. The PCR was performed using HotstarTaq polymerase from Qiagen and the GeneAmp PCR System 9700 (Applied Biosystems, Foster City, California, USA). A total volume of 20 µl containing 0.3 µmol/l primers, 1.5 mmol/l MgCl₂, ~50 ng DNA and 200 µmol/l of each dNTP was used. An initial 15 min denaturation step at 95°C was followed by 41 cycles of 15 s at 95°C, 30 s at 63°C and 15 s at 72°C. Once the cycles were completed, the reaction was incubated at 72°C for 7 min and then left at 4°C. The PCR product was genotyped using a Pyrosequencer PSQ 96 and the PSQ 96 SNP Reagent Kit (Pyrosequencing, Uppsala, Sweden). To identify the polymorphism +1444C>T 15 pmol of the sequencing primers 5'-AAT TCT GAT TCT TTT GGA C-3' was used. A total of 20 µl of PCR products was used for pyrosequencing according to the manufacturer’s instructions.

Personality assessment
The temperament of patients in suicidal cohort 1 was assessed by means of the KSP (Schalling et al., 1987) during the index period, that is within a few weeks of the suicide attempts. KSP is a self-report questionnaire based on 135 items forming 15 subscales, which in turn form four factors: extraversion (comprising the subscales impulsiveness and monotony avoidance), neuroticism (comprising the subscales somatic anxiety, muscular tension, psychic anxiety, psychasthenia, inhibition of aggression, guilt and socialization), psychoticism (comprising the subscales detachment and suspicion) and nonconformity (comprising the subscales verbal aggression, indirect aggression, irritability and social desirability). The KSP inventory has been used widely in studies involving biologically correlates of personality traits (Schalling et al., 1987; Gustavsson et al., 1996; Laakso et al., 2003; Suchankova et al., 2009).

Statistics
Before pooling suicidal cohort 1 and 2 as well as the two population-based cohorts, a Pearson χ²-test was carried out to ensure that there were no differences in distribution in +1444C>T genotype before the merging of cohorts, yielding one case and one control cohort. Cases and controls were compared with respect to genotype and allele distribution using the Pearson χ²-test. Odds ratios (OR) with a 95% confidence interval (CI) were calculated to determine the effect size.

The associations between the +1444C>T and the KSP factors in suicidal cohort 1 were assessed in a linear regression (one tailed) using age, sex and the primary axis diagnosis as covariates. A significant association between factor and polymorphism was further examined by analysing the subscales. The statistical analysis was carried out using the statistical software package SPSS for Mac (version 18.0.0, SPSS Inc., Chicago, Illinois, USA).

Results
The Pearson χ²-test showed no statistical difference in the genotype distribution of the polymorphism +1444C>T between suicidal cohorts 1 and 2 (P = 0.64) as well as between the two population-based cohorts (P = 0.39) before they were merged to yield one patient and one control group, respectively. There was no significant difference between patients and controls in terms of BMI after controlling for sex and age (data not shown). The genotype and allele frequencies for controls and cases are shown in Table 2. Compared with the +1444C allele, the +1444T allele was associated with an increased risk of suicidal behaviour (OR = 1.6, 95% CI = 1.2–2.2) (Table 2). Analysis of allele frequencies in patients with depressive disorders (i.e. major depressive disorder, dysthymic disorder, depressive disorder, not otherwise specified; n = 43) as well as bipolar disorders (i.e. bipolar I and bipolar II disorders; n = 16) and patients with other diagnoses (n = 38) compared with the control participants showed that the +1444T allele was significantly associated with depressive disorders (OR = 1.9, 95% CI = 1.2–3.0), but not with bipolar disorders or other diagnoses (Table 3).

For the analysis of the personality traits in suicidal cohort 1, the +1444CT group was merged with +1444TT in a dominant model on the basis of previous results reported between the SNP and KSP scores (Suchankova et al., 2009). The presence of the +1444T allele was significantly associated with higher scores in the factor extraversion compared with +1444C homozygotes in this cohort (Table 4). Further analysis of the subscales including this factor showed a significant association between the T allele and the personality trait impulsiveness.

The distribution of the genotypes did not differ significantly from the Hardy–Weinberg equilibrium in either of the cohorts (P > 0.05).

Discussion
The present study reports for the first time that the +1444T allele of CRP increases the risk for suicidal
behaviour; the T allele is more common among suicide attempters compared with controls. The aetiology of suicide attempts is multifactorial including both polygenic as well as environmental components and our study is the first to show the influence of a gene related to inflammation on suicidal behaviour. This is in accordance with several observations linking the immune system to suicidal behaviour. In addition, the presence of the +1444T allele in patients was associated with significantly higher scores in KSP impulsivity compared with +1444CC carriers. We have shown previously that the same allele of the CRP gene was associated with the trait impulsivity in the female cohort of healthy controls (Suchankova et al., 2009).

The molecular mechanism by which the +1444C > T polymorphism could influence the susceptibility to suicidal behaviour is not known at present. CRP is mainly synthesized by hepatocytes in response to cytokines such as tumour necrosis factor-α and IL-6 (Moshage et al., 1988), and its role in the brain has not been studied thoroughly. In Alzheimer’s disease, cerebral expression of CRP has been shown in a few studies (Duong et al., 1997; Yasojima et al., 2000; Kok et al., 2009). Moreover, CSF levels of CRP are detected in the CSF (Kanoh and Ohtani, 2001; Shameem et al., 2012); in addition, in bacterial meningitis, elevated levels of CRP are detected in the CSF (Kanoh and Ohtani, 2001; Shimetani et al., 2008), which indicates a possible upregulation of the protein in the brain. Potential mechanisms of transportation of CRP across the blood–brain barrier have yet to be established.

Nonetheless, a peripheral inflammation may activate an inflammatory response in the central nervous system, which in turn could interact with, for example serotonin metabolism (Raison et al., 2009). Moreover, CSF levels of cytokines in suicide attempters have been shown to correlate with monoamine metabolites (Lindqvist et al., 2009). Possibly, genetic variants of the CRP gene may affect the reactivity of the inflammatory response, which in turn may alter monoamine neurotransmission and

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**Table 2** Distribution of genotype and allele frequencies of the C-reactive protein +1444C>T polymorphism in suicide attempters and controls

<table>
<thead>
<tr>
<th>Genotype [n (%)]</th>
<th>Controls</th>
<th>Cases*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>TT</td>
<td>n=517</td>
<td>n=270</td>
<td>n=247</td>
</tr>
<tr>
<td>CT</td>
<td>54 (10.4)</td>
<td>33 (12.2)</td>
<td>21 (8.5)</td>
</tr>
<tr>
<td>CC</td>
<td>207 (40.0)</td>
<td>106 (39.3)</td>
<td>101 (40.9)</td>
</tr>
<tr>
<td>Allele [n (%)]</td>
<td>n=1034</td>
<td>n=540</td>
<td>n=494</td>
</tr>
<tr>
<td>T</td>
<td>315 (30.5)</td>
<td>172 (31.9)</td>
<td>143 (28.9)</td>
</tr>
<tr>
<td>C</td>
<td>719 (69.5)</td>
<td>368 (68.1)</td>
<td>351 (71.1)</td>
</tr>
</tbody>
</table>

Significant P-values are given in bold.

*Genotyping of one sample in cohort 2 failed.

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**Table 3** Distribution of allele frequencies of the C-reactive protein +1444C>T polymorphism in suicide attempters diagnosed with depressive disorders as well as bipolar disorder compared with controls

<table>
<thead>
<tr>
<th>Allele [n (%)]</th>
<th>Controls</th>
<th>Depressive disorders</th>
<th>Bipolar disorders</th>
<th>Other diagnoses</th>
<th>P-value1</th>
<th>P-value2</th>
<th>P-value3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>n=1034</td>
<td>n=86*</td>
<td>n=32*</td>
<td>n=76</td>
<td>0.004</td>
<td>0.11</td>
<td>0.25</td>
</tr>
<tr>
<td>C</td>
<td>315 (30.5)</td>
<td>39 (45.3)</td>
<td>14 (43.8)</td>
<td>28 (36.8)</td>
<td>0.071</td>
<td>0.178</td>
<td></td>
</tr>
</tbody>
</table>

Significant P-values are given in bold.

*Genotyping of four samples failed.

1P-value following the Pearson χ²-test between patients with depressive disorders and controls.

2P-value following the Pearson χ²-test between patients with bipolar disorders and controls.

3P-value following the Pearson χ²-test between patients with diagnoses other than depression and bipolar disorder, respectively, and controls.

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**Table 4** Statistics of suicide attempters (cohort 1) who had completed the Karolinska Scales of Personality questionnaire

<table>
<thead>
<tr>
<th>+1444CT+TT</th>
<th>+1444CC</th>
<th>P-value</th>
<th>df</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>n=27–29a</td>
<td>12</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sex, n (men/women)</td>
<td>19/14</td>
<td>5/7</td>
<td>0.558</td>
<td>–</td>
</tr>
<tr>
<td>Age [mean ±SD]</td>
<td>38.8 (10.0)</td>
<td>36.8 (10.3)</td>
<td>0.067</td>
<td>–</td>
</tr>
<tr>
<td>KSP [mean ±SD]</td>
<td>54.4 (8.9)</td>
<td>48.4 (10.7)</td>
<td>0.023</td>
<td>0.140</td>
</tr>
<tr>
<td>Extraversion</td>
<td>53.3 (9.3)</td>
<td>47.0 (11.7)</td>
<td>0.026</td>
<td>0.114</td>
</tr>
<tr>
<td>Impulsiveness</td>
<td>55.3 (11.9)</td>
<td>49.3 (11.0)</td>
<td>0.060</td>
<td>–</td>
</tr>
<tr>
<td>Monotony avoidance</td>
<td>80.6 (7.9)</td>
<td>63.5(7.7)</td>
<td>0.136</td>
<td>–</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>55.2 (8.7)</td>
<td>57.0 (10.3)</td>
<td>0.389</td>
<td>–</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>52.2 (7.0)</td>
<td>51.8 (6.6)</td>
<td>0.462</td>
<td>–</td>
</tr>
</tbody>
</table>

KSP scores grouped according to the dominant model (+1444CT+TT vs. +1444CC genotype).

All data are reported as mean (SD). The KSP factors are shown in regular fonts, with the subscales for extraversion written in italic. Personality trait scores have been standardized using normative data (T-scores).

P-values were obtained by linear regression (one tailed) controlling for age, sex and primary axis 1 diagnosis.

Significant P-values are given in bold.

*KSP data were missing for one patient and three patients had missing values in their personality profile.
thereby generate psychiatric symptoms in susceptible individuals.

The involvement of the immune system in processes implicated in brain development and plasticity (Boulanger, 2009) provides another possible explanation by which the +1444C>T polymorphism may influence mental functions. Findings on neurodevelopmental abnormalities in both personality disorders and psychopathy (Raine et al., 2010) may be a result of an influence of immune-related genes such as CRP and it is not far-fetched to also assume that the risk of suicidal behaviour is at least partially established under the development of the brain. Keeping in mind the previously reported association between the +1444T allele and a greater elevation of CRP serum levels following an inflammatory stimulus (D’aiuto et al., 2005), it is possible that this allele may result in a heightened inflammatory response also in the developing and/or developed brain, which in turn induces neurochemical changes (Yirmiya and Goshen, 2011). Also, CRP may have neurological regulatory properties that are not known at present. These suggestions are supported by the fact that we have shown associations between variants in genes related to the immune system and personality traits (Suchankova et al., 2009, 2012a, 2012b); personality dimensions are known to be relatively stable over time (Caspi et al., 2005) and may reflect structural variance in specific brain areas (Gardini et al., 2009).

A possible vascular contribution to the susceptibility to suicide may also be discussed. Polymorphisms in the CRP gene have been associated with cardiovascular diseases (Chen et al., 2005; Balistreri et al., 2006; Ekdund et al., 2008), and it is thus possible that genetic variations such as the +1444C>T SNP contribute towards the established association between mood and cardiovascular disorders (Halaris, 2009). In accordance with this relationship, strong associations between suicidal behaviour and cardiovascular disease have been reported (Placido and Sposito, 2009). Similar results have also been obtained in a population-based study in Finland in which the estimated risk of suicide for patients with coronary artery disease was two-fold compared with the general population (Mainio et al., 2010). Elevated serum levels of CRP have been associated with degradation of the microstructural organization of white matter as well as impaired cognitive function (Wersching et al., 2010), and have also been suggested to influence cerebrovascular events (Rizzo et al., 2008). Therefore, CRP could be associated with cerebral dysfunction increasing the risk for mood disorders and suicidal behaviour.

Several studies have shown previously that impulsivity is a major determinant together with psychiatric morbidity for suicide attempts (Crumley, 1979; Dumais et al., 2005; Neufeld and O’rourke, 2009). The linking of the +1444T allele to increased impulsivity scores both in a normal population and in suicide attempters allows us to suggest that this association may also be of interest in a wider sense. Thus, even if our current study may not show any causal relationships, we suggest that carriers of the CRP allele +1444T, which is of importance for impulsive behaviour, may subsequently be at a higher risk for developing suicidal behaviour.

The finding of the studied polymorphism and suicidal behaviour must be considered as preliminary until replicated. A general limitation of the present paper is the fact that we are studying a heterogeneous group of suicide attempters, with various underlying diagnoses, which may have potentially had an impact on the results from both the case-control and the personality trait study. In addition, the selection of suicide attempters was biased by the fact that all the patients were included after survival of the attempt; intoxication was the most commonly used method. Inclusion of patients with more violent suicidal methods may yield different results. The limitations in the case-control study include the modest cohort size, the possibility of a type I error and population stratifications. To minimize the possibility of the latter, we ensured that both cases and controls were unrelated and recruited from the same region of Sweden. We cannot rule out that the +1444C>T SNP is specifically associated with any other psychiatric disorder; however, our results showed that there were no differences in allele frequencies between patients with a depressive disorder and patients with a bipolar disorder (Table 3).

Nevertheless, the study would have benefited from the inclusion of a nondepressed suicidal patient cohort, especially following a recent study in which cytokine levels were reported to differ between suicidal patients and nonsuicidal depressed patients (Janelidze et al., 2011). The study would further have benefited from including variables on chronic illness and cardiovascular risk factors, given the association between such parameters and the risk of suicidal behaviour (Asellus et al., 2010; Ozek and Ekici, 2011). Because of the fact that the cohorts studied were analysed at different time-points and with respect to different parameters, we could not include these covariates in the analysis; however, no associations were found in either the population-based cohorts or cohort 1 (suicide attempters) between the studied genotype and cholesterol, triglyceride, HDL or LDL levels measured in serum or plasma. In addition, no association was found between genotype and diabetes or hypertension in either controls or patients. It still remains to be established whether the +1444C>T SNP is associated with other risk factors for suicidal behaviour that could have contributed towards the present results. An additional limitation is the fact that we did not have access to serum levels of CRP for all the patients and thus could not investigate whether there was an association between these and the SNP or whether patients differed from controls in terms of these levels. Some cases with

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different ethnic origin existed among both patients and controls. However, the exclusion of these patients from the analysis did not affect the outcome significantly (data not shown). The analysis of personality traits in the present study has limitations owing to the selection, the limited number of patients assessed, the variety of psychiatric diagnoses among the patients that may have resulted in state-dependent effects on reported personality traits and finally the use of a self-report measure. Although only a modest number of seven additional SNPs located in various candidate genes related to inflammation has been analysed in the cohorts, the issue of multiple testing should be raised. However, the consistency of the present results with our previously published findings (Suchankova et al., 2009) should be considered.

The observation that the +1444T allele in the gene encoding CRP is more frequent in patients with suicidal behaviour compared with controls is in agreement with our earlier findings of variations in genes related to the immune system and their relevance for mental functions (Suchankova et al., 2009). In addition, this allele is shown to be associated with higher personality scores of impulsivity both in patients and in controls. Nonetheless, the underlying molecular mechanisms are unknown, and further studies are warranted in the field of psychoneuroimmunology to understand the aetiology of suicidality.

Acknowledgements
The invaluable assistance of our research nurse Charlotta Sunnqvist is greatly acknowledged. The authors would also like to acknowledge the technical assistance of Gunilla Bourghardt and Inger Oscarsson.

This study was supported by the Swedish Research Council (Grant No. K2009-61X-21524-01-1, VR 2008-29611-56265-175), the Foundation for Psychosomatic and Clinical Research, the Swedish Brain Foundation, Soderstrom-Konig Foundation, Sjoberg Foundation, Fysiografiska Society and the province of Scania state grants (ALF). None of these organizations had any further role in the study or in the decision to submit the work for publication.

Conflicts of interest
There are no conflicts of interest.

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