The 5-HT₁A C(-1019)G polymorphism, personality and electrodermal reactivity in a reward/punishment paradigm

Anja Schmitz¹, Peter Kirsch², Martin Reuter³, Nina Alexander⁴, Eva Kozyra¹, Yvonne Kuepper¹, Roman Osinsky¹ and Juergen Hennig¹

¹ Department of Psychology, University of Giessen, Germany
² Central Institute of Mental Health, Mannheim, Germany
³ Department of Psychology, University of Bonn, Germany

Abstract

During past years the 5-HT₁A C(-1019)G polymorphism has been associated with vulnerability to depression, anxiety-disorder and personality traits related to negative emotionality (e.g. neuroticism). Many of these studies focused on case-control comparisons or associations between genetic markers and personality traits assessed by the use of questionnaires. In contrast, overt behaviour and physiological measures in experimental paradigms, although very promising, have seldom been the focus of studies investigating the role of the 5-HT₁A polymorphism for behaviour and psychopathology. To fill this gap, we examined the relationship between the 5-HT₁A C(-1019)G polymorphism and reaction times (in a reward/punishment paradigm) as well as electrodermal activity, as a marker of autonomic arousal, in 123 healthy subjects. This paradigm seems very promising, as sensitivity to punishment in particular, is strongly associated to traits related to negative emotionality. Carriers of the GG genotype, which is related to increased expression of 5-HT₁A autoreceptors, exhibited increased reaction times when they were able to win money (reward condition). In direct contrast to the reward condition, these subjects show faster reaction times in the punishment condition (losing money). Moreover, GG carriers are characterized by an enhanced electrodermal activity in all experimental conditions (win, lose and verbal feedback). Finally, the reaction-time pattern mentioned was related to higher scores on negative emotionality as revealed by self-reports. These findings demonstrate for the first time that the 5-HT₁A polymorphism is related to personality on the level of a triadic approach including behaviour, physiology and self-reports.

Received 2 April 2008; Reviewed 4 May 2008; Revised 15 July 2008; Accepted 12 August 2008;
First published online 17 September 2008

Key words: EDA, personality, polymorphism, serotonin, 5-HT₁A.

Introduction

In the last decades there have been numerous studies, demonstrating the critical role of serotonin in psychopathological diseases such as depression or anxiety disorders (Bell and Nutt, 1998; Deakin and Graeff, 1991). At the same time, personality theories evolved in which the biological basis has become a main focus of research, declaring the serotonergic system as one major component in regulating differences in emotion and behaviour, especially in various aspects of negative emotionality [e.g. the Behavioural Inhibition System (BIS), see Gray, 1970, and Harm Avoidance (HA), see Cloninger, 1987]. These two branches of research are strongly related to each other, due to the fact that psychopathology seems to be located at the endpoints of a shared continuum with personality (Donnelly, 1998). Nowadays, it is possible to detect polymorphisms in regions which code for neuropeptide proteins (e.g. receptors, reuptake sites), which are involved in psychopathology and personality.

Since the influential work of Lesch et al. (1996) who were able to relate a functional polymorphism of the serotonin transporter gene (5-HTTLPR) to Neuroticism and Harm Avoidance, many studies have been published with similar results. Accordingly, a first series...
of studies investigated associations between personality traits obtained from self-reports. Although these attempts were very fruitful and corroborated the importance of serotonin function in personality and psychopathology, results were often heterogeneous (for a review see Ebstein, 2006). There are various reasons which potentially lead to this heterogeneity. First, meta-analyses of association studies between single polymorphisms and personality traits show only small effect sizes (e.g. Munafo et al., 2005; Sen et al., 2005). Consequently, very large sample sizes are required, to detect these rather small effects. Second, gene × gene or gene × environment interactions might also lead to inconsistent results. For example, Caspi et al. (2003) were able to detect an interaction between 5-HTTLPR and life stress on the incidence of depression. Third, other confounding variables like gender or population stratification strategies cannot always be ruled out. Finally, personality traits, like neuroticism, cover a broad range of behaviour and emotional states and consist of many facets. Conceptual differences between different measurements and different subscales might lead to inconsistent results. It seems more likely that a single polymorphism is related to specific components than to a whole heterogeneous construct (Schmitz et al., 2007). There are two upcoming strategies to overcome these problems. One is the concept of ‘imaging genetics’ which was strongly influenced by the working group of Hariri and colleagues. Their work focused on the impact of 5-HTTLPR on neuronal reactivity to emotional cues assessed by the use of functional brain imaging. Studying the influence of genetic markers on the activation of distinct brain areas provides a much more proximate investigation of the consequences of a genetic variation to subsequent biological processes, which themselves affect behavioural output (Hariri et al., 2006). Therefore, much smaller sample sizes are sufficient to detect presumably stronger effects. A second strategy is the investigation of associations between genetic polymorphisms and behavioural and physiological responses (endophenotypes) to emotional stimuli in experimental paradigms. For example, Brocke and co-workers (2006) pursued this strategy and were able to associate 5-HTTLPR to a physiological measure of innate fear processing: the acoustic startle response and its modulation by emotional cues. Another interesting paradigm was applied by Kirsch et al. (2006), in which subjects had to react to cues indicating monetary punishment, reward or verbal feedback in a simple reaction-time (RT) task. In that study, the authors detected a significant relationship between reward system activation as measured by fMRI under dopamine agonist influence (bromocriptine) and a genetic polymorphism of the dopaminergic D2 receptor gene. This paradigm is very interesting since, in contrast to many other studies, it consists of two parts. On the one hand, emotional stimuli are presented to which the subjects have to respond, and on the other, direct consequences of the subjects’ behaviour are included (win or lose). Therefore, this task is of high relevance for the participants and potentially leads to strong commitment. Furthermore, sensitivity to punishment and sensitivity to reward are strongly related to basal personality dimensions (Gray, 1970) and considered to be involved in depression (Must et al., 2006). We, therefore, adapted this paradigm and focused on the association between reward and punishment anticipation, personality, the serotonergic system and physiological reactivity.

In contrast to the frequently studied 5-HTTLPR (see above), polymorphisms in the genetic region coding for the 5-HT1A receptor were seldom investigated, especially in the field of behavioural and physiological paradigms. This is somewhat surprising, since this receptor is a key region in the regulation of serotonergic activity. The 5-HT1A receptor is expressed inter alia as a somatodendritic autoreceptor especially, at the midbrain raphe cell bodies, and regulates serotonin release by terminating neuronal impulse flow (Barnes and Sharp, 1999; Raymond et al., 1999). It is thought to play a critical role in anxiety and depression, as indicated by the effects of partial 5-HT1A agonists, which have antidepressant and anxiolytic properties. The delay between application and clinical effects indicates that these effects are mainly due to desensitization of the 5-HT1A autoreceptors (Blier and de Montigny, 1990; Feighner et al., 1982). A similar mechanism is thought to be involved in SSRI functioning (Stahl, 1998). The 5-HT1A receptor is coded on the long arm of chromosome 5 (5q11.2-13) on an intronless gene (Kobilka et al., 1987). Several polymorphisms on this gene were identified, but most of them are either silent mutations or less frequent and, therefore, not promising for association studies. Wu and Comings (1999) were able to identify a C < G single nucleotide polymorphism (SNP) in the promoter region (C-1019G), which is frequent and seems to influence 5-HT1A receptor density by altering the binding of a single repressor, the nuclear DEAF-1-related (NUDR) protein (Lemonde et al., 2003). Thereby, the G allele leads to a significantly lower binding of the repressor and, therefore, to an increased expression of the 5-HT1A receptor, which in turn increases negative feedback.

Some studies were able to associate the G allele with psychopathological diseases such as depression or
suicide (Lemonde et al., 2003) and panic disorder with and without agoraphobia (Freitag et al., 2006; Lemonde et al., 2003; Rothe et al., 2004), while others were not (Arias et al., 2002; Serretti et al., 2007). Furthermore, several studies were able to relate the same allele to a worse response of patients with major depression to selective serotonin reuptake inhibitors (SSRI) such as fluvoxamine (Serretti et al., 2004), fluoxetine (Hong et al., 2006) and citalopram (Arias et al., 2005). Additionally, responses to combined therapy with different serotonergic medication (Lemonde et al., 2004) led to comparable results. Overall, it seems that there is some evidence that the G allele is related to a higher risk of developing an anxiety related psychopathological disease combined with a reduced therapeutic efficacy of serotonergic drugs.

Compared to this rather broad investigation of the C-1019G polymorphism and its associations to drug responses or psychopathology, only a few attempts were made to associate this polymorphism to related personality constructs like Neuroticism or Harm Avoidance. Strobel et al. (2003) were able to show that the G allele is related to higher scores in these particular traits, which is in accord with the results mentioned earlier. To our knowledge, there are only two other studies which investigated this relationship (Koller et al., 2005; Hettema et al., 2007) but both failed to show any associations. Therefore, the aim of this study was to investigate whether this functional polymorphism of the 5-HT1A receptor [C(-1019)G], is related to self-described personality measures and behaviour. Furthermore, electrodermal activity (EDA) was recorded during the reward/punishment paradigm, in order to measure autonomic arousal. EDA represents a relative proximal measure of the biological substrates of behaviour, and electrodermal hyporeactivity has been related to lower scores in neuroticism, BIS and trait anxiety (Fowles, 2000). Hence, EDA is a promising measure for physiological processes that might be related to personality and genetic markers.

Methods

Participants

Thirty-three males and 89 females (n=122; mean age = 22.5 yr, s.d. = 4.43 yr), who were all psychology students at the Justus-Liebig-Universität Gießen, participated in this study. Volunteers received course credits and were able to earn money during the experiment. All subjects had given written informed consent prior to the experiment. As part of the ‘Gießener Gene Brain Behaviour Project’, the study was approved by the Ethics Committee of the German Association for Psychology (DGPs).

Experimental design

Participants were seated in front of a monitor, with a distance of ~ 80 cm between the subject’s head and the monitor. The electrodes were attached to the left hand of the subjects (for more details, see below), and subjects were asked to find a comfortable position for their left arm and hand and to avoid moving during the experiment.

After this, subjects were informed that different kinds of arrows with varying meanings would be shown (see Figure 1). During the presentation of these arrows, a signal tone was presented to which the participants were instructed to react as fast as possible by pressing the space-bar of the computer keyboard.

An upwards pointing arrow indicated the reward condition: by pressing the space-bar ‘fast enough’, subjects were able to win €0.50. A downwards pointing arrow indicated the punishment condition. If the participants did not react ‘fast enough’, €0.50 were subtracted. In a third condition, a vertical arrow pointed in both directions and only a verbal feedback was given, if the subjects reacted ‘fast enough’ or if their reaction was too slow. To ensure that all subjects were able to win some money and to ensure their maximum performance, the threshold for a fast response was adapted for each subject and each trial. A slow response was followed by an increase in the threshold of 5%. A fast response resulted in lowering the threshold by 10%. Every stimulus was presented 20 times in randomized order with a varying inter-trial interval (6–9 s) resulting in a total number of 60 trials. Stimulus presentation and timing measurement were controlled by Presentation software (Neurobehavioral Systems, Albany, CA, USA).
Self-report measures

In order to cover a wide range of personality constructs and facets, which are related to negative emotionality, several questionnaires were administered. The Behavioural Inhibition System (BIS; Gray, 1970) was measured by use of the Carver and White BIS–BAS scales (Carver and White, 1994; German version: Strobel et al., 2001). Although Gray revised his personality theory in 2000 (Gray and McNaughton, 2000), we used the earlier scale since a questionnaire for the revised version is still lacking. In addition, neuroticism (N) was measured by use of the NEO-FFI (Neo Five-Factor Inventory; Costa and McCrae, 1992; German version: Borkenau and Ostendorf, 1993). Levels of Harm Avoidance (HA) were obtained by means of the Temperament and Character Inventory (TCI; Cloninger et al., 1994; German version: Richter et al., 1999). HA consists of the four subscales: HA1 (worry/pessimism), HA2 (fear of uncertainty), HA3 (shyness with strangers) and HA4 (fatigability and asthenia).

EDA

EDA was recorded by the Coulbourn V71-23 isolated skin conductance coupler of the modular LabLink V system (Coulbourn Instruments, Allentown, PA, USA). This module was connected via a V19-02 Wingraph Port with a Wingraph DI 400 ISA interface (Dataq Instruments, Akron, OH, USA) with a standard personal computer. An additional channel detected stimulus markers, which were controlled by a second computer. Registration and further processing of the EDA were carried out with Windaq Pro software (Dataq Instruments) and saved with a sample rate of 1000 Hz. A constant voltage calibration of 0.5 V was applied to the non-dominant hand (thenar and hypothenar) with Ag/AgCl electrodes (Marquette Hellige, Freiburg, Germany), which had a diameter of 22 mm and a contact area of 10 mm. A Unibase electrode paste was used (0.5% NaCl, PAR Medizintechnik GmbH, Berlin, Germany). AC coupling with a time constant of 5 s was used in order to assess the phasic fraction of EDA.

EDA was inspected visually, and all electrodermal responses to the experimental stimuli were computed as amplitude within a time-frame of 5 s after stimulus onset and an amplitude criterion >0.02 μS.

Genotyping

DNA was extracted from buccal cells and purification of genomic DNA was performed with a standard commercial extraction kit (MagNA Pure LC DNA Isolation kit I; Roche Diagnostics, Mannheim, Germany). Genotyping of the 5-HT₁A C(-1019)G polymorphisms was performed by real-time PCR using fluorescence melting-curve detection analysis by means of the Light Cycler System (Roche Diagnostics). For amplification and detection the following reaction mix was used: Light Cycler FastStart DNA Master Hybridization probes (Roche Diagnostics) consisting of: reaction buffer, dNTP mix and Taq DNA polymerase (0.5×) and additionally 1.6 mM magnesium chloride, 0.5 μM of each of the primers and 0.1 μM of each of the hybridization probes. The primers and hybridization probes used (TH Molbiol, Berlin, Germany) and the PCR protocols were as follows: forward primer (AATTATATGCTAATTAGTGGGAA-GTA), reverse primer (AGGGCTGGACTGTTAGATGA), anchor hybridization probe (LC Red640-AAGCTATTCTCTGCGCCA-PH), sensor hybridization probe (ACCGAGTGTGTCTTCTTAAAA). The PCR comprised an incubation period of 10 min to activate the FastStart Taq DNA polymerase of the reaction mix followed by 55 cycles of denaturation (95 °C, 0 s, ramp rate 20 °C/s), annealing (61 °C, 14 s, ramp rate 20 °C/s) and extension (72 °C, 10 s, ramp rate 20 °C/s). After amplification, a melting curve was generated by keeping the temperature constant at 40 °C for 2 min and then heating slowly to 75 °C with a ramp rate of 0.2 °C/s. The fluorescence signal was plotted against temperature to yield the respective melting points (Tₘ) of the two alleles. Tₘ for the G allele was 61.5 °C and for the C allele 54.4 °C.

Statistical analysis

First, a χ² test was calculated in order to detect deviations of the genotype distribution from Hardy–Weinberg equilibrium. Afterwards, mean RTs for each subject and condition were computed and differences between the experimental conditions were tested with t tests for dependent samples. In order to obtain a possible effect of the outcome of the preceding trial on subsequent RTs, mean reaction-time scores were calculated for trials following a loss and for trials following a gain for each participant. These mean scores were compared against each other with t tests for dependent samples. For further analysis, differences between all categories were calculated to account for differences in individual reaction speed. Furthermore, subjects were assigned to two groups, with a cut-off point of 0 in the win–lose difference value, resulting in one group of subjects, which reacted faster when able to win money in contrast to a possible loss...
of money, and one group of subjects which reacted faster in the losing condition in contrast to the winning condition. For almost all subsequent analyses ANOVAs were used in order to test an association between (a) the 5-HT1A polymorphism and RT, (b) the 5-HT1A polymorphism and skin conductance response (SCR) amplitudes, (c) the 5-HT1A polymorphism and personality measures, (d) the RT (win–lose difference score split at 0) and SCR amplitudes and (e) RT (win–lose difference score split at 0) and personality measures. The association between RT and personality measures was further analysed by means of Pearson correlations, as was the relationship between the SCR amplitudes and personality. All statistical analyses were carried out using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

**Results**

**Genetic sample characteristics**

The sample comprised of 34 GG (12 male, 22 female), 60 CG (14 male, 46 female) and 29 CC (7 male, 22 female) carriers. The genotype distribution was in Hardy–Weinberg equilibrium ($\chi^2 = 0.024, p = 1$). There were no gender differences between the genotype groups ($\chi^2 = 1.72, p = 0.42$).

**Money earned by the subjects**

The mean gain of the subjects in this experiment was €2.89 (S.D. = €1.15).

**RTs**

All trials of each subject with RTs differing by $> 2$ S.D. from the subject’s mean RT were defined as outliers and were rejected. By the same token, trials faster than 100 ms, which presumably do not represent valid reactions (Woodworth and Schlosberg, 1954), were removed (number of rejected trials per subject: mean = 3.56, S.D. = 1.13). Afterwards, RTs were averaged over all valid trials of one experimental condition (win, lose, verbal).

Altogether, subjects reacted faster when loss of money was indicated in contrast to the possibility of winning ($t = 4.61$, d.f. = 122, $p < 0.001$). Slowest RTs were obtained when only verbal feedback was given (win vs. verbal: $t = 4.30$, d.f. = 122, $p < 0.001$; lose vs. verbal: $t = 7.41$, d.f. = 122, $p < 0.001$) (see Figure 2). As described previously in the Statistical analyses section, mean scores were calculated for trials following both a loss and a gain for each participant, in order to obtain a possible effect of the outcome of the preceding trial on subsequent RTs. Mean RTs following a losing trial did not differ from mean RTs following a gain ($t = 0.25$, d.f. = 122, $p = 0.80$).

Gender was significantly related to RTs, with males reacting faster in the reward condition and showing smaller win–lose difference values (win: $F = 7.76, p = 0.006$; win–lose: $F = 6.94, p = 0.01$). In order to control for possible interactions, additional ANOVAs were carried out after all subsequent analyses with gender as a secondary independent variable.

**RTs and 5-HT1A**

ANOVA were carried out in order to assess the relationship between genotypes of the 5-HT1A C(-1019)G polymorphism and RTs and difference scores. We obtained no significant association on the genotype level (CC vs. CG vs. GG) but on the allele level [C + (CC and CG)] vs. C (GG)] (win: $F = 5.69$, d.f. = 1, 122, $p = 0.019$, $\eta^2 = 0.045$). Additionally, there was a significant relationship between the difference value win–lose (RTwin – RTlose) and the GG genotype, indicating that those subjects with the GG genotype tend to be slower in the win category compared to the lose category than subjects with at least one C allele ($F = 6.61$, d.f. = 1, 122, $p = 0.011$, $\eta^2 = 0.052$) (see Table 1). There were neither significant differences in RT means in the verbal and lose categories nor in other difference values. No interaction effects with gender could be obtained.

**5-HT1A and EDA**

Nine subjects did not show any EDA modulation during the experiment and, therefore, were identified...
as non-responders leading to their exclusion from all further analyses. For the remaining 114 subjects, an ANOVA was calculated in order to obtain electrodermal reactivity (EDR) differences between the three experimental conditions. There was a significant main effect of the experimental condition on EDA amplitudes ($F_{1, 113} = 66.62$, $p < 0.001$, $\eta^2 = 0.37$). Post-hoc tests revealed a significant difference between the reward and the verbal feedback condition ($p < 0.001$) and the punishment vs. the verbal feedback condition ($p < 0.001$). No differences between the reward and the punishment conditions in EDR could be determined (see Figure 3).

ANOVA$s$ were computed in order to test the association between EDR and the 5-HT$_{1A}$ polymorphism. Carriers of the GG genotype showed greater EDR in all three conditions compared to those of the CC or CG genotype (see Table 2 and Figure 3). Again, there were no differences on the genotype level. No interaction effects with gender could be determined.

### 5-HT$_{1A}$ and personality

No differences in personality traits obtained by means of self-report measures could be detected related to genotypes or alleles of the 5-HT$_{1A}$ polymorphism.

### RTs and EDR

ANOVA$s$ were computed in order to test the association between EDR and RTs. We computed difference scores (RTwin – RTlose) and defined two groups showing values $> 0$ [lose faster (78 subjects)] and $< 0$ [win faster (45 subjects)]. Subjects who reacted faster when they feared loss of money in contrast to the winning condition, showed greater EDR to all three experimental categories compared to subjects who reacted faster in the winning condition (see Table 3). No interaction effects with gender could be determined.
First, correlations were computed in order to assess the relationship between RTs and personality measures. A significant correlation was obtained between almost all assessed personality traits associated with negative emotionality (NEO-N, HA, HA1, HA2, HA4, BIS) and the difference value between RTs in the win and lose condition (see Table 4). Next, win–lose difference value 0-split group differences between personality traits were assessed via ANOVAs in order to test if persons who reacted faster in the reward condition differ significantly in personality from subjects who reacted faster in the punishment condition. In this analysis, a very similar pattern was obtained: subjects who reacted faster in the lose condition compared to the win condition showed greater values in nearly all traits related to negative emotionality (see Table 5). There were no associations between personality and simple RTs or other difference values.

Table 3. Difference score between the reward and the punishment conditions split at 0 (DSwin–lose 0-split) × electrodermal activity (EDA) amplitude ANOVA results

<table>
<thead>
<tr>
<th>DS win–lose 0-split Score</th>
<th>ANOVA</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (S.E.M.)</td>
<td>F</td>
</tr>
<tr>
<td>EDA verbal (µS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster RT</td>
<td>43</td>
<td>0.116 (0.018)</td>
<td></td>
</tr>
<tr>
<td>Lose faster RT</td>
<td>71</td>
<td>0.173 (0.014)</td>
<td></td>
</tr>
<tr>
<td>Win faster vs. lose faster</td>
<td>6.06</td>
<td>0.015</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F</td>
</tr>
<tr>
<td>EDA win (µS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster RT</td>
<td>43</td>
<td>0.167 (0.025)</td>
<td></td>
</tr>
<tr>
<td>Lose faster RT</td>
<td>71</td>
<td>0.254 (0.019)</td>
<td></td>
</tr>
<tr>
<td>Win faster vs. lose faster</td>
<td>7.56</td>
<td>0.007</td>
<td>0.063</td>
</tr>
<tr>
<td>EDA lose (µS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster RT</td>
<td>43</td>
<td>0.166 (0.026)</td>
<td></td>
</tr>
<tr>
<td>Lose faster RT</td>
<td>71</td>
<td>0.251 (0.020)</td>
<td></td>
</tr>
<tr>
<td>Win faster vs. lose faster</td>
<td>6.6</td>
<td>0.012</td>
<td>0.056</td>
</tr>
</tbody>
</table>

Table 4. Pearson correlations between win–lose difference scores (DSWL) and personality measures

<table>
<thead>
<tr>
<th>DSWL</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIS</td>
<td>0.284**</td>
<td>0.001</td>
</tr>
<tr>
<td>HA1</td>
<td>0.220*</td>
<td>0.015</td>
</tr>
<tr>
<td>HA2</td>
<td>0.264**</td>
<td>0.003</td>
</tr>
<tr>
<td>HA4</td>
<td>0.332**</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HA</td>
<td>0.298**</td>
<td>0.001</td>
</tr>
<tr>
<td>NEO-N</td>
<td>0.266**</td>
<td>0.003</td>
</tr>
</tbody>
</table>

EDA, Behavioural Inhibition System; HA 1–4, Harm Avoidance subscales; NEO-N, Neo Inventory – Neuroticism. *p<0.05, **p<0.01.

RT and personality

First, correlations were computed in order to assess the relationship between RTs and personality measures. A significant correlation was obtained between almost all assessed personality traits associated with negative emotionality (NEO-N, HA, HA1, HA2, HA4, BIS) and the difference value between RTs in the win and lose condition (see Table 4). Next, win–lose difference value 0-split group differences between personality traits were assessed via ANOVAs in order to test if persons who reacted faster in the reward condition differ significantly in personality from subjects who reacted faster in the punishment condition. In this analysis, a very similar pattern was obtained: subjects who reacted faster in the lose condition compared to the win condition showed greater values in nearly all traits related to negative emotionality (see Table 5). There were no associations between personality and simple RTs or other difference values.

Personality was significantly related to gender, with females exhibiting higher scores in BIS (F=7.09, p = 0.009), HA2 (F=10.89, p = 0.001), HA4 (F=15.44, p < 0.000) and HA (F=10.86, p = 0.001), which is in line with earlier findings relating gender especially to traits of negative emotionality (Jorm, 1987). However, no interaction effect of gender and RT on personality could be obtained.

EDA and personality

No correlations between SCR amplitudes and personality measures were detected.

Discussion

The present study investigated the relationship between the 5-HT1A C(-1019)G polymorphism and RTs in a reward/punishment paradigm. Furthermore, EDA was assessed during the anticipation of reward or punishment and different personality measures were used. The GG genotype of the 5-HT1A polymorphism was associated with slower RTs in the winning condition compared to the losing condition, and with an absolute slower RT when subjects were able to win money. No differences in RT could be obtained in any other condition.

These findings indicate that subjects carrying the GG genotype are not generally slower, but tend be more sensitive to the losing condition compared to the winning condition. These subjects are also characterized by higher scores in personality measures related to negative emotionality (BIS, HA and N). Therefore, a possible explanation for this RT pattern might be a general, pessimistic view of their winning chances. Subjects with high scores on Neuroticism and Harm Avoidance probably show less effort in a reward condition due to general anticipatory failure or specific attribution style.

Although the above-mentioned RT pattern is related to the GG genotype of the 5-HT1A polymorphism and to traits of negative emotionality, no association could be found between this genetic marker and any personality trait depicted from self-report measures. Former studies indicate a possible link between the
G allele of this polymorphism and Neuroticism and Harm Avoidance (Strobel et al., 2003). But our sample was presumably too small to provide sufficient statistical power. At any rate, the 5-HT1A polymorphism seems to be related to behaviour in an experimental reward/punishment paradigm, which in turn is associated with traits of negative emotionality. Future studies with sufficient sample sizes are required to clarify this relationship.

Furthermore, subjects with the GG genotype exhibit higher EDA amplitudes when anticipating either reward or punishment or a verbal feedback. Interestingly, this form of hyper-reactivity occurs in all experimental conditions. Thus, the 5-HT1A C(-1019)G polymorphism seems to be associated with generally higher autonomous arousal, regardless of whether reward or punishment or a verbal feedback is anticipated. Although these results seem to contradict our findings of the association between the GG genotype and differences in punishment and reward sensitivity, they are consistent with considerations that serotonin might be involved not only in the wide range of negative emotionality but might instead be a general modulator of behaviour including positive emotionality (Depue and Spoont, 1986). Lower serotonergic functioning, which has been speculated to be a consequence of carrying the GG genotype (Lemonde et al., 2003), may result in a disinhibition of noradrenergic activity, which in turn induces elevated autonomic arousal (Azmita and Whitaker-Azmita, 1997). Although only verbal feedback was given in one experimental condition, no clear neutral condition was employed, because verbal feedback includes an evaluation of task performance and might, therefore, not be emotionally neutral. Subsequent studies with similar paradigms and a condition without any feedback might be able to determine whether EDR is, in general, heightened in carriers of the GG genotype or only during anticipation of emotionally relevant stimuli. Previous studies suggest an association between electrodermal hyporeactivity and lower anxiety and neuroticism scores (Fowles, 2000), which could not be confirmed in the present study. Nevertheless, electrodermal hyper-reactivity is related to the reported RT pattern which, in turn, is associated with traits of negative emotionality.

Overall, a quite homogenous pattern emerges: subjects carrying the GG genotype show higher physiological arousal as measured by EDR and slower RTs in a reward condition compared to a punishment condition – a RT pattern which relates to negative emotionality. Carriers of the GG genotype exhibit enhanced negative feedback due to a higher density of 5-HT1A autoreceptors, resulting in a lower serotonergic activation (Lemonde et al., 2003). This form of enhanced negative feedback may predispose to higher negative emotionality, anxiety disorders and depression as already indicated by several studies (Freitag et al., 2006; Lemonde et al., 2003; Rothe et al., 2004). Furthermore, this study confirms the consideration that it appears worthwhile to study the association between behavioural and physiological data and genetic polymorphisms, because these variables seem to be strongly related to the biological basis of personality and psychopathology.

Table 5. Difference score between the reward and the punishment conditions split at 0 (DS win–lose 0-split) × personality ANOVA results

<table>
<thead>
<tr>
<th>DS win–lose 0-split</th>
<th>Score</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean (S.E.M.)</td>
</tr>
<tr>
<td>BIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster</td>
<td>45</td>
<td>19.844 (0.509)</td>
</tr>
<tr>
<td>Lose faster</td>
<td>78</td>
<td>21.718 (0.386)</td>
</tr>
<tr>
<td>Win faster vs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lose faster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HA1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster</td>
<td>44</td>
<td>3.773 (0.410)</td>
</tr>
<tr>
<td>Lose faster</td>
<td>78</td>
<td>4.833 (0.308)</td>
</tr>
<tr>
<td>Win faster vs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lose faster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HA2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster</td>
<td>44</td>
<td>3.818 (0.270)</td>
</tr>
<tr>
<td>Lose faster</td>
<td>78</td>
<td>4.949 (0.203)</td>
</tr>
<tr>
<td>Win faster vs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lose faster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HA4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Win faster</td>
<td>44</td>
<td>2.864 (0.329)</td>
</tr>
<tr>
<td>Lose faster</td>
<td>78</td>
<td>4.551 (0.247)</td>
</tr>
<tr>
<td>Win faster vs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lose faster</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| BIS, Behavioural Inhibition System; HA 1–4, Harm Avoidance subscales.
size might still be too small to detect an effect of the 5-HT_{1A} C(-1019)G polymorphism on personality traits measured via self-report. Second, the applied paradigm lacked a clear neutral condition, which might have provided further clarification of the association between the investigated genetic variation, RTs and EDR. Furthermore, it should be considered that the participants were performing a motor task, which might contribute additionally to the electrodermal response. Nevertheless, this effect should add equally to all experimental conditions and is, therefore, unrelated to differential effects.

In summary, these results corroborate the importance of the 5-HT_{1A} receptor in general, and the 5-HT_{1A} C(-1019)G polymorphism in particular for the impact of the serotonergic system on behaviour and physiological arousal which are associated to anxiety- and depression-related personality traits.

Acknowledgements

None.

Statement of Interest

None.

References


Costa PT, McCrae RR (1992). Revised NEO Personality Inventory and NEO Five-Factor Inventory. Odessa, Psychological Assessment Resources.


Hong CJ, Chen TJ, Yu YWY, Tsai SJ (2006). Response to fluoxetine and serotonin 1A receptor (C-1019G) polymorphism in Taiwan Chinese major depressive disorder. Pharmacogenomics Journal 6, 27–33.


