Divergent effects of increased serotonergic activity on psychophysiological parameters of human attention

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Abstract
Selective serotonin reuptake inhibitors (SSRIs) are frequently combined to the antipsychotic medication of schizophrenia patients, to treat their depressed, cognitive or negative symptoms. No convincing neurochemical theory exists for this combination. The role of serotonin in those psychophysiological parameters of attention that are already found to be disturbed in schizophrenia, e.g. processing negativity (PN), mismatch negativity (MMN) and P300 amplitude, is poorly understood. In the present study the effects of increased serotonergic activity on these psychophysiological parameters is investigated. In a balanced, double-blind, placebo-controlled, cross-over experiment 18 healthy male volunteers received an oral dose of either placebo or of 10 mg escitalopram (a highly specific SSRI) on two separate test days, after which they were tested in an auditory selective attention paradigm and a MMN paradigm. Escitalopram significantly increased PN and MMN compared to placebo, without affecting the P300 amplitude. Furthermore, administration of escitalopram resulted in a small, yet significant, reduction of task performance in the selective attention paradigm compared to placebo, while it did not affect reaction time. Contrary to what was expected, escitalopram enhanced PN and MMN, without affecting the P300 amplitude. The results are discussed in the light of dosage issues and subtypes of serotonergic receptors.

Introduction
Selective serotonin reuptake inhibitors (SSRIs) are frequently combined to the antipsychotic medication of schizophrenia patients, to treat their depressed, cognitive or negative symptoms. No convincing neurochemical theory does, however, exist for this combination, or for a possible positive effect of increased serotonin activity on information processing; on the contrary, increased central serotonergic transmission is believed in part to be responsible for the psychotomimetic effects of hallucinogens and numerous preclinical studies have demonstrated disruption of information processing by serotonin agonists whereas serotonin 5-HT\textsubscript{2A} receptor antagonists reverse such disturbances (Geyer et al., 2001). Given this possible relationship between serotonergic activity and information processing, it is important to investigate what influence SSRIs themselves have on cognition, especially on those parameters of attention that are already found to be disturbed in patients with schizophrenia such as prepulse inhibition of the startle response (PPI), processing negativity (PN), mismatch negativity (MMN) and the P300 amplitude. In a previous study from our laboratory, the influence of serotonergic activity on human PPI was investigated (Jensen et al., 2007). In the present study the relation between serotonergic activity and PN, MMN and the P300 amplitude was explored.

PN is a negative deflection which appears in the electroencephalogram (EEG) above the frontal areas of the brain, whenever healthy subjects are asked to selectively attend to stimuli defined by certain features, while ignoring others (e.g. focusing on a male voice, while ignoring a simultaneously speaking
female voice, or focusing on stimuli presented in the left ear, while ignoring simultaneously presented stimuli in the right ear). It is believed that PN reflects a cerebral matching process, by which the brain selects relevant stimuli from irrelevant stimuli for further processing (Näätänen, 1990). Currently, only one study has explored the role of serotonin in PN in healthy volunteers, in which no effects of acute depletion of tryptophan (which decreases brain serotonin synthesis) were found (Ahveninen et al., 2003). There are neither reports in the literature on effects of serotonergic agonists on PN, nor on correlations between PN and cognitive measures.

A P300 amplitude is elicited by infrequent stimuli (deviants) appearing in a sequence of frequent stimuli (standards). Maximum P300 amplitude is commonly found when the subject is requested to respond to these deviant stimuli, e.g. by pressing a button. The P300 amplitude is proportional to the amount of attentional resources that is employed in a given task (Grillon et al., 1991; Kramer and Strayer, 1988; Sutton et al., 1965; for reviews see Braff and Light, 2004; Polich and Kok, 1995). Moreover, there is evidence that the P300 amplitude is modulated by the vigilance (arousal) of a subject (for a review see Muller et al., 2001). In addition, attention-demanding conditions increase P300 amplitudes (Coull, 1998). On a cognitive level, the P300 is assumed to index online updating of attentional resources that is employed in a given task (Coull, 1998). An increase in MMN amplitude (Kahkonen et al., 2005). In a follow-up study of this same group it resulted in an increase in MMN amplitude (Kahkonen et al., 2005). In a third study, psilocybin (amongst others a 5-HT2A agonist) showed no effects on MMN amplitude of healthy volunteers (Umbricht et al., 2003).

In the present study, the effect of increased serotonergic activity on P300 amplitude as well as PN and MMN of healthy volunteers was further explored. Serotonergic activity was raised by a single, oral dose of 10 mg escitalopram. Escitalopram is the S-enantiomer of citalopram, which is believed to be the only pharmacologically active enantiomer of racemic citalopram (Hiemke and Hartter, 2000). Escitalopram is a highly potent and selective reuptake blocker of serotonin (SSRI), without affecting other major neurotransmitter systems that might be involved in the psychophysiological parameters of attention that are investigated in the present study, such as the dopaminergic and noradrenergic systems (Goodman-Gilman et al., 2001). Acute escitalopram challenge (10 mg and 20 mg) has been found to block the serotonin reuptake transporter (SERT) in the midbrain of humans similar to other clinically active SSRIs (Klein et al., 2005, 2006). Since MMN, PN and P300 amplitude are reduced in schizophrenia, and serotonergic activity is generally assumed to be increased in this disease, it was expected that escitalopram would reduce these psychophysiological parameters of attention in
healthy volunteers. In order to monitor the physiological effects of escitalopram, serum cortisol level was assessed, since citalopram is known to increase the level of cortisol (Bhagwagar et al., 2002). Blood pressure was monitored since orthostatic hypotension is one of the listed side-effects of escitalopram.

Methods

Subjects

Healthy male volunteers were recruited through university newspaper advertisements. The inclusion criteria were: physically healthy males, no prescription drugs, body mass index (BMI) between 19 and 25, no alcohol or other abuse drugs, no personal or (first-degree) DSM-IV family history of psychiatric illness. The study was approved by the Committee for Biomedical Research Ethics, Copenhagen, with respect to the statements for human research from Helsinki (Amendment of Edinburgh, 2000). Following both written and oral information, written informed consent was obtained from all subjects before enrolment in the study. Subsequently, subjects were interviewed with the Schedule for Clinical Assessment in Neuro-psychiatry, version 2.1 (SCAN; Wing et al., 1990), to ascertain absence of psychiatric illnesses. Subjects also underwent physical examination (including an electrocardiogram and a urine toxicology screen for drugs of abuse). In addition, volunteers were screened for hearing deficits at 500, 1000 and 6000 Hz. Subjects who could not detect tones at 40 dB were not included. Twenty-one subjects proceeded to the active phase of the study, of which two had to be excluded because they became severely nauseated. Due to hardware failure, the assessment of one treatment of a subject was lost, resulting in the entire removal of the subject’s data from the analysis. The remainder of the subjects (n = 18) had a mean age of 25.2 yr (s.d. = 2.5), a mean Quetelet (BMI) index of 23.3 (s.d. = 1.2) and all were right-handed.

Experimental design

In a randomized, double blind, placebo-controlled cross-over experiment subjects received a white, opaque gelatin capsule containing either escitalopram (Cipralex®, 10 mg) or placebo (calcium tablets) on two separate occasions, a minimum of at least 1 wk apart. Psychophysiological (PPI, P50 suppression, selective attention, MMN), neuroendocrine (cortisol), biochemical (serum escitalopram levels) and physiological (blood pressure and heart rate) measures were collected over a 4.5-h period during each session. The order of the tests in both treatment sessions was such that subjects always started with the hearing test (5 min) followed by either the PPI (25 min) or P50 suppression (21 min) paradigm (the order of which was balanced over the subjects, yet for each subject the same for both treatment sessions), which was followed by the selective attention (13 min) paradigm, and finally the MMN (12 min) paradigm. In order to keep the current report comprehensive, the results of the PPI and P50 suppression paradigms will be reported elsewhere.

Subjects arrived at the research ward of the Department of Psychiatry, Bispebjerg University Hospital at 08:15 hours, having fasted since 23:00 hours the previous day. At 08:45 hours, following initial (baseline) blood sampling and physiological assessments, a capsule containing either 10 mg escitalopram or placebo was administered. At 11:00 hours the subjects were prepared for psychophysiological assessments, i.e. attachment of electrocap and facial electrodes (see Signal recording section below).

The psychophysiological test battery was initiated at the expected time of T_{max} for plasma level of escitalopram, i.e. 210 min after oral administration of the capsules (Gutierrez and Abramowitz, 2000). Serum cortisol and serum escitalopram were measured at baseline (prior to administration of the capsule) and at 210 min and 285 min after oral administration of medication, which coincided with the start and end of the psychophysiological test battery. Blood pressure was measured four times during each test day (at 0, 30, 210 and 285 min following administration of the capsule). In addition, two questionnaires were administered to assess for potential adverse effects due to treatment, the Adverse Symptom Checklist (ASC) and the Adverse Event Record (AER). Blood samples were drawn at baseline (prior to administration of the capsule), and at 210 min and 285 min after oral administration of medication (coinciding with the start and end of the psychophysiological test battery). For cortisol sampling 5 ml blood was taken in a gelatin-containing sample glass, for escitalopram sampling 10 ml blood was taken in a heparinized sample glass, which was kept at 5 °C until the test day was complete after which they were centrifuged at 163 g for 10 min and stored at −20 °C until analysis.

Paradigms

Stimulus presentation

All auditory stimuli were presented by a computer running Presentation® (Neurobehavioral Systems
Inc., Albany, CA, USA) software (soundcard: Creative soundblaster® 1, 5.1) and presented binaurally through stereo insert earphones (Eartone ABR, C and H Distributors Inc., Milwaukee, WI, USA). The software and hardware settings were calibrated by means of an artificial ear (Brüel and Kjær, type 2133; Brüel and Kjaer, Naerum, Denmark) in order to ensure that the stimulus intensities at the subject’s ears were the intended intensities.

Selective attention

The selective attention paradigm consisted of 400 stimuli that were presented in a semi-random fashion (equally distributed) to the subject’s right and left ear. Two types of stimuli were presented: standard tones, which appeared in 80% of the cases, and deviant tones, which appeared in the resulting 20% of the cases (attended deviants were never presented immediately following each other). Subjects were required to push a button as quickly as possible if the deviant tone was perceived in the previously designated ear. Following this initial task, the subjects were presented an identically designed task, in which they had to monitor the other ear for deviant stimuli. Tone frequency was used as the attribute to define stimulus type: standard tones were 1000 Hz, deviant tones 1200 Hz. Duration and intensity of both stimuli were 50 ms and 75 dB respectively, while the interstimulus intervals (ISIs) were randomized between 700 and 900 ms. During the task, the subjects had to maintain their gaze at a fixed cross, situated at eye level on the opposite wall from which they were seated. Task performance was assessed by means of the number of hits and false alarms, as well as the mean reaction time to hits. Responses to target stimuli were classified as a hit if they occurred within 200–900 ms following presentation of the target stimulus. A miss was designated as a target not followed by a response, and a false alarm was a response to a non-target stimulus. Reaction time was measured as the latency of the response from the onset of the target.

MMN

In the MMN paradigm, stimuli were presented binaurally, and consisted of two types: 1000 Hz standard stimuli, presented with a probability of 90% and 1200 Hz deviant stimuli, presented with a probability of 10%. Intensity of all stimuli was 75 dB and they were 50 ms in length. A total of 1750 stimuli were presented, with an ISI randomized between 300 ms and 500 ms. Subjects were requested to ignore all stimuli.

Signal recording

EEG recordings were made with BioSemi® hardware (BioSemi, Amsterdam, The Netherlands) using a cap containing 64 Active Two electrodes (Metting van Rijn et al., 1996), arranged according to the 10–20 system. However, only data from the electrodes relevant for the present study were analysed [i.e. where the maximum activity for the investigated event-related potentials (ERPs) was to be expected]: the midline electrodes Fz and Pz. The left mastoid was used as a reference. A horizontal electro-oculogram (EOG) was recorded using Active Two electrodes placed to the outer canthus of each eye. Similarly, vertical EOG was recorded from electrodes placed infra-orbital and supra-orbital to the left eye. The right eye was used to record electromyography (EMG, startle reflex) of the orbiculus oculi. Sampling started as soon as an experimental block started, and lasted until the end of it (continuous recording). All signals were digitized online by a computer, at a rate of 4 kHz.

Signal analysis

EEG data from both the selective attention paradigm and MMN paradigm were analysed using BESA software (MEGIS Software GmbH, Gräfelfing, Germany). First, the data were resampled from the original 4 kHz to 250 Hz, to allow easier file handling. Second, the data were corrected for eye artifacts by using the adaptive method of BESA, as described by Ille et al. (2002). Third, the data were epoched (from 100 prestimulus to 900 post-stimulus) and corrected for movement (or other unrelated paradigm) artifacts, by removing those epochs from the database that contained amplitudes above or below 100 µV. In the case of the selective attention paradigm, the data were filtered (low-pass set to 40 Hz, 24 dB), collapsed over both ears, and averaged in the case of the P300 amplitude data. The individual processing-negativity difference waves were expressed as the average ERP of the subject to the attended standard stimuli, subtracted with the average ERP of this subject to the unattended standard stimuli. Similar to the data of the selective attention paradigm, the data of the MMN paradigm were filtered (low-pass set to 40 Hz, 24 dB), while the MMN was expressed as the average ERP of a subject to the deviant stimuli, subtracted with the average ERP of this subject to the standard stimuli. Finally, maximum P300 amplitude was scored at electrode PZ, separately for the four different stimuli [attended deviant (target), non-attended deviant, attended standard, non-attended standard], within a window between 250 and 500 post-stimulus;
maximum MMN and PN were scored at electrode Fz within windows between 50 ms and 200 ms and between 150 ms and 350 ms, respectively.

**Statistical analysis**

The P300 amplitudes were analysed by means of repeated-measures MANOVA (within-subject design), with factors ‘treatment’ (placebo or escitalopram), ‘attention’ (attended or unattended stimulus) and ‘stimulus type’ (standard or deviant). Similarly, a repeated-measures ANOVA with the factor ‘treatment’ (placebo or escitalopram) was used to analyse the data regarding the PN and MMN. Following pooling of the data over the left and right ears, task performance in the two treatments was analysed with paired-samples Student’s t tests for hits, false alarms and reaction time. To test whether the level of escitalopram was constant during the psychophysiological assessments, the two serum escitalopram levels from just before and after the start of the test battery were compared to each other with a paired-samples Student’s t test. Similarly, to test whether escitalopram affected cortisol level, the serum cortisol levels of the same two samples (just before and after the test battery) were compared between placebo and escitalopram treatment. Finally, blood pressure was analysed with an ANOVA with the factors ‘treatment’ and ‘time’ (expressed as a difference from zero), indicating enhanced processing activity of stimuli in the attended ear. In addition, a treatment main effect was found [F(1, 17) =6.07, p < 0.05], indicating an increased processing-negativity amplitude in the escitalopram session, compared to the placebo session (Figures 1a, 2, Table 2).

**Results**

**Biochemical, endocrinological and physiological measures**

Serum escitalopram level showed a sharp increase from baseline to T = 3.5 h, but was stable at 19.7 nmol/l (mean level) between times T = 3.5 h and T = 4.6 h, which was the time period in which the psychophysiological assessments took place.

Baseline (T = 0) serum levels of cortisol did not differ over the two treatments. Paired-samples Student’s t tests revealed a significant increased cortisol level at T = 3.5 h, following administration of escitalopram when compared to placebo (t = 2.69, p < 0.05). No further effects of treatment on serum cortisol level were found.

Analysis of systolic and diastolic blood pressure, revealed neither an effect of treatment nor of time.

**Performance**

A small, yet significant, decrease in the number of hits was found in the escitalopram treatment, when compared to the placebo treatment (t = 2.17, p < 0.05). Similarly, a small, but significant, increase in the number of false alarms was found in the escitalopram treatment, when compared to the placebo treatment (t = 2.17, p < 0.05). No effect of treatment was found on reaction time. Group means are presented in Table 1.

**ERP data**

**P300**

An attention main effect [F(1, 17) = 31.17, p < 0.001], a stimulus type main effect [F(1, 17) = 51.21, p < 0.001], and an attention × stimulus type interaction effect [F(1, 17) = 30.77, p < 0.001] were found. These effects indicated a higher P300 amplitude to attended stimuli than to non-attended stimuli, and a higher amplitude to deviant stimuli than to standard stimuli. No effect of treatment on P300 amplitude was found (Table 2). The distribution of the P300 amplitude shows a large P3b activity (parietal) and a smaller P3a activity (fronto-central) in the case of the attended deviant stimuli, in contrast to the P300 distribution of the non-attended deviant stimuli, in which this is the other way round (Figure 1a).

**PN**

PN was found [F(1, 17) = 109.91, p < 0.001], irrespective of treatment (expressed as a difference from zero), indicating enhanced processing activity of stimuli in the attended ear. In addition, a treatment main effect was found [F(1, 17) = 5.82, p < 0.05], indicating an increased processing-negativity amplitude in the escitalopram session, compared to the placebo session (Figures 1b, 2, Table 2).

**MMN**

Similar to PN, MMN was found [F(1, 17) = 145.95, p < 0.001], irrespective of treatment (expressed as a difference from zero), indicating enhanced processing of deviant compared to standard stimuli. In addition, a treatment main effect was found [F(1, 17) = 5.82,

### Table 1. Mean performance data of each treatment (s.e.m. in parentheses)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hits (n)</th>
<th>False alarms (n)</th>
<th>Reaction time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>39.8 (0.07)</td>
<td>0.41 (0.09)</td>
<td>407 (13.5)</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>39.5 (0.11)*</td>
<td>0.68 (0.15)*</td>
<td>406 (14.3)</td>
</tr>
</tbody>
</table>

* Significantly different from placebo (p < 0.05).
p < 0.05], indicating a higher MMN amplitude in the escitalopram session than in the placebo session (Figure 3, Table 2). The distribution of the P300 amplitude to deviant stimuli in the MMN paradigm shows a clear fronto-central distribution, indicative of P3a activity (Figure 1c).

Discussion

To our knowledge, this is the first human study in which the effects of the antidepressant escitalopram on psychophysiological parameters of selective attention were investigated in healthy volunteers. Escitalopram was found to increase both PN and MMN, while having no effect on P300 amplitude. Furthermore, escitalopram reduced task performance – slightly, yet significantly – while it did not affect reaction time.

The implication of the serotonergic system in the generation and/or modulation of PN has not been well documented. To our knowledge, only one study reports on this subject, in which no effects of reduced serotonergic activity on PN were found (Ahveninen et al., 2003), while no studies are available on the effects of increased serotonergic activity on PN in healthy volunteers. Furthermore, no literature is available on the effects of antipsychotics on the PN of patients with schizophrenia, although circumstantial evidence points towards no effect of antipsychotic...
treatment on PN, PN is reduced in patients with (Baribeau-Braun et al., 1983; Iwanami et al., 1998) or without (Michie et al., 1990; Ward et al., 1991) medication. The seeming contradiction that PN was enhanced in the present study by administration of escitalopram to healthy volunteers (which increases serotonergic activity), while it is reduced in patients with schizophrenia (in whom serotonergic activity is supposed to be increased), might be explained by a difference in the subtypes of 5-HT receptors that are addressed with escitalopram and those that are involved in schizophrenia. In schizophrenia the evidence points towards a predominant involvement of the 5-HT$_{2A}$ receptor, although other 5-HT receptor subsystems seem to be implicated as well (for reviews see Lieberman et al., 1998; Meltzer et al., 2003). Escitalopram on the other hand, blocks the serotonin transporter, and therefore increases serotonergic

Figure 2. Grand average difference waves for processing negativity (PN) specified for both pharmacological treatments; the inset shows the individual PN amplitudes. * Significantly increased PN in the escitalopram treatment (–––), compared to the placebo treatment (–––) ($p<0.05$).

Figure 3. Grand average difference waves for mismatch negativity (MMN) specified for both pharmacological treatments, displaying a significantly increased MMN in the escitalopram treatment (–––), compared to the placebo treatment (–––) ($p<0.05$); the inset shows the individual MMN amplitudes.
activity throughout the entire brain, regardless of receptor subtype. If different subtypes of the 5-HT receptor would have different (opposing) effects on PN, this would mean that potential serotonergic effects might have been masked in the present study. To verify this, agonists of certain serotonergic receptor subtypes should be investigated. Alternatively, or perhaps in addition to this line of thought, the relationship between (subtypes of) serotonergic activity and PN might be represented by an inverted U shape, with below-maximum serotonergic activity in healthy subjects under normal circumstances. If this were indeed true, the increase in serotonergic activity by escitalopram in the present study could have shifted the curve towards maximum, resulting in enhanced PN, while in schizophrenia the serotonergic activity could be even higher, pushing the PN over the maximum towards lower amplitudes. A simple way to test this latter hypothesis would be to increase the currently administered dose (10 mg) of escitalopram to push the PN towards more sub-maximum levels.

Similar to PN, MMN was significantly increased following administration of escitalopram. Naturally, the same lines of thought as mentioned above could apply for MMN: more than one subtype of the serotonergic receptor could be involved in the modulation of MMN with opposing effects, and/or the relationship between serotonin and MMN might be represented by an inverted U shape. From previous reports in literature, evidence for a serotonergic modulation of MMN is rather inconclusive: while in an initial study tryptophan depletion resulted in reduction of MMN in healthy volunteers (Ahveninen et al., 2002), it resulted in an increase in MMN in a follow-up study of this same research group (Kahkonen et al., 2005), probably due to methodological differences in the MMN paradigm, as correctly stated by the authors themselves. In a third study, psilocybin (amongst others a 5-HT2A agonist) showed no effects on MMN of healthy volunteers (Umbricht et al., 2003; for a review on other neurotransmitter systems which might be involved in MMN see Umbricht and Kruljes, 2005). Atypical antipsychotics (relatively potent 5-HT2A antagonists) seem to have no effect on the reduced MMN of patients with schizophrenia, this includes clozapine (Schall et al., 1998, 1999; Umbricht et al., 1998) and risperidone (Umbricht et al., 1999). Taking all this into account, the fact that escitalopram raised MMN amplitude in the present study supports the concept that increased serotonergic activity augments MMN, although probably not by means of the 5-HT2A receptor subtype. An alternative interpretation of the current data might be that MMN was enhanced by an interaction between the serotonergic and glutamatergic transmitter systems, since there is evidence that N-methyl-D-aspartic acid (NMDA) receptors are involved in MMN (Javitt et al., 1996; Umbricht et al., 2000).

In contrast to MMN and PN, literature on biochemical modulation of the P300 amplitude in healthy volunteers is abundant, although only a few studies report on serotonergic effects. Hansenne et al. (1998) reported a negative correlation between serotonergic activity and the P300 amplitude in healthy volunteers. Also clomipramine (a tricyclic antidepressant; TCA) and fluoxetine (a SSRI) were found to decrease P300 amplitude, while tianeptine (a serotonin reuptake enhancer) showed no effect (Liogier d’Ardhuy et al., 1999) following a single administration to healthy volunteers. In addition, venlafaxine (a combined serotonin, noradrenaline and dopamine reuptake inhibitor) and buspirone (a 5-HT1A and dopamine agonist) do not seem to affect P300 amplitude in healthy volunteers (Semlitsch et al., 1993; Unrug et al., 1997). The data of the present study do not support a reduction in P300 amplitude as a result of increased serotonergic activity, in spite of the fact that the highly specific SSRI escitalopram was used. Again, the current data may be explained by assuming that subtypes of the serotonin receptors have different, maybe even opposing, effects on the P300 amplitude, or alternatively, that the currently administered dose of escitalopram was simply too low. Currently, there is limited literature available on the effects of specific subtypes of the serotonergic receptor on the P300 amplitude in healthy volunteers. The few reports available, seem to focus on the 5-HT1 receptor subtypes: the 5-HT1A agonists flesinoxan (Hansenne et al., 1998) and buspirone (Unrug et al., 1997) seem to reduce P300 amplitude, which is also the case for zolmitriptan, a 5-HT1B/1D agonist (Hughes et al., 1999). Assuming that 5-HT1 receptor agonists in general do indeed reduce P300 amplitude, and given the negative results of the present study with escitalopram, it seems likely that additional serotonergic subtype receptors are involved in modulation of the P300 amplitude. If these additional receptor subtypes have a more beneficial effect on the P300 amplitude than the 5-HT1 receptor subtypes, than treatment with escitalopram (which has no specificity for serotonergic subtype receptors) would have activated all subtypes at the same time, thereby cancelling out each others’ effects.

The distribution of the P300 amplitude in the selective attention paradigm shows a large P3b activity and a small P3a activity in the case of the attended deviant stimuli, in contrast to the P300 distribution of
Besides PN, MMN and P300 amplitude also PPI, usually found to be distorted in schizophrenia. Physiological parameters of cognition, which are no effects at all on the currently investigated psychophysiological parameters that were investigated in the present study might also be affected in some patients suffering from other psychiatric illnesses, e.g. depression or obsessive–compulsive disorder (although it seems that the stability of the deficits over time as well as their combined presence is only characteristic of schizophrenia). Also these patients might benefit from treatment with highly specific SSRIs.

In summary, the present study shows that a low dose of escitalopram (10 mg) increases MMN and PN in healthy volunteers, while showing no effects on P300 amplitude. Since escitalopram is highly selective for the serotonergic system, but not selective for a specific subtype serotonergic receptor, this indicates that a non-specific increase in serotonergic activity increases both MMN and PN. Future research should focus on either higher dosages of escitalopram, or more to specific subtypes of the serotonin receptor targeting agonists in healthy volunteers. In addition, chronic effects of escitalopram on parameters of cognition should be studied in clinically relevant populations.

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Statement of Interest

None.

References


