Neurophysiological mechanisms of auditory information processing in adolescence: a study on sex differences

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Abstract

To date, little is known about sex differences in the neurophysiological correlates underlying auditory information processing. In the present study, auditory evoked potentials were evoked in typically developing male (n=15) and female (n=14) adolescents (13-18 years) during an auditory oddball task. Girls compared to boys displayed lower N100 and P300 amplitudes to targets. Larger N100 amplitudes in adolescent boys might indicate higher neural sensitivity to changes of incoming auditory information. The P300 findings point towards sex differences in auditory working memory and might suggest that adolescent boys might allocate more attentional resources when processing relevant auditory stimuli than adolescent girls.
Introduction

The ability to distinguish between relevant and irrelevant stimuli of the environment and to detect significant changes of incoming information is important for effective information processing and adaptive behaviour. This cognitive ability has been subjected to extensive research, which focused, among others, on the auditory domain of sensory processing and its underlying neural mechanisms. Although the distinction between relevant and irrelevant auditory stimuli is a basic mechanism, there is evidence that individuals show considerable individual differences in this skill. For example, there is evidence that men and women process task-relevant and task-irrelevant auditory stimuli in different ways (Jaworska et al., 2013). An often applied approach to study the neural mechanisms of auditory information processing are auditory evoked potential (AEP) studies using the auditory oddball task. In the standard two-tone auditory oddball task, participants have to respond to an infrequent (deviant) target tone presented in the background of frequent non-target (standard) tones. This task requires the differentiation of relevant and non-relevant stimuli and a selective response to the target stimulus (Polich, 2007).

The AEPs elicited during auditory information processing can roughly be related to exogenous (highly stimulus-dependent) or endogenous (cognitive) processes. Exogenous AEPs, including the N100 and P200, depend largely on stimulus properties like pitch, length and frequency, and indicate early stimulus differentiation processes. The N100 is considered to reflect early extraction of information during stimulus perception (Näätänen & Picton, 1987) and the P200 is likely to be related to the automatic inhibition of irrelevant sensory information (Johnstone, Barry, & Anderson, 2001). The later components N200 and P300 reflect mostly endogenous processes which require voluntary attention (Johnstone, Barry, Anderson, & Coyle, 1996; Polich, 1986, 2007) and rely on corticothalamo-limbic feedback (Rennie, Robinson, & Wright, 2002). The N200 component is related to response selection...
processes (Barry, Johnstone, & Clarke, 2003) whereas the P300 (also called P3 or P3b) reflects working memory processes, like the allocation of processing resources to the relevant tone or the revision of the mental stimulus representation (Polich, 2007).

These AEPs show strong sex differences. A number of electrophysiological studies that have applied the auditory oddball paradigm in adults to examine sex differences in auditory information processing reported higher P300 amplitudes to targets in females compared to males (e.g., Hoffman & Polich, 1999; Jaworska et al., 2013). Given that P300 generation is related to the inter-hemispheric transmission of auditory information, it has been tentatively suggested that this sex difference might be attributed to the fact that females have a larger corpus callosum than males (Jaworska et al., 2013). However, findings on sex differences in the target-related P300 in auditory oddball tasks are not consistent, as one study failed to find an effect of sex on the P300 (Polich, 1986). Differences between the results of these studies might be drawn back to methodological issues, including electroencephalogram (EEG) recording and sample characteristics. Findings on other AEP components elicited during oddball tasks are also equivocal. For example, one study found reduced P200 and increased N200 peak amplitudes in males compared to females (Nagy, Potts, & Loveland, 2003), which was interpreted as an attentional bias toward novelty in males. However, another study using single stimulus and oddball tasks reported smaller amplitudes in males both in the P200 and the N200 component compared to females (Hoffman & Polich, 1999).

In contrast to the fair amount of investigations on sex differences in adults on auditory information processing, there is a scarcity of studies which examined sex differences in this field of research in adolescents. However, there are considerable difficulties transferring findings from the adult population on auditory information processing to adolescent samples: Between the age of approximately 13 and 18 years, huge reorganisations occur in the auditory system due to the effect of gonadal hormones (Fuchigami et al., 1993; Sisk & Zehr, 2005). These neural changes are highly sex-specific (Sisk & Zehr, 2005), and result in particularly
pronounced sex differences in information processing during adolescence (Brumback, Arbel, Donchin, & Goldman, 2012; Rubia, Hyde, Halari, Giampietro, & Smith, 2010).

The most extensive AEP study on sex differences in auditory information processing in adolescents was conducted by Sumich et al. (2012). This study applied a two-stimulus oddball paradigm in different age groups of boys and girls (early childhood: 6-8 years; late childhood: 9-11 years; early adolescence: 12-14 years; and late adolescence: 15-17 years) and examined the endogenous AEPs N200 and P300. They found higher P300 amplitudes in boys than in girls during childhood and early adolescence. However, this difference was equated by late adolescence due to greater developmental effects on the P300 amplitudes in adolescent girls: Anterior P300 amplitudes generally increased with age in the group of girls, whereas this development was restricted to right frontal sites in boys. Based on their results, the authors assumed a sex based cognitive cross-over effect in the way that girls exhibit greater developmental changes in attentional control and working memory than boys during adolescence. The N200 component did not show sex differences. With regard to behavioural performance, reaction times were found to be slower in girls than in boys across all age groups (Sumich et al., 2012). Of note, as the study by Sumich et al. (2012) did not explore potential sex differences in exogenous AEPs, it remains unclear whether sex differences are also present at the early stages of auditory information processing in adolescent samples.

Studies in adolescents that have examined sex differences in both endogenous and exogenous AEP components based on an auditory oddball paradigm are scarce and provide conflicting results (Segalowitz & Barnes, 1993; Friedmann et al., 1984). Segalowitz and Barnes (1993) applied a standard two-tone auditory oddball paradigm based on a small adolescent sample comprising 10 males and 9 females. They found longer N100 latencies in the group of adolescent boys than in the group of adolescent girls. Friedman et al. (1984) elicited AEPs in male and female adolescents using a three-stimulus auditory oddball task. Among other findings, the authors reported higher N100 in response to standard tones in adolescent boys.
than in adolescent girls, whereas P200 amplitudes were higher in girls than in boys in this condition. It is important to note that the studies by Segalowitz and Barnes (1993) and Friedman et al. (1984) did primarily focus on research issues apart from sex-related differences. Supposedly for this reason, demographic characteristics for the sex groups were not separately reported and it remains unclear whether the male and female adolescents in these studies were comparable with regard to demographic variables. Moreover, both studies did not provide behavioural data for the sex groups, thus leaving the question open as to whether the reported group differences in AEPs might also be associated with differential behavioural findings.

Taken together, studies on sex differences in AEPs during adolescence yielded inconsistent results and are in part difficult to interpret for methodological reasons. Besides methodological issues, reasons for the heterogeneity of findings might include differences between the studies in the oddball paradigm applied and the AEP analyses conducted. Moreover, previous investigations in this domain differ with regard to the age range investigated. This might be of particular relevance as prior studies found evidence for differential age-related result patterns in AEPs in adolescent males versus females (e.g., Sumich et al., 2012; Friedman et al., 1984). More precisely, these studies found that sex differences in N100 amplitude are more prominent at age 15 than at other adolescent ages, with higher amplitudes in males compared to females (Friedman et al., 1984). Moreover, P300 amplitudes in girls were found to increase until late adolescence, while P300 amplitudes of boys peak during early adolescence (Sumich et al., 2012).

Studies on sex differences in the neural bases of auditory information processing during adolescence can further promote the understanding of well-established differences between the sexes in auditory functioning. For example, there is evidence that young males outperform young females in pitch discrimination (Rammsayer & Troche, 2012). As similarly advocated by Rammsayer et al., sex differences in basic auditory skills might impact on sex-related
differences in domains beyond basic auditory processing, including higher-order cognitive skills such as auditory working memory. Moreover, studying sex differences with regard to basic neurophysiological processing can also contribute to the understanding of the broader field of individual differences in brain organisation and functioning. Normal variations in the neurophysiological processes, such as the variation due to sex, can provide information about how particular biological characteristics can enhance or restrict particular functional and cognitive abilities (Kimura & Harshman, 1984).

Given the scarcity and heterogeneity of studies on sex-related differences in auditory information processing during adolescence, it is difficult to interpret the existing findings in a coherent way. Moreover, due to the fact that most previous studies did not report behavioural data for the sexes, it is important to conduct a study integrating neurophysiological and behavioural measures of auditory information processing. Thus, using the standard two-tone oddball paradigm, the aim of the present investigation was to investigate sex-related differences in auditory information processing during adolescence. In the present AEP study, we applied an auditory oddball task in male and female adolescents between the ages of 13-18 years. In contrast to previous approaches using the traditional two-tone-oddball design, both exogenous (N100, P200) and endogenous (N200, P300) AEPs were examined along with behavioural data, thus extending prior studies. Based on the most extensive prior study (Sumich et al., 2012), we expected to find smaller P300 amplitudes in girls compared to boys, but no sex differences in N200 amplitudes. Due to the heterogeneity of findings on endogenous components and the difficulties in interpreting these results, we did not impose any hypotheses regarding these AEPs.

Methods

Participants
Twenty-nine typically developing adolescents (14 females and 15 males) between the ages of 13-18 years and an IQ > 85 took part in the study. There were no significant differences between the sex groups in age, intelligence or handedness (all ps > .05; for details see Table 1 and Measures section).

All participants were Caucasian. More than the average of the parents had a high-school diploma or a higher degree (52.2% of the fathers and 62.5% of the mothers; German reference population 27.3%; Federal Statistical Office, 2014). Participants were recruited from a contact list containing names of families that had expressed interest in participating in studies within the department. In return for their participation, participants received coupons. Only participants without any personal history of psychiatric or neurological disorders were included in the study. None of the participants received any medication or suffered from any relevant neurological or somatic disorders. Altogether, three participants could not be included into the final study sample since the participants met the criteria for one or more psychiatric disorder(s) as assessed by a standardized instrument (see Measures section). Moreover, one participant was not included in the final sample based on an IQ score ≤ 85. Application of inclusion criteria resulted in a final total sample size of N=29 (as described above).

In order to ensure that our sample size was large enough to detect sex differences in AEPs as observed in prior studies that also applied a two-tone auditory oddball task in adolescents (Sumich et al., 2012; Segalowitz & Barnes, 1993), we conducted a power analysis. Segalowitz and Barnes (1993) reported a large effect size for sex-related differences in the N100 and Sumich et al. (2012) reported medium-to-large effect sizes for sex-related differences in the P300. Based on these effect sizes, calculation of the minimal required
sample size to detect a significant group difference in AEPs using a repeated measures ANOVA with an alpha error=0.05 and a power of 0.80 revealed that our sample size was sufficient.

The study was approved by the institutional review board of the local ethics committee and was performed in accordance with the latest version of the Declaration of Helsinki and in compliance with national legislation. All participants were informed in detail about the experimental procedures and the aims of the study, and provided written informed assent. Written informed consent was obtained by at least one parent/legal custodian, after the parent(s)/legal custodian(s) had been informed about all aspects of the study.

Measures

IQ of participants was assessed by the revised German version of the Culture Fair Intelligence Test (CFT-20-R; Weiß, 2006). The CFT-20-R is a non-verbal and culture-fair test which assesses fluid intelligence based on four subtests (sequence completion, classification, matrices and topological reasoning) in a multiple-choice format. The subtests have an increasing level of difficulty and a time limit. The CFT-20-R can be applied in children/adolescents (8-19 years) and adults. The instrument has good reliability (internal consistency=0.95; test-retest reliability=0.80-0.82) and correlates well with other IQ tests (Weiß, 2006).

Handedness was assessed via participants´ self-report of global handedness (i.e., participants were asked for their handedness and globally indicated their handedness as “left”, “right” or “ambidextrous”).

Socioeconomic status and ethnicity were assessed via parental report based on a short internal questionnaire which is routinely used within our department. In this questionnaire, the highest completed education level of both parents was assessed as an indicator of the socioeconomic status. Moreover, the ethnicity of both parents and the child was reported.
**Diagnostic interview.** In order to exclude psychiatric disorders, a standardized semi-structured interview for psychiatric disorders in children and adolescents (Diagnostic Interview for Mental Disorders in Children and Adolescents, “Kinder-DIPS”; Schneider et al., 2009) was administered to the participants and one of the participants’ caregiver by experienced clinicians. The Kinder-DIPS assesses psychiatric disorders according to both ICD-10 and DSM-IV diagnostic criteria and is suitable for children and adolescents aged 6-18 years. The Kinder-DIPS is a well-established German instrument with high retest-reliabilities (Cohens’s Kappa =.85-94 for all DSM-IV diagnoses) and has demonstrated good validity (Schneider, 2009).

**Experimental procedure**

Participants completed a standard two-tone auditory oddball task while the electroencephalogram (EEG) data was collected. This task required participants to respond to target (deviant) tones (1000 Hz) as fast as possible and ignore non-target (standard) tones (500 Hz). The tones were presented binaurally via headphones. Responses were made by pressing the computer mouse button with the dominant hand. A total amount of 340 tones (280 non-target and 60 target tones) were presented in a pseudorandom order which took approximately 8 minutes. The tones were presented for 200 ms and were separated by an interstimulus interval of 1350 ms. During the experiment, a fixation cross remained on the middle of the computer screen and participants were instructed to fixate this point. Before the experimental session, participants completed a practice session consisting of 34 trials (28 non-target and 6 target tones).

**EEG recordings and processing**

EEG was recorded using 128-channel Geodesic Sensor Net (128-channel HCGSN) and a NetAmps 300 amplifier (Electrical Geodesics Inc.; EGI, Eugene, OR; Tucker, 1993) with a
sampling rate of 500 Hz and Cz as the reference electrode (*Figure 1*, electrode REF). The impedance was kept below 50 kΩ during recording.

Further processing steps were performed with Brainvision Analyzer (Brain Products GmbH, Gilching, Germany). After visual inspection of the data and offline filtering with a 0.5 to 40 Hz band-pass (Butterworth zero phase, 24 dB/Oct) and 50 Hz notch filter, an independent component analysis (ICA) was run to identify components representing electrooculogram (EOG) artefacts, and to remove those before back-projection of the residual components. Subsequently, all electrodes were re-referenced to the averaged mastoids and the continuous EEG of each participant was segmented into epochs (event related potentials, ERPs) from -300 ms to 1000 ms relative to stimulus onset. The 300 ms pre-stimulus period was used for baseline correction. Artefacts apart from EOG artefacts were defined as amplitudes exceeding +100 μV or -100 μV, bursts of electromyographic activity (maximal allowed voltage step: 50 μV/ms) and any activity lower than 0.1 μV in intervals of 100 ms. These artefacts were excluded from further processing. Correct trials with respect to non-targets were defined as trials on which the subject made no response; correct trials in the target tone condition were defined as trials on which the subject made a response in the time interval from 100–1000 ms after stimulus onset. ERPs of correct trials were averaged separately for each participant and condition (target or non-target tone). For the inclusion into the final analysis, participants had to meet two criteria: (1) a minimum of 30 artefact-free trials in each trial condition, and (2) a minimum of 80% correct responses in the non-target and target condition, respectively. None of the participants had to be excluded based on these two criteria. The average number of artefact-free trials was 255.54±20.30 in the non-target tone condition and 54.82±5.31 in the target tone condition.
There was no difference in the average number of artefact-free trials between the groups ($p=.132$ for non-target tones and $p=.219$ for target tones).

**Data analysis**

**ERP data analysis**

Similar to previous studies (e.g., Nagy, Potts, & Loveland, 2003, Bell & Cuevas, 2012), we defined regions of interests (ROIs) for the N100, P200, N200 and P300 around Fz (electrode 11), Cz (electrode 129) and Pz (electrode 62). The frontal ROI included the electrodes 4, 5, 11, 12, 16 and 19, the central ROI the electrodes 7, 31, 55, 80, 106 and 129 and the parietal ROI the electrodes 61, 62, 67, 72, 77 and 78 (see Fig. 1). The individual latencies of the four components were determined as the time point of the maximum deflection (peak amplitude) within a predefined time window. The time windows were set individually for each ERP component based on visual inspection of the grand average potentials: N100 (70-120 ms), P200 (140-220 ms), N200 (190-270 ms), P300 (270-360 ms). To determine individual mean amplitudes, we exported the mean values within the above specified fixed time windows separately for each component. N100 and P200 amplitudes were exported both to the non-target and the target tones. As the N200 and the P300 were only reliably elicited to targets, N200 and P300 amplitudes were only exported for the target condition (similar to previous investigations, e.g., Kemp et al., 2009; Kemp et al., 2010).

Variables exceeding values more than 3 standard deviations apart from the mean of each sex group were removed from further analysis (less than 5% of the cases).

**Statistical analysis**

Statistical analyses of both the ERP and behavioural data were conducted with IBM SPSS Statistics 20. For all analyses, the significance level was set to $p=.05$ (two-tailed). In addition to p-values, the effect size measure partial eta squared ($\eta_p^2$) is reported, which ranges from 0
to 1 and describes the proportion of the variance in the dependent variable that is accounted for by the independent variable, partialling out other factors (classification of partial eta squared: .01=small effect; .06=medium effect; .16=large effect) (Ellis, 2010).

**ERP data**

N100 and P200 amplitudes and latencies were analysed using repeated measures ANOVAs with the between-subject factor sex (female, male) and the within-subject factors stimulus type (non-target, target) and ROI (frontal, central, parietal). In line with other studies (Kemp et al., 2009; Kemp et al., 2010), N200 and P300 components were only reliably elicited in the target tone condition. Thus, these components were only analysed to target tones and 2(sex) × 3(ROI) repeated measures ANOVAs were conducted.

Due to the focus of the present study, we report only main effects of sex or interactions effects involving the factor sex. In case of significant interaction effects involving the factor sex, further post-hoc comparisons were conducted with adjusted p values (p’, adjustments according to the Holm procedure). When sphericity was violated, the degrees of freedom were corrected using Greenhouse-Geisser’s procedure.

In case of significant differences between the sex groups in ERP parameters, we further explored whether differential age-related patterns in the ERP amplitudes have influenced the results (see e.g., Sumich et al., 2012). Therefore, the respective ERP parameters were correlated (Pearson coefficient; two-sided) with the age of participants (separately for both groups) at the most relevant ROIs (frontal and central ROI for the N100 and central and parietal ROI for the P300 amplitude). The most relevant ROIs were selected based both on prior literature (Jaworska et al., 2013; Sumich et al., 2008) and data inspection.

**Behavioural data**
Behavioural performance (reaction times (RTs) to hits, hit rates, false alarm rates) was compared between the groups using independent-samples t-tests. Reaction times were only included in the analysis if a response followed on a target tone in a time interval of 100-1000 ms after stimulus onset.

Results

Behavioural results

There were no significant reaction time difference between girls (388.7±15.8 ms) and boys (380.2±17.1 ms, t(27)=-.36, p=.724; $\eta^2_p=.00$). Similarly, the analysis of the hit rates (M$_{girls}$=100.0±0.0% vs. M$_{boys}$=99.4±1.0%; t(27)=-2.02, p=.055; $\eta^2_p=.13$) revealed no differences between the groups. Moreover, there was no sex difference in the false alarm rate (M$_{girls}$=0.18±0.34% vs. M$_{boys}$=0.26±0.25%; t(1, 27)=0.76, p=.454; $\eta^2_p=.02$).

Auditory evoked potentials

AEPs elicited in response to target and non-target stimuli are presented in Figure 2, separately for each sex group. Group means of amplitudes and latencies of the AEP components are reported in Table 2.

------Insert Figure 2 and Table 2 about here------

N100

A significant main effect of sex associated with N100 amplitudes ($F(1, 25)=7.09$, $p=.013$; $\eta^2_p=.22$) was observed. Irrespective of the other factors, N100 amplitudes were more negative in boys (-5.65±1.50 μV) than in girls (-4.03±1.67 μV). Moreover, we found a significant interaction between the factors stimulus type and sex ($F(1, 25)=5.12$, $p=.033$; $\eta^2_p=.17$). After
applying the correction for multiple testing, between-group comparisons of N100 amplitude revealed significant sex differences in the target tone condition ($M_{girls}=-4.5\pm2.0$ $\mu$V vs. $M_{boys}=-7.3\pm2.4$ $\mu$V; $t(27)=-3.42$, $p'=.002$; $\eta_p^2=.30$), but not the non-target tone condition ($p'=.026$). None of the remaining interactions with the factor group was significant (all $ps>.275$). We found no significant sex differences in N100 latency ($F(1, 27)=1.62$, $p=.214$; $\eta_p^2=.06$). A significant interaction between ROI and sex ($F(2, 54)=6.91$, $p<.001$; $\eta_p^2=.20$) was revealed. However, between-group comparisons of N100 latency separately for each region did not survive correction for multiple comparisons (all $ps>.045$). The remaining interactions with the factor group were all non-significant (all $ps>.079$).

**P200 and N200**

There were no significant sex differences in P200 and N200 amplitudes and latencies, and interaction effects between sex and the other factors were all non-significant (all $ps>.354$).

**P300**

There was a main effect of sex associated with P300 amplitudes ($F(1, 26)=12.85$, $p=.001$; $\eta_p^2=.33$) with higher P300 amplitudes in boys ($6.03\pm2.98$ $\mu$V) than in girls ($1.68\pm3.43$ $\mu$V). The interaction effect between ROI and sex was non-significant ($F(1.36, 35.27)=0.09$, $p=.830$; $\eta_p^2=.00$). Sex groups were comparable with regard to P300 latency ($F(1, 26)=0.53$, $p=.471$; $\eta_p^2=.02$) and no significant interaction effect was revealed between the factors sex and ROI ($F(2, 52)=1.07$, $p=.350$; $\eta_p^2=.04$).

**Relationship between AEP parameters and age**

Correlational analyses revealed that in girls, age significantly correlated with their frontal and central N100 (averaged across stimulus type) amplitudes ($r=-.67$, $p=.009$ and $r=-.66$, $p=.009$;
respectively), suggesting more negative N100 amplitudes with increasing age. In contrast, no significant correlation was found between age and N100 amplitudes (averaged across stimulus type) in the group of boys ($r=-.06$, $p=.844$ and $r=.03$, $p=.922$; respectively) (see Fig. 3). Moreover, correlational analysis revealed a significant positive correlation between individual age and girls’ central P300 amplitudes ($r=.55$, $p=.040$). However, there was no correlation between age and girls' parietal P300 amplitudes ($r= .357$, $p=.210$). In boys, there was no significant correlation between age and central and parietal P300 amplitudes ($r=-.12$, $p=.681$ and $r=-.24$, $p=.407$; respectively) (see Fig. 3).

To examine the possibility that the relationship between age and ERP parameters might not be linear, we also fitted the data to a quadratic model. However, for the relationships described above, the linear model resulted in a better fit with two exceptions: in boys, the quadratic model fit explained the relationship between age and N100 amplitudes at the frontal and central ROI better than the linear model. However, neither the linear nor the quadratic model fit reached significance in boys (all $ps>.096$).

Discussion

The aim of the present AEP study was to examine sex differences in the neurophysiological correlates of auditory information processing using a two-stimulus oddball paradigm. In sum, we found that the N100 and P300 amplitudes were smaller in girls than in boys. Moreover, in the group of girls, age was positively related to N100 and P300 amplitudes, while no such relationships were found in the group of boys.

Behavioural data
In the present study, we did not find any behavioural differences between the sex groups. Since faster RTs of males compared to females, as previously reported (Sumich et al., 2012), seem to be more pronounced during early and late childhood than during adolescence, the difference between our findings and Sumich et al. (2012) can be most probably attributed to the much broader age range of this prior study (6-17 years).

**ERP data**

In the present study, target-related N100 amplitudes were found to be higher in adolescent boys than in adolescent girls. To our knowledge, this study is the first to report sex-related differences in the target N100 amplitude during two-stimulus auditory oddball task in adolescents. A previous two-stimulus auditory oddball study in adolescents (Segalowitz & Barnes, 1993) did not find sex-related N100 amplitude differences between the sexes but reported shorter N100 latency in boys compared to girls. However, as the authors point out, the sample size for the comparison of the sexes was small, what might explain why the results differ from the present study. With respect to findings from the adult literature, one study that applied the two-tone auditory oddball paradigm found higher N1-P2 interpeak amplitudes in males compared to females (Gölgeli et al., 1999), what can be roughly brought in line with our findings, although in the previously mentioned study, N100 and P200 amplitude heights were not separately reported.

N100 amplitude enlargement during attentional tasks is considered to reflect stimulus dependent, exogenous processes interpreted as generally greater sensory sensitivity or increased arousal (Burkhart & Thomas, 1993; Näätänen & Picton, 1987). Moreover, it has been suggested that the N100 component may be influenced also by intentional discrimination processing and can reflect selective attention to basic stimulus characteristics (Sanders & Astheimer, 2008). Based on our findings of higher N100 amplitudes in adolescent boys than in girls, we suggest that the early auditory sensory processing system of boys is more
sensitive to changes in the incoming information. Our results are in line with results that show superior performance of boys and young men compared to females in sensitivity to auditory changes, such as pitch discrimination (Rammsayer & Troche, 2012; Zaltz, Roth, Gover, Liran, & Kishon-Rabin, 2014).

Interestingly, we found an increase of N100 amplitude with age in girls, but not in boys. Thus, although our findings need to be replicated in longitudinal studies, it might be the case that the development of the N100 is nearly complete in boys already at the age of 13, whereas girls still undergo major changes until the age of 18. Our findings of a sexually dimorphic N100 age pattern during adolescence may help to reconcile former inconsistent findings from developmental studies in the field of auditory processing: Some AEP studies have shown age-related increase in the N100 component, while others failed to find such a developmental effect (for a review see Wunderlich & Cone-Wesson, 2006). Such inconsistency in the findings might be due to the fact that the factor sex was not adequately accounted for.

The finding of lower P300 amplitudes to targets in girls compared to boys across all electrode sites can be brought in line with the results of Sumich et al. (2012), who also found smaller P300 amplitudes in girls than in boys during early adolescence (12-14 years), although the sex difference in the former study was restricted to anterior sites. The P300 component is an endogenous component, reflecting working memory processes including the allocation of processing resources to the relevant tone or the update of the internal representation of the previous stimulus (Johnstone et al., 1996; Polich, 2007). Our findings indicating larger P300 amplitudes in boys might suggest that boys allocate more attentional resources to relevant auditory stimuli compared to girls.

Similar to the observed age-related pattern for the N100 amplitude, we found age-related differences in the P300 amplitudes only in adolescent girls. This pattern is consistent with the results provided by Sumich et al. (2012), who also found age-related differences in the P300 amplitudes of girls, but not in boys. Again, our finding of age-related differences during
adolescence in the P300 amplitudes of girls as opposed to boys might help to reconcile conflicting findings from previous neurophysiological studies, with some of these studies reporting age-related increases in the P300 component (Johnstone et al., 1996; Polich, Ladish, & Burns, 1990), while others failed to find an effect of age (Fuchigami et al., 1993; Johnson, 1989; Ladish & Polich, 1989). Furthermore, the findings of sex differences in the P300 maturational trajectory concur with behavioural observations of a sex-based cognitive cross-over maturational effect, although this effect is typically reported earlier than in our study. During childhood, girls show poorer performance in tasks measuring executive function including working-memory (e.g., in the digit span test). Later in early adolescence, girls start to outperform boys in these tasks and this pattern persists until later adolescence (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Klenberg, Korkman, & Lahti-Nuuttila, 2001). To be able to paint a clear picture of the implications of sex-related differences in endogenous and exogenous AEPs during adolescence, it seems promising to both record AEPs during the oddball task and additionally assess behavioural parameters that are thought to be related to the respective AEP components.

Limitations and conclusions

It should be noted that we only included participants with an IQ > 85 and without any psychiatric disorder to avoid confounds associated with low cognitive abilities and psychopathology. Moreover, the parents of the study participants had a comparatively high educational status (suggesting a comparatively high socioeconomic status of the study participants). Although explorative analyses did not suggest that our main results were influenced by these sample characteristics, future studies should examine whether the results from the present study can be generalized across a more representative adolescent sample. It should be mentioned that the IQ test version used in the present study (CFT-20-R; Weiß, 2006) is somewhat dated, which might have led to a slight overestimation of IQ scores. Future
studies should acknowledge this aspect be applying an IQ measure with a more current standardization status. The sample size of the present study was rather small. However, as a power analysis proved it as sufficient to find the expected sex-related AEP differences, this issue is of secondary importance.

It should be stated that similar to most prior studies (e.g., Sumich et al., 2012, but see Friedman et al., 1984), the pitch height of our target and non-target stimuli was not counterbalanced. As the N100 component is influenced by stimulus properties (Polich, 1986; 2007), it might be argued that the sex differences are rather related to the recognition of high pitch stimuli than to the relevance of the stimulus. However, as there is evidence that males and females process high and low pitch sounds in similar ways (Shenvi & Balasubramanian, 1994), the former explanation seems rather unlikely. Notwithstanding this issue, in future studies, it would undoubtedly be advantageous to counterbalance the pitch height across target and non-target tones to be able to strictly separate effects of stimulus relevance from auditory stimulus height. Despite these limitations, this study is the first to examine sex-related differences in endogenous and exogenous AEP components elicited by the traditional two-stimulus oddball paradigm along with its behavioural correlates in adolescents.

In sum, our finding of an enhanced N100 in male participants might suggest greater sensory sensitivity in adolescent boys compared to their female counterparts. Moreover, increased P300 amplitudes in boys may point to a greater ability of adolescent boys compared to girls to allocate their attention to significant auditory stimuli in the environment. The differential relationship between the N100 and P300 components and age in the two sexes might imply that the development of the neurophysiological bases underlying auditory information processing is more complete in adolescent boys, whereas girls undergo a protracted development in this phase. However, given that our findings are based on a cross-sectional design, a replication of our findings in a longitudinal study is warranted.
Sex differences in the neurophysiological mechanisms of auditory information processing and sex specific developmental changes in endogenous and exogenous AEPs are presumably the result of a complex interplay between hormonal influences, neurotransmitter systems and maturational functional as well as structural changes in the brain (Fuchigami et al., 1993; Sisk & Zehr, 2005). It was beyond the scope of the present study to investigate these factors. However, future studies should apply methodological approaches beyond AEPs to yield a more comprehensive understanding of sex differences in auditory processing between adolescent boys and girls.

A number of brain-related psychiatric disorders, including depression (e.g., Kemp et al., 2009) and schizophrenia (e.g., Wood et al., 2006) show abnormal neurophysiological mechanisms underlying auditory information processing. Findings of sex-related differences in auditory processing as found in the present study stress the importance of considering potential influences of sex when examining neural mechanisms of auditory information processing in these disorders.
References


### Table 1. Characteristics of the groups

<table>
<thead>
<tr>
<th></th>
<th>Females (n=14)</th>
<th>Males (n=15)</th>
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<td>.58</td>
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^a Assessed by the CFT-20-R. ^b Assessed via self-report of global handedness (recorded as “left”, “right” or “ambidextrous”; none of the participants indicated to be ambidextrous).
Table 2. Amplitudes and latencies of N100, P200, N200 and P300 separately for each condition and group

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<tr>
<th></th>
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Figure 1. Electrical Geodesic Inc. 128-channel system: Regions of interest (ROI) were defined (1) in the frontal region (green) including the electrodes 4, 5, 11=Fz, 12, 16 and 19, (2) in the central region (yellow) including the electrodes 7, 31, 55, 80, 106 and 129=REF=Cz and (3) in the parietal region (blue) including the electrodes 61, 62=Pz, 67, 72, 77 and 78.
Figure 2. AEPs elicited to (A) target and (B) non-target tones, depicted separately for each ROI. The black line represents the group of boys (n=15), the red line represents the group of girls (n=14).
Figure 3. Correlations between the individual testing age and the N100 (at the frontal and central ROI, averaged across different stimulus types) and P300 (at the central and parietal ROI) mean amplitudes in the two groups.