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# **40Hz auditory steady-state response: the impact of handedness and gender**

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## *Abstract*

The 40Hz auditory steady-state response (ASSR) is a periodic response to a periodic stimulation. Its sources are located in the primary auditory cortex and the asymmetry of the planum temporale has previously been associated with hand preference and gender-related differences; thus subject's handedness and gender could potentially influence ASSRs. Nevertheless, electrophysiological studies of ASSRs are mainly dominated by right-handed participants and the observed findings can only be generalized to the right-handed populations. However, for a potential use of 40Hz ASSR as a translational biomarker of neuropsychiatric disorders, it is important to investigate the response in association to handedness and gender.

We included an equal number of left-handed and right-handed males and females and recorded EEG responses during left-ear, right-ear and both ears stimulation. The results of the study suggest that the processing of 40Hz auditory stimulation depends on the subjects' gender and handedness: significantly lower phase-locking and strength of 40Hz ASSRs were observed in left-handed females as compared to left-handed males, but right-handers did not differ in 40Hz ASSRs.

Our observation of the opposite impact of gender in the examined handedness groups stresses the importance of careful consideration of handedness and gender factors when evaluating the determinants of inter individual variability of 40Hz ASSRs. This finding is of particular importance for clinical studies in psychiatry and neurology.

## *Keywords*

Auditory steady-state response; 40Hz; gender; handedness

## *Introduction*

The auditory steady-state response (ASSR) is a periodic response to a periodic stimulation that is measured with EEG/MEG (Picton et al. 2003). The largest response magnitudes are achieved with stimulus presentation rates at around 40Hz (Galambos et al. 1981). The 40Hz ASSRs are increasingly used in neuropsychiatric populations (schizophrenia, bipolar disorder, autism) and show abnormal synchronization processes in the brain (Light et al. 2006; Spencer et al. 2008; Rass et al. 2010). In schizophrenia, the 40Hz ASSR was proposed to serve as one of the biological markers of the disorder (O'Donnell et al. 2013) with a recent meta-

analysis proving its utility (Thuné et al. 2016). Another important application of ASSRs stands in the field of language studies, where ASSRs serve as an index of sensitivity of the auditory cortex to particular frequencies (De Vos et al. 2017). Finally, ASSRs are frequently utilized in brain-computer interface applications, due to their sensitivity to attentional demands (Hill and Schölkopf 2012).

Functional imaging studies localized the origin of the 40Hz ASSRs in the primary auditory cortex (Pantev et al. 1996; Gutschalk et al. 1999; Brugge et al. 2009). The auditory cortex shows both anatomical (Herve et al., 2006) and functional (Penhune et al., 1996.; Schonwiesner et al., 2006) asymmetry in the healthy human brain. Importantly, the 40Hz ASSR is somewhat asymmetric across the hemispheres, with several studies showing a right-hemispheric dominance (Ross et al., 2005; Draganova et al., 2008) in healthy subjects. However, in both schizophrenia and bipolar disorder, a diminished left-right hemispheric asymmetry for the 40Hz ASSRs has been shown (Teale et al. 2003; Reite et al. 2009; Tsuchimoto et al. 2011). This is in line with an overall reduction of brain asymmetry on both the structural and functional level in neuropsychiatric disorders (Wang et al. 2013; Ribolsi et al. 2014; Royer et al. 2015; Delvecchio et al. 2017).

Handedness is considered to be a behavioral manifestation of individual differences in hemispheric cerebral asymmetry (Hellige 2001). In Western countries ~ 85-90 percent of the population are right-handed and ~10-15 percent are left-handed (Harris 1990). The elevated prevalence of non-right-handedness in psychiatric disorders as compared with healthy population is a true empirical effect (Deep-Soboslay et al. 2010; Hirnstein and Hugdahl 2014; Ravichandran et al. 2017). A few meta-analyses have reported that the odds of being non-right-handed are approximately 1.5 times higher in people with schizophrenia than in controls (Sommer et al., 2001; Hirnstein and Hugdahl, 2014). Moreover, Saugstad (1998) and Hollinger et al. (1999) pointed out that in schizophrenia, structural brain abnormalities differ in right-handed vs. left-handed subjects (Saugstad, 1998; Hollinger et al., 1999). Nevertheless, electrophysiological studies of auditory responses (both in healthy and clinical populations) are dominated by right-handed participants and the observed findings can only be generalized to right-handed populations.

Thus, for a potentially translational biomarker such as the 40Hz ASSR, it is important to investigate this response in association with handedness. Firstly, because the main sources for

the 40Hz ASSR are located in the primary auditory cortex and the asymmetry of the planum temporale (PT) has previously been associated with hand preference: the PT showed more leftward asymmetries in right-handed subjects (Herve et al., 2006) and no asymmetry was observed in left-handers (Foundas et al. 1995). In addition, the primary auditory cortex is larger on the left in males, but is of equal size in both hemispheres in females (Rademacher et al. 2001) and there is a slightly higher proportion of left-handedness in males than females (Peters et al. 2006; Sommer et al. 2008), suggesting that gender may be an additional confounding factor.

Given this background and because the 40Hz ASSRs were found to be asymmetric across the hemispheres for right-handers, we sought to investigate whether the parameters of the 40Hz ASSR differ between left and right-handed participants. In this study, we aimed to compare phase-locking index and event-related spectral perturbation of the 40Hz ASSRs between right-handed and left-handed subjects, as this has not been done before. We included an equal number of males and females to capture potential associations with gender. The evaluation of both handedness and gender would be of particular importance for clinical studies in psychiatry and neurology and for BCI applications.

## *Methods*

### *Subjects*

Forty-four healthy subjects were enrolled. First, the recruitment of left-handed subjects was performed by advertisements distributed in the public library, social media webpages, or by word of mouth. Further, right-handed group was recruited. We aimed for two well-differentiated groups of left-handers and right-handers; thus before the admission to the study, all participants filled in the Edinburgh Handedness Inventory (Oldfield 1971) and assigned themselves as right-handed (61 to 100 score) or left-handed (-100 to -61). Ambidextrous subjects were not included to the study. To prove right or left handedness, we also used the Target Test (Borod et al. 1984). The details on these tests are presented as Supplementary material. Twenty two left-handed (mean age 23 (3.7) years, 11 females; further referred to as LH) and 22 right-handed (mean age 22 (1.8) years, 11 females; further referred to as RH) participants were invited for an EEG study, all of them being university students. Subjects did not receive any financial reward for their participation.

The hearing thresholds of all subjects were within the norm range (i.e. with less than 20 dB HL on pure tone audiometry performed at 125, 250, 500, 1000, 2000, 4000 and 8000 Hz) measured with a screening audiometer AS608 (Interacoustics, Denmark). Subjects were asked not to consume caffeine-containing drinks and not to smoke up to one hour before the experiment. Naturally cycling female subjects were invited during their follicular phase (2 to 7 days from the start of menses). The study was approved by the Lithuanian Bioethics Committee, in accordance with the Declaration of Helsinki and all participants gave their written informed consent.

### *EEG recordings and stimulation*

The EEG was recorded with the 64 Ag/AgCl WaveGuard Cap and using ANT device (ANT Neuro, The Netherlands). Mastoids were used as a recording reference. Impedance was kept below 20 k $\Omega$  and the sampling rate was set at 1024 Hz.

Stimuli were 500 ms duration trains of 40Hz clicks. 20 identical clicks (1.5 ms bursts of white noise) were presented 60 times through Sennheiser HD 280 PRO headphones in three ways in a random order: 1) to the right ear, 2) to the left ear and 3) to both ears simultaneously. The sound pressure level of the sounds was adjusted to 60dBA with a DVM 401 decibel meter (Velleman, USA).

### *EEG analysis*

The off-line processing of EEG data was performed in EEGLAB and ERPWAVELAB for MatLab<sup>©</sup> (Delorme and Makeig 2004; Mørup et al. 2007). The power-line noise was removed using multi-tapering and Thomas F-statistics implemented in the CleanLine plugin for EEGLAB. Channels with substantial noise throughout the recording were rejected. An independent component analysis (ICA) was performed on the remaining channels with the ICA-implementation of EEGLAB ('runica' with default settings) and independent components related to eye blinks were removed. Epochs of 700 ms were created, starting 100 ms prior to the stimulus onset and lasting for 600 ms post-stimulus onset, and inspected for remaining artifacts. The removed channels were reconstructed using a spherical spline interpolation (Perrin et al. 1989). The common mode average reference was used for further processing. The data were baseline-corrected to the mean of the pre-stimulus period.

A wavelet transformation (WT; complex Morlet wavelet; frequencies represented from 10 to 80 Hz, 1 Hz intervals between each frequency, cycle=7) was performed. Phase-locking index (PLI, corresponding to the phase consistency over epochs) and event-related spectral perturbation (ERSP, corresponding to the average power over epochs) measures (more details can be found in Mørup et al. 2007) were calculated within 38-42 Hz and -100 -0 and 200-500 ms windows, the former resulting in a baseline measure and the latter corresponding to the late-latency gamma (Tada et al. 2016). Response window from 200 ms was chosen in order to exclude the impact of onset and capture both the maximum response and the steady-state part, as previously done in (Rojas et al. 2011; Griskova-Bulanova et al. 2016). The wavelet-transform derived measures of the late-latency gamma response were normalized by subtracting the mean of the baseline.

To assess the laterality effect, the electrodes were grouped to the left site (F3, FC1, C3, F1, FC3, C1), center (Fz, FCz, Cz) and right site (F4, FC2, C4, F2, FC4, C2). The laterality index ( $L_i$ ) was calculated according to the formula:  $L_i = (L - R) / (L + R)$ , where L indicated the left site responses and R – right site responses accordingly; the  $L_i$  value of -1 indicating a right-lateralized response, 0 indicated no laterality and 1 indicated a left-lateralized response.

### *Statistical evaluation*

Statistical evaluation was performed in STATISTICA, version 10 (Stat Soft, Inc., 2011). Data were normally distributed as indicated by the Shapiro-Wilk test. Mixed model ANOVAs with factors STIMULATION (left vs. both vs. right) and SITE (left vs. centre vs. right) as within-subject factors and HANDEDNESS (left-handed vs. right-handed) and GENDER (males vs. females) as between-subject factors were performed on the mean PLI and ERSP values. Subsequent post-hoc testing using the Fisher LSD method was applied and adjusted p-values are reported. Separate mixed-model ANOVA with the factors STIMULATION (left vs. both vs. right) as a within-subject factor and HANDEDNESS (left-handed vs. right-handed) and GENDER (males vs. females) as between-subject factors were conducted on the laterality indices of PLIs and ERSPs.

### *Results*

All three types of stimulation resulted in the observation of a fronto-central activation. The grand-averaged topography plots of PLI across 38-42Hz and the 200-500ms window for both groups (left-handed and right-handed subjects) for females and males separately in each stimulation condition are depicted in Figure 1. The means and standard deviations of the phase-locking index and event-related spectral perturbation values for each group and each site are presented in Table 1.

### *Phase-locking index*

A significant crossover interaction of GENDER\*HANDEDNESS was observed for PLIs ( $F(1, 40) = 7.465$ ,  $p = 0.009$ ,  $\text{partial } \eta^2 = 0.157$ ), pointing to lower PLIs in LH females as compared to LH males ( $p=0.007$ ) and somewhat lower PLIs as compared to RH females ( $p=0.059$ ). This interaction effect was independent of STIMULATION used ( $F(2, 80) = 0.025$ ,  $p = 0.975$ ,  $\text{partial } \eta^2 < 0.001$ ) and the main effect of STIMULATION was not significant for PLI estimates ( $F(2, 80) = 2.073$ ,  $p = 0.132$ ,  $\text{partial } \eta^2 = 0.049$ ). Although PLI's differed according to the SITE of measurement ( $F(2, 80) = 66.348$ ,  $p < 0.001$ ,  $\text{partial } \eta^2 = 0.624$ ) and were strongest over the central area ( $p < 0.001$ ), the SITE\*GENDER\*HANDEDNESS interaction was not significant ( $F(2, 80) = 1.239$ ,  $p = 0.295$ ,  $\text{partial } \eta^2 = 0.030$ ). However, a significant interaction of GENDER\* SITE emerged ( $F(2, 80) = 3.477$ ,  $p = 0.036$ ,  $\text{partial } \eta^2 = 0.080$ ), revealing that in both males ( $p < 0.001$ ) and females ( $p < 0.001$ ) the PLIs were largest over the centre.

None of the factors or their combinations assessed had a significant effect on the laterality indices of PLIs.

The least square means of PLI values and corresponding 95% bars over the right, central and left brain areas for all stimulation types in the right-handed and left-handed subjects separately for males and females are presented in Figure 2. Additionally, least square means of laterality indices are presented for each group.

### *Event-related spectral perturbation*

The significant crossover interaction of GENDER\*HANDEDNESS was observed for ERSPs ( $F(1, 40) = 10.595$ ,  $p = 0.002$ ,  $\text{partial } \eta^2 = 0.209$ ). Post hoc tests revealed that LH females had lower ERSPs as compared to RH females ( $p = 0.012$ ) and LH males ( $p = 0.005$ ); the difference between LH and RH males was on a trend level ( $p=0.054$ ), suggesting somewhat

higher ERSPs in RH males. This was independent from stimulation used ( $F(2, 80) = 2.177, p = 0.120$ , partial  $\eta^2 = 0.052$ ), although the main effect of STIMULATION significantly influenced ERSP values ( $F(2, 80) = 4.060, p = 0.021$ , partial  $\eta^2 = 0.092$ ): highest ERSP values were obtained during bilateral stimulation as compared to the left ear stimulation ( $p = 0.038$ ) and right ear stimulation ( $p = 0.008$ ). However, the area of measurement had significant impact on ERSPs: the main effect of SITE of measurement ( $F(2, 80) = 11.226, p < 0.001$ , partial  $\eta^2 = 0.219$ ) pointed to overall stronger response over the central site in comparison to the left ( $p = 0.015$ ) and right ( $p < 0.001$ ) sites. The interaction among SITE\*GENDER\*HANDEDNESS ( $F(2, 80) = 10.933, p < 0.001$ , partial  $\eta^2 = 0.215$ ) revealed that ERSPs over the central sites were higher than those over the left and right areas in LH males (all  $p < 0.001$ ) and RH females ( $p < 0.05$ ) only. The significant difference in ERSPs was observed between the right-sided responses in RH and LH females ( $p = 0.005$ , lower in LH females) and between the right-sided and left-sided responses in LH females ( $p < 0.001$ , higher on the left).

A significant GENDER\*HANDEDNESS interaction was observed for ERSP laterality indices:  $F(1, 40) = 8.378, p = 0.006$ , partial  $\eta^2 = 0.173$ ). Post hoc analysis revealed that LH females had more leftward lateralised responses than RH females ( $p = 0.007$ ) and LH males ( $p = 0.004$ ). No other effects or interactions were observed.

Least square means of ERSP values and corresponding 95% bars over the right, central and left brain areas for all stimulation types in the right-handed and left-handed subjects separately for males and females are presented in Figure 3. Additionally, least square means of laterality indices are presented for each group.

### *Discussion*

Most electrophysiological studies exclusively include right-handed subjects. However, knowledge of the effects of handedness becomes important where electrophysiological measures are being considered as candidate biomarkers. To the best of our knowledge, this is the first study comparing a recently proposed biomarker for schizophrenia – the 40Hz auditory steady-state response - in right-handed and left-handed young healthy subjects. This study highlights several important aspects: (1) bilateral 40Hz stimulation with clicks resulted in the largest activation and no differences between the responses to the left-ear and right-ear stimulation were observed; (2) both unilateral and bilateral stimulation resulted in a fronto-central activation with

no effect on laterality; (3) a significant difference in the phase-locking and strength of 40Hz ASSR between genders was revealed in the left-handed group (lower in females), but right-handers did not differ in their 40Hz ASSRs.

The bilateral stimulation used in our study resulted in a more pronounced 40Hz ASSR as compared to the left and right ear stimulation conditions. This was true for ERSPs; however, no such effect was observed on PLIs. The finding that binaural stimulation produces strongest activation is in line with previous reports (Poelmans et al. 2012; Luke et al. 2017; Gransier et al. 2017). Luke et al. (2017) proposed that this effect indicates an increased cortical activity with bilateral stimulation (Luke et al. 2017). The finding of a higher response over fronto-central locations is consistent with previous studies (Yamasaki et al. 2005); this is considered to be due to the electrical dipoles of ASSRs (toward the vertex) (Mäkelä and Hari 1987; Pastor et al. 2002). However, the lack of contralateral response dominance with monaural stimulation contradicts some of the earlier observations (Pastor et al. 2002; Yamasaki et al. 2005; Ross et al. 2005b; Lazzouni et al. 2012) where authors found larger responses in the hemisphere contralateral to the stimulated ear.

Stronger 40Hz ASSRs over the right hemisphere were reported in numerous studies (Ross et al., 2005; Draganova et al., 2008; Lamminmäki et al., 2014; Tan et al., 2015; Luke et al., 2017); however, both the opposite effect was also shown (Müller et al. 2009) and some studies employing EEG provided contradictory results (Mahajan et al. 2014; Edgar et al. 2017). Importantly, the majority of studies showing pronounced laterality effects with 40Hz stimulation used MEG that is capturing tangential sources only (Ahlfors et al. 2010). The 40Hz ASSR is generated in the medial primary auditory cortex (PAC) (Brugge et al. 2009). Recently, Shawn et al. (2013) explained the lower 40Hz ASSRs over the left hemisphere as a result of signal cancelation in the left cortex due to the anatomic features (Shaw et al. 2013). As suggested by Edgar et al. (2017), EEG analysis at the sensor level might be suboptimal to detect the laterality effect (Edgar et al. 2017). Using similar EEG processing settings as done in the current study, Edgar et al. (2017) failed to show the right side dominance for both the power and phase-locking of 40Hz ASSRs, the result being in accordance to our current observation (Edgar et al. 2017). Moreover, the rightward lateralization of ASSRs is normally reported at the group level, whereas single subjects can show strong lateralization to the left. The high level of inter-individual variability in both response strength and phase-locking measures can be seen from our results

(Figures 2 and 3). The laterality indices of PLIs did not differ between groups or stimulation conditions, and the centrally obtained responses were higher as compared to the left- and right-sided responses. Noteworthy, we also show that the most leftward responses are observed in the LH females, pointing to the handedness and gender influence (Figure 3).

The crossover interaction between handedness and gender for 40Hz ASSR measures points to the fact that both of these factors should be considered. A significant difference in phase-locking and ERSPs between genders was observed in the left-handed group, but right-handers did not differ in 40Hz ASSRs parameters. A very limited number of studies addressed gender differences of ASSRs in the right-handed groups: both Zakaria et al. (2016) and Kirihara et al. (2012) found somewhat larger 40Hz ASSRs in females as compared to males, but no effect was observed on the phase-locking index (Kirihara et al. 2012; Zakaria et al. 2016). In a recent study Larsen et al (2017) failed to show any differences between males and females in the 40Hz ASSR measures (Larsen et al. 2017). However, there is some indication that observations can depend on stimulation settings (Zakaria et al. 2016). Our results suggest that it is not only gender that influences 40Hz ASSRs, but a combination of gender and handedness.

Yamasaki et al. (2005) have suggested that the auditory 40Hz information is predominately processed in the left PAC (Yamasaki et al. 2005) that is specialized for the processing of temporal aspects of the auditory stimuli (Penhune et al. 1996). Histological studies provided no indications that, on the group level, PAC is larger on the left (Galaburda and Sanides 1980; Rivier and Clarke 1997). However, some data point to a leftward asymmetry of the planum temporale in the right-handed subjects (Herve et al., 2006) and no asymmetry in the left-handers (Foundas et al. 1995). Moreover, as shown by Rademacher et al. (2001), gender may play a role: in their study, the PAC was larger on the left than in right in males, but was indifferent in females (Rademacher et al. 2001). Evidence exists that women exhibit a greater degree of inter individual variability in functional cortical asymmetries, whereas functional cortical asymmetries in males are rather robust (Hausmann et al. 1998). Nevertheless, our data suggest relatively similar variability of 40Hz ASSRs in both right-handed and left-handed males and females (Table 1), advising that the observed effects on 40Hz ASSRs cannot be solely explained by the potential differences in the anatomy and functioning of the PAC.

It has been shown that 40 Hz stimulation results in a synchronized activation (Yamasaki et al. 2005) of bilateral auditory areas that are strongly connected through the corpus callosum

(CC) (Clarke et al. 1995; Wallace and Harper 1997). Thus, the observed cross interaction between gender and handedness for 40Hz ASSRs could be the result of combined differences in both the PAC and connections through the corpus callosum. Although the results on the differences in CC size and structure between males and females are controversial, effects gender and handedness cannot be fully ignored (Bishop and Wahlsten 1997). For example, Westerhauser et al. (2004) found increased anisotropy along with lower mean diffusion within the CC in the left-handed subjects and in males (Westerhausen et al. 2004). In the present study, a somewhat larger response was observed in LH males as compared to RH males and to LH females, potentially resulting from a more efficient involvement of both left and right hemispheres during processing of 40Hz stimulation. Similarly, lower 40Hz ASSRs in LH females as compared to RH females and LH males could be the result of less efficient participation of both hemispheres. This could potentially result from the limited involvement of the right hemisphere, as indicated by the largest leftward lateralization of ERSPs in LH females. Indeed, the importance of inter hemispheric synchrony can be inferred by previous studies showing that inter hemispheric disconnection produces severe dichotic suppressions in the left ear (Milner et al. 1968; Rubens et al. 1985; Risse et al. 1989; Sugishita et al. 1995). Similarly, Mulert et al (2011) observed a decreased phase synchrony between left and right primary auditory cortices in schizophrenia during 40 Hz ASSRs (Mulert et al. 2011) along with the reduced 40Hz ASSRs in the left sources but not in the right sources (Spencer et al. 2009).

The 40Hz ASSRs are sensitive to the excitation/inhibition balance in the brain and the possible influence of the different levels of glutamatergic and GABAergic processes on the current observations needs to be considered. The synchronization per se is hypothesized to be propagated through networks in a cycle of GABA-A-mediated inhibition (Gonzalez-Burgos and Lewis 2008). The left-right asymmetry in glutamate and GABA levels after auditory stimulation was shown by Chen et al. (Chen et al. 2013). The different patterns of 40Hz ASSR in males and females in the current study suggest a potential involvement of sex steroids and the influence of sex hormones on the functioning of the GABAergic system has been established (Carta et al. 2012; Huang and Woolley 2012). Previously, we reported 40Hz ASSR sensitivity to the hormonal background in females – more pronounced responses were observed with higher estradiol levels (Griskova-Bulanova et al. 2014). To control for this factor, we enrolled healthy young females during their early follicular phase (menses, with expected low estradiol levels), as

estimated by self-reports. One limitation of the current study could be that we did not quantify hormone levels. However, as shown by Negrev et al. (2000) during normal menopause (low level of sex hormones), estradiol and progesterone levels were much lower in the left-handed females as compared to the right-handed women (Negrev et al. 2000). In our group, left-handed females showed somewhat less expressed 40Hz ASSRs. The effect could result from potentially lower levels of estradiol and potentially lower GABA level within the left PAC. In the future studies, it would be interesting to evaluate potential differences in 40Hz ASSRs across the menstrual cycle in the left-handed and right-handed naturally cycling females, and in females on hormonal contraception.

Our observation of the opposite impact of gender in the examined handedness groups stresses the importance to carefully consider handedness and gender factors when evaluating the determinants of inter individual variability of 40Hz ASSRs. This is an important finding for neurodiagnostical applications in populations where both the prevalence (Sánchez et al. 2010; Bao and Swaab 2010; Weafer and de Wit 2014) and the severity of the symptoms (Sánchez et al. 2010; Barajas et al. 2015) differ between genders and a high proportion of non-right handedness is observed. Additionally, the field of speech studies, where ASSRs are frequently used, could benefit from these results as the left-hemisphere dominance for speech in males and more frequent bilateral or right hemisphere speech lateralization in females was reported (Miller et al. 2005) with the rightward shift of language dominance shown in the left-handed subjects (Knecht et al. 2000). Further research, including larger gender-balanced groups of right-handed and left-handed participants and covering broader age-span are necessary, together with the evaluation of individual anatomical PAC features, careful estimation of individual sex hormones and GABA levels.

### *Conclusions*

The results of the study suggest that the processing of 40Hz auditory stimulation depends on the subjects' gender and handedness. Significantly lower phase-locking and event-related spectral perturbation values of 40Hz ASSRs were observed the left-handed females as compared to the left-handed males, but right-handers did not differ in 40Hz ASSRs.

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*The Authors declare that there is no conflict of interest.*

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### *Figure Legends*

Figure 1. Grand-averaged topography plots of PLIs within 38-42Hz and 200-500ms window for all stimulation types and study groups – right-handed (RH) and left-handed (LH) subgroups separated by gender. In the centre, a plot of electrodes used for the statistical analysis is depicted: central electrodes (Fz, FCz, Cz) are represented in blue; left-side electrodes (F3, FC1, C3, F1, FC3, C1) are colored in green, and right-side electrodes (F4, FC2, C4, F2, FC4, C2) are marked in orange.

Figure 2. Least square means of phase-locking index (PLI) values and PLI laterality indices with corresponding 95% bars. PLIs obtained over the right, central and left brain areas for all stimulation types in the right-handed (RH) and left-handed (LH) subjects plotted separately for males (blue color) and females (red color). The prominent significant interaction between gender and handedness can be seen. PLI laterality indices for all stimulation types in right-handed (RH) and left-handed (LH) subjects are plotted separately for males in blue and females in red. No significant laterality differences were observed.

Figure 3. Least square means of event-related spectral perturbation (ERSP) values and ERSP laterality indices with corresponding 95% bars. ERSP obtained over the right, central and left brain areas for all stimulation types in the right-handed (RH) and left-handed (LH) subjects separately for males (blue) and females (red). The prominent significant interaction between gender and handedness can be seen. (PLI laterality indices are presented for all stimulation types in right-handed (RH) and left-handed (LH) subjects separately for males in blue and females in red. LH females had significantly more rightward responses as compared to other groups.

**Figure 1**

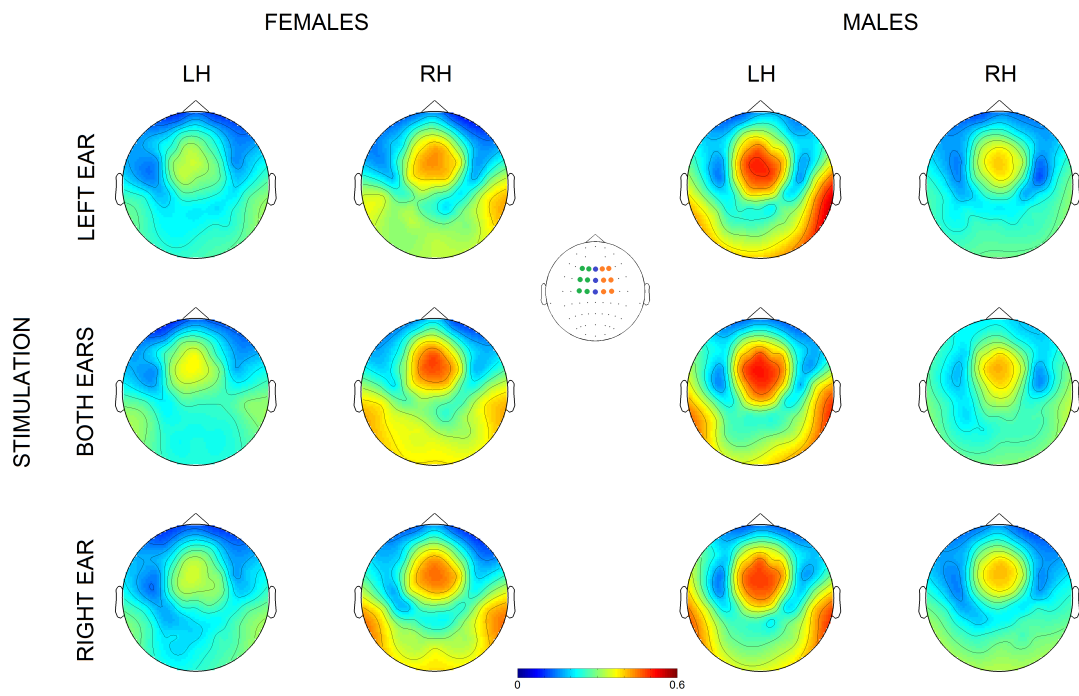


Figure 2

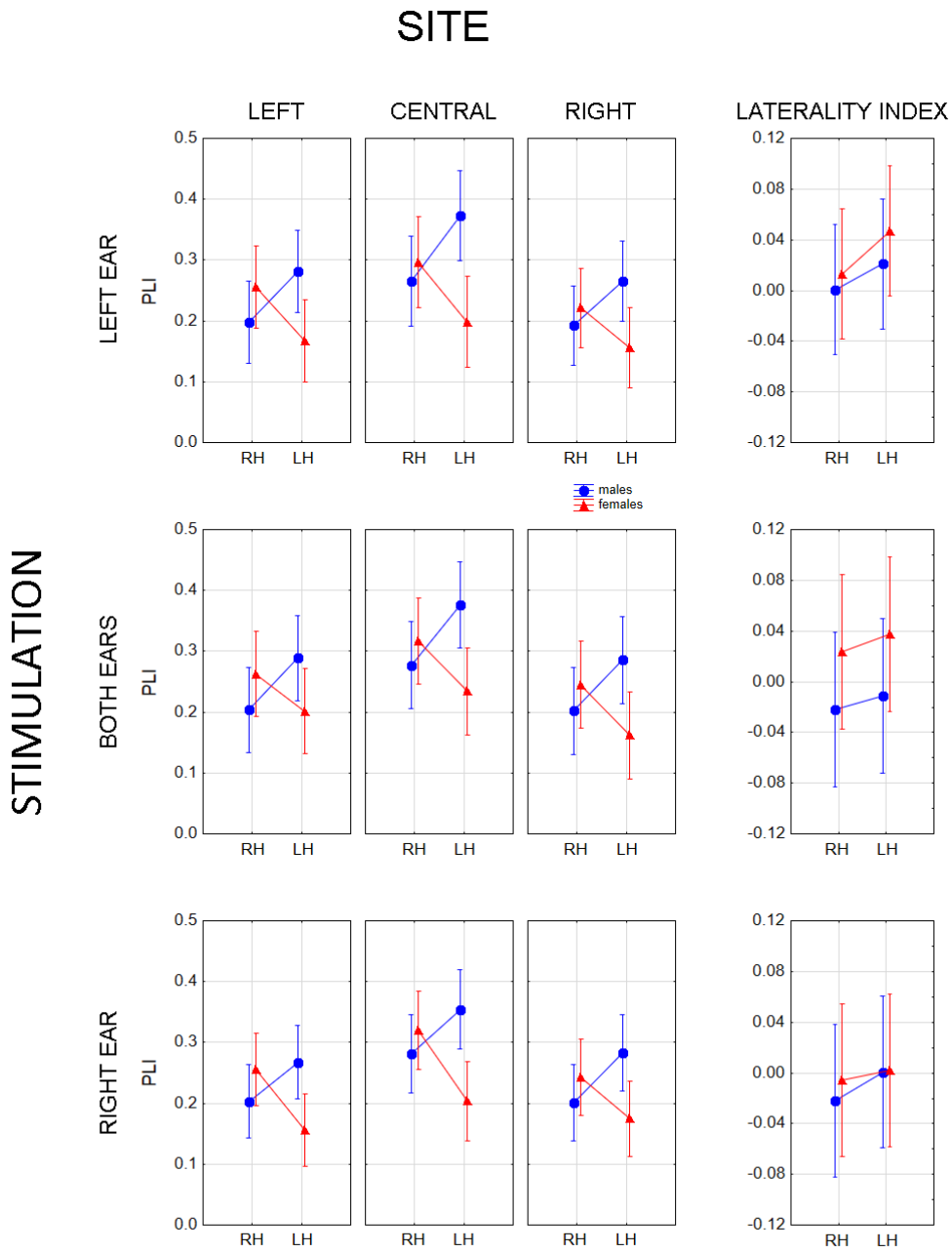


Figure 3

