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Non-stimulus-evoked activity as a measure of neural noise in the frequency-following response

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ABSTRACT

Background: The frequency-following response, or FFR, is a neurophysiologic response that captures distinct aspects of sound processing. Like all evoked responses, FFR is susceptible to electric and myogenic noise contamination during collection. Click-evoked auditory brainstem response collection standards have been adopted for FFR collection, however, whether these standards sufficiently limit FFR noise contamination is unknown. Thus, a critical question remains: to what extent do distinct FFR components reflect noise contamination? This is especially relevant for prestimulus amplitude (i.e., activity preceding the evoked response), as this measure has been used to index both noise contamination and neural noise.

New method: We performed two experiments. First, using >1000 young-adult FFRs, we ran regressions to determine the variance explained by myogenic and electrical noise, as indexed by artifact rejection count and electrode impedance, on each FFR component. Second, we reanalyzed prestimulus amplitude differences attributed to athletic experience and socioeconomic status, adding covariates of artifact rejection and impedance.

Results: We found that non-neural noise marginally contributed to FFR components and could not explain group differences on prestimulus amplitude.

Comparison with existing method: Prestimulus amplitude has been considered a measure of non-neural noise contamination. However, non-neural noise was not the sole contributor to variance in this measure and did not explain group differences.

Conclusions: Results from the two experiments suggest that the effects of non-neural noise on FFR components are minimal and do not obscure individual differences in the FFR and that prestimulus amplitude indexes neural noise.

1. Introduction

The frequency-following response (FFR) is a neurophysiologic response to sound generated primarily in the auditory midbrain that reflects distributed and integrated processing occurring concertedly throughout the auditory system (Bidelman, 2018; Chandrasekaran and Kraus, 2010; Coffey et al., 2019; Kraus and White-Schwoch, 2015; Liang-Fa et al., 2006; White-Schwoch et al., 2019). In humans, this subcortical evoked potential is captured with scalp electrodes, resulting in a response that is microvolts in amplitude (Chandrasekaran and Kraus, 2010). Given its small size, a stimulus, such as speech, is presented to the participant several hundred to thousand times to generate an FFR (Skoe and Kraus, 2010). The large number of stimulus presentations enables the time-locked response to be averaged above the non-evoked noise (Don et al., 1984; Elberling and Don, 1984; Krizman and Kraus, 2019; Skoe and Kraus, 2010). The FFR captures high-fidelity encoding of multiple distinct sound features, including timing of landmark peaks, fundamental frequency and harmonic energies, as well as non-stimulus-evoked electrical activity (Krizman and Kraus, 2019; Krizman et al., 2020b; Skoe and Kraus, 2010; Skoe et al., 2013).

Like any other far-field evoked potential, the FFR is susceptible to noise. For many years, the amplitude of non-stimulus-evoked activity measured over the prestimulus interval (i.e., the silent gap between successive stimulus presentations) was considered a measure of noise

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contamination of the response (Hyde et al., 1998; Junius and Dau, 2005; Musacchia et al., 2006). The contamination was thought to be dominated by non-neural sources, including ambient room noise seeping in through electrodes or muscle movement from fidgety participants. Therefore, a number of previous studies used prestimulus amplitude as an index of FFR recording quality (Musacchia et al., 2006; Russo et al., 2004, 2005). For these studies, the goal was to equate individuals or recording sessions on prestimulus amplitude to ensure that findings, such as group differences or training effects, could not be attributed to variation in data quality. Others, however, have referred to prestimulus amplitude as a measure of background EEG (Dembon et al., 1989; Galbraith et al., 1997), suggesting it is a measure of neural, rather than a measure of non-neural noise. Given these two interpretations, a critical need exists to determine whether prestimulus amplitude reflects non-neural or neural noise.

Though prestimulus amplitude has been used, and still is considered by many, as a measure of non-neural noise, the actual contribution of different noise sources to this measure, or any FFR component, is unknown. Currently, to mitigate the influence of noise, FFR studies apply stringent artifact rejection criteria and very low electrode impedance (Krizman and Kraus, 2019). Artifact rejection count is a record of how many recording epochs had an amplitude too large to be attributable to an evoked response and whose large size was likely due to myogenic or external electric contamination (Hall, 2007; Hood, 1998). With respect to electrode application, the lower the impedance value, and hence, the better the connection between scalp and electrode, the less external noise bleeds in at the scalp-electrode connection (Hall, 2007; Kappenman and Luck, 2010; Luck, 2014; Teplan, 2002). The values used for FFR testing have been based on other classes of subcortical electrophysiological recordings, such as auditory brainstem responses to simple sounds, including clicks and tones (Hall, 2007; Hood, 1998). However, whether these parameters are sufficient or overly stringent to mitigate non-neural noise influences to the FFR has never been empirically tested. Moreover, whether these parameters and the influence of non-neural noise affect distinct FFR components differently is unknown.

To better understand the contributions of non-neural noise sources to distinct FFR components, we ran regressions on individual FFR components from over 1000 young adults to determine the contribution of artifact rejection count and electrode impedance on these components. We hypothesized that contributions of non-neural noise to the FFR are minimal, but that the greatest influence would be to the prestimulus amplitude component of the FFR. Additionally, to understand the magnitude of the effects of non-neural noise on FFR components, we also included age and sex in the regressions, two factors that have been shown to influence FFR components distinctly (Krizman et al., 2012, 2019, 2020a). We did not have any a-priori expectation for how sex, age, impedance, and artifact rejection would influence one another when contributing to distinct FFR components. Therefore, we entered these values into the same regression rather than treating the biological and recording factors separately. By analyzing these measures together, we can determine their independence from one another and also identify how much variance is independently accounted for by each measure.

Understanding the contributions of neural and non-neural noise on FFR recordings is important because a number of measures show effects that are presumed to arise from experience. Most notably, differences in prestimulus amplitude have been linked to athletic experience and, separately, linguistic deprivation associated with low socioeconomic status (Krizman et al., 2020b; Skoe et al., 2013). To conclude that these effects are indeed experiential and not driven by differences in recording quality, a thorough examination of whether these effects can be explained by non-neural noise is warranted. Though electrical and myogenic contamination may contribute to FFR components, particularly prestimulus amplitude, we hypothesized these differences arise from individual differences in *neural* rather than non-neural, noise. If so, then ongoing neural activity would contribute more to prestimulus amplitude than myogenic or electric noise. To test the hypothesis that prestimulus amplitude reflects individual differences in neural noise and not differences in the recording environment, we re-ran analyses exploring the effects of athletic experience and socioeconomic status on prestimulus amplitude covarying for electrode impedance and artifact rejection count. We predicted that differences in prestimulus amplitude would persist when accounting for these non-neural noise sources.

2. Methods

2.1. Participants

2.1.1. Experiment 1

We considered all data previously collected from young adults aged 17–28 years. Data were collected on the Biologic NavPro system between July 2006 and October 2018. Of the 1214 available data points, 60 were missing impedance information and excluded. The remaining 1154 data points included in the analyses were from 1045 participants, of which 961 contributed a single data point, 68 contributed 2, 9 contributed 3, and 7 contributed 4 or more. Multiple recordings were from participants completing more than one study in the lab or participating in longitudinal studies.

2.1.2. Experiment 2

Experiment 2 is a reanalysis of two published datasets (Krizman et al., 2020b; Skoe et al., 2013). In these studies, we reported that prestimulus amplitude varies with sports participation and maternal education level, a proxy for socioeconomic status. Specifically, athletic expertise corresponded with lower levels of prestimulus activity while lower maternal education corresponded with greater activity. Here we reanalyzed these published findings, including electrode impedance and artifact rejection percentage into the analyses, to determine the extent to which non-neural factors can account for group differences in prestimulus activity.

Only participants with both artifact rejection and impedance values were used in these analyses. This resulted in a final group size of 464 athletes (226 female, 20.05 ± 1.3 years of age) and 418 non-athletes (232 female, 19.96 ± 1.98 years of age). The maternal education groups consisted of 27 high-maternal education adolescents (13 female, 14.56 ± 0.31 years) and 30 low-maternal education adolescents (13 female, 14.58 ± 0.36 years).

2.2. Stimulus and recording parameters

The stimulus and recording parameters were consistent across experiments 1 and 2. Stimulus presentation and frequency-following response (FFR) collection were performed with Bio-logic Navigator Pro AEP (Natus Medical Inc., Mundelein, IL). FFRs were recorded in response to ‘da’, a 40 ms, five-formant synthesized speech sound (Klatt, 1980), previously described in detail (Krizman et al., 2012; Skoe and Kraus, 2010). FFRs, were collected using Ag/AgCl electrodes applied in an ipsilateral vertical montage, with active at Cz referenced to the right ear lobe, and ground on the forehead. Preceding and following ‘da’ FFR collection, auditory brainstem responses to a 100 μs broadband click presented in rarefaction at 31.25 Hz were collected to confirm stable ear insert placement during the recording session and normal peripheral function (i.e., click V latency within lab-internal norms (Krizman et al., 2019)).

The FFR was passively recorded while the participant sat comfortably in a darkened, quiet room. The participant was allowed to watch a movie or relax during the recording session. The ‘da’ was presented to the right ear in alternating polarity at 10.9 Hz and 80 dB SPL through a shielded insert earphone (ER-3A, Natus Medical Inc., Mundelein, IL). FFRs were collected over an epoch window that began 15.8 ms prior to stimulus onset to capture non-evoked activity. FFRs were filtered online from 100 to 2000 Hz and artifact rejected online at ±23.8 μV. The final average for each participant consisted of 6000 artifact-free

presentations, 3000 of each polarity. Presenting 'da' in alternating polarity allowed us to generate an average by adding the responses to the two polarities (i.e., 'add') and by subtracting the responses to the two polarities (i.e., 'subtract'). Adding accentuates the envelope and lower frequencies of the response, whereas subtracting accentuates high-frequency FFR components (Aiken and Picton, 2008; Krizman and Kraus, 2019).

During data collection, to minimize the effects of non-neural noise, we maintain electrode impedance at $\leq$5 kΩ and artifact rejection count below 10% (i.e., <600 rejections). Traditionally, data not meeting these metrics are removed from analyses. While this is true for the data analyzed in experiment 2, because the goal of experiment 1 was to determine how these two sources of non-neural noise impact FFR components, data exceeding these standards were included. With respect to electrode impedance, of the 3462 electrode applications (3 electrodes applied per participant for each of the 1154 recordings), only 74 of the electrode applications from 64 recordings (10 recordings had 2 electrodes exceeding impedance limits) exceeded our criterion, ranging between 6 and 35 kΩs. Artifact rejection count had more variability across recordings, with 92 of the 1154 recordings having artifact rejection counts exceeding our criterion. These recordings had counts ranging from 611 to 5804 rejected epochs. Thirteen recordings exceeded both the impedance and artifact rejection criteria, thus 12.4% (143 of 1154) of the FFRs used in these analyses were outside of lab collection standards. Across all recordings, impedance averaged 1.85 ± 1.35 and artifact rejection averaged 206.89 ± 371.25.

2.3. Data analyses

2.3.1. Experiment 1

The FFR is the sum of many parts (Krizman and Kraus, 2019). Within the added FFR, neural timing precision is captured through absolute peak latencies and lag differences between stimulus and neural onset. Pitch encoding is reflected in the amplitude of the fundamental frequency in the added FFR, while timbre encoding is reflected in the amplitude of harmonic frequencies in both the added and subtracted responses. The size of the response reveals the magnitude of synchronous neural firing evoked by the stimulus and response consistency measures the level of synchrony of the neural firing. The size of the activity over the prestimulus region corresponds to the level of non-evoked activity, and based on previous definitions of prestimulus amplitude, the level of non-neural noise present in the response (Elberling and Don, 1984; Hyde et al., 1998; Junius and Dau, 2005). The goal of experiment 1 was to determine the contribution of two sources of non-neural noise, namely, artifact rejection and electrode impedance, on each of these FFR measures. We also included age and sex in these models to determine whether the contribution of non-neural noise sources was comparable to biological factors known to influence FFR measures (Jalaei et al., 2017; Krizman et al., 2012, 2019, 2015; Liu et al., 2017, 2016; Skoe et al., 2015; Vander Werff and Burns, 2011).

For each FFR component, we ran a stepwise regression to determine the contribution of non-neural and biological factors to the variability seen across participants within each component. Because these analyses were performed on previously collected data, some participants had more than one FFR collected across past studies. Rather than arbitrarily exclude a recording, we included all data. To account for this, the first step in the regression was participant identifier, to control for some participants having multiple recordings. To reduce the number of impedance values for each participant, the impedance at each electrode (Cz, Right ear, and Ground) was entered into a factor analysis, which yielded a single impedance factor (Table 1). Because impedance and artifact rejection count had skewed distributions, they were log transformed. The remaing factors were entered into the regression in the following order: age, sex, electrode impedance, and artifact rejection count. The percent variance of each of the 27 FFR components accounted for by each factor (i.e., ID, sex, age, electrode impedance, artifact rejection count) was entered into an ANOVA to determine if the five factors differed in the amount of FFR variance they explained. These differences were followed up with *t*-tests to determine which factors differed from the others in variance explained. Statistics were run in SPSS v. 26 and data were processed using custom routines in Matlab.

Table 1
Factor weighting for impedance at each electrode.

Experiment 1	
All Young Adults (n = 1154)	
Cz	0.586
R ear	0.726
Ground	0.640
Experiment 2	
Athlete (n = 464) v. Non-athlete (n = 418)	
Cz	0.615
R ear	0.692
Ground	0.719
High- (n = 27) v. Low-SES (n = 30)	
Cz	0.778
R ear	0.127
Ground	0.776

2.3.2. Experiment 2

We investigated whether artifact rejection count and electrode impedance could explain differences in prestimulus amplitude seen in athletes vs. non-athletes and low- vs. high-SES (Krizman et al., 2020b; Skoe et al., 2013). As in experiment 1, the impedance covariate was determined by entering the impedance value at each of the three electrodes (Cz, Right ear, and Ground) into a factor analysis. The values loaded onto a single factor (Table 1). The impedance and artifact values were log-transformed for these data to normalize their distributions. Because we were unable to obtain specific impedance values for some participants (see participants section above), we first ran a repeated-measures ANOVA (RMANOVA) for 'add' and 'subtract' prestimulus noise, to establish that these slightly smaller groups showed the prestimulus group difference. We then ran a second RMANOVA covarying for artifact rejection count and impedance to determine if the differences could be accounted for by these non-neural factors. Statistics were run in SPSS v. 26 and data were processed using custom routines in Matlab.

3. Results

Across both experiments, we found that non-neural noise was not a major factor in explaining variability within FFR components. In young adults, biological differences, namely participant sex, had a more pervasive influence on FFR measures than non-neural sources of noise contamination (Fig. 1). Furthermore, when reanalyzing group differences in prestimulus amplitude (Fig. 2), these differences persist when controlling for electrode impedance and myogenic artifact (Fig. 3).

3.1. Experiment 1

For the FFR components, ID, age, sex, impedance, and artifact rejection in total accounted for an average 9.2% of the variance (±4.39%, range: 1.9–18.3%, Fig. 1, Table 2). Across all FFR components, the five factors differed in the amount of variance each explained ($F_{(4, 130)} = 17.658$, $p < .0005$). Participant sex had the largest contribution, affecting 26 of the 27 components measured (5.23 ± 2.75%, range: 0–13.3%), with females showing earlier and larger responses than males. Sex had the greatest influence on peak latencies, response magnitude, and high-frequency encoding. The second largest influence was artifact rejection count, affecting 19 components (2.9 ± 4.65%, range: 0–16.9%). The difference in contribution between these two factors was significant ($t = 2.027$, $p = .048$, $d = 0.552$). Electrode impedance had minimal contribution, affecting only 9 components

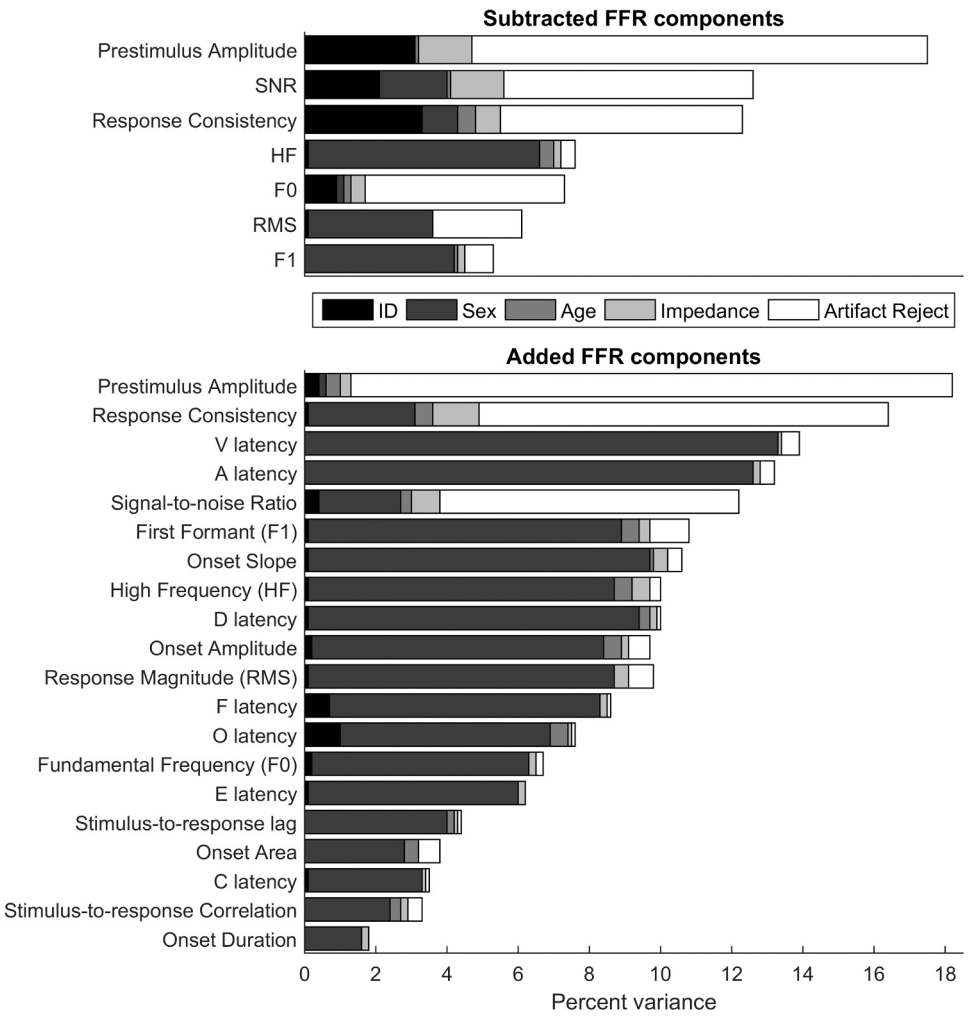

Fig. 1. Percent variance explained by each factor for distinct FFR components. ID (i.e., how many FFRs the participant had, black bars) had a moderate effect on subtracted FFR components but little effect on added components. Additionally, age (medium gray bars) had little effect on FFR components. These small effects are likely due to the limited amount of multiple recordings from the same participant and the narrow age range and relative stability over age seen in young adults. Impedance (light gray bars) also had small effects, which may be due to the majority of data points falling within a strict impedance criterion. Artifact rejection count (white bars) had the second largest contribution to FFR variability, though it was largely driven by its contribution to prestimulus amplitude, response consistency, and signal-to-noise ratio. Sex (dark gray bars) had the largest and most pervasive effect on FFR components. Subtracted FFR components are plotted above the legend and added FFR components are plotted below. Each section is sorted in order of most variance to least variance explained across the five factors. Note that the x-axis maximum value is 18%, indicating that only a small proportion of the variance of these FFR measures can be accounted for by the factors analyzed here.

(0.39 ± 0.42%). Artifact rejection count and electrode impedance had the largest effect on prestimulus amplitude, signal-to-noise ratio (SNR), and response consistency for both the subtracted and added FFR (Fig. 1). However, the combined magnitude of these non-neural noise sources on variability of FFR components was quite small (1.65 ± 2.47%). Given that the fundamental frequency is an envelope-driven response (Aiken and Picton, 2008; Krizman and Kraus, 2019), it is not surprising that the response over the fundamental frequency in the subtracted response also shows a larger noise influence: by subtracting the two polarities, the F0 response is canceled out, leaving only noise (Krizman and Kraus, 2019). Furthermore, it is not surprising that SNR was affected by artifact rejection count given that it is calculated by dividing the response amplitude (RMS) by prestimulus amplitude (Krizman and Kraus, 2019).

3.2. Experiment 2

When comparing only the athletes and non-athletes with artifact rejection count and impedance data, the group differences remained such that athletes had lower levels of prestimulus activity than non-athletes ($F_{(1, 880)} = 26.428$, $p < .0005$, $\eta p^2 = .029$; Figs. 2, 3). This effect did not differ by polarity ($F_{(1, 880)} = 0.049$, $p = .826$, $\eta p^2 = 0$) and there was no polarity by group interaction ($F_{(1, 880)} = 1.992$, $p = .158$, $\eta p^2 = .002$). The addition of electrode impedance and artifact rejection count as covariates in the RMANOVA strengthened the group differences ($F_{(1, 878)} = 43.398$, $p < .0005$, $\eta p^2 = .047$; Fig. 3), even though both impedance and artifact rejection contributed to prestimulus amplitude (Impedance: $F_{(1, 878)} = 8.705$, $p = .003$, $\eta p^2 = .010$; Artifact: $F_{(1, 878)} = 177.607$, $p < .0005$, $\eta p^2 = .168$). There was no effect of polarity ($F_{(1, 878)} = 1.895$, $p = .169$, $\eta p^2 = .002$) and the interaction of polarity and group was not significant ($F_{(1, 878)} = 2.296$, $p = .130$, $\eta p^2 = .003$).

Similarly, the subset of adolescents showed group differences consistent with the original finding, with adolescents in the high-maternal education group having smaller prestimulus amplitude than the adolescents in the low-maternal education group ($F_{(1, 56)} = 7.135$, $p = .01$, $\eta p^2 = .113$, Figs. 2, 3). Again, the effect did not differ by polarity ($F_{(1, 55)} = 1.507$, $p = .225$, $\eta p^2 = .027$) and there was no polarity by group interaction ($F_{(1, 55)} = 0.287$, $p = .594$, $\eta p^2 = .005$). Group differences still had a large effect size after adding in electrode impedance and artifact rejection count as covariates in the RMANOVA ($F_{(1, 53)} = 5.514$, $p = .023$, $\eta p^2 = .094$; Fig. 3). Artifact rejection count had a trending influence on prestimulus amplitude ($F_{(1, 53)} = 3.948$, $p = .052$, $\eta p^2 = .069$), while impedance had no effect ($F_{(1, 53)} = 0.199$, $p = .657$, $\eta p^2 = .004$). There was no effect of polarity ($F_{(1, 53)} = 3.093$, $p = .084$, $\eta p^2 = .055$) and the interaction of polarity and group was not significant ($F_{(1, 53)} = 0.694$, $p = .408$, $\eta p^2 = .013$).

4. Discussion

In this study, we find that stimulus artifact and electrode impedance cannot account for individual differences in the FFR. Rather, the impact of these two sources of non-neural noise on each FFR component is minimal. As demonstrated in experiment 1, sex, a biological factor, had the strongest and most pervasive influence on FFR components; and, as demonstrated in experiment 2, differences in prestimulus amplitude,

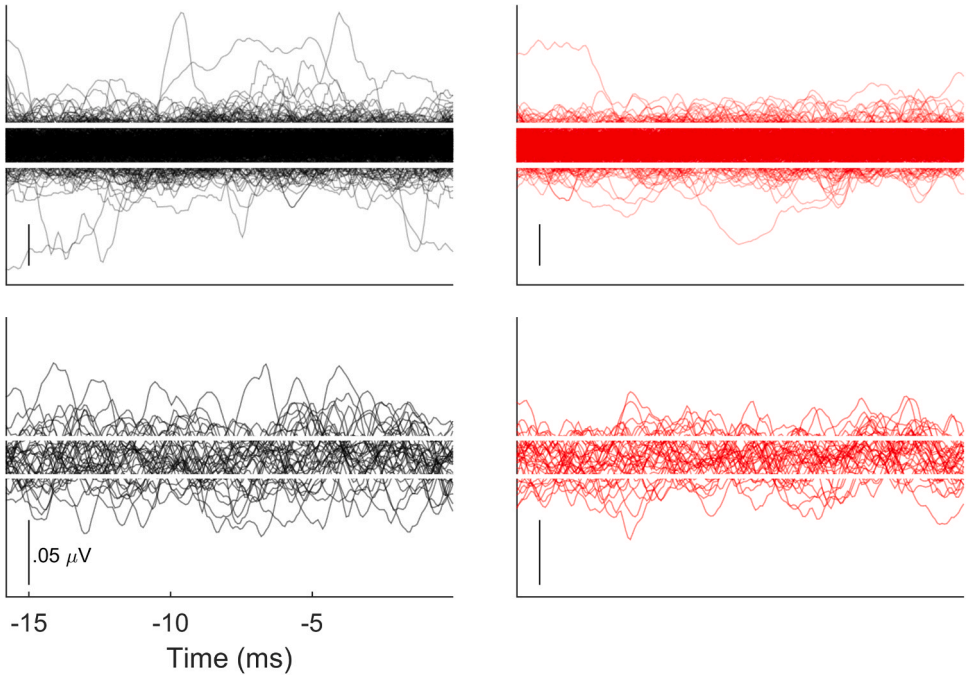

Fig. 2. Prestimulus amplitude varies by experience. Prestimulus amplitude is plotted for non-athlete (top left, black) and athlete (top-right, red) young adults and low-SES (bottom left, black) and high-SES (bottom-right, red) adolescents. Only individuals with impedance and artifact rejection values are plotted. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

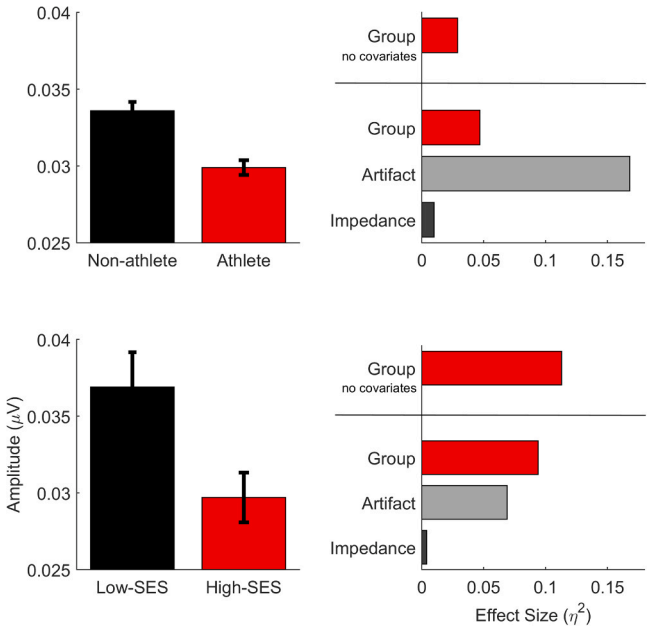

Fig. 3. Prestimulus amplitude differences between groups persist when accounting for sources of non-neural noise. The vertical bars on the left show the averaged prestimulus amplitude for the non-athletes and low-SES participants (black) and athletes and high-SES participants (red). The horizontal bars on the right show the effect size for the group without (top red) and with (bottom red) non-neural noise covariates of artifact rejection count (light gray) and electrode impedance (dark gray). Group differences between athletes and non-athletes are strengthened by adding non-neural noise covariates and SES differences are minimally impacted by these covariates (as indicated by the difference in red horizontal bars). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

which had been attributed to differences in life experience, persisted when controlling for non-neural noise. In fact, on average, electric and myogenic noise only accounted for 1.65% of the variance of FFR components, suggesting that just over 98% of FFR variance is coming from other biological and experiential differences among participants.

The observed sex differences were consistent with previously reported differences, such that females had earlier and larger responses than males (Krizman et al., 2012, 2019, 2020a). While the finding that males and females differ on FFR components is not new, what is new is the comparison between sex and external noise on different FFR components. From these analyses, we find that sex has the greatest influence on the largest number of components and that the influence of sex and artifact rejection on FFR components appear complementary: FFR components that showed a large sex effect showed a small non-neural noise effect (e.g., peak V latency), while components showing a larger non-neural noise effect showed a small sex effect (e.g., prestimulus amplitude). These findings underscore the importance of considering sex as a biological variable in any FFR study.

Prestimulus amplitude has been used as a measure of recording noise (i.e., non-neural noise) and, elsewhere, as a measure of background neural activity (i.e., neural noise; Don et al., 1984; Musacchia et al., 2006; Skoe et al., 2013; Xiao and Braun, 2008). Here we identified the contribution of these different noise sources to each FFR component, including prestimulus amplitude. With respect to non-neural noise, we found that electrode impedance accounted for 0.3% and artifact rejection count explained 16.9% of the prestimulus amplitude variance across participants. This small contribution of impedance and artifact rejection count could not explain the differences in prestimulus amplitude observed between athletes and non-athletes and high- and low-SES adolescents. Together, results from experiments 1 and 2 demonstrate that prestimulus amplitude may be less of an indicator of external noise than previously thought.

Given that non-neural noise contributes minimally to prestimulus amplitude, variability in this measure must be driven in large part by the remaining factor: background neural activity. Thus, prestimulus amplitude differences observed between groups in experiment 2 result from individual differences in life experience, namely athletic

Table 2
Final model beta weights for each factor, total R^2, model F and significance from regression analyses of FFR components.

FFR variable	ID β	Sex β	Age β	Impedance β	Artifact Reject β	R^2	F $_{(df)}$	p
Added FFR								
Onset Duration	-0.015	.129***	-0.023	.049~	-0.012	.019	$4.4_{(5, 1148)}$	.001
Stimulus-to-response Correlation	.001	-0.147***	-0.056~	-0.031	-0.064*	.032	$7.599_{(5, 1148)}$	<0.0005
C latency	-0.045	.183***	-0.015	.041	-0.036	.037	$8.597_{(5, 1133)}$	<0.0005
Onset Area	-0.016	-0.167***	-0.059*	-0.025	.079**	.038	$9.166_{(5, 1148)}$	<0.0005
Stimulus-to-response lag	-0.022	.204***	-0.043	.029	-0.033	.043	$10.282_{(5, 1148)}$	<0.0005
E latency	-0.048	.246***	-0.007	.048~	-0.021	.063	$15.45_{(5, 1146)}$	<0.0005
Fundamental Frequency (F0)	-0.036	-0.251***	.015	-0.054~	.050~	.068	$16.685_{(5, 1148)}$	<0.0005
O latency	-0.104***	.235***	.073*	-0.027	.031	.075	$18.558_{(5, 1143)}$	<0.0005
F latency	-0.092**	.277***	.002	.046	-0.032	.085	$21.371_{(5, 1147)}$	<0.0005
Response Magnitude (RMS)	-0.023	-0.296***	-0.007	-0.070*	.083**	.096	$24.519_{(5, 1148)}$	<0.0005
Onset Amplitude	.044	-0.285***	-0.064*	-0.058*	.080**	.097	$24.786_{(5, 1148)}$	<0.0005
D latency	-0.032	.304***	.049~	.054~	-0.039	.101	$25.582_{(5, 1141)}$	<0.0005
High Frequency (HF)	.033	-0.292***	-0.068*	-0.077**	.058*	.101	$25.722_{(5, 1148)}$	<0.0005
Onset Slope	-0.042	.311***	.026	.069*	-0.065*	.106	$27.182_{(5, 1148)}$	<0.0005
First Formant (F1)	.023	-0.296***	-0.064*	-0.070*	.105***	.107	$27.581_{(5, 1148)}$	<0.0005
Signal-to-noise Ratio	.099***	-0.134***	-0.071*	-0.048~	-0.296***	.122	$31.845_{(5, 1148)}$	<0.0005
A latency	-0.024	.361***	-0.024	.058*	-0.065*	.133	$35.201_{(5, 1148)}$	<0.0005
V latency	-0.020	.370***	-0.014	.037	-0.075**	.140	$37.273_{(5, 1148)}$	<0.0005
Response Consistency	.075**	-0.154***	-0.089**	-0.069*	-0.346***	.166	$45.301_{(5, 1148)}$	<0.0005
Prestimulus Amplitude	-0.100***	-0.070**	.087**	.002	.420***	.183	$51.358_{(5, 1148)}$	<0.0005
Subtracted FFR								
F1	.019	-0.209***	-0.017	-0.056~	.093**	.054	$13.019_{(5, 1148)}$	<0.0005
RMS	-0.047	-0.192***	-0.013	-0.020	.161***	.061	$14.994_{(5, 1148)}$	<0.0005
F0	-0.115***	-0.059*	.055~	.027	.241***	.072	$17.803_{(5, 1148)}$	<0.0005
HF	.034	-0.253***	-0.059 *	-0.048~	.068*	.076	$18.883_{(5, 1148)}$	<0.0005
Response Consistency	.209***	-0.083**	-0.083**	-0.049~	-0.266***	.123	$32.111_{(5, 1148)}$	<0.0005
SNR	.182***	-0.123***	-0.041	-0.088**	-0.270***	.126	$33.184_{(5, 1148)}$	<0.0005
Prestimulus Amplitude	-0.217***	-0.005	.046~	.072**	.364***	.174	$48.448_{(5, 1148)}$	<0.0005

Beta weights:
* <.05, ~<0.1.
** <.01.
*** <.005.

experience and socioeconomic status. These findings indicate that background neural activity measured at the scalp in humans is malleable with experience. Evidence in animals supports this conclusion. Indeed, we know that experience living in a noisy environment or noise exposure, even at low levels, can lead to an increase in background neural activity and spontaneous neural firing (Costalupes et al., 1984; Mulders and Robertson, 2013; Norena and Eggermont, 2003; Pienkowski and Eggermont, 2012; Seki and Eggermont, 2003). In the auditory midbrain, the predominate generator of the electrophysiologically recorded FFR (Bidelman, 2018; Coffey et al., 2016, 2019), the increase in background noise results from a change in the balance of firing of excitatory and inhibitory neurons (Ma et al., 2020). It is possible that malleability of this excitatory-inhibitory balance in humans is captured in the prestimulus amplitude measured at the scalp. Interestingly, while these findings suggest that certain experiences can shape non-neural noise, as indexed by prestimulus amplitude, non-neural noise is unaffected by some biological factors, such as sex (Krizman et al., 2019, 2020a). Future research should investigate the malleability of non-neural noise to different experiential and biological factors.

By virtue of these data being pulled from previous studies, the majority of the data included in experiment 1 and all of the data included in experiment 2 fell within the strict collection criteria for electrode impedance value and artifact rejection count used in our lab. In experiment 1, only ~12% of all recordings had impedance values of >5 kΩs for at least one electrode and/or artifact rejection counts exceeding 600 epochs (i.e., >10% of the total of clean epochs collected). While these values have been adopted from standards set for recording other evoked potentials, their ability to minimize the influence of non-neural noise on FFR components was untested. The present analyses conclusively demonstrate that applying these data collection standards can successfully minimize the influence of non-neural noise on FFR components, and that for some FFR components, these standards may be relaxed to speed up data collection. This study motivates a new line of research to systematically investigate what level of artifact rejection and electrode impedance results in the various FFR components becoming overwhelmed by sources of non-neural noise. Moreover, this study answers a long-standing question about the role non-neural noise plays in previously reported findings of experiential differences on FFR components. Across all components, we find that the role of non-neural noise is minimal and cannot explain previous results.

4.1. Conclusion

In conclusion, we examined contributions of non-neural noise to FFR components across two experiments. We found that electric and myogenic noise, as measured by electrode impedance and artifact rejection count, had minimal effects on FFR components. These findings suggest that differences measured across test sessions or participants for distinct FFR components reflect differences in biology and experience, rather than differences in recording quality. These results support the FFR as a measure of experiential and developmental plasticity in humans.

CRediT authorship contribution statement

Jennifer Krizman: Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Visualization, Writing – original draft. **Silvia Bonacina:** Data curation, Investigation, Validation, Writing – review & editing. **Rembrandt Otto-Meyer:** Data curation, Investigation, Writing – review & editing. **Nina Kraus:** Conceptualization, Funding acquisition, Methodology, Resources, Validation, Writing – review & editing.

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Declaration of Competing Interest

The authors report no declarations of interest.

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