

Review

Enhanced brainstem phase-locking in low-level noise reveals stochastic resonance in the frequency-following response (FFR)

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ABSTRACT

In nonlinear systems, the inclusion of low-level noise can paradoxically improve signal detection, a phenomenon known as stochastic resonance (SR). SR has been observed in human hearing whereby sensory thresholds (e.g., signal detection and discrimination) are enhanced in the presence of noise. Here, we asked whether subcortical auditory processing (neural phase locking) shows evidence of SR. We recorded brainstem frequency-following-responses (FFRs) in young, normal-hearing listeners to near-electrophysiological-threshold (40 dB SPL) complex tones composed of 10 iso-amplitude harmonics of 150 Hz fundamental frequency (F0) presented concurrent with low-level noise (+20 to -20 dB SNRs). Though variable and weak across ears, some listeners showed improvement in auditory detection thresholds with subthreshold noise confirming SR psychophysically. At the neural level, low-level FFRs were initially eradicated by noise (expected masking effect) but were surprisingly reinvigorated at select masker levels (local maximum near ~ 35 dB SPL). These data suggest brainstem phase-locking to near threshold periodic stimuli is enhanced in optimal levels of noise, the hallmark of SR. Our findings provide novel evidence for stochastic resonance in the human auditory brainstem and suggest that under some circumstances, noise can actually benefit both the behavioral and neural encoding of complex sounds.

1. Introduction

Noise is typically considered to be unpleasant, loud, and disruptive, particularly for speech communication. However, under some circumstances, the addition of low-level noise can be beneficial to aspects of hearing (e.g., tinnitus masking treatments; sleep aids). A salient example of noise-related improvements in auditory processing (e.g., signal detection, discrimination), is a phenomenon known as stochastic resonance (Moss, 1994; Stufflebeam et al., 2000; Ward et al., 2002; Zeng et al., 2000). Stochastic resonance (SR) was first used to explain the periodic recurrence of ice ages (Benzi et al., 1981; Benzi et al., 1982; Nicolis, 1982; Nicolis, 1993) but has since been widely observed throughout nature in both physical and biological systems (Chiou-Tan et al., 1996; Collins et al., 1996a; Douglass et al., 1993; Henry, 1999; Stufflebeam et al., 2000). SR is observed in non-linear systems when noise is added at optimal levels and produces a counterintuitive enhancement in signal representation (Benzi et al., 1981; Moss, 1994; Ward et al., 2002). While large increases in noise intensity reduce signal detectability (expected masking effect), for *subthreshold* stimuli, the

addition of optimal levels of noise can actually improve signal detection. For example, when appropriate levels of wide-band noise are added to a periodic stimulus otherwise too faint to detect, the mixture can be said to “resonate” and become discernible (Gammaitoni et al., 1998; Wiensfeld and Moss, 1995).

In accordance with the highly non-linear nature of the human auditory system and basic non-linearity of neurons, several studies have documented evidence of SR in various aspects of audition. For example, Morse and Evans (1996) used nerve stimulation (simulating a cochlear implant) in animal models and found that the addition of select levels of noise resulted in marked improvement in neural responses to different vowel sounds. Despite obvious differences in the transduction mechanisms of electrical hearing, such findings were later applied in translational interventions in order to improve the neural encoding of subsequent perception of speech in cochlear implant patients by including low-level noise into the stimulating electrodes (Brown et al., 1990; Middlebrooks et al., 2005; Morse and Evans, 1996; Morse and Evans, 1999; Morse et al., 2007; Stocks et al., 2002). Similarly, in related psychophysical work, Zeng et al. (2000) found that adding an optimal

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level of noise improved tone detection and frequency discrimination thresholds in individuals with normal and electrical hearing (e.g., cochlear/brainstem implants). These benefits of noise on behavior have been replicated in other psychophysical studies using a variety of tasks (Ries, 2007; Shepherd and Hautus, 2009; Ward et al., 2001).

Electrophysiological studies have shed light on possible neural manifestations of these behavioral SR effects. Neural recordings in animals show SR at the level of first-order sensory neurons in crayfish (Douglass et al., 1993), cricket (Levin and Miller, 1996), shark (Braun et al., 1994), and rat (Collins et al., 1996b). SR has also been observed via noise-related increases in phase locking of cochlear nerve fiber activity in Mongolian gerbils (Henry, 1999). In humans, neuromagnetic (i.e., MEG) recordings from auditory cortex show increased correlation between single-trial evoked potentials and grand average responses recorded to near-threshold tones (6 dB SL) in optimal noise levels compared to no-noise conditions (Stufflebeam et al., 2000). Similarly, Ward et al. (2010) found that optimal noise enhanced the 40-Hz auditory cortical response and alpha/gamma neural synchronization between auditory and linguistic brain areas (e.g., bilateral auditory cortex, left posterior cingulate cortex, and left superior frontal gyrus). Thus, while SR is clearly present at both behavioral and cortical levels of auditory processing, it remains unclear whether such noise-related enhancements in auditory coding can emerge at more peripheral stages of the auditory system (e.g., brainstem).

Here, we asked whether human *subcortical* auditory processing shows evidence of SR. To this end, we recorded brainstem frequency-following-responses (FFRs) in the presence of a range of sub- and supra-threshold noise to assess whether subcortical phase-locking to near-threshold periodic stimuli is enhanced in optimal levels of noise. FFRs are scalp-recorded neurophonic potentials that reflect sustained neural phase-locking to the spectrotemporal properties of complex sounds (Kraus et al., 2017; Krishnan, 2007). When recorded via EEG, FFRs are emitted primarily from brainstem structures (i.e., midbrain inferior colliculus) (Bidelman, 2015; Bidelman, 2018; Bidelman and Momtaz, 2021; Sohmer and Pratt, 1977; Sohmer et al., 1977) and are thus an ideal platform to identify the presence of SR in pre-attentive, subcortical auditory processing. Our hypothesis for the existence of brainstem SR was based on the highly replicated observation that FFRs to lower fundamental frequencies (F0s) are surprisingly robust to noise (Bidelman and Krishnan, 2010; Bidelman et al., 2018; Prevost et al., 2013; Russo et al., 2004; Smalt et al., 2012). As postulated in the literature (Bidelman, 2017; Bidelman and Momtaz, 2021; Prevost et al., 2013), such resilience (and even increment) of the FFR amidst certain noise characteristics might reflect a form of brainstem stochastic resonance, a possibility we herein test empirically. Our findings demonstrate that FFR phase-locking to near-threshold sounds is enhanced in optimal levels of noise, providing novel evidence that SR occurs prior to conscious awareness and as early as the auditory brainstem pathways.

2. Materials & methods

2.1. Participants

A total of 15 young adults (mean age 28.3 ± 3.9 years; 7 males, 8 females) participated in the study. All had normal hearing (i.e., pure tone thresholds ≤ 25 dB HL; 250–8000 Hz) and no history of neuropsychiatric illnesses. They were from mixed race and ethnicity. Eight of the participants were bilingual (English as second language; mean age 26.75 ± 3.07) and three participants had musical training (mean 3.3 ± 6.2 years). All were paid and gave written informed consent in accordance with a protocol approved by the University of Memphis IRB.

2.2. Stimuli

FFRs were recorded to a 200 ms tone complex composed of 10 iso-amplitude harmonics of 150 Hz fundamental frequency (F0) (cf.

Bidelman and Powers, 2018). This F0 is above the phase-locking limit of auditory cortical neurons (Joris et al., 2004) and observable FFRs in cortex (Bidelman, 2018; Bidelman and Momtaz, 2021; Brugge et al., 2009; Gorina-Careta et al., 2021; Guo et al., 2021), and thus ensured that FFRs would be of brainstem origin (Bidelman, 2018). All tokens were gated with $10 \text{ ms } \cos^2$ ramps. To ensure a measurable FFR, tone stimuli were presented at 40 dB SPL, which is roughly 5–10 dB above the electrophysiological threshold for low-frequency FFRs (Bidelman and Powers, 2018; Marsh et al., 1974; Stillman et al., 1976)¹. In addition to the “no-noise” condition, low-level FFRs were recorded in the presence of concurrent masking noise presented between 20 and 60 dB SPL (7 noise levels). Thus, the effective signal-to-noise ratio (SNR) of stimuli ranged from +20 to –20 dB SNR. The masker was a broadband white noise (50–10000 Hz) presented continuously such that it provided a constant backdrop of interference without being time-locked to the stimulus. This ensured FFR measurements (see Section 2.5) were due to phase-locking to the stimulus tone itself and not due to synchronization to the noise. Noise conditions were randomized within and between participants.

Stimulus presentation was controlled by MATLAB® 2019 (The MathWorks, Inc.) routed to a TDT RP2 signal processing interface (Tucker-Davis Technologies). Listeners heard 2000 repetitions of each stimulus presented with fixed, rarefaction polarity² (ISI = 10 ms) delivered binaurally through electromagnetically shielded ER-2 insert earphones (Etymotic Research) (see Fig. S2 in Price and Bidelman, 2021). Stimulus level was calibrated using a Larson-Davis SPL meter (Model LxT) measured in a 2-cc coupler (IEC 60126).

2.3. FFR recording procedures

All testing was carried out in a double-walled, sound-attenuating booth (Industrial Acoustics Company, Inc., Bronx, New York). EEGs were recorded differentially between Ag/AgCl disc electrodes placed on the scalp at the mid-hairline referenced to linked mastoids (A1/A2) (mid-forehead = ground). This montage is ideal for recording FFRs of midbrain origin (Bidelman, 2015; Chandrasekaran and Kraus, 2010). Impedance was kept $\leq 5 \text{ k}\Omega$. EEGs were digitized at 10 kHz (Neuroscan SynAmps RT amplifiers) using an online passband of DC – 4000 Hz. Neural signals were then epoched (–5–205 ms window) and averaged in the time domain to derive FFRs for each condition. Sweeps $> \pm 50 \mu\text{V}$ were rejected as artifacts prior to averaging. On average (across all subjects and conditions), 1899 ± 62 trials survived artifact rejection. Importantly, trial counts did not differ between masker conditions ($F_{7,98} = 0.86, p = 0.54$) indicating FFRs had similar SNR and did not differ in their intrinsic noise level. FFRs were then bandpass filtered (120–1500 Hz; zero-phase –48 dB/oct) for subsequent analysis. Thus, in addition to the high F0 of our stimuli (150 Hz), this high-pass cutoff effectively eradicated cortical activity from our FFRs thereby isolating brainstem responses.

2.4. Behavioral task

We used a 3AFC paradigm to measure tone-in-noise detection thresholds and confirm SR behaviorally. The task was based on customized routines adapted from the PsyAcoustX package for MATLAB (Bidelman et al., 2015). A 2-down, 1-up adaptive tracking procedure

¹ I/O functions (i.e., level dependence) of the FFR suggest a threshold of 30 dB SPL at 150 Hz (Bidelman and Powers, 2018).

² FFR F0 is not affected by stimulus polarity manipulations (Kumar et al., 2014). In contrast, the common approach to add responses to alternating (ALT) phase reversed stimuli distorts the representation of the FFR and reduces it to an envelope following potential containing minimal fine structure (Aiken and Picton, 2008). Contrary to popular belief, ALT polarity also does not allow full separation of the cochlear microphonic (CM) (Chimento & Schreiner, 1990).

estimated the 70.7% correct point on the psychometric function (Levitt, 1971). The target stimulus was a 200 ms, 150 Hz complex tone presented in various amounts of noise as in the FFR experiment. The target tone was randomly placed in one of the three intervals (ISI = 400 ms); the remaining two contained only noise. Interval presentation was demarcated with lights and soft buttons on the computer screen (Bidelman et al., 2015), which helped cue listeners to the timing and sequence of interval presentation even if the stimuli became inaudible (i.e., near threshold). Participants clicked the button corresponding to the interval in which they heard the tone. Trial-by-trial feedback was provided via another graphical light (green = correct; red = incorrect). The next trial commenced 650 ms after listeners' response. The target tone was initially presented at 60 dB SPL. Following two correct responses (detection), the level was decreased by 10 dB for the subsequent trial; it was increased 10 dB following a single incorrect response. Step size was 10 dB for the first four reversals (5 dB step size thereafter). The geometric mean of the last 8 out of 14 reversals was used to compute listeners' tone in noise detection threshold. Separate thresholds were measured in each of 9 masker levels ranging from inaudible (-15 dB SPL) to clearly audible (40 dB SPL) noise (see Fig. 1a). We also measured thresholds in a no-noise (i.e., "clean" condition) to assess baseline (unmasked) tone thresholds. Unmasked thresholds were measured using an identical 3AFC task except the two nontarget intervals contained silence rather than noise (the target tone was placed randomly in the remaining interval). Condition order was randomized within and between participants. Stimulus presentation was controlled by MATLAB and delivered binaurally through Sennheiser HD 280 Pro headphones.

2.5. Data analysis

2.5.1. Behavioral data

We measured threshold shifts relative to the unmasked condition by subtracting no-noise and tone-in-noise thresholds for each noise level. Improvement in the tone detection threshold at any particular noise level (SNR) compared to no-noise indicates SR.

2.5.2. Electrophysiological data

We computed the FFT from each FFR waveform (2048-point FFT). From each spectrum, we measured the magnitude of the response F0, relative to the surrounding noise floor, to quantify the degree of neural phase-locking to pitch-relevant information (e.g., Bidelman and Powers, 2018; Bidelman et al., 2014). Because of the short duration of the pre-stimulus interval, we instead estimated the noise floor from the (post-stimulus) response spectrum. We used a 20-point moving average filter to smooth the FFTs. This eradicated harmonics of the evoked FFR response from the spectrum, providing an estimate of the resting-state EEG noise spectrum (see Fig. 2b). F0 was then identified as the spectral amplitude in the FFT nearest 150 Hz (i.e., the stimulus F0). Amplitudes were then expressed relative to the noise floor. Tracking changes in F0 across noise levels allowed us to assess whether near-threshold FFRs showed an enhancement in signal amplitude at certain noise levels and thus evidence of SR.

2.6. Statistical analysis

We analyzed the data using one-way, mixed-model ANOVAs in R (v1.3.1073) (lme4 package; Bates et al., 2015). The fixed effect was noise level [9 levels for behavioral threshold shift (Fig. 1a); 8 levels for FFR (Fig. 2c)]. Subjects were modeled as a random factor by allowing for a random intercept per subject [i.e., $\text{FFRamp} \sim \text{noiseLevel} + (1|\text{subject})$]. Stochastic resonance is defined as a facilitatory improvement in response amplitude under select levels of noise (McDonnell and Abbott, 2009; McDonnell and Ward, 2011). To test for this specific s-shaped pattern in the data, following the omnibus ANOVA, we used cubic polynomial contrasts (coefficients determined by the emmeans package; Lenth, 2020) [behavior threshold shifts = (-14, 7, 13, 9, 0, -9, -13, -7,

14); FFR amplitude = (-7, 5, 7, 3, -3, -7, -5, 7)] to explicitly model whether behavioral and neural variables conformed to this pattern (i.e., amplitude change to a local maxima/minima, return to baseline, then increasing indefinitely). Additionally, we also used one tailed t-tests to assess whether low-level maskers induced an improvement in tone detection relative to the unmasked baseline condition (i.e., threshold shifts differed from 0) and similarly, whether FFR strength was greater than the noise floor. These *a priori* t-tests were uncorrected for multiple comparisons. Initial diagnostics (QQ- and residual plots) confirmed normality and heterogeneity of variance assumptions for parametric ANOVAs. A priori significance level was set at $\alpha = 0.05$. Effect sizes are reported as η_p^2 .

3. Results

3.1. Behavioral data

Threshold shifts for tone detection relative to the unmasked condition are shown in Fig. 1a. Thresholds varied strongly with low-level noise [$F_{8,112} = 180.08$, $p < 0.0001$, $\eta_p^2 = 0.93$] (Fig. 1a). Detection worsened (i.e., thresholds elevated) once noise became audible (~20 dB), an expected masking effect. However, in low-level subthreshold noise, listeners showed improvements (negative threshold shifts) at certain masker levels [cubic contrast: $t_{112} = 8.94$, $p < 0.0001$, $\eta_p^2 = 0.42$]. This dip (i.e., local threshold improvement) is indicative of SR. SR was more apparent at the individual rather than group level. Subject S5, for example, showed ~5 dB improvement in tone detection with inaudible noise at -10 dB SPL. However, the SR effect was subject to stark individual differences. Across our sample, the strength of SR ranged ~5 dB (Fig. 1b) and occurred at different levels of subthreshold noise (Fig. 1c). On average, listeners showed SR characterized by a ~2.5 dB threshold improvement for noise levels between ± 15 dB SPL (t-test against 0 dB threshold shift, one-tailed; $t_{14} = -5.84$, $p < 0.0001$, $\eta_p^2 = 0.71$), always below the threshold of the masker (t-test against 19.3 dB SPL³, one-tailed: $t_{14} = 8.69$, $p < 0.0001$, $\eta_p^2 = 0.84$). Though, this comparison would likely be more accurate had noise-only thresholds been measured per listener³.

We note these behavioral thresholds shifts are small. However, the null hypothesis predicts that no (i.e., 0 dB) threshold shift should occur for tones in inaudible noise. Any departure from the 0 dB in Fig. 1a is evidence of SR. Still, one question that arises is whether the small magnitudes of these shifts are greater than noise floor of the task itself. To address this issue, we used the within-subject standard error in listeners' thresholds (no-noise condition) to estimate the reliability and thus noise level of each participant's threshold estimate in the task (Saber and Green, 1996). Average standard error in these thresholds across listeners was 1.48 dB across listeners given the parameters of our adaptive tracking procedure (see shading, Fig. 1b)⁴. This suggests the magnitude of threshold shift (i.e., SR effect) was outside the noise floor of the task (i.e., shading in Fig. 1b) for 10/15 (66%) of participants. The magnitude of SR observed here (0–5 dB), while subtle, is also consistent with the magnitude and noise levels reported to elicit SR in previous psychoacoustic studies (Zeng et al., 2000). These data confirm the counterintuitive phenomenon that optimal levels of subthreshold noise can enhance auditory signal detection in some listeners.

³ 19.3 dB SPL reflects the absolute threshold for the noise alone determined in $n=2$ pilot subjects.

⁴ In their model simulations of adaptive psychophysical tracking procedures, Saber and Green (1996) report that for a 2-down 1-up tracking rule and step size of 5 dB (as used here), the standard error of threshold estimate is 1.41 dB ($=4 \text{ dB}/\sqrt{N_{\text{reversals}}}$; here $N_{\text{reversals}}=8$; see their Fig. 3). This theoretical estimate of the task's inherent noise agrees closely with our empirical data, where the average standard error in listeners' threshold estimates was 1.48 dB.

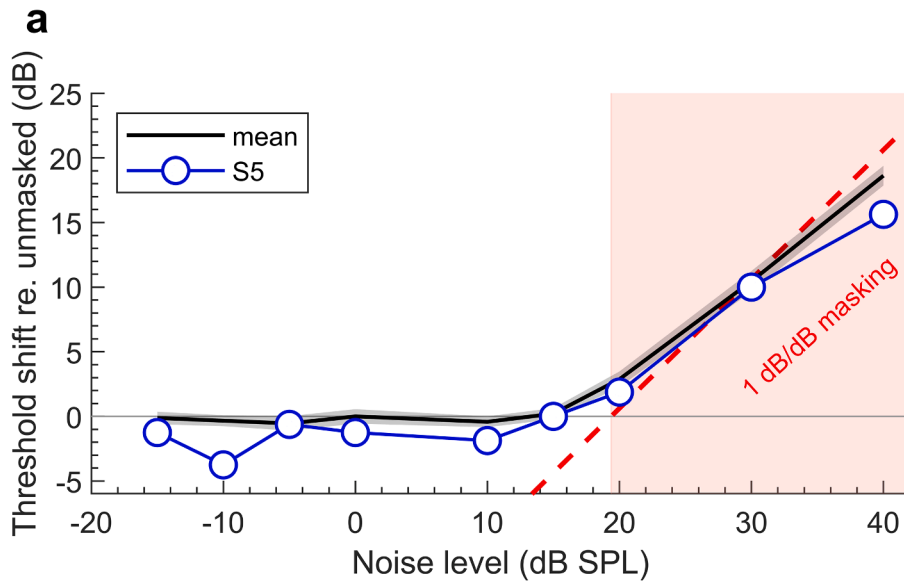


Fig. 1. Behavioral thresholds reveal stochastic resonance in hearing. (a) Tone detection thresholds relative to the no-noise (unmasked) condition. Black line, grand average data ($n = 15$); Blue \circ = representative subject. Red shading = audible noise levels that produce masking, elevating thresholds 1 dB/dB (dotted line). Gray shading = ± 1 s.e.m. Tone in noise thresholds are generally stable for inaudible (sub-threshold) maskers. However, listeners show 2–5 dB of threshold improvement at certain optimal masker levels (e.g., -10 dB SPL for subject S5). (b) Maximum threshold improvement across listeners. SR benefits range from 0 to 5 dB across the sample and occur at different subthreshold noise levels. Shading, estimated noise level of the task computed from the standard error of threshold measurements in the last 8 reversals of the adaptive track (Saberi and Green, 1996). Most (66%) participants' threshold shifts (i.e., SR magnitude) fall outside the noise floor of the task. (c) Noise level at SR corresponding to the maximum threshold shift as observed in panel b. Listeners showed SR below the estimated threshold for the noise alone (19.3 dB SPL, red dotted line). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

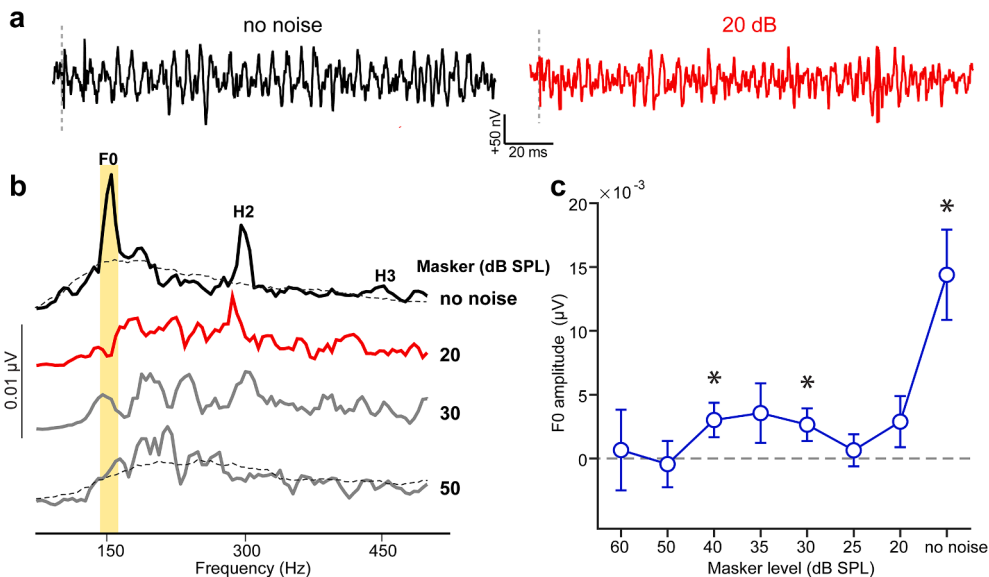
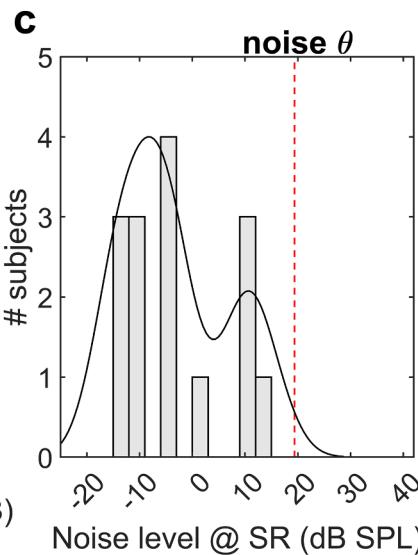
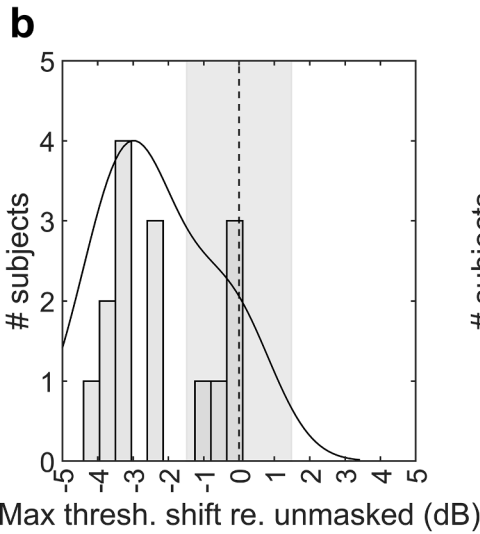


Fig. 2. FFRs reveal stochastic resonance in human auditory brainstem responses. (a) Grand average FFR waveforms elicited by near-threshold (40 dB SPL) complex tones (no-noise and 20 dB masked conditions). Note the reduced periodicity in noise, indicating weaker phase-locking to the stimulus F0. (b) Grand average FFR spectra across select masking conditions. Yellow shading, spectral window for F0 quantification. Red trace, 20 dB response shown in panel a. Dotted lines = noise floor estimate. (c) FFR amplitudes across noise levels. Dotted line = noise floor. Certain masker levels (e.g., see 30 dB SPL) boost the low-level FFR above the noise floor ($*p < 0.05$; one tailed t -test against 0), suggesting brainstem phase-locking is enhanced in optimal levels of noise (i.e., SR). error bars = ± 1 s.e.m. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.2. Frequency-following responses (FFRs)

Grand average FFR waveforms and spectra elicited by near-threshold (40 dB SPL) complex tones are shown in Fig. 2a and b, respectively. The introduction of noise expectedly decreased neural phase locking at F0. Nevertheless, low-level FFRs were strongly modulated by the level of concurrent noise [$F_{7,98} = 4.33, p = 0.00032, \eta_p^2 = 0.24$]. More critically, responses were enhanced in the presence of specific intensities of low-level noise (between 40 and 30 dB SPL), consistent with SR. The small neural effect was confirmed via a polynomial contrast, which suggested a localized “bump” (i.e., improvement) in absolute FFR amplitudes around ~ 35 dB SPL of noise [cubic contrast: $t_{98} = 2.71, p = 0.0077, \eta_p^2 = 0.07$]⁵. Despite noise initially decreasing neural phase locking, FFRs emerged significantly above the noise floor in 30- and 40-dB SPL of noise (i.e., 0 dB and + 10 dB SNR) (one tailed t-tests against 0; $p < 0.05$; Fig. 2d). Importantly, noise floor amplitudes did not significantly differ across conditions [$F_{7,98} = 2.03, p = 0.06, \eta_p^2 = 0.13$], confirming changes in FFR F0 strength were due to phase-locking to the stimulus F0 and not simply a raising or lowering of the noise of recorded responses. However, the correlation between behavioral (Fig. 1c) and FFR amplitude (mean of 40 and 30 dB SPL where SR was observed neurally; see * in Fig. 2c) was not significant.

We further tested for SR effects via a secondary assay of neural synchronization strength by measuring inter-trial phase locking (ITPL) (Anderson et al., 2021; Jenkins et al., 2018; Lachaux et al., 1999; Zhu et al., 2013). In contrast to F0 amplitude, which is computed on each listener’s ensemble (trial-wise) averaged FFR, ITPL considers the phase synchronization of the response across single trials of the data (see *Supplemental Materials*). Mirroring F0 results, FFR phase-locking at the F0 (i.e., ITPL) showed a boost in strength at similar masker levels (cf. Fig. 2c and Fig. S1) despite responses initially being masked at more favorable SNRs. Collectively, these findings suggest brainstem phase locking is enhanced at optimal levels of noise resulting in SR.

4. Discussion

In the present study, we found evidence of SR in both behavioral and brainstem electrophysiological responses. Behaviorally, we found tone detection slightly improved in low-level, subthreshold noise, though this perceptual effect was small and variable across ears. Paralleling these perceptual benefits, electrophysiological recordings of tone evoked FFRs showed enhanced brainstem phase locking in optimal low-level noise. Our findings establish a neural correlate of SR at subcortical levels of the auditory system and suggest that under some circumstances, noise benefits both the behavioral and neural encoding of complex periodic sounds.

4.1. Behavioral SR: Noise aids tone-in-noise detection

Behaviorally, we found an average of ~ 2.5 dB threshold improvement for noise levels between ± 15 dB SPL, always *below* the detection threshold of the masker itself. These results are consistent with the magnitude and noise levels reported to elicit SR in previous psychoacoustic studies (Zeng et al., 2000). They also confirm the counterintuitive phenomenon that optimal levels of subthreshold noise can enhance auditory signal detection. Although we confirmed noise-related improvements in perception, the magnitude of this effect was relatively small (2–5 dB). One explanation for the small behavioral effect is the stark individual differences we observed in SR. This could be because

⁵ Note that the “bump” in FFRs is due to the increase in absolute amplitude above the noise floor. This contrasts the behavioral data which plot thresholds relative to the clean condition making the putative perceptual SR “bump” (i.e., threshold improvement) a downward change in the response.

internal noise already present in the auditory system (i.e., spontaneous neural activity) interacts with the externally presented physical noise (Hanna et al., 1986). Indeed, detection and intensity discrimination of sinusoidal signals elicit shallower psychometric functions in noise compared to quiet (Hanna et al., 1986). Thus, perception in quiet might be limited to internal noise whereas, perception in external noise (as in our study) might be influenced by interactions between both intrinsic and extrinsic noise sources (cf. Gold et al., 2004; Lutfi et al., 2017; Schölvinck et al., 2012). In support of this notion, and despite major differences in acoustic vs. electrical hearing, differences in threshold improvement between individuals with normal hearing (2 dB) compared to individuals with cochlear/brainstem implants (2–6 dB) might be due to a reduction of internal noise in the latter group due to hearing impairment (Zeng et al., 2000).

4.2. Subcortical SR: Noise enhances brainstem FFR phase locking

By measuring near-threshold brainstem FFRs in low-level noise, we show significant enhancements in phase locking at optimal levels of noise resulting in SR. Our FFR results are consistent with previous cortical electrophysiological studies (Stufflebeam et al., 2000) which found enhanced evoked responses by a weak stimulus when low-level background noise was added. Even though introducing noise initially decreased neural phase-locking from the no-noise condition, surprisingly, FFRs emerged above the noise floor at select noise levels. FFRs were especially prominent above the noise floor in 30- and 40-dB SPL of noise (i.e., 0 dB and + 10 dB SNR). Though the amplitude of F0 for the noise conditions was above the noise floor, it was always smaller than the no-noise condition. Thus, we find an initial diminishment of near-threshold FFRs with the introduction of some noise—an expected masking effect. FFR phase-locking is then partially reinstated at more moderate noise levels (e.g., “mid-level bump”, Fig. 2c)—suggestive of SR. FFRs are then subsequently eradicated to the noise floor at increasingly higher noise levels—indicative of (over)masking.

The range of values over which SR emerged was slightly smaller for FFRs (~25 dB range; Fig. 2) compared to what we observed behaviorally (~30 dB range; Fig. 1). Differences in the “operating point” of SR presumably reflect the fact that FFRs were recorded with suprathreshold tones whereas the behavioral SR was measured at thresholds. Though typically described as a near-threshold phenomenon, it is conceivable that SR can emerge for suprathreshold stimuli as observed in our FFRs if low spontaneous rate auditory neurons, which have higher thresholds, are more engaged by the suprathreshold stimuli in our task. Single unit recordings in animals would be needed to test this possibility by assessing SR in sub-populations of neurons.

Theoretically, it has been suggested that greater stochastic resonance is observed when noise (i.e., spontaneous activity) among different neurons is uncorrelated (Collins et al., 1996a; Parnas, 1996). In contrast, external noise might partially correlate cross-channel neuronal activity (Collins et al., 1996a; Parnas, 1996) thereby worsening signal detection at threshold—as observed in the visual system (e.g., Gutnisky et al., 2017; Schölvinck et al., 2012). Also, studies using intracellular recordings have shown that adding an optimal amount of noise increases the information flow in the auditory nerve (Stufflebeam et al., 2000). At a cortical level, these effects have been shown to manifest as a decrease in latency rather than an increase in the amplitude of cortical responses (Collins et al., 1996a; Stufflebeam et al., 2000). Our use of single polarity stimuli and a mastoid reference electrode also suggests our FFRs likely contained some pickup of the cochlear microphonic (CM) (Chimento and Schreiner, 1990)—though auditory nerve contributions to the FFR are more likely (Bidelman, 2015; Bidelman, 2018; Bidelman and Momtaz, 2021). This raises the intriguing possibility that SR might be observed even more peripherally than the midbrain generators of the FFR (e.g., Henry, 1999), perhaps as early as the cochlea. Future studies are needed to test this possibility.

We did not find a correlation between the behavioral and the FFR

measures of SR. In addition to the large inter-subject variability, several explanations might account for this null brain-behavior correspondence. First, given the mismatch between behavioral and electrophysiological thresholds, neural and behavioral SR were measured at different overall sound levels—though both near their respective thresholds. In addition, behavior engages the entire auditory system (including higher-level perceptual systems), well beyond the midbrain and lower neural generators which primarily drive the FFR (Bidelman, 2015; Bidelman, 2018; Bidelman and Momtaz, 2021). Thus, even if an SR effect is observed in the FFR, higher-level “signal detection” systems may not be affected by the addition of noise in the same manner. Relatedly, the neural code used to behaviorally detect a near-threshold stimulus likely extends beyond the mere brainstem temporal phase-locking that underlies the FFR and may require a different coding strategy entirely (e.g., rate-based rather than temporal representation). Lastly, listeners combine information across harmonics to construct a unitary pitch percept (Bidelman and Krishnan, 2009; Gockel et al., 2007; Terhardt et al., 1982). Consequently, behavioral SR likely depends on the physiological response to all tone harmonics, and not just at F0 where FFR phase-locking was quantified. This point might also account for the stronger SR effects observed in F0 amplitude (Fig. 2) vs. ITPL measures (Fig. S1); the former is driven by FFRs to all harmonically related components of the signal F0 whereas the latter reflects phase-locking primarily at the F0. The aforementioned factors may also account for why the behavioral results did not completely mirror electrophysiological responses in our study.

5. Conclusion

Our findings provide novel evidence for stochastic resonance in the human auditory brainstem and suggest that under some circumstances, noise can benefit both the behavioral and neural encoding of complex sounds. The presence of SR at pre-attentive, subcortical levels of human auditory processing, coupled with previous observations in cochlear and cortical physiological responses, indicates neural resonance phenomena are likely widely distributed across the auditory hierarchy. More broadly, SR may reflect an intrinsic mechanism of brain function, a form of entrainment that aids sensory-perceptual coding (Bidelman and Patro, 2016; Coffey et al., 2021; Gourévitch et al., 2020).

Future avenues of work could investigate how the objective indices of SR observed here are altered with experiential factors known to enhance (e.g., musicianship) or hinder (e.g., hearing loss) the processing of noise-degraded acoustic signals (e.g., Anderson et al., 2012; Bidelman and Krishnan, 2010; Bidelman and Yoo, 2020; Bidelman and Momtaz, 2021; Price et al., 2019; Song et al., 2011). Moreover, speech-in-noise listening abilities vary substantially among even normal hearing listeners (Bidelman, 2017; Bidelman et al., 2018; Song et al., 2011). Future studies could test the possibility that noise deficits in otherwise “normal-hearing” individuals vary according to the degree to which their auditory neural responses express more or less SR.

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Appendix A. Supplementary data

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References

Aiken, S.J., Picton, T.W., 2008. Envelope and spectral frequency-following responses to vowel sounds. *Hearing Research*. 245 (1-2), 35–47.

- Anderson, S., Parbery-Clark, A., White-Schwoch, T., Kraus, N., 2012. Aging affects neural precision of speech encoding. *Journal of Neuroscience*. 32 (41), 14156–14164.
- Anderson, S., Bieber, R., Schloss, A., 2021. Peripheral deficits and phase-locking declines in aging adults. *Hearing Research*. 403, 108188. <https://doi.org/10.1016/j.heares.2021.108188>.
- Bates, D., et al., 2015. Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*. 67, 1–48.
- Benzi, R., Sutera, A., Vulpiani, A., 1981. The mechanism of stochastic resonance. *Journal of Physics A: Mathematical and General*. 14 (11), L453–L457.
- Benzi, R., Parisi, G., Sutera, A., Vulpiani, A., 1982. Stochastic resonance in climatic change. *Tellus*. 34 (1), 10–15.
- Bidelman, G., Powers, L., 2018. Response properties of the human frequency-following response (FFR) to speech and non-speech sounds: level dependence, adaptation and phase-locking limits. *International Journal of Audiology*. 57 (9), 665–672.
- Bidelman, G.M., Krishnan, A., 2009. Neural correlates of consonance, dissonance, and the hierarchy of musical pitch in the human brainstem. *Journal of Neuroscience*. 29 (42), 13165–13171.
- Bidelman, G.M., Krishnan, A., 2010. Effects of reverberation on brainstem representation of speech in musicians and non-musicians. *Brain Research*. 1355, 112–125.
- Bidelman, G.M., Weiss, M.W., Moreno, S., Alain, C., 2014. Coordinated plasticity in brainstem and auditory cortex contributes to enhanced categorical speech perception in musicians. *European Journal of Neuroscience*. 40 (4), 2662–2673.
- Bidelman, G.M., 2015. Multichannel recordings of the human brainstem frequency-following response: Scalp topography, source generators, and distinctions from the transient ABR. *Hearing Research*. 323, 68–80.
- Bidelman, G.M., Jennings, S.G., Strickland, E.A., 2015. PsyAcoustX: A flexible MATLAB® package for psychoacoustics research. *Frontiers in Psychology*. 6, 1–11.
- Bidelman, G.M., Patro, C., 2016. Auditory perceptual restoration and illusory continuity correlates in the human brainstem. *Brain Research*. 1646, 84–90.
- Bidelman, G.M., 2017. Communicating in challenging environments: Noise and reverberation. In: Kraus, N., Anderson, S., White-Schwoch, T., Fay, R.R., Popper, A. N. (Eds.), *Springer Handbook of Auditory Research: The frequency-following response: A window into human communication*. Springer Nature, New York, N.Y.
- Bidelman, G.M., 2018. Subcortical sources dominate the neuroelectric auditory frequency-following response to speech. *NeuroImage*. 175, 56–69.
- Bidelman, G.M., Davis, M.K., Pridgen, M.H., 2018. Brainstem-cortical functional connectivity for speech is differentially challenged by noise and reverberation. *Hearing Research*. 367, 149–160.
- Bidelman, G.M., Yoo, J., 2020. Musicians show improved speech segregation in competitive, multi-talker cocktail party scenarios. *Frontiers in Psychology*. 11, 1–11.
- Bidelman, G.M., Momtaz, S., 2021. Subcortical rather than cortical sources of the frequency-following response (FFR) relate to speech-in-noise perception in normal-hearing listeners. *Neuroscience Letters*. 746, 135664. <https://doi.org/10.1016/j.neulet.2021.135664>.
- Braun, H.A., Wissing, H., Schäfer, K., Hirsch, M.C., 1994. Oscillation and noise determine signal transduction in shark multimodal sensory cells. *Nature*. 367 (6460), 270–273.
- Brown, C.J., Abbas, P.J., Gantz, B., 1990. Electrically evoked whole-nerve action potentials: data from human cochlear implant users. *The Journal of the Acoustical Society of America*. 88 (3), 1385–1391.
- Brugge, J.F., Nourski, K.V., Oya, H., Reale, R.A., Kawasaki, H., Steinschneider, M., Howard, M.A., 2009. Coding of repetitive transients by auditory cortex on Heschl's gyrus. *Journal of Neurophysiology*. 102 (4), 2358–2374.
- Chandrasekaran, B., Kraus, N., 2010. The scalp-recorded brainstem response to speech: Neural origins and plasticity. *Psychophysiology*. 47, 236–246.
- Chimento, T.C., Schreiner, C.E., 1990. Selectively eliminating cochlear microphonic contamination from the frequency-following response. *Electroencephalography and Clinical Neurophysiology*. 75, 88–96.
- Chiou-Tan, F.Y., et al., 1996. Enhancement of subthreshold sensory nerve action potentials during muscle tension mediated noise. *International Journal of Bifurcation and Chaos* 06 (07), 1389–1396.
- Coffey, E.B.J., Arseneau-Bruneau, I., Zhang, X., Baillet, S., Zatorre, R.J., 2021. Oscillatory entrainment of the frequency-following response in auditory cortical and subcortical structures. *Journal of Neuroscience* 41 (18), 4073–4087.
- Collins, J.J., Imhoff, T.T., Grigg, P., 1996a. Noise-enhanced tactile sensation. *Nature*. 383 (6603), 770.
- Collins, J.J., Imhoff, T.T., Grigg, P., 1996b. Noise-enhanced information transmission in rat SA1 cutaneous mechanoreceptors via aperiodic stochastic resonance. *Journal of Neurophysiology*. 76 (1), 642–645.
- Douglass, J.K., Wilkens, L., Pantazelou, E., Moss, F., 1993. Noise enhancement of information transfer in crayfish mechanoreceptors by stochastic resonance. *Nature*. 365 (6444), 337–340.
- Gammaitoni, L., Hänggi, P., Jung, P., Marchesoni, F., 1998. Stochastic resonance. *Reviews of Modern Physics*. 70 (1), 223–287.
- Gockel, H.E., Moore, B.C.J., Carlyon, R.P., Plack, C.J., 2007. Effect of duration on the frequency discrimination of individual partials in a complex tone and on the discrimination of fundamental frequency. *Journal of the Acoustical Society of America*. 121 (1), 373–382.
- Gold, J.M., Sekuler, A.B., Bennett, P.J., 2004. Characterizing perceptual learning with external noise. *Cognitive Science*. 28, 167–207.
- Gorina-Careta, N., Kurkela, J.L.O., Hämäläinen, J., Astikainen, P., Escera, C., 2021. Neural generators of the frequency-following response elicited to stimuli of low and high frequency: A magnetoencephalographic (MEG) study. *NeuroImage*. 231, 117866. <https://doi.org/10.1016/j.neuroimage.2021.117866>.
- Gourévitch, B., Martin, C., Postal, O., Eggermont, J.J., 2020. Oscillations in the auditory system and their possible role. *Neurosci Biobehav Rev*. 113, 507–528.

- Guo, N., Si, X., Zhang, Y., Ding, Y., Zhou, W., Zhang, D., Hong, B.o., 2021. Speech frequency-following response in human auditory cortex is more than a simple tracking. *NeuroImage*. 226, 117545. <https://doi.org/10.1016/j.neuroimage.2020.117545>.
- Gutnisky, D.A., et al., 2017. Cortical response states for enhanced sensory discrimination. *eLife* 6, e29226.
- Hanna, T.E., von Gierke, S.M., Green, D.M., 1986. Detection and intensity discrimination of a sinusoid. *The Journal of the Acoustical Society of America*. 80 (5), 1335–1340.
- Henry, K.R., 1999. Noise improves transfer of near-threshold, phase-locked activity of the cochlear nerve: evidence for stochastic resonance? *Journal of Comparative Physiology A*. 184 (6), 577–584.
- Jenkins, K.A., et al., 2018. Effects of amplification on neural phase locking, amplitude, and latency to a speech syllable. *Ear and Hearing*. 39, 810–824.
- Joris, P.X., Schreiner, C.E., Rees, A., 2004. Neural processing of amplitude-modulated sounds. *Physiological Reviews*. 84 (2), 541–577.
- Kraus, N., et al., 2017. *Springer Handbook of Auditory Research: The frequency-following response: A window into human communication*. Springer Nature, New York, N.Y.
- Krishnan, A., 2007. Human frequency following response. In: Burkard, R.F., Don, M., Eggermont, J.J. (Eds.), *Auditory evoked potentials: Basic principles and clinical application*. Lippincott Williams & Wilkins, Baltimore, pp. 313–335.
- Kumar, K., Bhat, J.S., D'Costa, P.E., Srivastava, M., Kalaiah, M.K., 2014. Effect of Stimulus Polarity on Speech Evoked Auditory Brainstem Response. *Audiology research*. 3 (1), 52–56.
- Lachaux, J.-P., Rodriguez, E., Martinerie, J., Varela, F.J., 1999. Measuring phase synchrony in brain signals. *Human Brain Mapping*. 8 (4), 194–208.
- Lenth, R., 2020. *emmeans: Estimated Marginal Means, aka Least-Squares Means. R package version 1.5.2-1*. <https://CRAN.R-project.org/package=emmeans>.
- Levin, J.E., Miller, J.P., 1996. Broadband neural encoding in the cricket cercal sensory system enhanced by stochastic resonance. *Nature*. 380, 165–168.
- Levitt, H., 1971. Transformed up-down methods in psychoacoustics. *Journal of the Acoustical Society of America*. 49 (2B), 467–477.
- Lutfi, R., Tan, A., Lee, J., 2017. Individual differences in cocktail party listening: The relative role of decision weights and internal noise. *Proceedings of Meetings on Acoustics*. 30, 050010.
- Marsh, J.T., Brown, W.S., Smith, J.C., 1974. Differential brainstem pathways for the conduction of auditory frequency-following responses. *Electroencephalography and Clinical Neurophysiology*. 36, 415–424.
- McDonnell, M.D., Abbott, D., 2009. What is stochastic resonance? Definitions, misconceptions, debates, and its relevance to biology. *PLOS Computational Biology*. 5 (5), e1000348.
- McDonnell, M.D., Ward, L.M., 2011. The benefits of noise in neural systems: bridging theory and experiment. *Nature Reviews Neuroscience*. 12 (7), 415–425.
- Middlebrooks, J.C., Bierer, J.A., Snyder, R.L., 2005. Cochlear implants: the view from the brain. *Current Opinion in Neurobiology*. 15 (4), 488–493.
- Morse, R.P., Evans, E.F., 1996. Enhancement of vowel coding for cochlear implants by addition of noise. *Nature medicine*. 2 (8), 928–932.
- Morse, R.P., Evans, E.F., 1999. Additive noise can enhance temporal coding in a computational model of analogue cochlear implant stimulation. *Hearing research*. 133 (1-2), 107–119.
- Morse, R.P., Morse, P.F., Nunn, T.B., Archer, K.A.M., Boyle, P., 2007. The effect of Gaussian noise on the threshold, dynamic range, and loudness of analogue cochlear implant stimuli. *Journal of the Association for Research in Otolaryngology*. 8 (1), 42–53.
- Moss, F., 1994. Stochastic Resonance: From the Ice Ages to the Monkey's Ear. In: *Contemporary Problems in Statistical Physics. Other Titles in Applied Mathematics. Society for Industrial and Applied Mathematics*, pp. 205–253.
- Nicolis, C., 1982. Stochastic aspects of climatic transitions—response to a periodic forcing. *Tellus*. 34 (1), 1–9.
- Nicolis, C., 1993. Long-term climatic transitions and stochastic resonance. *Journal of Statistical Physics*. 70 (1-2), 3–14.
- Parnas, B.R., 1996. Noise and neuronal populations conspire to encode simple waveforms reliably. *IEEE transactions on biomedical engineering*. 43 (3), 313–318.
- Prevost, F., Laroche, M., Marcoux, A.M., Dajani, H.R., 2013. Objective measurement of physiological signal-to-noise gain in the brainstem response to a synthetic vowel. *Clinical Neurophysiology*. 124 (1), 52–60.
- Price, C.N., Alain, C., Bidelman, G.M., 2019. Auditory-frontal channeling in α and β bands is altered by age-related hearing loss and relates to speech perception in noise. *Neuroscience*. 423, 18–28.
- Price, C.N., Bidelman, G.M., 2021. Attention reinforces human corticofugal system to aid speech perception in noise. *NeuroImage*. 235, 118014. <https://doi.org/10.1016/j.neuroimage.2021.118014>.
- Ries, D.T., 2007. The influence of noise type and level upon stochastic resonance in human audition. *Hearing Research*. 228 (1-2), 136–143.
- Russo, N., Nicol, T., Musacchia, G., Kraus, N., 2004. Brainstem responses to speech syllables. *Clinical Neurophysiology*. 115 (9), 2021–2030.
- Saberi, K., Green, D.M., 1996. Adaptive psychophysical procedures and imbalance in the psychometric function. *J. Acoust. Soc. Am.* 100 (1), 528–536.
- Schölvinc, M.L., Friston, K.J., Rees, G., 2012. The influence of spontaneous activity on stimulus processing in primary visual cortex. *NeuroImage*. 59 (3), 2700–2708.
- Shepherd, D., Hautus, M.J., 2009. Evidence of stochastic resonance in an auditory discrimination task may reflect response bias. *Attention, Perception, & Psychophysics*. 71 (8), 1931–1940.
- Smalt, C.J., Krishnan, A., Bidelman, G.M., Ananthakrishnan, S., Gandour, J.T., 2012. Distortion products and their influence on representation of pitch-relevant information in the human brainstem for unresolved harmonic complex tones. *Hearing Research*. 292 (1-2), 26–34.
- Sohmer, H., Pratt, H., 1977. Identification and separation of acoustic frequency following responses (FFRs) in man. *Electroencephalography and Clinical Neurophysiology*. 42 (4), 493–500.
- Sohmer, H., Pratt, H., Kinarti, R., 1977. Sources of frequency-following responses (FFR) in man. *Electroencephalography and Clinical Neurophysiology*. 42 (5), 656–664.
- Song, J.H., et al., 2011. Perception of speech in noise: Neural correlates. *Journal of Cognitive Neuroscience*. 23, 2268–2279.
- Stillman, R.D., Moushegian, G., Rupert, A.L., 1976. Early tone-evoked responses in normal and hearing-impaired subjects. *Audiology* 15 (1), 10–22.
- Stocks, N.G., Allingham, D., Morse, R.P., 2002. The application of suprathreshold stochastic resonance to cochlear implant coding. *Fluctuation and Noise Letters*. 2, L169–L181.
- Stufflebeam, S.M., Poeppel, D., Roberts, T.P., 2000. Temporal encoding in auditory evoked neuromagnetic fields: stochastic resonance. *Neuroreport* 11, 4081–4085.
- Terhardt, E., Stoll, G., Seewann, M., 1982. Algorithm for the extraction of pitch and pitch salience from complex tonal signals. *Journal of the Acoustical Society of America*. 71, 679–687.
- Ward, L.M., et al., 2001. Noise can help as well as hinder seeing and hearing. *Bull Am Phys Soc*. 46, N23.
- Ward, L.M., MacLean, S.E., Kirschner, A., 2010. Stochastic resonance modulates neural synchronization within and between cortical sources. *PloS One* 5 e14371–e14371.
- Ward, L.M., Neiman, A., Moss, F., 2002. Stochastic resonance in psychophysics and in animal behavior. *Biological Cybernetics*. 87, 91–101.
- Wiesenfeld, K., Moss, F., 1995. Stochastic resonance and the benefits of noise: from ice ages to crayfish and SQUIDS. *Nature*. 373 (6509), 33–36.
- Zeng, F.G., Fu, Q.J., Morse, R., 2000. Human hearing enhanced by noise. *Brain Research*. 869, 251–255.
- Zhu, L., et al., 2013. A comparison of spectral magnitude and phase-locking value analyses of the frequency-following response to complex tones. *Journal of the Acoustical Society of America*. 134 (1), 384–395.