

The effect of stimulation rate on cervical vestibular evoked myogenic potential quality

Faten S. Obeidat (Corresponding Authors)

Institute of Sound and Vibration Research

University of Southampton

Highfield, Southampton, United Kingdom

SO17 1BJ

Fso1e13@soton.ac.uk

Steven L. Bell

Institute of Sound and Vibration Research

University of Southampton

Highfield, Southampton, United Kingdom

SO17 1BJ

S.L.Bell@soton.ac.uk

Conflict of Interest Statement: University of Jordan provided financial support for this research.

The present study explored the effect of repetition rate on the quality, amplitude and presence of the cervical vestibular evoked myogenic potentials (cVEMPs) at a fixed tone-burst level.

cVEMPs are short-latency electromyographic (EMG) potentials elicited by stimulating the ear with high-level sound (around 95 dBA) and can provide diagnostic information about the vestibulocollic reflex pathway. cVEMP is an inhibitory biphasic potential with an early positive-negative component arising at 13-23 ms after stimulus presentation (P13-N23 or P1-N1). The conventional approach for evaluating the presence of cVEMP responses is visual inspection by the audiologist of two or more runs to identify replications of significant peak and trough components in the waveform. This visual evaluation of the response is problematic when the signal-to-noise ratio is poor due to a small response relative to the physiological background noise. Elberling and Don. (1984) proposed the F_{sp} statistic as an objective estimate of response quality that increases with signal-to-noise ratio.

Although some previous studies have subjectively explored the effects of rate on air conduction cVEMPs by measuring peak-to-peak amplitude and peak latency, none have used objective methods to assess the quality of responses. Previous work (Carnaúba et al., 2013; van Tilburg et al., 2016; Wu & Murofushi, 1999) have looked at parameters of the cVEMP such as amplitude, latency or threshold as a function of rate. However, these authors have not directly measured response quality. For a given cVEMP response, the response can contain high or low noise. Indeed a potential problem with subjective estimates of amplitude or latency is that noise and response can be confused and introduce measurement variability. By using the F_{sp} , an objective measure of quality is obtained.

Such objective response metrics as a function of rate have not been used before with cVEMP. van Tilburg et al. (2016) only looked at two rates and did not map the rate function over many rates. They did not use objective methods to determine when a response was present.

Wu & Murofushi, (1999) did look at several rates, but only measured amplitude and latency subjectively and they did not measure quality objectively. Brantberg and Fransson (2001) attempted to objectively indicate response presence for the cVEMP. However they did not use statistical metrics of quality that can be compared across rates, such as the F_{sp} and their method for response detection is not a standard one for evoked response detection. They also only explored a limited set of rates. Our approach of bootstrapping the F_{sp} to obtain a p value is a more statistically robust measure of quality than previous approaches. Our work is therefore the first to objectively quantify response quality as a function of rate.

We also explored the effect of very high repetition rates on the cVEMP response. High repetition rates require a shorter recording time than low repetition rates for the same number of averages, so using high rates in evoking cVEMP could potentially lessen fatigue and the need to maintain neck tension for the subject. The number of epochs was fixed ($N=150$) for all rates, so the duration of recording varied from rate to rate. As the peak level of the stimulus was fixed, if we had fixed the recording duration then high rate recordings would have resulted in excessive noise exposure for subjects. Quality would have increased for high rates recordings as more averages were taken in a fixed time, but at the cost of a high noise dose for subjects. In the current study we instead explored whether increasing rate could reduce recording time, but still obtain 100% detection of responses.

The present study was conducted using subjects with normal hearing and vestibular function and approved by the Human Experiment Safety and Ethics Committee of the University of Southampton's Institute of Sound and Vibration Research (ISVR). Responses were recorded from 18 subjects (18 ears) in the age range of 25-48 years.

The equipment used in this study to deliver the stimuli for VEMP measurement was the Cambridge Electronic Design CED 1401 data acquisition system and a signal software. A sampling rate (input and output) of 10 KHz was used. The output from the Digital to Analogue Converters (DAC) port was routed through a headphone amplifier (OBH-21) to control the intensity of the stimulus. The stimuli were administered to the subjects using insert earphones (ER-3A). Amplification of the signals was performed using an isolated amplifier (CED 1902) with a 1-3000 Hz bandpass filter and 1000 gain. The calibration of the stimuli was carried out through a Brüel and Kjar (B&K) type 2260 sound level meter (SLM), attached to the ear simulator (IEC-711). The cVEMP responses were recorded using three surface electrodes: active on the belly of the ipsilateral SCM muscle, reference on the upper sternum of the test side and ground on lower forehead. The EMG activity of the SCM muscle was visually monitored on an oscilloscope and kept between 80 and 100 mV.

500 Hz 1:2:1 (one cycle rise/fall and two cycles plateau) tone-bursts stimuli were presented using insert earphones (Etymotic ER-3A) for repetition rates from 1 to 100 Hz at 119.2 dB PeSPL. 150 epochs were collected for all rates, so recording duration reduced with rate. The order of presentation was randomised.

Recording response quality was assessed using the F_{sp} . Although an F_{sp} threshold can be defined for a group to indicate response presence, the significance of a given F_{sp} value can vary across individuals as the degrees of freedom of subject data can vary. Response presence was therefore determined from bootstrapping methods based on random resampling of the data, to indicate whether the F_{sp} of a given recording was significantly different from that of random noise (Lv et al., 2007).

Figure 1 shows the number of subjects with a significant cVEMP response ($p < 0.05$) as a function of rate. Response rate was 100% for 1, 5 and 10 Hz stimulation and then decreased as rate increased beyond 10 Hz.

* suggest insert Figure 1 here

In the current study, the clarity of cVEMP waveform deteriorated as repetition rate increased above 35 Hz. At high rates the duration of cVEMP response is greater than that of the stimulus interval, producing overlap (superposition) between stimuli. Hence it becomes difficult to identify the VEMP waveform. An example of typical subject cVEMP waveforms across repetition rates is shown in Figure 2.

*suggest insert Figure 2 here

From bootstrap analysis, most subjects did not show cVEMP responses at repetition rates above 60 Hz. Therefore, these rates were not included in the F_{sp} , peak-to-peak amplitude, and peak latency analysis. Rates of 45 and 50 Hz were not included in the analysis due to difficulty in finding the significant peaks resulting from the overlap between stimuli at high rates. A Friedman's test showed a significant effect of repetition rates on the F_{sp} value and peak-to-peak amplitude ($p < 0.05$). One-Way Repeated Measures ANOVA showed that the mean peak latencies of cVEMP did not differ significantly between repetition rates, $p_{13} [F(3.069, 81.250) = 1.108, p = 0.369]$.

Figure 3 shows the variation in mean cVEMP F_{sp} with rate. Wilcoxon signed-rank testing revealed that there was no significant difference between 1, 5 and 10 Hz but these rates produced significantly larger F_{sp} values than all other rates ($p < 0.05$).

*suggest insert Figure 3 here

Figure 4 shows the peak-to-peak amplitude of cVEMP as a function of rate. Wilcoxon signed-rank testing revealed that the 1 Hz rate produced significantly higher amplitude than

rates 25 to 40 Hz. 5 and 10 Hz stimulation rates produced significantly higher amplitudes than 35 and 40 Hz rates. No statistically significant differences were observed in cVEMP amplitude between the other remaining rates.

* suggest insert **Figure 4** here

The motivation behind this work was to improve the quality of cVEMP responses by exploring how they adapt to high repetition rates. Response rate was 100% for rates up to 10 Hz and decreased progressively for higher rates. There was a trend of progressive decrease in amplitude and F_{sp} with rate. Rates up to 10 Hz produced higher quality than all others. Rates up to 10 Hz produced higher amplitude of cVEMPs than 35 and 40 Hz rates. Carnáuba et al. (2013) evaluated the effect of rates on amplitude and reported a progressive decrease in amplitude with rate similar to that of the current study. The reduction in the response rate and amplitude of cVEMPs with repetition rate may be attributed to the refractory period of the SCM muscle fibres. The mean firing rates of human neck muscles motor units are normally between 10 and 15 spikes per second (Schomacher et al., 2012). Stimulus rates up to 15 Hz are within the physiological responding time of the SCM muscle fibres whereas higher stimulation rates will not be.

In the present study, we expected that subjects with high-rate cVEMP may have larger cVEMP at low rates compared with subjects without high-rate cVEMP. This is because having a larger cVEMP response at low repetition rates could be the reason the continued responses at high repetition rates. Therefore, the amplitude of cVEMP at a 5 Hz repetition rate was compared between subjects with and without high-rate cVEMP. The results revealed that the amplitude of cVEMP responses for subjects with responses at high rates was not statistically higher than for those without high-rate VEMPs. Therefore, subjects with high

rate cVEMPs did not have larger cVEMPs at low rates compared with subjects without high-rate cVEMPs.

Skeletal muscles consist of varying percentages of fast-twitch and slow-twitch muscle fibres (Hall, 2016, p. 1090). Slow-twitch fibres are structured for endurance whereas fast-twitch fibres can fire more rapidly but fatigue more quickly. Variation in percentages of fast- and slow twitch- fibres across subjects might explain why in the current study a few subjects showed responses at very high repetition rates but the majority did not.

In summary, this study demonstrated that responses can be recorded from the SCM muscle to 500 Hz tone-bursts at high rates, but only in a few subjects. We had hoped that recording at very high rates might reduce recording times, but this is not possible in the majority of subjects. Evoking cVEMP using 1, 5, and 10 Hz repetition rate produced the maximum response rate and highest F_{sp} . The rate of 10 Hz requires considerably shorter time for recording compared to 1 and 5 Hz rates but still gives 100% response detection, so appears to be the optimal trade-off between recording time and response detection for the majority of subjects.

References

- Brantberg, K., & Fransson, P. A. (2001). Symmetry measures of vestibular evoked myogenic potentials using objective detection criteria. *SCAND AUDIOL*, 30 (3), 189-196.
<http://www.tandfonline.com/doi/abs/10.1080/010503901316914566>
- Carnaúba, A. T. L., Lins, O. G., Soares, I. D. A., Andrade, K. C. L. D., & Menezes, P. D. L. (2013). The impact of stimulation rates in vestibular evoked myogenic potential testing. *BRAZ J OTORHINOLAR*, 79(5), 594–598. <http://doi.org/10.5935/1808-8694.20130106>
- Elberling, C., & Don, M. (1984). Quality estimation of averaged auditory brainstem responses. *SCAND AUDIOL*, 13(3), 187-197.
<http://www.tandfonline.com/doi/pdf/10.3109/01050398409043059?needAccess=true>
- Hall, J. (2016). *Guyton and Hall textbook of medical physiology* (13th ed). Barcelona: Elsevier.
- Lv, J., Simpson, D. M., & Bell, S. L. (2007). Objective detection of evoked potentials using a bootstrap technique. *MED ENG PHYS*, 29(2), 191-198. <http://doi.org/10.1016/j.medengphy.2006.03.001>.
- Schomacher, J., Dideriksen, J. L., Farina, D., & Falla, D. (2012). Recruitment of motor units in two fascicles of the semispinalis cervicis muscle. *J NEUROPHYSIOL*, 107(11), 3078-85. <http://doi.org/10.1152/jn.00953.2011>.
- van Tilburg, M. J., Herrmann, B. S., Guinan Jr, J. J., & Rauch, S. D. (2016). Increasing the Stimulation Rate Reduces cVEMP Testing Time by More Than Half with No Significant Difference in Threshold. *OTOL NEUROTOL*, 37(7), 933-936.
<https://www.ncbi.nlm.nih.gov/pubmed/27295442>

Wu, C. H., & Murofushi, T. (1999). The effect of click repetition rate on vestibular evoked myogenic potential. *ACTA OTO-LARYNGOL*, 119(1), 29-32.
<http://doi.org/10.1080/00016489950181891>

Figure Captions

Figure 1. Percentage of subjects with a cVEMP response as a function of repetition rates.

Figure 2. The waveforms of cVEMP across repetition rates for a typical subject. In the images, the upward peak (positive, p13) and downward peak (negative, n23) of the VEMPs are labelled.

Figure 3. F_{sp} values of cVEMP as a function of repetition rates. Error bars display ± 1 SE of the mean. The F_{sp} values of the non-responsive ears were set to unity for missing data (on average this is the F_{sp} obtained when no response is present in data).

Figure 4. Peak-to-peak amplitude of cVEMP as a function of repetition rates. Error bars display ± 1 SE of the mean. The amplitude values of recordings that did not show a significant response on bootstrap analysis was set to zero for the analysis of amplitude values.

Figure 1
[Click here to download high resolution image](#)

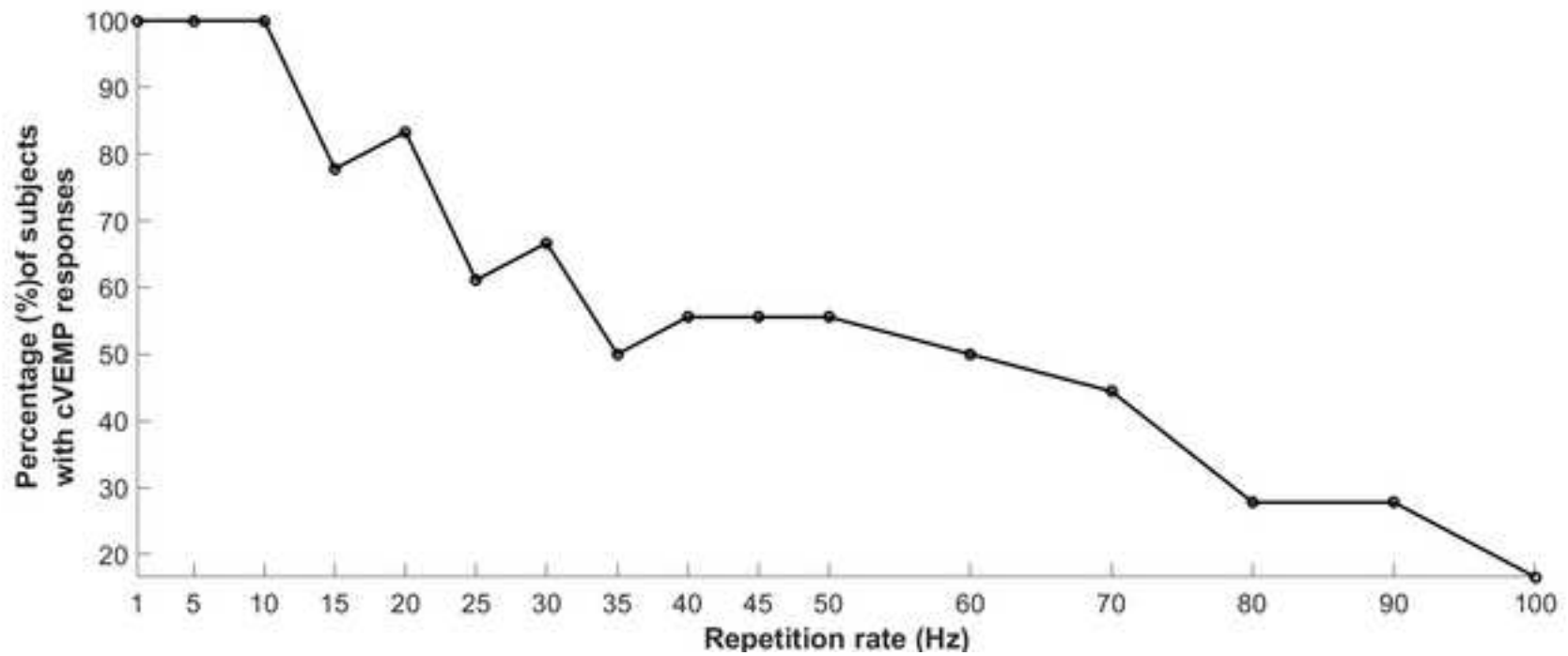


Figure 2
[Click here to download high resolution image](#)

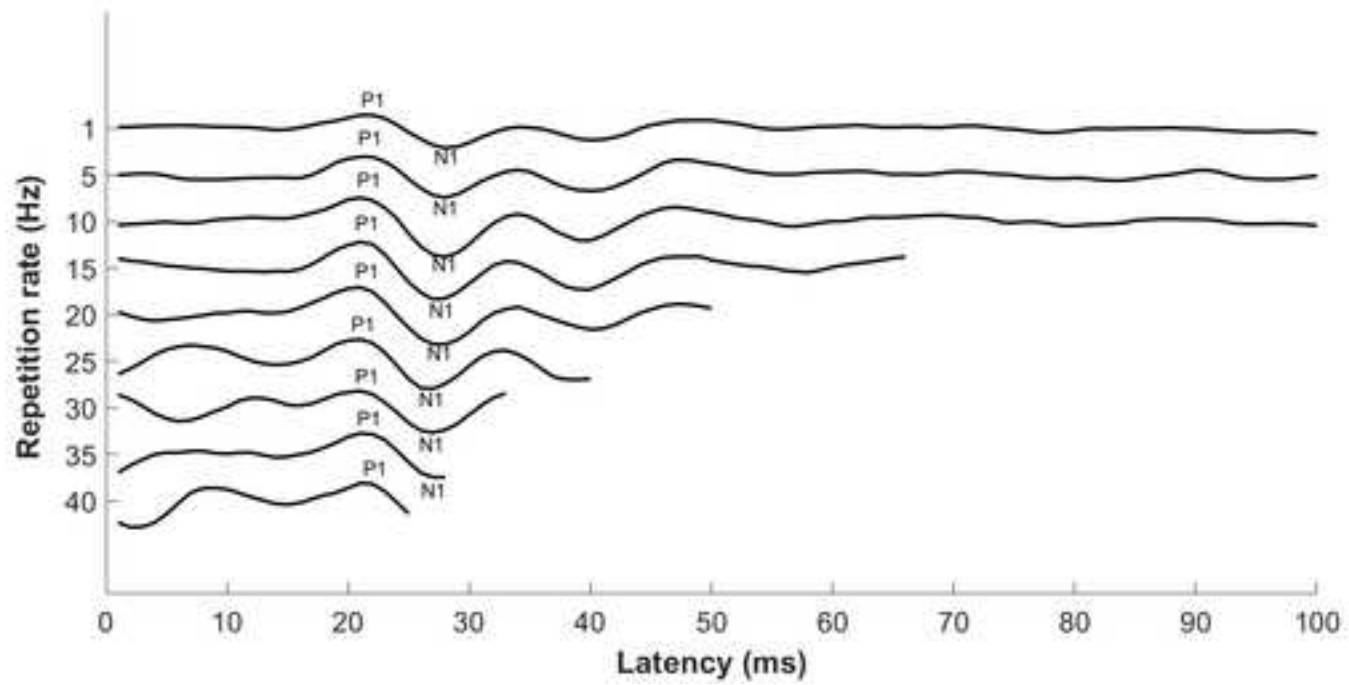


Figure 3
[Click here to download high resolution image](#)

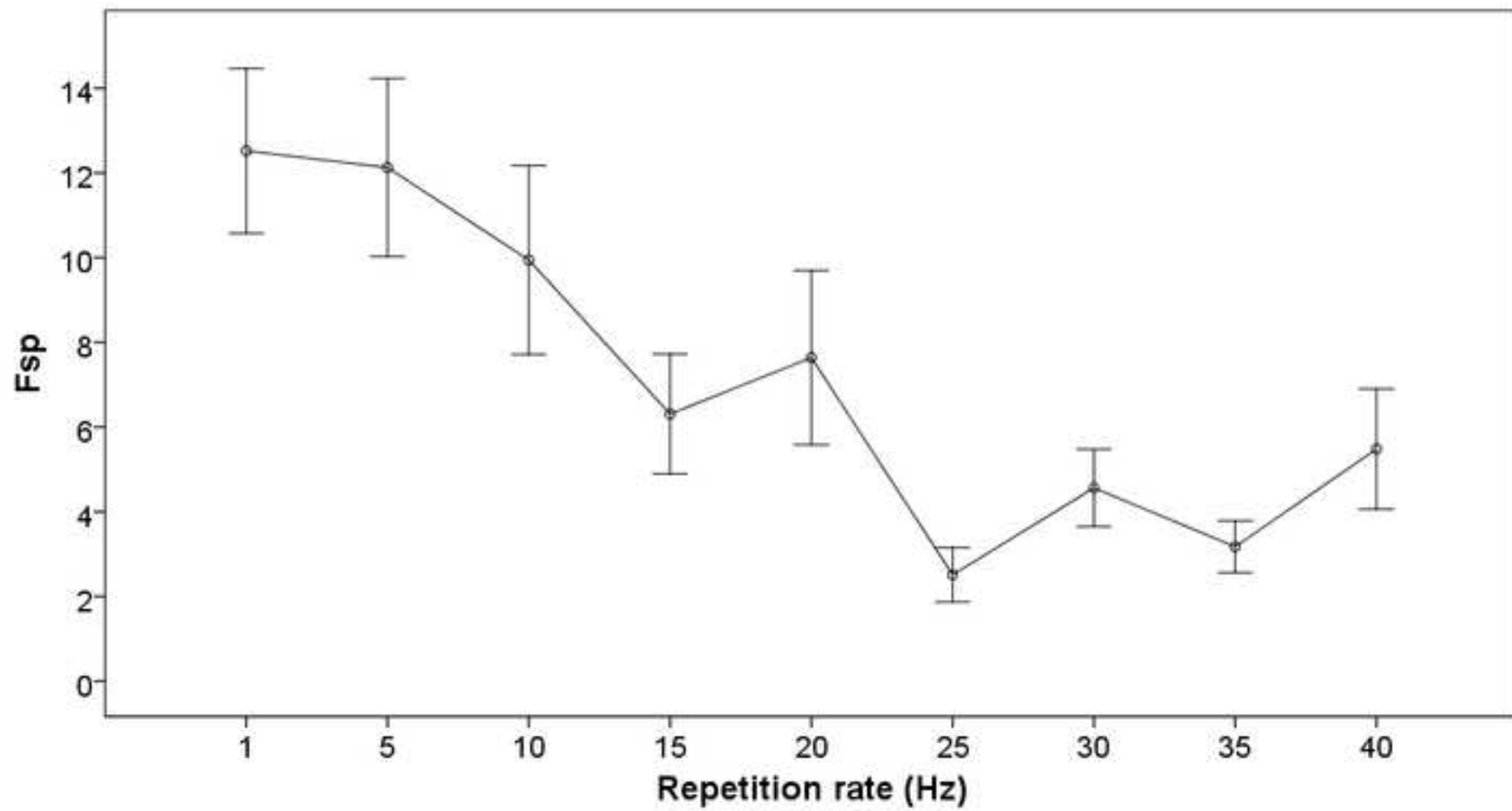


Figure 4
[Click here to download high resolution image](#)

