The Effects of Caffeine on Ocular Vestibular Evoked Myogenic Potentials in Adults Over 50

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Abstract: Clinicians often ask patients to avoid caffeine prior to undergoing vestibular testing as well as electrophysiologic testing. This study investigated the effect of caffeine on ocular vestibular evoked myogenic potentials (oVEMP), specifically, N1-P1 peak-to-peak amplitudes in adults 50 years or older. Participants were asked to refrain from caffeine at least 24 hours prior to oVEMP testing. Following initial non-caffeinated oVEMPs, participants consumed 20 oz. of commercially brewed coffee (~410 mg caffeine) and waited 15-20 minutes before the next oVEMP recordings. In addition, participants also completed a caffeine questionnaire to assess daily consumption. Results showed statistically significant findings between non-caffeinated and caffeinated N1-P1 peak-to-peak amplitudes in participants who were considered light-moderate caffeine users (<400 mg/day), whereas daily consumers of more than 400 mg/day had no differences. As one of the clinical manifestations of oVEMP testing is to diagnose superior semicircular canal dehiscence (SSCD), patients who are complaining of sound- or pressure-induced dizziness or vertigo should refrain from caffeine for 24 hours prior to oVEMP testing.

Keywords: ocular; vestibular evoked myogenic potentials; caffeine; older adults

1. Introduction

Older adults are more prone to issues relating to vestibular function with dizziness, vertigo and falls being one of the number one complaints this population makes to their primary care physicians. Research shows that up to 85% of balance dysfunction could be inner ear related [1]. The balance system involves integration of information from our vestibular, visual, and proprioceptive systems. The vestibular test battery includes a variety of tests to stimulate each of these systems to decipher which one is impaired. Ocular vestibular evoked myogenic potentials (oVEMPs) is a diagnostic test that could be included in the test battery. oVEMP testing evaluates the ascending vestibular pathway via the vestibulo-ocular reflex (VOR). The VOR is responsible for maintaining a clear image during head movement. During this test, high intensity sound stimuli is presented into one ear to stimulate the utricle. Neurons are then sent from the superior vestibular nerve to the contralateral extraocular muscles via the medial longitudinal fasciculus. The oVEMP response consists of a negative peak (N1) with a mean latency of ~11 milliseconds (ms) followed by a positive peak (P1) with a mean latency of ~15 ms. Clinical application of oVEMPs are associated with the diagnosis of superior canal dehiscence by the presence of oVEMP responses to sound stimuli at lower threshold levels and of increased N1-P1 peak-to-peak amplitudes. It has also been found that patients who have multiple sclerosis will present with delayed N1 and P1 latencies [2].

Prior to vestibular testing, clinicians often ask their patients to refrain from caffeine and certain medications 24 hours prior to the administration of tests. McNerney et al. [3] evaluated the effect of caffeine on cervical VEMP (cVEMPs) and the somatosensory organization test (SOT) on young healthy adults with a mean age of 23.28. The cVEMP test assesses the function of the saccule and the inferior vestibular nerve, while the SOT is a test of postural stability across a variety of measures. There was no significant effect found on either test between non-caffeinated and caffeinated responses, yet there was a trend of better performance from participants in the caffeinated SOT. In another study involving cVEMPs, de Souza and Suzuki [4] had participants refrain from caffeine consumption for 24 hours and then administered 420 mg of caffeine in two capsules. They, too, found no statistically significant difference in cVEMP values pre- and post-caffeine consumption. In a recent systematic review, de Souza et al. [5] found the same two studies that met eligibility criteria, focusing only on cVEMP. Most recently, Tavanai et al. [6] conducted a double-blind placebo-controlled study examining the effect of caffeine on the auditory brainstem response (ABR) and cVEMP in young adults. Although they found a latency difference in the ABR, those who consumed caffeine did not have a statistically significant difference compared to the placebo group for cVEMP.

The above cVEMP studies suggest that caffeine does not appear to have an effect on young adults. However, there is a paucity of information about the effect of caffeine on oVEMPs and in older adults. Thus, the purpose of the present study was to determine, in adults over 50, if there is an effect of caffeine on oVEMP testing with the hypothesis being that N1-P1 peak-to-peak amplitudes will increase after caffeine consumption. Findings would be used to determine whether to ask older patients to refrain from caffeine consumption prior to oVEMP testing.

2. Materials and Methods

2.1. Participants

Participants who completed the study included sixteen individuals (6 males, 10 females) from 56 to 76 years of age (62.9±4.9). Inclusion criteria included normal middle ear status due to reduced or absent oVEMP responses being found in patients who have a conductive hearing loss. Two of the 16 participants had histories of prosthetic stapes surgery (right ear) and vestibular neuritis (left ear), respectively, so those ears were removed from analyses leaving a total of 30 ears. Informed consent was obtained from all participants. This study received prior approval by the Institutional Review Board at the University of Arkansas at Little Rock (#16-033).

2.2. Instrumentation

Tympanometry was measured using an Interacoustics Titan tympanometer (Eden Prairie, MN). oVEMP recordings were performed in a quiet testing room using the Biologic Navigator Pro (Natus Medical, Inc., Schaumburg, IL). oVEMP response recordings were measured using ER-3A insert earphones and disposable electrodes placed on the participants' foreheads and cheeks. For all 2-channel oVEMP recordings, the non-inverting electrodes were placed approximately 1 cm below the lower eyelid of each eye, and the inverting electrodes were placed directly underneath the non-inverting electrodes without overlapping the conductive pads of each electrode. The ground electrode was placed on the forehead (Fpz). As the oVEMP is a contralateral response, all measures were taken from the eye opposite to the side of auditory stimulation. Air conduction stimuli consisted of 200 sweeps of 500 Hz tone bursts with a presentation rate of 5.1/s with an intensity level of

95 dB nHL. Rarefaction polarity with a Blackman envelope (two cycles plateau and one cycle rise and fall times) was used. Recordings were bandpass filtered 30-2,000 Hz and amplified 100,000x. Electrode impedances did not exceed 5 kΩ. The initial ear of stimulation was quasi-randomized from the first to last participant, and all oVEMPs were replicated in each ear. Prior to marking N1 and P1 components for collection of latencies and peak-to-peak amplitude, a weighted-average waveform was obtained for replicated responses in each ear.

2.3. Procedures

Participants were required to refrain from caffeine for 24 hours prior to testing. Participants were asked to fill out the 2014 version of the Caffeine Consumption Questionnaire [see e.g., 7] regarding the average milligrams of caffeine consumed per day (mg/day). An upward gaze creates the most prominent oVEMP amplitudes; therefore, participants were asked to gaze upward at a fixed point on the wall during testing [8]. Participants consumed 20 oz. of Starbucks Breakfast Blend coffee (Seattle, WA), which is approximately ~410 mg of caffeine. Since caffeine reaches peak levels in the bloodstream around 30-60 minutes after consumption [6,9], oVEMP responses were obtained approximately 15 minutes after participants had consumed the entire 20 oz. of coffee

2.4. Statistical Analysis

Raw data was in the form of N1 and P1 latencies (ms) and N1-P1 peak-to-peak amplitudes (μV) in non-caffeinated and caffeinated oVEMP testing sessions as well as the average milligrams per day of caffeine from each participant's questionnaire. Raw data for each participant was transferred to a Microsoft Office Excel spreadsheet for descriptive statistics, and two-tailed, paired *t*-tests were performed using the VassarStats website (vassarstats.net) with the alpha level set at 0.05.

3. Results

Results from the caffeine questionnaire revealed that participants of this study consumed an average amount of 440.1 mg/day (SD = 314.8) ranging from 125 to 1320 mg/day. **Table 1** shows the descriptive statistics for latencies and peak-to-peak amplitudes. When oVEMPs from both right and left ears of stimulation were combined: 1) N1 and P1 latencies were not statistically different between non-caffeinated and caffeinated conditions (t (29) = -0.57, $p > .05$ and t (29) = +1.29, $p > .05$, respectively), and 2) a statistically significant difference was found for N1-P1 peak-to-peak amplitudes between non-caffeinated and caffeinated conditions (t (29) = -2.3, $p < .05$). When ear specific oVEMPs were compared in both non-caffeinated and caffeinated conditions, right ear oVEMPS were not statistically different (t (14) = -1.12, $p > .05$), while left ear oVEMPs were statistically different (t (14) = -2.55, $p < .05$).

Although not the focus of the study, two observations were made: First, in the fourteen participants with oVEMP data on both ears, there does appear to be asymmetry in averaged N1-P1 peak-to-peak amplitudes (right ear > left ear). Using the Jonkees formula (100 x ((right ear - left ear)/right ear + left ear)) for amplitude ratio, 7 of 14 non-caffeinated ears and 5 of 14 caffeinated ears exceeded 40%, a common criteria for oVEMP asymmetry.

Second, further examination of caffeine consumption variability revealed that 9 of 16 participants were considered light-moderate caffeine consumers with an average of 236.8 mg/day (SD = 109.8) and the remaining participants were considered heavy caffeine consumers with an average of 701.4 mg/day (SD = 302.4). Though the sample sizes are considerably smaller than when participants are combined, light-moderate caffeine drinkers had a statistically significant difference (t (17)

= -2.93, $p < .05$) between non-caffeinated and caffeinated conditions, whereas heavy caffeine drinkers did not (t (11) = -0.41, $p > .05$).

Table 1. Means and standard deviations for non-caffeinated and caffeinated N1 and P1 latencies and N1-P1 peak-to-peak amplitudes in right, left, and combined ears.

		Latency (ms)		Amplitude (μV)
	Ear(s)	**N1**	**P1**	**N1-P1**
Non-Caffeinated	Right (n=15)	10.75 (0.99)	15.03 (1.68)	4.36 (3.36)
	Left (n=15)	10.84 (0.71)	14.69 (1.42)	2.35 (1.44)
	Combined (n=30)	10.79 (0.85)	14.86 (1.54)	3.36 (2.74)
Caffeinated	Right (n=15)	10.74 (1.11)	14.64 (1.47)	4.68 (3.96)
	Left (n=15)	11.04 (1.64)	14.71 (1.21)	2.78 (1.70)
	Combined (n=30)	10.89 (1.38)	14.67 (1.32)	3.73 (3.14)

Figure 1 displays the average differences between non-caffeinated and caffeinated N1-P1 peak-to-peak amplitudes across all participants (0.40 μV difference), light-moderate caffeine consumers (0.54 μV difference), and heavy caffeine consumers (0.15 μV difference). **Figure 2** shows an example of non-caffeinated and caffeinated oVEMP waveforms in a participant who consumes <400 mg of caffeine per day.

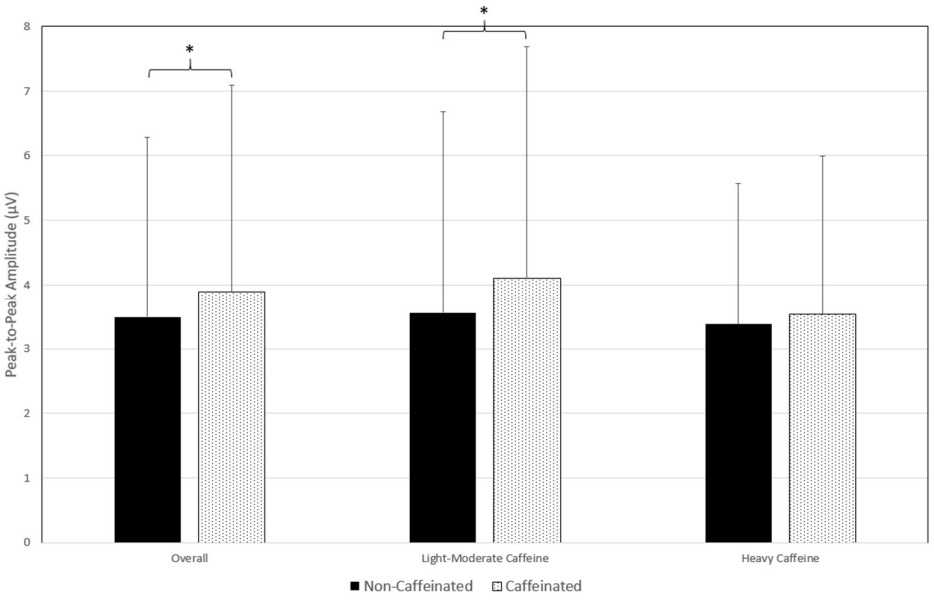

Figure 1. Average N1-P1 peak-to-peak amplitudes for all participants compared with heavy caffeine users and moderate caffeine users in Non-Caffeinated (NC) and Caffeinated (C) sessions.

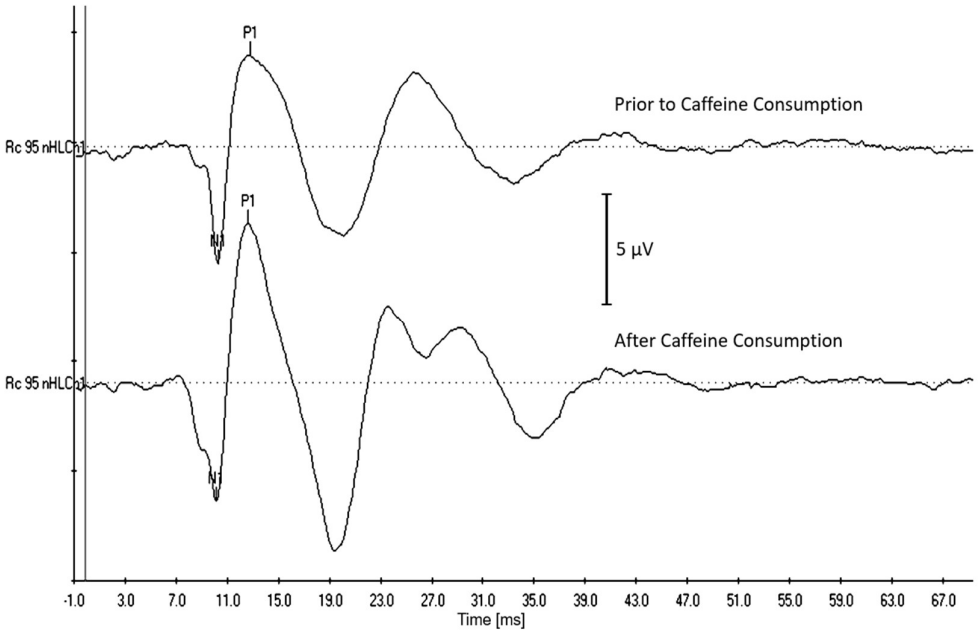

Figure 2. Example non-caffeinated (top) and caffeinated (bottom) oVEMP responses in a light-moderate caffeine user (<400 mg/day).

4. Discussion

The purpose of this study was to evaluate if caffeine had an effect on vestibular testing in adults over the age of 50. Non-caffeinated and caffeinated oVEMP responses were obtained from sixteen adults > 50 years. The findings of this study suggests that caffeine consumption has an impact on oVEMP responses, specifically, N1-P1 peak-to-peak amplitudes in adults > 50 years. After further analyzing the results from the caffeine questionnaire, it was concluded that consuming ~410 mg of caffeine only has an impact on N1-P1 peak-to-peak amplitudes in adults who are light-moderate caffeine consumers. oVEMP responses were not found to have an effect on adults > 50 years who are heavy caffeine users.

Some limitations of the study are noted: First, the amount of time participants took to consume the 20 oz. of coffee varied. The physiological effects of caffeine begins as early as 15 minutes and reaches its highest concentration in blood plasma between 30 and 60 minutes. While we waited 15-20 minutes after each participant finished their coffee to retest oVEMP responses, the amount and peak of central nervous system stimulation is likely variable among participants. Caffeine pills would be a more consistent option in future studies. Second, oVEMPs were obtained using 200 sweeps. A recent study by Mallinson et al. [10] demonstrated that as few as 26 sweeps can be used for oVEMPs that helps to minimize recording time, minimizes cochlear insult, and maximizes the amplitude of the response (which decreases with more sweeps and is already smaller in older adults).

Ingestion of caffeine prior to vestibular electrophysiological measures has not been proven to negatively affect test results by lowering amplitudes or delaying latencies. Based on this study,

oVEMP results could cause a false elevation of N1 and P1 amplitudes if one consumes more caffeine than their usual dosage. Since one of the clinical applications of oVEMP testing is the diagnosis of superior semicircular canal dehiscence (SSCD) by an increase in N1-P1 peak-to-peak amplitudes, patients who are complaining of pressure- or sound-related vertigo should refrain from consuming caffeine 24 hours prior to administering oVEMP testing. By use of a caffeine withdrawal questionnaire, McNerney et al. [3] found that cessation of individuals' normal caffeine consumption can have negative withdrawal symptoms. There was no caffeine withdrawal questionnaire in the present study; however, participants were vocal about the negative effects they had experienced caused by a lack of caffeine consumption. Vestibular testing is already usually uncomfortable for many patients; therefore, with the exception of pressure- and sound-related vertigo, patients should not be asked to refrain from caffeine prior to undergoing vestibular electrophysiological testing.

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References

1. Gans, R. Dizziness, vertigo and falls: issues for older adults and practitioners. ENT & Audiology News 2011, 20, 66-68.
2. Felipe, L.; Kingma, H. Ocular vestibular evoked myogenic potentials. International Archives of Otorhinolaryngology 2014, 18.
3. McNerney, K.; Coad, M. L.; Burkhard, R. The influence of caffeine on the sensory organization test. Journal of the American Academy of Audiology 2014, 25, 521-528.
4. de Souza, A.M.A.; Suzuki, F.A. Effect of caffeine on cervical vestibular-evoked myogenic potential in healthy individuals. Brazilian Journal of Otorhinolaryngology 2014, 80, 226-230.
5. de Souza, M.E.D.C.A.; da Costa, K.V.T.; de Lemos Menezes, P. Effect of caffeine on vestibular evoke myogenic potential: a systematic review with meta-analysis. Brazilian Journal of Otorhinolaryngology 2018, 84, 381-388.
6. Tavani, E.; Farahani, S.; Ghahraman, M.A.; Soleimanian, S.; Jalaie, S. Effects of caffeine on auditory- and vestibular-evoked potentials in healthy individuals: a double-blind placebo-controlled study. Journal of Audiology and Otology 2020, 24, 10-16.
7. Preston, J.; Mura, A. Lessons from neuropsychologist John Preston, Psy.D. on stress, sleep, energy, and solutions that backfire. International Journal of Coaching in Organizations 2006, 4, 16-21.
8. Welgampola, M.S.; Migliaccio; A.A.; Myrie, O.A.; Minor, M.B.; Carey, J.P. The human sound-evoked vestibulo-ocular reflex and its electromyographic correlate. Clinical Neurophysiology 2009, 120, 158-166.

9. Liguori, A.; Hughes, J.R.; Grass, J.A. Absorption and subjective effects of caffeine from coffee, cola and capsules. Pharmacology Biochemistry and Behavior 1997, 58, 721-726.
10. Mallinson, A., Kuijpers, A., & Longridge, N. Optimum number of sweeps in clinical OVEMP recording; how many sweeps are necessary? Journal of International Advanced Otology 2018, 14, 72-76.