Effect of betel nut chewing on the otolithic reflex system

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Abstract

Objective: This study investigated the effect of betel nut chewing on the otolithic reflex system.

Methods: Seventeen healthy volunteers without any experience of chewing betel nut (fresh chewers) and 17 habitual chewers underwent vital sign measurements, ocular vestibular-evoked myogenic potential (oVEMP), and cervical VEMP (cVEMP) tests prior to the study. Each subject then chewed two pieces of betel nut for 2 min (dosing). The same paradigm was repeated immediately, 10 min, and 20 min after chewing. On a different day, 10 fresh chewers masticated chewing gum as control.

Results: Fresh chewers exhibited significantly decreased response rates of oVEMP (53%) and cVEMP (71%) after dosing compared with those from the predosing period. These abnormal VEMPs returned to normal 20 min after dosing. In contrast, 100% response rates of oVEMP and cVEMP were observed before and after masticating chewing gum. In habitual chewers, the response rates of oVEMP and cVEMP were 32% and 29%, respectively, 20 min after dosing.

Conclusion: Chewing betel nuts induced a transient loss of the otolithic reflexes in fresh chewers but may cause permanent loss in habitual chewers.

Significance: Chewing betel nuts can cause a loss of otolithic reflex function. This creates a risk for disturbed balance and malfunction, for instance, during driving.
Betel nut chewing may cause a series of symptoms such as euphoria, palpitation, salivation, sweating, diaphoresis, heightened alertness, warm sensation in the body, and increased capacity to work. These psychological and neurological effects of betel nut may be attributed to the presence of arecoline, with parasympathomimetic properties acting on both muscarinic and nicotinic receptors (von Euler and Domeij, 1945; Chu, 2002). In addition, betel nut chewing increases the plasma concentrations of norepinephrine and epinephrine and thus may affect both the central and autonomic nervous systems (Chu, 2001).

Autonomic response and vestibular symptoms are closely related. Patients with acute vertigo often have concomitant distressing autonomic symptoms such as nausea, vomiting, pallor, and sweating, implying that an efferent vestibular influence markedly affects the sympathetic outflow (Lin et al., 2012). Vomiting during caloric irrigation is common in those with anxiety/panic symptoms, which implies that the vestibulo-ocular reflex (VOR) shares synapses with the vestibulo-sympathetic reflex (Yates and Bronstein, 2005).

By stimulating the ear with loud sound or bone vibration, the vestibular-evoked myogenic potential (VEMP) can be recorded on contracted neck muscles, termed cervical VEMP (cVEMP), and on the extraocular muscles, termed ocular VEMP (oVEMP) (Colebatch et al., 1994; Rosengren et al., 2005). These two emerging tests have been widely adopted in clinical practice for assessing the dynamic otolithic function (Young, 2013). The oVEMP primarily originates from the utricular macula, through the crossed VOR, along the superior vestibular nerve to the opposite extraocular muscles (Curthoys, 2010). In contrast, the cVEMP is evoked by air-conducted sound and primarily assesses the sacculo-colic reflex, whereas bone vibration-evoked cVEMPs probably assess both saccular and utricular vestibulo-collic projections. Although the psychological and neurological effects of betel nut have been substantially investigated (Chu, 2002), the impact of betel nut chewing on the otolithic reflex system has never been explored. This study performed oVEMP and cVEMP tests to investigate the effect of betel nut chewing on the otolithic reflex system.

2. Methods

2.1. Participants

Initially, 22 healthy volunteers without a history of betel nut chewing participated in this study. Contamination from other psychoactive drugs or alcohol was excluded. Subjects who failed to complete the examination were also excluded. Finally, 17 healthy volunteers were enrolled and assigned to the fresh chewer group (15 males and 2 females; mean age = 28 years, range 24–39). None of the participants had any systemic disease or ear disorders and were further checked by otoscopy and audiometry.

In the predosing period, baseline vital signs including body temperature, heart rate, and blood pressure were measured in each volunteer. Thereafter, each subject was administered with two pieces (one by one) of betel nut, called “Ching-a” (Fig. 1), for chewing for 2 min. Each piece of betel nut weighed 3.8 ± 0.6 g. One gram of betel nut contained four major alkaloids: arecoline (7.5 mg), arce-cadine (1.5 mg), guvacoline (2.0 mg), and guvacine (2.9 mg) (Wang et al., 1997). The rationale for chewing two pieces of betel nut is that facial flushing is noted in all volunteers (100%) after chewing two pieces (one by one) but in only 24% of the volunteers after chewing one piece.

Immediately after chewing (dosing period), vital sign measurements followed by oVEMP and cVEMP tests were repeated. Then, all the subjects rested in a quiet room, and 10 and 20 min after dosing (postdosing I and II, respectively), all the subjects underwent the same paradigm. Fig. 2 illustrates the flow chart of the testing procedure.

On a different day, 10 subjects from the fresh chewer group repeated the same paradigm; however, this time betel nut was replaced by chewing gum (control group). Each subject underwent oVEMP and cVEMP tests before and after dosing.

This study was approved by the institutional review board of the university hospital, and each subject signed the informed consent form before participation.

2.2. oVEMP test

The subject was seated and gazed upward at a fixed target that was >2 m from the eyes during recording (Smart EP 3.90; Intelligent Hearing Systems, Miami, FL). Two active surface electrodes were attached 1 cm below the lower eyelids. The other two reference electrodes were 1–2 cm below the active ones, and a ground electrode was placed on the sternum. Each response had duration of 50 ms for analysis, with a stimulation rate of 5/s, and 30 responses were averaged for each run.

The operator held the vibrator (Minishaker 4810; Bruel & Kjaer Co., Nærum, Denmark) and tapped on the subject’s skull on the forehead. The input signal was 500 Hz sine wave, with the initial peak driving voltage about 144 dB force level.

The initial negative–positive biphasic waveforms were termed waves nl and pl, respectively. Consecutive runs were undertaken to confirm the reproducibility of the nl–pl waveform, and oVEMPs
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