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The effects of aging on lifetime of auditory sensory memory in humans

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ABSTRACT

The amplitude change of cortical responses to repeated stimulation with respect to different interstimulus intervals (ISIs) is considered as an index of sensory memory. To determine the effect of aging on lifetime of auditory sensory memory, N100m responses were recorded in young, middle-aged, and elderly healthy volunteers ($n = 15$ for each group). Trains of 5 successive tones were presented with an inter-train interval of 10 s. In separate sessions, the within-train ISIs were 0.5, 1, 2, 4, and 8 s. The amplitude ratio between N100m responses to the first and fifth stimuli (S5/S1 N100m ratio) within each ISI condition was obtained to reflect the recovery cycle profile. The recovery function time constant (τ) was smaller in the elderly (1.06 ± 0.26 s, $p < 0.001$) and middle-aged (1.70 ± 0.25 s, $p = 0.009$) groups compared with the young group (2.77 ± 0.25 s). In conclusion, the present study suggests an aging-related decrease in lifetime of auditory sensory memory.

1. Introduction

Neuronal refractoriness or habituation is a process by which the cortical response to repeated stimulation decreases over time, which is partially determined by neural memory traces (Fruhstorfer et al., 1970; Ritter et al., 1992; Budd et al., 1998; Rosburg, 2004). During repetitive stimulation at a certain ISI, if neuronal representations greatly decay, the response strength to subsequent stimuli is approximate to the preceding response. However, if the sensory memory traces continue to be present, the cerebral reactivity is attenuated to filter redundant sensory inputs and to avoid information overload (Lu et al., 1992; Uusitalo et al., 1997).

The preservation of sensory memory encoded in cerebral cortices is crucial for humans to integrate successive perceptual information from various external and internal sensory inputs. Longer maintenance of sensory memory lifetime results in increased efficiency of the brain to process information, as evaluated by the current signal compared with previously stored sensory representations of auditory, visual, and somatic stimuli (Lu et al., 1992; Sams et al., 1993; Uusitalo et al., 1996, 1997; Hamada et al., 2002).

An aging-related impairment in retaining a large amount of information probably results from a deficit in memory storage and information processing (Adams and Victor, 1989). Pre-attentive sensory memory storage has been suggested to involve in echoic or iconic memory (Cowan, 2010). It is of importance to study the sensory memory because the early response component may be involved in ensuing higher-order perceptual operations. The mismatch negativity (MMN), elicited by infrequent deviants mismatching with previously stored sensory representations, was proposed as an objective index of pre-attentive auditory sensory memory (Näätänen et al., 2007). The maintenance of auditory sensory memory lifetime in healthy adults was approximately 10 s (Cowan et al., 1993; Sams et al., 1993), which was consistent with behavioral studies using a tone-comparison paradigm (Cowan et al., 1997) and unattended spoken syllables (Cowan et al., 1990). The effects of aging on the decay of neural memory traces, which diminished with an increase in the ISI and vanished when the sensory memory for standard stimuli was completely decayed, have been investigated with this MMN protocol (Pekkonen et al., 1993, 1996; Kazmerski et al., 1997; Gaeta et al., 1998). The above findings suggest that elderly adults might have difficulty maintaining sensory representation over time. However, the lifetime of sensory memory in each aging individual is uncertain from the MMN paradigm because the MMN estimates the approximate duration of sensory

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memory based on the specific ISI used (for example, 3 s), in which no MMN is observable (Hari et al., 1984; Pekkonen, 2000; Näätänen et al., 2007; Hsiao et al., 2009). To obtain a more definite lifetime of the neuronal activation traces *in each individual* (for example, 1.75 s or 3.50 s in each case), the time constant (τ) derived from auditory recovery functioning provides an alternative approach.

By measuring N100m responses to acoustic stimulation in various ISI conditions, Lu et al. (1992) have proposed the first evidence of a time constant (τ) of neuronal activation traces. Notably, the time constant correlated well with the behaviorally measured lifetime of auditory sensory memory. This approach has been used in previous studies on visual (Uusitalo et al., 1996, 1997) and somatosensory systems (Hamada et al., 2002). However, to the best of our knowledge, the time constant of auditory sensory memory in aging subjects has not been addressed. It is of scientific importance to characterize the profile of neuronal activation traces in auditory cortices in elderly population because a better understanding of the dynamics of sensory memory decay would aid in unraveling the deficits of neurophysiological processing in patients with neurodegenerative diseases.

We recorded auditory evoked fields (AEFs) in response to stimulation trains at several different ISIs and calculated the time constant (τ) of the recovery function. We hypothesized that the time constant would be significantly smaller in elderly adults compared with young adults because ample evidence has suggested aging-associated memory decline, even in pre-attentive situations (Pekkonen et al., 1993, 1996; Alain et al., 2004; Cooper et al., 2006). Furthermore, we predicted that the recovery function time constant changes as a function of age by means of a correlation examination.

2. Methods

This study was approved by the Institutional Review Board of the Taipei Veterans General Hospital, and the procedures were in accordance with the Declaration of Helsinki. All subjects were recruited through advertisements posted at older adult community centers, the bulletin board system on Taipei Veterans General Hospital, and National Yang-Ming University.

2.1. Participants

Forty-five healthy volunteers participated in the study after giving their informed consent. They were categorized into young (n = 15, mean age 26.6 ± 0.6 years, 6 women), middle-aged (n = 15, mean age 50.3 ± 1.0 years, 9 women; 1 left-handed man), and elderly groups (n = 15, mean age 72.2 ± 2.1 years, 6 women). None of the participants had hearing problems, neurological diseases and psychiatric disorders, as determined by a careful examination. Mini-Mental Status Exam (MMSE) scores ≥ 27 were also required to exclude the possibility of dementia.

2.2. Stimulation and procedures

The auditory stimuli were 800 Hz pure sinusoidal tones of 25-ms duration (including 5-ms rise and fall times), with a binaural presentation at an intensity of 65–70 dB above the subjects' hearing threshold through plastic earphones. Stimulus trains with different onset-to-onset ISIs of 0.5, 1, 2, 4, and 8 s were presented in separate experimental sessions, and the sequence was counterbalanced across subjects. Each train consisted of 5 identical stimuli, and the inter-train interval (ITI) was 10 s. The N100m was the target component with respect to individual stimuli within a train (from S1 to S5, respectively) because this component exhibits a better signal-to-noise ratio for the source estimate compared with the P50m or P200m components (Godey et al., 2001).

To reduce the vigilance effect on N100m responses, 20–25 trains were presented for each ISI condition. Short breaks were offered to the participants between experimental sessions. During the recordings, the subjects were instructed to concentrate on watching a self-chosen movie presented silently in front of them at a distance of approximately 1 m.

2.3. MEG recordings and source modeling

A whole-head 306-channel MEG, consisting of 102 magnetometers and 204 orthogonal planar gradiometers (Vectorview, Elekta Neuromag, Helsinki, Finland), was used for magnetic measurements. The recording epochs were 530 ms with a 50-ms pre-stimulus baseline. The online recording bandpass was 0.1–130 Hz, with a sampling rate of 400 Hz. Exaggerated eye movements, monitored by electrooculograms (EOGs) attached above the left orbit and below the right orbit, were discarded (EOG > 150 μV) (Cheng et al., 2010; Hsiao et al., 2010). To reduce brain artifacts originating inside the helmet and external interferences outside the sensor array, we applied Maxwell Filtering from the Neuromag software system (Vectorview, Elekta Neuromag, Helsinki, Finland) based on the "signal space separation" theory (Taulu et al., 2004, 2005). The length of the raw data buffer and the subspace correlation limit were set at 7 s and 0.98, respectively. The final responses were digitally filtered with a bandpass between 1 and 30 Hz offline (Gaal et al., 2007; Cheng et al., 2010). According to the presentation sequence of individual stimuli (S1–S5) within a train, 5 sets of N100m responses (N100m_S1, N100m_S2, N100m_S3, N100m_S4, and N100m_S5) were obtained at each ISI condition. The peak N100m response was identified within a time window of 70–150 ms after the stimulus onset (Näätänen and Picton, 1987).

We analyzed the cerebral sources of N100m signals by using equivalent current dipole (ECD) modeling, in which all 204 gradiometers were included in a time-varying multiple model. The two best-fit equivalent dipoles, one from each hemisphere, were calculated by a least-square search using subsets of 20–30 channels around the maximal signals. The goodness-of-fit value represented a determination of how well the measured signals were explained by estimated ECDs, and only a value that was larger than 80% at the selected time periods in a subset of channels was accepted for further analysis. The ECD modeling approach has been previously addressed in detail (Hämäläinen et al., 1993).

2.4. Data analysis and statistics

The amplitude ratio of the N100m_S5 over the N100m_S1 was obtained for each ISI condition, and the value is referred to as the S5/S1 N100m amplitude ratio in this paper. Accordingly, the recovery function profile was defined as the change of the S5/S1 N100m amplitude ratio as a function of ISI (Hamada et al., 2002). The auditory recovery cycle time constant (τ) for each participant was estimated from the modified mathematical equation (Lu et al., 1992):

$$R(1 - e^{-(\mathrm{ISI}-t_0)/\tau}),$$

where R is the S5/S1 N100m amplitude ratio, t_0 is the time of decay onset.

All data were expressed as the mean ± standard error of the mean (SEM). Lifetimes of auditory sensory memory were evaluated by a two-way analysis of variance (ANOVA), with the group (young, middle-aged, elderly) as the between-subject factor and the hemisphere (left, right) as the within-subject factor. The ECD locations of the N100m_S1 within a train of 1 s ISI were examined by a two-way ANOVA (between-subject factor: group; within-subject factor: hemisphere) in terms of x-, y-, and z-coordinates. A Greenhouse-Geisser correction was applied when appropriate. A Bonferroni procedure was used for *post hoc* analysis. Spearman's rank correlation was also used to determine the relationship between age and recovery function time constant.

All the statistical analyses were performed with the SPSS statistical package (version 13.0). $p < 0.05$ was considered statistically significant.

3. Results

3.1. Aging effects on the S5/S1 N100m amplitude ratio at a group level

The upper panel of Fig. 1 shows a main effect of the group on the S5/S1 N100m amplitude ratio ($F_{2,42}$ = 13.45, $p < 0.001$) through the two-way repeated measures ANOVA (group by hemisphere). The ratio was larger in the elderly group ($p < 0.001$) than in the young and middle-aged groups. The grand-averaged N100m responses to each stimulus (S1–S5) with 1 s ISI in each group supports the statistical results (see lower panel of Fig. 1). The two selected channels with the maximal N100m amplitude in each hemisphere are presented. The topographic maps show similar spatial distributions of N100m_S1 activation at individual peak latencies in the young (119 ms), middle-aged (120 ms), and elderly (124 ms) groups.

Fig. 2 and Table 1 show the averaged S5/S1 N100m amplitude ratio as a function of ISI in the young, middle-aged, and elderly groups. The amplitude ratio between the fifth and first N100m responses reflects the extent to which the sensory memory traces remained in the primary auditory cortex: a ratio closer to 1 (the plateau level of this exponential function) indicates an obvious decay in lifetime of neuronal activation traces. The S5/S1 N100m amplitude ratio increased to 1 faster (ISI = 1–2 s) in the elderly group than in the young (ISI = 4–8 s) and middle-aged (ISI = 2–4 s) groups. Except for the ISI of 8 s ($F_{2,42}$ = 0.723, p = 0.491), significant