



## Positive Slow Wave of P3b is Significantly Enhanced in Post TGA Subjects

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### Abstract

Modern imaging studies have shown that Transient Global Amnesia (TGA) is associated with structural changes in the hippocampus. We investigated the Slow Wave (SW) component following P3b of visual Event Related Potentials (ERP) in nine post TGA subjects and sixteen age-matched controls in attempt of identifying objective electrophysiological evidence of changes in memory processing in TGA subjects. While P3b was comparable in both groups, SW in TGA subjects was significantly enhanced in the frontal regions. The findings strongly support the concept that SW enhancement reflects frontal hyperactivity in high load conditions, and represent an objective sign that clinical recovery of TGA likely reflects neural reorganization.

### Introduction

Transient Global Amnesia (TGA) is a syndrome characterized by complete clinical recovery, which led to earlier views that TGA is a functional rather than organic disease process. Modern imaging techniques, however, demonstrated focal abnormalities involving the hippocampus in the majority of TGA cases [1-5]. It is now generally believed that TGA constitutes a clinical syndrome with a variety of etiologies. Nevertheless, the basis for the clinical recovery remains unknown. It would appear that in the cases in which structural abnormalities are detected, clinical recovery suggests functional reorganization through neural plasticity.

A sensitive index for detecting subtle processing differences in memory function is the Slow Wave (SW) of Event Related Potentials (ERPs), originally described as posterior positivity following P3b in response to attended rare stimuli [6]. It is suggested that SW correlates with processing demands [7], especially those involving rehearsal in short-term memory [8]. In this study, we investigated visual ERPs in post-TGA subjects using conditions optimized for detecting SW alteration, accomplished by recording P3b over the entire scalp and using a low-cut filter optimized for detecting slow activities.

### Materials and Methods

#### Subjects

Nine subjects who had TGA, seven females (age range 63 to 74 years) and two males (age range 58 to 76 years), participated in the study. All subjects met the proposed clinical diagnostic criteria for TGA [1,2]. Any subject with a history of significant medical comorbidities, including myocardial infarction or stroke, was excluded. Subjects who had more than two episodes of an amnestic event were also excluded from this study. Participating subjects had their TGA event at least six months prior to this study, and none reported recurrence of memory disturbance within this interval. All subjects underwent neuropsychological evaluations prior to the study, the results of which are summarized in (Table 1). Sixteen age-matched volunteers (10 female, 6 male) with no history of either neurological or psychiatric disorders participated in the study as normal controls. Informed consents were obtained from all study participants. The study was carried out in accordance with the human research guidelines of the Internal Review Board of University of Niigata.

#### ERPs

All subjects were confirmed to possess 20/20, or better, corrected vision. The following visual paradigm was utilized. Standard (70%, upward) and target (20%, downward) stimuli were white triangles presented on a half-gray background. Novel stimuli (10%), animals or flowers, were in 256 colors. All stimuli subtending 2 degrees of the visual angle were presented on the center point of a 21 inch CRT monitor using a STIM system (Neuroscan Labs Inc., El Paso, US) [9]. All stimuli

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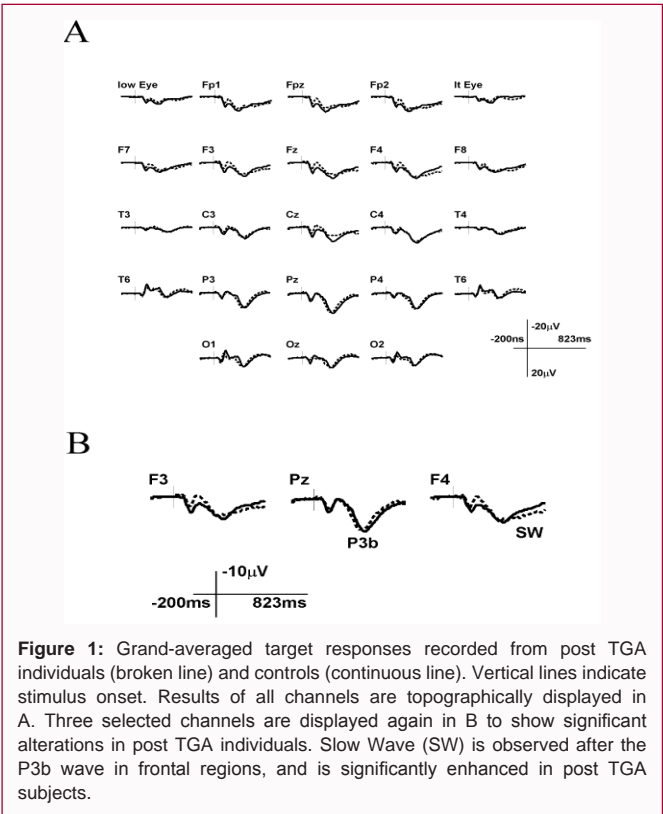
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had 200-millisecond duration and stimulus onset asynchrony was randomized between 1.1 and 1.3 seconds. Subjects were instructed to press a button when the target appeared and subject reaction times were measured.

Subjects were seated in a comfortable chair, in an air conditioned, normally lit room. Silver electrodes were attached on Fp1, Fp2, Fp3, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, O1, O2 and Oz, following the international 10-20 method. Two additional electrodes were attached lateral to the left eye (horizontal electro-oculogram, hEOG) and below the left eye (vertical electro-oculogram, vEOG) to monitor eye movements. All channels were referred to linked earlobe electrodes with impedances kept below 5 kΩ during the recording sessions. Using a 32-channel SynAmp (Neuroscan Labs Inc., El Paso, US), 16-bit electroencephalogram (EEG) data were acquired at a gain of 500, sampled at a rate of 1 kHz and filtered with a band pass of 0.05 to 100 Hz. EEG data were stored digitally. EEG data were segmented to set the analysis period from 200ms prior to 823ms after the onset of each stimulus. After the baseline was corrected by subtracting the average of the pre-stimulus period, artifact rejection was performed with a threshold of ± 100 µV from the baseline at Fp1, Fp2, Fp3, F7, F8, T3, T4, hEOG and vEOG. ERPs were obtained by averaging EEG segments time-locked to stimulus onset for each stimulus type, and subsequently all averages were low-pass filtered at 30 Hz (24dB/oct).

P3b amplitude was defined as the mean within a period starting 380 ms and ending 420 ms after stimulus onset. SW amplitudes were measured as the mean voltage within a period starting 770 ms and ending 800 ms after stimulus onset. Statistical comparison was performed by repeated measure analysis of variance with the design of 1 between factor (subject groups) and 1 within factor (components: P3b, SW) at F4 employing the Geisser-Greenhouse correction of degrees of freedom.

Results

Reaction time

Behavioral analyses revealed comparable results between groups for both reaction times (controls 454±38ms vs. post TGA subjects 432±41 ms,  $t=1.34$ ,  $p>0.1$ ) and error rates ( $t=1.33$ ,  $p>0.1$ ).

ERPs

Figure 1 summarizes the group average of target responses (broken line for post-TGA subjects and continuous line for controls), clearly revealing P3b with parietal maximum distribution. There is a clear-cut difference in positive SW following P3b between the two groups, especially at bilateral frontal regions. Repeated analysis of ERP amplitudes variance measures showed a significant main effect of component ( $F(1,23)=51.0$ ,  $p<0.01$ ), but a non-significant main effect of the subject groups ( $F(1,23)=2.01$ ,  $p>0.1$ ). The interactions between the two factors were significant ( $F(1,23)=4.55$ ,  $p<0.05$ ). P3b amplitude was not significantly different between groups ( $F(1,23)=0.0$ ,  $p>0.1$ ). SW amplitude was significantly different between the two groups ( $F(1,23)=7.27$ ,  $p<0.03$ ). No statistical differences were detected between SW amplitudes and neuropsychological scores (Table 1).

Discussion

Multiple studies regarding P3 components and TGA have been published [10-13]. Some studies indicate that P3 abnormalities are detectable, even in the acute phase of TGA. However, the abnormal findings are not consistent across the studies. Grand averaged ERP also did not show consistent P3 abnormalities [10-13]. The inconsistencies may be in part due to the varying etiologies behind the clinical syndrome of TGA. The current study clearly shows abnormality in SW without significant P3 abnormalities in grand averaged ERPs. The study owes its success to optimization of recording setting compared to prior ERP studies on TGA [14].

SW of the visual Event-Related Potential (ERP) is significantly enhanced in post-TGA subjects compared to controls, unequivocally showing alteration in neural processing in post-TGA individuals. Enhancement of frontal positive SW has been demonstrated as an alteration of prefrontal activities associated with memory processing in the elderly. The sustained positivity is believed to reflect frontal hyperactivity in an attempt to maintain memory performance.

Table 1: Subject profiles and neuropsychological scores performed prior to ERP studies.

Age	Gender	TGA duration(hour)	BVRT	MRT		
				1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>
63	F	8	7	10		
71	F	4	7	9	10	
66	F	6	8	7	9	10
58	M	7	7	7	10	
76	M	1	4	8	10	
74	F	5	7	7	10	
69	F	1	5	6	9	9
66	F	5	6	9	10	
65	F	1	9	9	10	

BVRT: Benton visual retention test.  
MRT: Miyake's verbal retention test (Ten pairs of Japanese words are given. Trials are repeated three times. Data are shown in series, with trials separated by hyphens. Normative values are 8.5-9.8-10 for related pairs, and 4.5-7.6-8.5 for unrelated pairs).

in a high load condition[15,16]. Our findings in post-TGA subjects are in strong agreement with these ERP findings, indicating similar neural substrates underlying SW enhancement and suggesting that memory processing post TGA is in “higher load” for maintaining memory performance.

Even though much remains to be clarified, the current study nevertheless further confirms that TGA is likely associated with disruption in the neural network responsible for memory processing. Like aging, TGA results in a reduction in neural capacity, consequently leading to overload conditions in prefrontal cortical activities. The frontal SW enhancement observed in this study indicates that the post TGA period requires neural reorganization for regaining normal memory function.

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