

## ORIGINAL ARTICLE

## Effect of purposeful activity-based electrical stimulation on auditory event-related potential in a stroke survivor with a severely paretic upper limb

Seigo MINAMI,<sup>1</sup> Yoshihiro FUKUMOTO,<sup>2</sup> Ryuji KOBAYASHI,<sup>3</sup> Kenji ISHIKAWA,<sup>4</sup> Nobuyuki SANNO,<sup>5</sup> Mitsumasa HIDA,<sup>6</sup> Hideaki AOKI,<sup>7</sup> Tomoki AOYAMA<sup>8</sup>

<sup>1</sup>Department of Occupational Therapy, Gunma Paz University, <sup>2</sup>Faculty of Rehabilitation, Kansai Medical University, <sup>3</sup>Graduate School of Human Health Sciences, Tokyo Metropolitan University, <sup>4</sup>Department of Occupational Therapy, Osaka Kawasaki Rehabilitation University, <sup>5</sup>Department of Occupational Therapy, Fukuoka International University of Health and Welfare, <sup>6</sup>Department of Physical Therapy, Osaka Kawasaki Rehabilitation University, <sup>7</sup>Graduate School of Medicine, Wakayama Medical University, <sup>8</sup>Human Health Science, Graduate School of Medicine, Kyoto University

*Correspondence:* Seigo Minami, OTR, PhD, Gunma Paz University, 1-7-1 Tonyamachi, Takasaki city, Gunma 370-0006, Japan. Tel: +81-27-365-3366 E-mail: minami@paz.ac.jp

*Disclosure:* The authors have no potential conflicts of interest to disclose.

**Key words:** cognitive function, P300 latency, hemiplegia, stroke

### INTRODUCTION

Surviving a stroke is the most common reason to discharge a patient to their home (Alexander, 1994), where survivors are expected to continue the process of recovery. Previous findings have shown that stroke survivors that have severe hemiplegic upper limb disorders typically show no recovery of functional movement during hospitalization (Nakayama, 1994); these patients are refractory and difficult to treat (Hendricks, 2002). The challenge of rehabilitating these survivors is that no effective program has been developed to provide advanced rehabilitation at home without additional burden on the patient or their caregivers.

Purposeful activity-based electrical stimulation therapy (PA-EST) is a short-term rehabilitation program designed to alleviate severely hemiparetic upper limbs in stroke survivors. This intervention includes assigning purposeful activities combined with and/or assisted by an electrical stimulation therapy

### Abstract

**Objectives:** The objective of this case study was to determine the effect of purposeful activity-based electrical stimulation therapy (PA-EST) on cognitive function using auditory event-related potentials (ERPs) in chronic stroke survivors.

**Methods:** The participant was a female patient in her late 60s who presented with left-sided paresis. She had a subarachnoid haemorrhage about 20 years prior and a right thalamic haemorrhage five years prior. The participant received four phases of the PA-EST program (three months for each phase). Auditory ERPs, Fugl-Meyer Assessment (FMA), Motor Activity Log (MAL), Goal Attainment Scaling-Light (GAS-L), and Mini-Mental State Examination (MMSE) were used for evaluation before administration of the PA-EST intervention and following phases II and IV.

**Results:** The P300 latency component of auditory ERPs (Fz, Cz, and Pz) shortened after phase II compared to the initial evaluation and did not change remarkably afterwards. FMA for the upper extremity, MAL amount of use, quality of movement, and GAS-L demonstrated improvements following phases II and IV. FMA for the upper extremity showed drastic improvement until phase II with minimal differences observed after this phase. There was a minimal difference in the MMSE scores during the observation period.

**Conclusion:** The PA-EST program for survivors of chronic stroke with severe upper limb paresis may contribute to improvements in cognitive function.

device. It is hypothesized that this intervention may enhance the individual's ability to re-integrate cognitive functions during the post-discharge period. A previous study suggested that PA-EST, with a focus on life adaptation (for example, picking up a towel in the bathroom with the paretic limb), may expand the range of activity in chronic stroke survivors (Minami, 2020a). Another study indicated that PA-EST may serve as an efficient intervention for rehabilitation, which allows the affected limbs to transition from 'severe' to 'moderately severe' paresis (Minami, 2021). Other studies have also reported that therapeutic interventions induce changes in brain activities as well as functional improvements in the paretic upper limb in chronic stroke survivors (Sasaki, 2012; Carey, 2002). Therefore, it is highly possible that PA-EST improves the brain's ability; however, the benefits of PA-EST have not been validated in terms of functional changes in the brain during this transition period in chronic stroke survivors.

Auditory event-related potentials (ERPs) are a measure of functional changes in the brain. Auditory ERPs are the response of the central nervous system to a constant stimulus and are recorded over the scalp as an evoked potential (Steven, 1983). Among auditory ERPs, the positive potential that appears at a latency of about 300 msec (250 to 500 msec), widely known as “P300 latency,” is associated with subjective brain activities, such as prediction, expectation, attention, and judgement (Sutton, 1965; Squires, 1976; Duncan-Johnson, 1981; Goodin, 1983). Previous studies have reported that stroke survivors show extended P300 latency values compared to healthy individuals due to disruptions in the information processing activities (Gunmow, 1986; Goodin, 1978). Dejanovic (2000) reported that P300 latency in stroke survivors who attend rehabilitation centres was shortened between 3 and 12 months after stroke onset. It is possible that PA-EST contributes to improvement in cognitive functions, such as prediction and expectations, and this consequently leads to a shortening of P300 latency values. The objective of this case study was to determine the effect of PA-EST on cognitive function, measured by evaluating auditory ERPs, in a survivor of chronic stroke.

## METHODS

### Participant

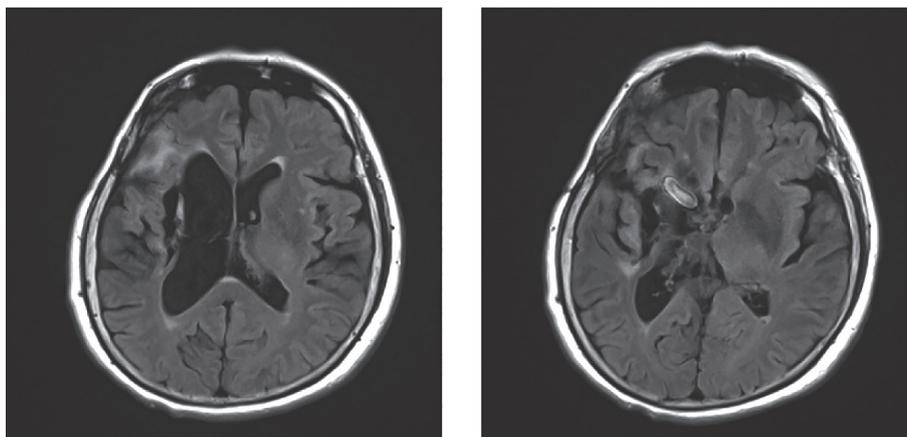
The participant was a female patient in her late 60s who presented with left sided paresis. She had a subarachnoid haemorrhage approximately twenty years prior, in addition to a right thalamic haemorrhage that occurred five years prior (Figure 1). The goal of her

daily living activity was to “open the sliding door with her left hand (paretic side)”.

### PA-EST intervention

The PA-EST program consists of four phases. In each phase, the participant received the PA-EST for three months, and a one-month rest period was observed between the intervention phases. Thus, about 15 months of rehabilitation were observed in this study.

PA-EST is a program that elicits the reaction of a specific movement following a session of purposeful activity and subsequently executes parts of the movement at the time of electrical stimulation (Minami, 2020b). Electrical stimulation was applied to the forearm of the paretic upper limb. For example, during the program, the patient was asked to emulate the movement of her hand on the door, stretching the elbow when the electrically stimulated wrist begins to dorsiflex. In our study, the intensity of the electrical stimulation was determined based on the degree of the wrist joint movement and absence of pain. In the last two phases, an assisted electrical stimulator (NESSH200®, Bioness Co., Ltd., Valencia, CA, USA) was used (10 min/1–2 times daily, three times or more a week). In the first two phases, after confirming voluntary movement in the forearm on the paretic side, a voluntary assistance-type electrical stimulator (WILMO®, SK-Electronics Co., Ltd., Kyoto, Japan) was used (5–10 min/1–2 times daily, three times or more a week). Appropriate instructions and demonstrations were provided at the beginning of the occupational therapy session. The patient underwent unsupervised PA-EST at least three days a week and an additional



**Figure 1.** Initial magnetic resonance imaging. She had a subarachnoid haemorrhage approximately twenty years prior, in addition to a right thalamic haemorrhage that occurred five years prior.

session of PA-EST that was supervised by an occupational therapist at least once a week.

### Outcome measures

The evaluation was performed a total of three times: an initial evaluation and then after phases II and IV. The evaluation comprised Fugl-Meyer Assessments (FMAs), Motor Activity Logs (MALs), Goal Attainment Scaling-Light (GAS-L), Mini-Mental State Examination (MMSE), and auditory ERPs. Part of the FMA is illustrated in Figure 2-A and Figure 2-B. Auditory ERPs were recorded using electroencephalography (Neuro-pack II MEB-5100, NIHON KOHDEN, Tokyo, Japan). To measure auditory ERPs, silver electrodes were referenced to linked ears from Fz, Cz, and Pz, according to the international 10–20 system of electrode placement. The electroencephalogram was amplified and digitised at a sampling frequency of 250 Hz. An auditory oddball paradigm was used to elicit the P300 latency component of auditory ERPs (Ishikawa, 2011). The measurements were conducted after the participant received a random sequence of discriminative stimuli of 1000 Hz and 2000 Hz of auditory stimuli. Stimulation was given to both ears from earphones at intervals of 1300–1700 ms. The participant was instructed to press a button with her thumb immediately after the target sound was heard. The reaction time was recorded on a 2000 Hz sound target, after which Fz, Cz, and Pz were measured. In addition, achievement of the goal of her activity of daily living (i.e., “to open the sliding door with her paretic hand”) was visually assessed (Figure 2-C).

### Ethical considerations and consent

This study was conducted in accordance with

the principles of the Declaration of Helsinki and the Ethical Guidelines for Clinical Research and was approved by the Ethics Committee of Osaka Kawasaki Rehabilitation University (OKRU19-A023) with the intent to evaluate cognitive benefits of PA-EST.

## RESULTS

The results of the initial evaluation and those performed after phases II and IV are shown in Table 1 and Figure 2. Compared with the initial evaluation (Fz=448; Cz=425; and Pz=421), the P300 latency component of auditory ERPs was shortened after phase II (Fz=646; Cz=642; and Pz=730) and did not show a remarkable change afterwards (Fz=471; Cz=458; and Pz=437).

The participant’s MAL amount of use (MAL-AOU), quality of movement (QOM), and GAS-L measurements appeared to have improved from the initial evaluation (MAL-AOU=0.36; MAL-QOM=0.29; GAS-L=27) to phase II (MAL-AOU=0.43; MAL-QOM=0.43; GAS-L=31.7) and phase IV (MAL-AOU=1.08; MAL-QOM=1.08; GAS-L=45). FMA for the upper extremity showed drastic improvement from the initial evaluation (13 points) to phase II (16 points) with minimal differences observed after phase IV (17 points). The MMSE showed almost no change during the observation period. Regarding the goal of activities of daily living, the participant could not touch the door with the paretic hand at the initial evaluation. However, following phase II, she showed motor function improvement as she could touch the door but could not open it. After phase IV, she was able to fully open the door with her paretic hand.

**Table 1.** The effect of PA-EST on measures of cognitive function

	FMA		MAL		GAS-L	MMSE	ERPs		
	upper	lower	AOU	QOM			Fz (ms)	Cz (ms)	Pz (ms)
Initial evaluation	13	8	0.36	0.29	27	30	448	425	421
After phase II	16	10	0.43	0.43	31.7	28	646	642	730
After phase IV	17	10	1.08	1.08	45	30	471	458	437

FMA: Fugl Meyer Assessment, MAL: Motor Activity Log, AOU: Amount of Use, QOM: Quality of Movement, GAS-L: Goal Attainment Scaling-Light, MMSE: Mini-Mental State Examination, ERPs: Auditory Event-Related Potentials

	Initial evaluation	After phase II	After phase IV
A. Shoulder flexion 0 - 180° elbow at 0° pronation-supination 0°			
B. Shoulder abduction 0 - 90° elbow at 0° forearm neutral			
C. Living act scene. ※Open the door	She could not touch the door.  (no photo)		

A part of the FMA is illustrated in A and B. In addition, the achievement of the goal of her activity of daily living, i.e., “open the sliding door with her paretic hand” was visually assessed (C).

**Figure 2.** Assessment of paretic upper limbs and activities of daily living

## DISCUSSION

In healthy adults, while Fz, Cz, and Pz of P300 latency have been found to lag with age, they are usually <500 ms (Polish, 1996, 2004). Our findings indicated that the participant exhibited extended values of Fz (646 ms), Cz (642 ms), and Pz (730 ms) at P300 latency at the initial evaluation. In phase II and phase IV evaluations, following the administration of the PA-EST intervention, P300 latency was reduced to <500 ms. These results suggest that chronic stroke survivors with severe upper limb paresis who undergo the PA-EST program can experience improved motor function in the paretic limb. In addition, the patient in this study showed improvements in MAL-AOU and QOM (as measures of the frequency of use and the quality of movement of the paretic upper limbs) and GAS-L (as a measure of goal achievement). The results imply that these functional improvements in the paretic upper limb may be associated with improvement in cognitive function as shown by measurements of the P300 latency.

The P300 latency was not reduced between phase II and phase IV, whereas MAL and GAS-L greatly improved during this period. These results suggest that improvements in brain activity measured by P300 latency reaches a plateau at a relatively early phase of the intervention, while the function of the paretic upper limb continuously improves during the

intervention. After the implementation of PA-EST, the P300 latency was shortened to 500 ms or less in phase II, and it was possible to maintain these values until phase IV. Combining intentional activity-based training with electrical stimulation therapy has been suggested to have the potential of enriching the daily life of chronic stroke survivors by shortening and maintaining P300 latency.

A previous study has shown that it is difficult to restore motor function in the severe hemiplegic upper extremity three months after a stroke (Nakayama, 1994). To ensure recovery of motor function and for the hemiplegic upper limb to re-adapt to daily life, it is suggested that the brain requires intentional exercise planning. Furthermore, it is presumed that the cognitive processing speed increases even in patients with severely hemiplegic upper limbs, due to the patient's environment, the will of their intended action, and constant processing.

## Limitations

The limitation of this study is that we evaluated only a single case; therefore, these findings cannot be generalized and further studies with larger numbers of participants, such as randomized controlled trials, are needed to verify the findings of our study. Several factors may influence how patients respond to PA-EST such as their cognitive function, the degree of

injury, and their daily engagement in purposeful activities.

## ACKNOWLEDGMENTS

The authors would like to thank Mr. Hidetoshi Nakagawa and Mr. Takahito Takemoto, the occupational therapists who evaluated the subject.

## FUNDING

This work was supported by JSPS KAKENHI (Grant Number 19k12895).

## REFERENCES

- Alexander M Stroke rehabilitation outcome a potential use of predictive variables to establish levels of care. *Stroke* 25, 128–134, 1994
- Carey JR, Kimberley TJ, et al. Analysis of fMRI and finger tracking training in subjects with chronic stroke. *Brain* 125, 773–788, 2002
- Duncan-Johnson CC P300 latency: a new metric of information processing. *Psychophysiology* 18, 207–215, 1981
- Goodin DS, Squires KC, et al. Age-related variations in evoked potentials to auditory stimuli in normal human subject. *Electroencephalogr Clin Neurophysiol* 44, 447–458, 1978
- Goodin DS, Squires KC, et al. Variations in early and late event-related components of the auditory evoked potential with task difficulty. *Electroencephalogr Clin Neurophysiol* 55, 680–686, 1983
- Hendricks H, Limbeek J, et al. Motor recovery after stroke: a systematic review of the literature. *Arch Phys Med Rehabil* 83, 1629–1637, 2002
- Ishikawa K, Yamaguchi M, et al. Relationship between hand dexterity and cognitive function: utility of event-related potential upon MCI detection and relationship between visual memory and upper-extremity movement capability. *Bulletin of Health Sciences Kobe* 27, 9–17, 2011
- Minami S, Aoki H, et al. Transition of a severely hemiparetic upper limb to a supporting upper limb: development of a purposeful activity–electrical stimulation therapy rehabilitation programme (A report of three cases). *Japanese Academy of Health Sciences* 23, 14–24, 2020a
- Minami S, Fukumoto Y, et al. Effect of home-based rehabilitation of purposeful activity-based electrical stimulation therapy for chronic stroke survivors: a crossover randomized controlled trial. *Restor Neurol Neurosci* 39, 173–180, 2021
- Minami S, Kobayashi R, et al. Program for rehabilitation of the chronic severe hemiparesis upper extremity of cerebral stroke survivors: application of purposeful activities and an electrical stimulation therapy program. *Cognition & Rehabilitation* 1-1, 74–82, 2020b
- Nakayama H, Jorgensen H, et al. Compensation in recovery of upper extremity function after stroke: the Copenhagen Stroke Study. *Arch Phys Med Rehabil* 75, 852–857, 1994
- Polish J Meta-analysis of P300 normative aging studies. *Psychophysiology*, 33, 334–353, 1996
- Polish J Clinical application of the P300 event-related brain potential. *Phys Med Rehabil Clin N Am* 15, 133–61, 2004
- Sasaki K, Matsunaga T, et al. Effect of electrical stimulation therapy on upper extremity functional recovery and cerebral cortical changes in patients with chronic hemiplegia. *Biomedical Research* 33, 89–96, 2012
- Steven A, Hillyard, et al. Electrophysiology of cognitive processing. *Ann Rev Psych* 34, 33–61, 1983
- Squires KC, Wickens C, et al. The effect of stimulus sequence on the waveform of the cortical event-related potential. *Science* 193, 1142–1146, 1976
- Sutton S, Braren M, et al. Evoked potential correlates of stimulus uncertainty. *Science* 150, 1187–1188, 1965