Effects of music therapy accompanied by transcranial direct current stimulation on the recovery from aphasia following stroke: A single-center retrospective cohort study

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Received August 5, 2022; Accepted November 15, 2022

DOI: 10.3892/wasj.2022.177

Abstract. Aphasia is the difficulty in reproducing or understanding speech, and affects 21-38% of patients with stroke immediately after onset. In addition, disregarding improvement in the first weeks after stroke, ~20% of patients present with chronic deficiencies 6 months later. Consequently, speech and language therapy appears to be the optimal choice of treatment for chronic aphasia. The present study aimed to systematically investigate the effects of experimental/traditional music therapy (MT) in combination with transcranial direct current stimulation (tDCS) on improving aphasia in patients following a stroke in regular stroke rehabilitation services. For this purpose, 98 eligible participants who had suffered a single cerebrovascular accident were divided into three groups as follows: Group A, no MT or tDCS (only standard treatment); group B, daily MT; group C, combined treatment with daily MT and tDCS at a 1:1.21:1.28 ratio for the three groups, respectively. Statistically significant differences between groups were found either in terms of the interval of the Aachen Aphasia Test [(T_1-T_0) mean] ($P<0.05$) or in terms of the mean cerebral blood flow in the damaged regions ($P=0.042$), the mean mini-mental test ($P<0.05$) and the mean Barthel index ($P=0.004$). On the whole, the present study demonstrates that following a stroke, recovery from aphasia can by promoted by a regular exercise, training and rehabilitation program, as well as an improved acoustic environment and tDCS.

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Key words: stroke, rehabilitation care, music therapy, transcranial direct current stimulation

Introduction

Aphasia is the inability to reproduce or understand speech and occurs in 21-38% of patients immediately following a stroke (1-4). Furthermore, when considering recovery in the first weeks following a stroke, chronic deficits persist in ~20% of patients 6 months later (5,6). Therefore, speech and language therapy (SLAT) remains the ideal treatment option for patients with chronic aphasia (7). However, whether intensive speech therapy is useful or not remains controversial (8,9).

Non-invasive brain stimulation methods, such as transcranial direct current stimulation (tDCS), have exhibited clinical benefits in improving the efficacy of regular SLAT in aphasia rehabilitation conditions (10). However, there are some technical limitations to these possible benefits of tDCS in different clinical trials, such as the lack of randomization and the small size of the samples (10-17).

Clinical studies have gradually used an alternative treatment of experimental/traditional music during exercise to manage post-stroke rehabilitation, with positive outcomes for patients (18,19). In addition, music during exercise increases desire, decreases cognition during exercise (20), and alleviates feelings of fatigue (21). Nevertheless, data on the mechanisms through which the renewal environment following a stroke affects brain plasticity are limited. Music therapy, on the other

hand, is difficult to judge and predict in terms of its importance (22).

Therefore, the present study systematically investigated the effects of tDCS and traditional/experiential music therapy (MT) on the recovery of patients with aphasia following a stroke who were attending a regular stroke rehabilitation program.

Patients and methods

Study design. The present retrospective cohort study investigated the clinical effectiveness of tDCS in combination with MT for improving aphasia following a stroke. All participants had suffered a single stroke diagnosed by computed tomography perfusion (CTP). In the present 5-year follow-up cohort study (from February, 2015 to February, 2020), 98 patients, with a mean age of 68.4±5 years (55 males, 56.1%), who met the requirements, were divided into three groups as follows: Group A, no MT or tDCS (only standard treatment); group B, daily MT; group C, combined treatment with daily MT and tDCS at a 1:1.21:1.28 ratio for the three groups, respectively. The study was conducted at the University Hospital of Larissa, Greece and was based on anonymized hospital records. The Institutional Review Board (IRB) of the University of Larisa, Greece/The School of Medicine/School of Health Sciences approved the study (IRB no. 2492/19-01-2015, finalized by the 9th General Assembly on 28/01/2015).

Furthermore, all the patients received the usual care for a stroke, including medical care and rehabilitation. All patients who suffered a cerebrovascular accident (CVA) underwent neuropsychological assessment (including questionnaires and cognitive tests) and a mini-mental test (mMT) to assess cognitive deficits at baseline, during admission and at 6 months following the CVA. CTP was performed at 3 to 6 days (control) and at 6 months, and CTP scores [cerebral blood flow (CBF)] were assessed. The Barthel Index (BI) was used to assess impairment in daily living activities. All cases were screened and assessed for language ability before taking the Aachen Aphasia Test (AAT). Speech presentation was assessed using four subscales: Repetition, Token test, naming and comprehension. Writing (due to hemiparesis) and spontaneous speech (as construct validity was not sufficient) were not included as AAT subscales. Normally distributed t-scores were the AAT scores averaged over the subscales. Patients were scored three points for correctly naming target words; two points for correctly or incorrectly pronouncing target words on the second try, but with syntactically correct or phonologically related expressions; and one point for any other expressions or omissions. The average total score was expressed as a t-score based on these scores. In a repeated measures design, language testing was performed 1 day before (T0) and at 6 months after tDCS +/or MT (T_1). All reported alterations in language performance were described using the interval between two test phases of the AAT [Δ (T1-T0)] (Table I).

The severity of aphasia was categorized into subgroups, as presented in Table II (conduction aphasia: Good repetition of words/phrases; difficulty in word-finding; use of generic word fillers (e.g., 'thing') or circumlocutions; Broca's aphasia: High ability to repeat; possible difficulty responding to questions spontaneously; Wernicke's aphasia: capability of repeating words or phrases; repeats questions instead of providing answers (echolalia); substantial disability in both expressive and receptive language; can interact by gestures, intonation, and facial expressions).

Inclusion and exclusion criteria. The inclusion criteria were as follows: Patients with a first clinical onset of stroke 6 months prior; ab age between 18-75 years; a BI score ≥50 (possible score of 100) (23); modified Ashworth scale of ≤II; Greek-speaking; patients who were previously right-handed in all daily activities and were not forced to switch hands as children.

The exclusion criteria were the following: An inability to participate in an entire testing session; pre-stroke illiteracy; neuropsychological sequelae of brain injury likely to impair test performance (e.g., severe memory or visual perceptual impairment); no patients were diagnosed with other psychiatric or neurological disorders or depression. Additionally, all patients were native Greek speakers. The medical records of each patient were used to determine any issues with their central nervous system.

Procedures

MT. The patients in the exercise groups took part in a music-based exercise program for 6 months. There were four 45-min sessions per week. Patients in group C were subjected to a combined treatment (tDCS 20 min/MT 20 min) for 40 min daily. Patients were instructed to sit near a table and place their upper limbs on it. The primary instructor used simple and precise instructions in a verbal form in combination with continuous visuals. The number of medical students was the same as the number of patients. This made it possible to provide each patient with the assistance and care they needed on a one-to-one basis. In order to pique the interest and promote the involvement of the older patients, experiential/traditional music that was popular when they were young and was thus maintained in their minds for a long period of time was selected.

The study session began with 5-min warm-up exercises involving breathing and flexibility. The main part of the session consisted of moderately difficult exercises to strengthen the upper and lower limbs, as well as exercises to improve coordination and balance, while sitting or standing. Finally, during a 5- to 10-min cool-down period, the subjects moved slowly in a circle, while holding their hands and listening to music.

tDCS. The tDCS procedure was performed after the MT session for each patient. The neuroConn DC stimulator PLUS class II (neuroCare Group GmbH) was used, and two electrodes measuring 7x5 cm were placed and fixed on the head. The most common electrode configuration was used, i.e., anodal tDCS over the left inferior frontal gyrus (IFG) localized as F5, compared to sham tDCS. The cathode was placed in the contralateral supraorbital area localized as Fp2.

During each intervention, anodal tDCS was applied over the left IFG (1 mA for 20 min; experimental condition), or sham tDCS was applied over the same region (control condition) in the combined therapy group (group C).

In the sham tDCS condition, stimulation commenced with a 15-sec fade-in, just like in the experimental condition, but stimulation was turned off for the control group. In addition, both the patient and therapist were blinded to the stimulation condition.

CTP. Two radiologists performed the DTP. CTP parameters, i.e., CBF and cerebral blood volume (CBV) values were recorded

Table I. Aphasia test results.

Parameters	T_0 (baseline)	T_1 (after 6 months)	$\Delta(T_1-T_0)$	P-value
Group A, n=28				
Token test, mean	2.4	3.9	1.5	0.398
Repetition, mean	5.1	5.5	0.4	0.561
Naming, mean	5.3	11.2	5.9	0.080
Comprehension, mean	3	11	8	0.293
Sum, mean ± SD	3.9±2	8.6±3	3.9±2	0.293
Group B, n=34				
Token test, mean	2.1	7.3	5.2	
Repetition, mean	4.4	9.2	4.8	
Naming, mean	2.3	8.7	6.5	
Comprehension, mean	3.8	11.8	8	
Sum, mean ± SD	2.5±1	9.2±1	6.1±2	
Group C, n=36				
Token test, mean	2.5	10.5	8	
Repetition, mean	1.2	12	10.8	
Naming, mean	1.3	12	10.7	
Comprehension, mean	1.6	12	8.4	
Sum, mean ± SD	1.6±1	11.6±1	9.4±2	
AAT t-scores, mean	2.6±1	9.8±2	6.4±2	0.001[a]

[a]AAT, Aachen Aphasia Test; T_0, testing took place 1 day before transcranial direct current stimulation +/or music therapy (baseline); T_1, testing took place 6 months after the transcranial direct current stimulation +/or music therapy; $\Delta(T_1-T_0)$=interval between two trial phases of AAT; P-value for $\Delta(T_1-T_0)$.

Table II. Severity of aphasia in the subgroups.

Parameters	Conduction	Wernicke's	Broca's	Global	Sum
T_0 (baseline), n=98					
Group A, n (%)	3 (3.0)	9 (9.1)	14 (14.2)	3 (3.0)	28
Group B, n (%)	5 (5.1)	7 (7.1)	20 (20.4)	2 (2.0)	34
Group C, n (%)	2 (2.0)	8 (8.1)	22 (22.4)	4 (4.0)	36
All, n (%)	10 (10.2)	24 (24.4)	56 (57.1)	9 (9.1)	98
T_1 (after 6 months, n=36)					
Group A, n (%)	1 (1.0)	7 (7.1)	11 (11.2)	3 (3.0)	22
Group B, n (%)	1 (1.0)	1 (1.0)	6 (6.1)	2 (2.0)	10
Group C, n (%)	0	0	2 (2.0)	2 (2.0)	4
All, n (%)	2 (2.0)	8 (8.1)	19 (9.1)	7 (7.1)	36

T_0, testing took place 1 day before transcranial direct current stimulation +/or music therapy (baseline); T_1, testing took place 6 months after the transcranial direct current stimulation +/or music therapy.

and assessed using two consecutive 10-mm slices focused at the region of the basal ganglia and with the identical angulation as the native CT. A power injector administered a bolus dose of 50 ml non-ionic contrast medium (Imeron 400, Bracco Imaging Deutschland GmbH) through a central venous line at a flow rate of 4 ml/sec, followed by the administration of 30 ml of saline. A set of 40 images were collected at each slice level at a rate of two frames per second, 4 sec after intravenous contrast was administered (120 kV, 110 mAs, matrix 512x512). These values were measured utilizing post-processing software (Perfusion CT, Siemens), and the CTP color maps were evaluated for their quality using a visual rating scale. A positive visual score was recorded for side-to-side asymmetries or evident bilateral defects, demonstrating a reduction in CBF, CBV and the mean transit time (MTT), which were related to the central volume principle: CBF=CBV/MTT (24). CBV was calculated in milliliters of blood per 100 g of brain tissue and determined as the volume of inbound blood for a specific brain volume (25).

Table III. Baseline characteristics of the study participants.

Parameters	All patients, n=98 (100%)	Group A, n=28 (28.5%)	Group B, n=34 (34.6%)	Group C, n=36 (36.7%)	P-value
Age, years	68.4±5	68.0±5	68.5±4	68.8±5	0.430
Sex (male), n (%)	55 (56.1)	13 (13.2)	23 (23.4)	19 (19.3)	0.221
CBF mean in affected area, cm/sec	15.1±4	12.7±2	16.5±4	15.6±5	0.007
mMT mean	25.0±1	23.7±1	26.1±1	25.0±1	0.001
BI mean	78.7±5	77.3±4	81.0±5	77.7±5	0.002
Clinical characteristics					
Hemiparesis (yes), n (%)	73 (74.4)	20 (20.4)	26 (26.5)	27 (27.5)	0.902
Handedness					
Right, n (%)	83 (84.6)	26 (26.5)	28 (28.5)	29 (29.5)	0.333
Left, n (%)	13 (13.2)	2 (2.0)	5 (5.1)	6 (6.1)	
Ambidextrous, n (%)	2 (2.0)	0 (0)	1 (1.0)	1 (1.0)	
CT findings					
Ischemic or hemorrhage, (ischemic), n (%)	35 (35.7)	9 (9.1)	12 (12.2)	14 (14.2)	0.858
Lesion size, max diameter in cm	29.9±5	29.4±4	29.7±5	30.5±5	0.758
Damage location					
MCA, n (%)	53 (54.0)	13 (13.2)	21 (21.4)	19 (19.3)	0.395
ACA, n (%)	38 (38.7)	13 (13.2)	12 (12.2)	13 (13.2)	
PCA, n (%)	7 (7.1)	2 (2.0)	1 (1.0)	4 (4.0)	
Type of aphasia (after 6 months)					
Conduction, n (%)	2 (2.0)	1 (10)	1 (1.0)	0 (0)	0.533
Wernicke's, n (%)	8 (8.1)	7 (7.1)	1 (1.0)	0 (0)	0.002
Broca's, n (%)	19 (19.3)	11 (11.2)	6 (6.1)	2 (2.0)	0.003
Global, n (%)	7 (7.1)	3 (3.0)	2 (2.0)	2 (2.0)	0.692
Sum	36 (36.7)	22 (22.4)	10 (10.2)	4 (4.0)	

CT, computer tomography; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; mMT mean, mini-mental test; BI mean, Barthel index; CBF mean, cerebral blood flow.

Table IV. Outcomes of the patients in the present study.

Parameters	All patients, n=98 (100%)	Recovery, n=62 (63.2%)	No recovery, n=36 (36.7%)	P-value
AAT $\Delta(T_1\text{-}T_0)$ mean	6.4±2	7.5±1.9	5.1±1.8	0.001
CBF mean in affected area, cm/sec	15.1±4.5	15.6±4.6	14.4±4.3	0.353
BI mean	78.7±5.1	79.6±5.4	77.2±4.0	0.027
mMT mean	25.0±1.7	25.5±1.6	24.2±1.7	0.001
Type of aphasia (after 6 months, n=98)				
Conduction, n (%)	10 (10.2)	8 (8.1)	2 (2.0)	0.061
Wernicke's, n (%)	24 (24.4)	16 (16.3)	8 (8.1)	0.001
Broca's, n (%)	56 (57.1)	37 (37.7)	19 (19.3)	0.001
Global, n (%)	9 (9.1)	2 (2.0)	7 (7.1)	0.001

AAT, Aachen Aphasia Test; $\Delta(T_1\text{-}T_0)$, interval between two trial phases of AAT; mMT mean, mini-mental test; BI mean, mean Barthel index; CBF mean, mean cerebral blood flow.

Outcome measures

Primary endpoints. AAT $\Delta(T_1\text{-}T_0)$: The intermediate period between two phases of the AAT study. Patients were assessed 1 day before (AAT0) and 6 months after therapy (AAT1). As shown in Table II, rehabilitation was defined as the improvement of aphasia in the subgroups.

Table V. Univariate analysis for recovery.

Parameters	Recovery, n=62 (63.2%)	No Recovery, n=36 (36.7%)	P-value
Age, years	68.4±4	68.5±5	0.944
Sex (male), n (%)	34 (34.6)	21 (21.4)	0.737
Clinical characteristics			
Hemiparesis (yes), n (%)	46 (46.9)	27 (27.5)	0.930
Handedness			
Right, n (%)	50 (51.0)	33 (33.6)	0.282
Left, n (%)	10 (10.2)	3 (3.0)	
Ambidextrous, n (%)	2 (2.0)	0 (0)	
CT findings			
Ischemic or hemorrhage, (ischemic), n (%)	25 (25.5)	10 (10.2)	0.211
Lesion size, max diameter in cm	29.7±5	30.2±5	0.687
Damage location			
• MCA, n (%)	32 (32.6)	21 (21.4)	0.781
• ACA, n (%)	25 (25.5)	13 (13.2)	
• PCA, n (%)	5 (5.1)	2 (2.0)	
CBF mean in affected area, cm/sec	15.6±4	14.4±3	0.353
mMT mean	25.5±1	24.2±1	0.001
BI mean	79.6±5	77.2±4	0.027
Groups			
Group A, n(%)	6 (6.1)	22 (22.4)	0.001
Group B, n (%)	24 (24.4)	10 (10.2)	
Group C, n (%)	32 (32.6)	4 (4.0)	
Type of aphasia (after 6 months, n=98)			
Conduction, n (%)	8 (8.1)	2 (2.0)	0.061
Wernicke's, n (%)	16 (16.3)	8 (8.1)	0.001
Broca's, n (%)	37 (37.7)	19 (19.3)	0.001
Global, n (%)	2 (2.0)	7 (7.1)	0.001

CT, computed tomography; MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery; mMT mean, mean mini-mental test; BI mean, mean Barthel Index; CBF, mean, mean cerebral blood flow.

Secondary outcomes. The mean values [mean=(V1 + V0)/2] of i) CBF mean [mean CBF=(V1-CBF + V0-CBF)/2] from CTP conducted 3-6 days (V0-CBF) and 6 months after admission (V1-CBF); ii) mMT mean [mean mMT=(V1-mMT + V0-mMT)/2] were used to assess cognitive deficits. BI mean [mean BI=(V1-BI + V0-BI)/2] was used to measure performance in activities of daily living; first as a pre-screening test at admission to the rehabilitation center (baseline) (V0-mMT) (V0-BI), and 6 months after the CVA (V1-mMT) (V1-BI).

Statistical analysis. Data are expressed as the mean ± SD. Data were examined for regularity using the Shapiro-Wilk test and analyzed using one-way ANOVA. Categorical data were analyzed using the Chi-squared test or Fisher's exact test. The Bonferroni test was used following one-way ANOVA. A multivariable analysis model was used to assess variables significantly associated with the univariate analysis. A P-value <0.05 was considered to indicate a statistically significant difference. The discriminative ability of significant variables was evaluated using the area under the receiver operating characteristic curve (ROC). Statistical analyses were executed using Statistical Product and Service Solutions software, version 15 (SPSS Inc.).

Table VI. Multivariate analysis for recovery.

Parameter	OR	95% CI, lower-upper	P-value
BI mean	0.013	0.002-0.024	0.022
mMT mean	0.030	-0.003 to -0.064	0.074
Groups, n (%)	0.304	0.232-0.376	0.001
Type of Aphasia (after 6 months)			
Wernicke's, n (%)	-0.407	-0.621 to -0.192	0.001
Broca's, n (%)	-0.814	-1.010 to -0.618	0.001
Global, n (%)	-0.885	-1.157 to -0.614	0.001

mMT mean, mean mini-mental test; BI mean, mean Barthel Index; CI, confidence interval; OR, odds ratio.

Table VII. ROC analysis.

Parameters	Area	Std. error	95% CI, lower-upper	P-value
AAT $\Delta(T_1\text{-}T_0)$ mean/recovery	0.807	0.047	0.715-0.900	0.001
BI mean/recovery	0.615	0.057	0.503-0.727	0.058
MMT mean/recovery	0.707	0.055	0.599-0.816	0.001
Type of aphasia (after 6 months)				
Wernicke's, n (%)	0.611	0.062	0.490-0.733	0.068
Broca's, n (%)	0.611	0.062	0.490-0.733	0.068
Global, n (%)	0.556	0.062	0.434-0.677	0.361

ROC, receiver operating characteristic; AAT, Aachen Aphasia Test; $\Delta(T_1\text{-}T_0)$, interval between two trial phases of AAT; BI mean, mean Barthel Index; CI, confidence interval; mMT mean, mean mini-mental test; Std. error, standard error.

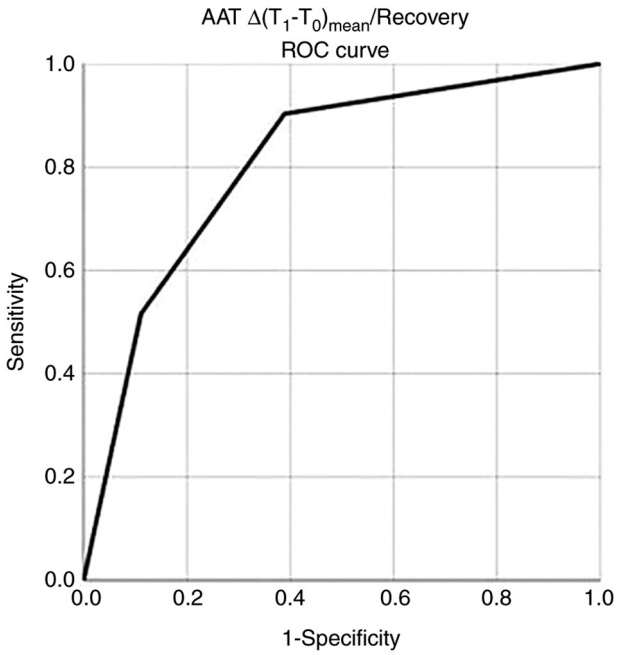

Figure 1. ROC analysis revealed that: AAT $\Delta(T_1\text{-}T_0)$/recoverybetween two trial phases of 1 day before (AAT_0) and 6 months after the music therapy and transcranial direct current stimulation (AAT_1), was the most accurate measure with which to identify recovery with an area under the curve (standard error) of 0.807 (0.047), P<0.05, whereas an AAT $\Delta(T_1\text{-}T_0)$/recovery value >7.7 presented with 90% sensitivity and 89% specificity for recovery. ROC, receiver operating characteristic; AAT Δ(T1-T0), Aachener Aphasie Test interval.

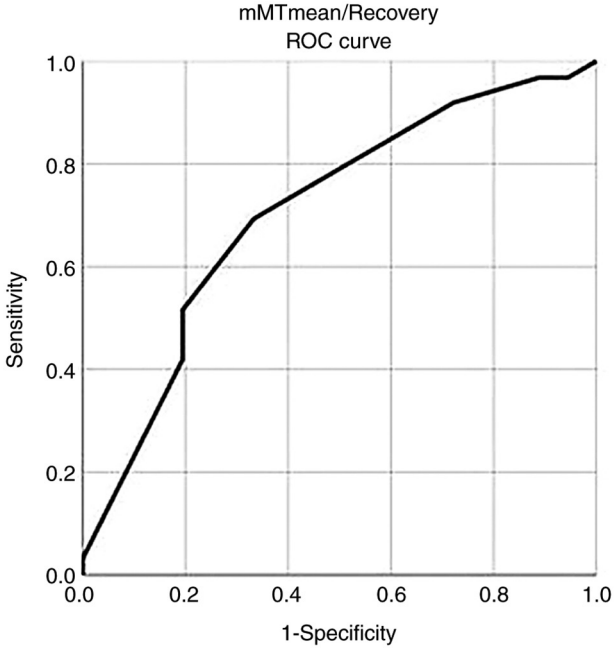

Figure 2. ROC analysis revealed that the mMT mean/recovery between two trial phases of 1 day before (mMT_0) and 6 months after the therapy (mMT_1), could predict the recovery and a mMT mean/recovery value >23.5 demonstrated better dispersion with 91.9% sensitivity and 67% specificity for recovery with an area under the curve (standard error) of 0.707 (0.055) P=0.001. ROC, receiver operating characteristic; mMT, mini-mental test.

Results

Baseline data. A total of 98 patients were enrolled in the present study, and their baseline data are presented in Table III. Statistically significant differences between groups were found for AAT $\Delta(T_1\text{-}T_0)$ mean (P<0.05) (Table I), CBF mean in affected areas (P=0.007), mMT mean (P<0.05) and BI mean (P=0.002) (Table III).

Wernicke's, Broca's and global aphasias were the only statistically significant aphasia types for recovery (P=0.001; Table IV). The overall recovery rate was 63.2% (62 of 98 patients). A higher recovery rate was documented in group C (32.6%) compared with groups B (24.4%) and A (6.1%), and the difference was statistically significant (P=0.001; Table V).

Univariate analysis. Univariate analysis demonstrated that the mMT mean, BI mean, Wernicke's, Broca's and global aphasia groups were associated with recovery (P=0.001, 0.027, 0.001, 0.001 and 0.001, respectively; Table V).

Multivariate analysis. Multivariate analysis revealed that only the parameters, BI mean (OR, 0.013; 95% CI, 0.002-0.024; P=0.022), groups (OR, 0.304; 95% CI, 0.232-0.376; P<0.05), and Wernicke's (OR, -0.407; 95% CI, -0.621 to -0.192; P<0.05), Broca's (OR, -0.814; 95% CI (-1.010 to -0.618; P<0.05) and

global aphasia (OR, -0.885; 95% CI, -1.157 to -0.614; P<0.05) were independent predictors of improvement (Table VI).

ROC analysis. Following ROC analysis, AAT $\Delta(T_1-T_0)$/recovery was the most accurate measure for discriminating recovery with a standard error of area under the curve [AUC (SE)] of 0.807 (0.047), P<0.05, while an AAT $\Delta(T_1-T_0)$/recovery value of >7.7 exhibited a sensitivity of 90% and a specificity of 89% for recovery (Fig. 1 and Table VII).

In addition, a mMT mean/recovery value >23.5 exhibited a sensitivity of 91.9% and a specificity of 67% for recovery with an AUC (SE) of 0.707 (0.055) P=0.001 (Fig. 2 and Table VII).

Discussion

The present retrospective cohort study on patients with post-stroke aphasia found that when MT and tDCS were added to the exercise rehabilitation program, the patients in group C (32.6%) recovered to a greater extent than those in groups B (24.4%) and A (6.1%). In addition, the AAT (T_1-T_0) mean was one of the most important independent predictors of the recovery of patients with CVA who completed a post-stroke rehabilitation program accompanied by MT and tDCS (group C), and an AAT $\Delta(T_1-T_0)$ mean >7.7 had better dispersion in predicting recovery. Moreover, according to the results, patients with a mMT mean >23.5 could also expect clinical recovery. Furthermore, the BI mean could also predict recovery in patients post-stroke.

It is generally accepted that music activates various neural networks in brain structures important for emotions, cognition and motor functions (19,26,27). In a number of studies on tDCS in the chronic phase, the use of electrode configuration (anodal tDCS over the left IFG compared to sham tDCS) was most commonly used in conjunction with disorder-oriented aphasia treatment (28-31). It appears to enhance the rate of language improvement (32).

It has been suggested that tDCS improves learning via long-lasting synergism, i.e., long-term synaptic plasticity (29). However, the debate on the effect of tDCS on recovery from aphasia is still ongoing (33). The present study found that the recovery rate was higher when the rehabilitation program was conducted with MT and tDCS using one electrode configuration. Although the present study demonstrated positive (albeit minor) effects, the influence of different parameters is currently unknown. Parameters, such as the type of aphasia or the size/location of the lesion probably play a significant role in the response to tDCS treatment.

The AAT is a reliable test for detecting aphasia. It can categorize aphasia into four subgroups, also assessing the speakers' language performance to provide more accurate information about the severity of the disorder (34). In the present study, the AAT $\Delta(T_1-T_0)$ mean was one of the most important independent predictors of improvement in patients with CVA who participated in a post-stroke rehabilitation program accompanied by MT and tDCS. Indeed, a change in AAT >7.7 at T0=0 and T1=6 months predicted clinical improvement with 90% sensitivity and 89% specificity.

In clinical practice, it is helpful to predict recovery in patients who have suffered a stroke. However, as predictive factors are variable, it is complex to assess the prediction of improvement in aphasia (35). The most accurate components are the severity of aphasia, lesion size and location (35). In the present study, the mean mMT score was one of the main factors for improvement, and patients with a score >23.5 can expect clinical improvement.

tDCS is a procedure that can alter brain functions temporarily (36). Furthermore, there is evidence to indicate that other brain regions (e.g., the non-damaged right hemisphere) can also promote speech recovery after stroke (36). However, it is unclear whether different stimulation sites affect specific parts of language function differently (37). Previous studies on healthy participants have demonstrated significant and long-term gains in cognitive and motor learning that were maintained for up to 12 months, and indicated that the effects of tDCS during the follow-up period may be more robust in older participants than in younger ones (38,39). In the present study, the long-term effects of tDCS were maintained for up to 12 months due to the advanced age of the patients.

The present study has some limitations. First, the intervention duration was relatively brief. However, the intensity and treatment duration used were consistent with studies (37-39) that have demonstrated an effect of tDCS in chronic aphasia following a stroke. Secondly, the present study was a single-center study. For this reason, the positive effect of MT and tDCS on recovery from aphasia following stroke cannot be generally assumed. However, the results presented herein may serve as a basis for future, more comprehensive clinical studies.

In conclusion, the present study aimed to elucidate the synergistic effects of an exercise rehabilitation program, an enriched acoustic environment, and tDCS leading to better recovery from aphasia following a stroke. Although the present study revealed positive (albeit minor) effects, the impact of different parameters, such as the size/location of the lesion or the type of aphasia, is likely to play a significant role in the response to MT and the tDCS treatment. These encouraging results also suggest that more non-invasive treatments for aphasia following a stroke need to be tested in large, multicenter, double-blind, randomized control trials.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

GF, AAF and VEG conceptualized the study. VEG, AAF, SC, PP, PS, NT, NM and KT made a substantial contribution to data interpretation and analysis, and wrote and prepared the draft of the manuscript. DAS, VEG and GF analyzed the data and provided critical revisions. VEG and GF confirm the

authenticity of all the data. All authors contributed to manuscript revision and have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The Institutional Review Board (IRB) of University of Thessaly, Greece/The School of Medicine/School of Health Sciences approved the study (IRB no. 2492/19-01-2015, finalized by the 9th General Assembly on 28/01/2015). The study was in line with the Declaration of Helsinki (1995; as revised in Edinburgh 2000). Due to the retrospective design of the study, a waiver for informed consent was granted by the Institutional Review Board.

Patient consent for publication

Not applicable.

Competing interests

DAS is the Managing Editor of the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article.

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