Research article
Ερευνητική εργασία

Effects of anodal transcranial direct current stimulation on cognitive dysfunction in patients with progressive supranuclear palsy

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Progressive supranuclear palsy (PSP) is a tauopathy characterized by motor, neurobehavioral and disabling brainstem deficits. No disease-modifying therapeutic options exist. The therapeutic potential of transcranial direct current stimulation (tDCS) has been highlighted in studies on patients with other neurodegenerative diseases. Therefore, by drawing upon the limited tDCS literature on PSP, we conducted a pilot study in order to evaluate the effect of tDCS over motor and premotor cortex in patients with PSP, with a particular emphasis on cognitive dysfunction. Eight patients affected by PSP were included (4 males and 4 females with mean age 67.4±7.4 years, range: 55–80 years and mean disease duration: 4.6±3.3 years, range: 1–11 years). The mean Unified Parkinson's Disease Rating Scale Part III (UPDRS III) was 49±16.1 and the mean Hoehn & Yahr (H&Y) scale was 3.9±1 at baseline. All pharmacological treatments (L-dopa, pramipexole, rotigotine, rasagiline, amantadine) were maintained stable during the study. We aimed at evaluating along with the motor outcome (as it is reflected on a disease-specific rating scale), the post-tDCS cognitive status after the completion of the intervention. The clinical evaluation involved the PSP-Rating Scale, the UPDRS III and the Timed Up and Go test. Neuropsychological assessment focused on auditory-verbal memory and learning, episodic memory, visuo-motor coordination and speed of information processing, executive functions and verbal fluency (phonemic and semantic). Anodal tDCS was applied over primary motor and pre-motor cortices in 10 daily sessions. During the tDCS stimulation a constant current of 2 mA was delivered for 30 minutes. Clinical evaluations were performed at baseline, day 11, day 30 and at day 90. The PSP-Rating score (total and sections I & III) improved significantly on day 11 compared to baseline and similarly on day 30. A positive effect was also seen on action tremor. In addition to the global mental status improvement, patients showed increases in neuropsychological performance in the domains of visuo-motor co-ordination and processing speed, auditory-verbal learning, episodic memory,phonological and semantic flu-

ency (access and retrieval from lexical memory, selective inhibition and lexical access speed). Our results suggest that tDCS has a beneficial effect on Progressive Supranuclear Palsy patients' bulbar and motor symptoms, cognitive dysfunction, as well as daily activities, which lasts beyond the duration of the treatment.

Key words: Progressive supranuclear palsy, transcranial direct current stimulation, motor function, neuropsychoogical dysfunction.

Introduction

Progressive supranuclear palsy (PSP) is a neurodegenerative parkinsonian disorder of tau protein aggregation. It is almost entirely sporadic, with a prevalence of 5–6 persons per 100,000, mean onset age of 63 and median survival of approximately 7 years.[1] The clinical spectrum of the disease is now known to be wider than originally described. Bradykinesia, postural instability, nuchal rigidity, frontal behavioral and cognitive changes, vertical gaze palsy, and other disabling brainstem deficits are some of the clinical features of PSP1. PSP is likely to present more diffuse prefrontal impairment as compared to Parkinson's disease (PD), with recent evidence showing prefrontal degeneration, beyond its known subcortical nuclei degeneration.[2] The diagnosis remains mainly clinical.

To date, no disease-modifying therapeutic options have been identified. The response to levodopa is transient and poor and treatment approaches focus on neurotransmitter replacement strategies with discouraging results.[1]

Transcranial direct current stimulation (tDCS) is a non-invasive and safe method of neuromodulation. Several studies highlight the therapeutic potential of tDCS in patients with neurological diseases including PD. Their results confirmed that tDCS application over the motor cortex had beneficial effect on bradykinesia and gait and postural control in advanced PD patients.[3–6]

In order to test the hypothesis that anodal tDCS could have beneficial effects in PSP we conducted an open label study without a control set-up. We applied the stimulation over primary motor and pre-motor cortices in 8 PSP patients. The aims of this study were the evaluation of the motor outcome as it is reflected on a disease-specific rating scale and the identification of the potential cognitive function outcome after the therapeutic sessions.

Material and method

Participants

Eight patients affected by PSP according to the current clinical criteria[7] were included in our study. The participants had no other relevant neurologic or psychiatric disease. Other exclusion criteria were implanted electrical medical device, such as a pacemaker, defibrillator, or deep brain stimulator; suspected or diagnosed epilepsy or other seizure disorder and pregnancy. The ethical committee of the Evangelismos Hospital approved the study and informed consent was obtained.

Instruments

All subjects underwent a clinical evaluation which involved the PSP-Rating Scale (PSP-RS)[8] which was used as the primary end point. This scale is divided in six sections: activities of daily living, behavior, bulbar, ocular motor, limb motor and gait.

The Unified Parkinson's Disease Rating Scale (UPDRS) III[9] and the Timed Up and Go test (TUG) (timed in seconds)[10] were also administrated. The time that the patient took to rise from an office chair with arms, walk three meters, turn around, walk back to the chair, and sit down was measured according to standard practice. Neurological evaluations also included the Schwab and England[11] and the Hoehn & Yahr[12] scales.

In order estimate cognitive functioning we used Mini Mental State Examination (MMSE) for a brief and raw assessment of the patient's general mental state.[13] Auditory-verbal memory and learning was estimated with Rey's Auditory Verbal Learning Test (RAVLT).[14] Visuo-motor activity and processing speed were evaluated with Digit Symbol Substitution Test-Wechsler Adult Intelligence (DSST-WAIS-III).[15] We

used Digit Span (Forward & Backward) to measure working memory and Trail Making Test (TMT-A) to assess concentration and visuo-motor activity.[15,16] Episodic memory has been evaluated by means of the Babcock Story Recall Test (BSRT)[17] while Verbal Fluency Test (Phonemic & Semantic) was also included to tap aspects of executive functions and language.[18]

Study Design/tDCS

Direct current was applied through a saline-soaked pair of surface sponge electrodes surface (35 cm^2) and delivered by a battery-driven, constant current stimulator (Sooma tDCSTM, Finland). During the tDCS stimulation a constant current of 2 mA was delivered for 30 minutes. To stimulate motor and premotor cortices the anode electrode was placed centrally across the scalp 8 mm anterior to Cz. Cathode was positioned over the right mastoid. tDCS was applied for 10 days over two weeks (Monday to Friday) with a weekend interval washout period.[19] Clinical evaluations were performed on day 0 (baseline), day 11, month 1 and month 3.

Statistics

Descriptive statistics were obtained for all parameters. Within group differences between baseline and follow-up values were compared by paired t-test. Comparisons were two-sided and $p<0.05$ was set as the level of statistical significance. All calculations were done in R version 3.5.1.

Study size

We calculated the required sample size based on the primary endpoint (PSP-R). Based on the published literature,[20] the minimum clinically important change in PSP-R over time is 5.7 and the anticipated standard deviation 3.7, which corresponds to an effect size Cohen d=1.51. Thus, the required sample size for a paired t-test to detect such a difference with a 0.8 power at a significance level of 0.05 is 6 patients.

Results

Patient demographics

Eight patients affected by PSP according to the current clinical criteria were included in our study; 4 males and 4 females with mean age 67.4±7.4 years, range: 55–80 years and mean disease duration: 4.6±3.3 years, range: 1–11 years. The mean Unified Parkinson's Disease Rating Scale Part III (UPDRS III) was 49±16.1 and the mean Hoehn & Yahr (H&Y) scale was 3.9±1 at baseline.

All pharmacological treatments (L-dopa, pramipexole, rotigotine, rasagiline, amantadine) were maintained stable during the study. The L-dopa equivalent dose was 738.5±235.6 mg.

Clinical outcome

PSP-Rating Scale total score was significantly decreased by 17.4% on day 11 and by 9% on month 1, compared to baseline (table 1). At the end of tDCS application all the patients reported a significant amelioration of dysarthria and dysphagia (PSP-RS III) ($p<0.05$). The therapeutic gain was retained for at least 1 month after the therapy. Significant improvement was noticed in daily activities (PSP-RS I) at day 11 and 1 month follow up visits ($p<0.05$).

Three out of the eight participants were not able to consummate the TUG evaluation. The disability due to the disease deteriorated after the 1st month in another patient. Therefore, we finally calculated TUG in 4 patients. The time required to complete the test was reduced by 31.3% compared to baseline at day 11, 32.8% at 1 month and 26.1 % at 3 months respectively (table 2). These results indicate a non-significant trend towards a reduction of TUG on follow up evaluations compared to baseline. We observed a 7% reduction of UPDRS total score on day 11 compared to baseline, which reached borderline statistical significance ($p=0.06$). This effect did not persist on months 1 and 3 (table 2). tDCS treatment exerted a significant reduction in action tremor (45.5%, $p<0.05$) at the end of the stimulation protocol (table 1).

No adverse events were reported.

Cognitive outcome

In the domain of auditory-verbal learning for not semantically organized material (lists of words) as measured by the RAVLT it has been showed an increase by 41.9% at day 11, by 30.7% at 1 month and later on in the course of the intervention a slight decrease by 22.8% at 3 months compared to baseline ($p<0.05$) though still maintaining therapeutic profits. There was a significant amelioration in the Phonemic

Table 1. The study outcomes during the 3 months follow- up (Mean +/– Standard Deviation).

	Baseline	11 days	1 month	3 months
PSP-RS (total)	47.6±16.3	39.3±13.1*	43.3±14.1*	45.1±15.3
PSP-RS-I	13.9±5.8	9.5±5.1*	11.3±5.5*	12.1±5
PSP-RS-II	0.5±1	0.4±0.7	0.4±0.7	0.6±1
PSP-RS-III	4.9±2.6	3.1±1.7*	3.4±2*	5±2.4
PSP-RS-IV	10.4±3.2	8.6±4	9.5±3.2	9.1±3.5
PSP-RS-V	7.4±3	7.8±2.8	7.6±3.2	8.1±3
PSP-RS-VI	11.1±7.1	10.3±6.4	11.5±6.2	11±6.6
UPDRS III	49±16.1	45.5±14.8	47.6±14.9	47.6±16.11
UPDRS rest tremor	0.4±1	0.5±1	0.3±0.7	0.1±0.4
UPDRS action tremor	1.1±1.1	0.6±0.9*	0.5±0.9	0.9±0.6
UPDRS rigidity	9±3.6	8.3±4.5	9.9±4	9±3.4
UPDRS upper bradykinesia	15.3±5.2	15±4.9	14.9±4.2	14.8±4.5
UPDRS leg agility	5.6±2	5.4±1.3	5.3±1.7	5.1±2
UPDRS-III-28	2.4±1.4	2.3±1.3	2.1±1.3	2.3±1.2
UPDRS-III-31	3±0.9	2.6±1	3±0.9	3.1±0.83
MMSE	23.0±5.4	26.2±3.5*	24.7±3.4	23.6±4.5
DSST-WAIS-III	17.2±9.1	21.6±10.8*	19.9±9.6	16.9±8.5
BSRT-immediate recall	8.7±2.6	10.0±2.7	9.1±2.4	7.7±2.3
BSRT- delayed recall	4.3±1.3	5.5±1.1	5.1±1.0	4.6±1.2
RAVLT	21.5±15.5	30.5±19.2*	28.1±18.6*	26.4±18.3*
Trail Making-A	234.0±81.5	217.0±98.7	211.3±103.9	220.2±95.5
Phonemic fluency	9.8±9.5	13.8±10.1*	13.8±10.8	12.7±10.1
Semantic fluency	15.3±10.9	17.4±12.0	19.3±10.8*	17.6±11.6

*Statistically significant changes compared to baseline at $p<0.05$
PSP-RS: PSP-Rating Scale, UPDRS: Unified Parkinson's Disease Rating Scale, MMSE: Mini Mental State Examination, DSST-WAIS-III: Digit Symbol Substitution Test-Wechsler Adult Intelligence Scale III, BSRT: Babcock Story Recall Test, RAVLT: Rey's Auditory Verbal Learning Test

fluency (access and retrieval of verbal information from lexical memory and selective inhibition) performance at the end of the tDCS application (increased performance by 40.8%), ($p<0.05$). Interestingly, we observed a significant therapeutic effect in the Semantic fluency test (executive function and access to semantic memory) during the 1 month visit too (table 1). Measures of verbal fluency assess the ability to retrieve specific information within restricted search parameters. Successful retrieval requires executive control over cognitive processes such as continuous updating, selective attention, selective inhibition, mental set shifting, internal response generation, and self-monitoring.[21]

Significant improvement was also observed in visuo-motor coordination and speed of information processing as measured by Symbol Coding-WAIS-III and in patients' global cognitive functioning as measured by MMSE (increase by 25.6% and 13.9% respectively). However, the positive effect was not maintained on the 1 and 3 months follow up evaluations (table 1). We noticed a reduction of BSRT scores (immediate and delayed recall of semantically organized verbal material) on day 11 and 1 month post-intervention which reached borderline statistical significance (table 1). Of no statistical significance were pre- and post-rehabilitation test performance in Trail Making-A (visual scanning and concentration).

Table 2. The TUG scores during the 3 months follow-up (time in seconds).

	Baseline	11 days	1 month	3 months
1	27	175	na	na
2	29	18	20	23
3	9	6.3	7.3	8.3
4	14	12.9	13.5	11.8
5	12.3	11.5	10.5	11.5
6	na	na	na	na
7	na	na	na	na
8	na	na	na	na
Average	18.26+/–9.1	13.24+/–4.8	12.1+/–1.5	10.5+/–.1,9

na: not available
TUG: Timed Up and Go test

Discussion

To our knowledge, the present study is the first to investigate the neuromodulation effects of anodal tDCS stimulation over the motor and pre-motor cortices in PSP patients' cognitive performance. Apart from our findings in motricity, meaning the improvement of PSP Rating Scale, in particular the bulbar function and the activities of daily living, as well as a post-tDCS effect on motor function as it reflected in UPDRS III and TUG performance, our PSP patients showed a post-tDCS neuropsychological improvement in the domains of visuo-motor coordination and processing speed (Symbol Coding-WAIS-III), auditory-verbal learning (RAVLT), episodic memory (BSRT immediate- and delayed -recall), phonemic fluency (access and retrieval of verbal information from lexical memory and selective inhibition), semantic fluency (executive function and access to semantic memory l, as well a global cognitive status improvement as suggested by the MMSE.

The improvement of dysarthria and dysphagia items is in line with a previous study.[22] Brusa et al, who employed cerebellar stimulation in PSP patients via 10 intermittent theta burst stimulation (TBS) sessions and reported amelioration of dysarthria symptoms. Interestingly, the authors,[22] reported a halting in paradoxical facilitation of cerebellar inhibition (CBI), probably counteracting pathological cerebellar inhibitory projections expected in these patients. The increased caudate nucleus' fMRI activivation as a consequence of thalamic stimulation is a possible explanation. Since caudate nucleus atrophy has been demonstrated in PSP,[23] tDCS stimulation likely promotes the induction of dopamine release in the caudate nucleus via the glutamatergic corticostriatal pathways, as has also been showed in animal studies.[24–26]

Current literature underlines the involvement of the cerebellum in PSP pathophysiology, while atrophy constitutes a common morphological finding encountered in the white and grey matter of the cerebellar peduncles. There is evidence that atrophy of specific grey matter regions correlates with postural instability and phonological changes, oculomotor deficits, affective and memory functions.[27] Besides cerebellar atrophy, PSP patients demonstrate significant gray matter volumetric reductions in both cortical and subcortical regions, including the frontal motor cortices, paralimbic (including anterior cingulate cortex and insula,) and lateral prefrontal cortices, superior temporal gyrus, striatum (putamen and caudate nucleus), thalamus and midbrain.[28] According to published studies there is evidence suggesting a tDCS modulating contribution on the functional connectivity of the corticostriatal and thalamo-cortical circuits in the human brain.[29]

The possible neuromodulating effects of tDCS on cortical excitability has raised interest in the application of the technique for the promotion of cognitive and executive function in either PSP or Multiple

System Atrophy (MSA) as it has been shown in the emerged studies of the last decade.[19,30]

Moreover, in the realm of psychopathology, since obesity is associated with decreased prefrontal cortex (DLPFC) activity, tDCS likely modifies cortical excitability and may facilitate improved control of eating. A recent study[31] emphasized the role played by left DLPFC in obesity and food intake and the potential application of anodal tDCS to facilitate weight loss.

The post-tDCS cognitive improvements are likely to reflect a functional improvement of both noradrenergic, glutaminergic, and dopaminergic neurotransmission leading to performance improvements in the domains of processing speed, memory and executive functions respectively, since PSP is likely to affect multiple neurotransmitter systems as a result of multiple sites of pathology.[32] It should be noted that memory disorders in PSP are seen as secondary (systemic) executively-induced disorders and as such not exclusively linked to cholinergic neurotransmission, as in the case of primary memory disorders.

The post-tDCS executive improvement seen in our patients, as reflected by improved verbal fluency performance, links to a possible functional upgrade of prefrontal cortex (PFC) since tDCS stimulation promotes dopamine release in the caudate nucleus, thus counterbalancing to some extend PSP-related gray matter loss of medio-lateral aspects of PFC.[33] Moreover, processing speed increases as suggested by patients' post-tDCS performance on Symbol Coding-WAIS-III, may strongly contribute to the observed post- tDCS phonological fluency improvement, since t processing speed is one of the many functional parameters f shaping phonological fluency performance.[34]

Episodic memory (BSRT) and auditory-verbal learning (RAVLT) post-tDCS increases may be interpreted in the light of a more general executive-frontal improvement (in terms of learning and retrieval strategies), since PSP is characterized by disruption of similar frontal-subcortical connections,[35] giving rise to executive-dependent (secondary) memory disorders, as well as other dysexecutive symptoms (e,g., apathy, working memory, reasoning, problem solving, conceptualization, planning, and social cognition deficits) strongly associated with frontal-executive dependent memory dysfunction.

By synthesizing all the pieces of evidence presented above, we hypothesize that the beneficial effect of tDCS that we observed in our patients was mediated by an improvement of the cerebello-thalamocortical functional connectivity.

Nevertheless, it has to be considered that changes in functional connectivity may not be strictly related to tDCS induced modulation of the cerebello-thalamocortical circuit. In PSP patients there is evidence of loss of cortical interneurons in the presupplementary motor area (SMA), primary motor cortex (M1) and motor thalamus,[36] resulting in the loss of γ-aminobutyric (GABA-A) intracortical inhibitory interneurons and possibly to a M1 disinhibition because of the reduced pallido-thalamic inhibitory input. Thus, tDCS may adjust resting membrane potentials mediated by changes in N-methyl-d-aspartate-receptor activation and GABAergic inhibition, as previously suggested.[37–40] Moreover, the tDCS long-term effects on motor performance as it was reflected in UPDRS III and TUG score could be a possible result of the stimulation and the induced M1 neuroplasticity. Of course, the relationship between dynamically interacting motor and cognitive circuitries connectivity should be addressed by future studies to disentangle the multifaceted nature of post-tDCS improvements.

Taking in to account that the minimal clinically important worsening on the PSPRS is 5.7 points, corresponding to the mean decline over 6 months,[20] our data suggest that tDCS might slow the progression of neurodegenerative process. Thus, tDCS in PSP appears to have a beneficial effect on motor (bulbar) and cognitive function which lasts beyond the duration of the treatment.

A main limitation of the present study is the open label design and the absence of a control group. Nevertheless, the conduction of an appropriate trial is difficult due to the rarity of the disease and, consequently, of the absence of optimal stimulation protocols with regard to the period of the therapy and the stimulation parameters (intensity, duration, repetition of treatment).

tDCS neuromodulation seems to be a promising therapy with a safe profile but larger randomized

controlled trials are needed to corroborate these encouraging results. Future research should address the putative interactions among motor and cognitive dysfunction parameters, since many cognitive domains share common cortico-subcortical circuitries with motor ones.

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Η επενέργεια της διακρανιακής διέγερσης συνεχούς ρεύματος στη νοητική δυσλειτουργία ασθενών με προϊούσα υπερπυρηνική παράλυση

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Η προϊούσα υπερπυρηνική παράλυση είναι μια tau-πάθεια που χαρακτηρίζεται από κινητικές, νευροσυμπεριφορικές διαταραχές και στελεχιαία ελλείμματα. Δεν υπάρχουν νευροτροποποιητικές θεραπευτικές επιλογές. Οι θεραπευτικές δυνατότητες της διακρανιακής διέγερσης συνεχούς ρεύματος (transcranial direct current stimulation, tDCS) είναι γνωστές από μελέτες ασθενών με άλλα νευροεκφυλιστικά νοσήματα. Γι' αυτόν τον λόγο, ορμώμενοι από την περιορισμένη αρθρογραφία tDCS επί του επίμαχου κλινικού πληθυσμού, πραγματοποιήσαμε μία πιλοτική μελέτη με σκοπό να εκτιμήσουμε την επίδραση της εφαρμογής του tDCS στον κινητικό και προ-κινητικό φλοιό σε ασθενείς με Προϊούσα Υπερπυρηνική Παράλυση και με επικέντρωση στη νοητική δυσλειτουργία. Οκτώ ασθενείς με Προϊούσα Υπερπυρηνική Παράλυση συμμετείχαν στη μελέτη (4 άνδρες και 4 γυναίκες με μέση ηλικία 67,4±7,4 έτη, εύρος: 55–80 έτη και μέση διάρκεια νόσου: 4,6±3,3 έτη, εύρος: 1–11 έτη. Κατά την ένταξη στη μελέτη παρουσίαζαν μέση τιμή στην κλίμακα Unified Parkinson's Disease Rating Scale Part III (UPDRS III) ίση με 49±16,1 και στην κλίμακα Hoehn & Yahr (H&Y) ίση με 3,9±1 αντίστοιχα. Η φαρμακευτική αγωγή (L-dopa, pramipexole, rotigotine, rasagiline, amantadine) παρέμεινε σταθερή σε όλους τους ασθενείς κατά τη διάρκεια της μελέτης. Σκοπός της παρούσας μελέτης ήταν, πέραν της εκτίμησης του κινητικού αποτελέσματος, ο προσδιορισμός της πιθανής βελτίωσης της νοητικής λειτουργίας μετά τις θεραπευτικές συνεδρίες. Για την κλινική αξιολόγηση των κινητικών συμπτωμάτων χρησιμοποιήθηκαν οι κλίμακες PSP-Rating Scale, UPDRS III και Timed Up and Go test. Η νευροψυχολογική αξιολόγηση περιλάμβανε δοκιμασίες ακουστικής-λεκτικής μνήμης και μάθησης, μνήμης επεισοδίων, οπτικοκινητικής συνεργίας και ταχύτητας επεξεργασίας των πληροφοριών, προσοχής και επιτελικών λειτουργιών, λεκτική ροή (φωνημική και σημασιολογική). Ανοδική διακρανιακή διέγερση εφαρμόστηκε στον κινητικό και προ-κινητικό φλοιό των ασθενών για 10 συνεδρίες. Κατά τη διάρκεια της διέγερσης, εφαρμόστηκε συνεχές ανοδικό ρεύμα 2 mA για 30 λεπτά. Η κλινική εκτίμηση πραγματοποιήθηκε πριν την έναρξη της εφαρμογής, τις ημέρες 11, 30 και 90 μετά την εφαρμογή αντίστοιχα. Σημειώθηκε σημαντική βελτίωση στην κλίμακα PSP-Rating score (συνολικά και στις υποενότητες I & III) που αφορούσε στην ημέρα 11 και 30 συγκριτικά με τη θεραπευτική συνεδρία (μετρήσεις αφετηρίας). Επίσης, παρατηρήθηκε θετική θεραπευτική επενέργεια στον τρόμο ενεργείας.

Πέραν της σφαιρικής βελτίωσης της νοητικής κατάστασής τους, οι ασθενείς παρουσίασαν μετα-αποκαταστασιακή πρόοδο στον οπτικοκινητικό συντονισμό και την ταχύτητα επεξεργασίας των πληροφοριών, στην ακουστική-λεκτική μάθηση μη σημασιολογικά οργανωμένου υλικού και στη μνήμη επεισοδίων, στις επιτελικές λειτουργίες, στη συνειρμική φωνολογική και σημασιολογική λεκτική ροή (προσπέλαση και ανάσυρση πληροφοριών από τη λεξικολογική μνήμη, επιλεκτική αναστολή και ταχύτητα λεξικολογικής προσπέλασης). Τα αποτελέσματα μάς καταδεικνύουν τη θετική επίδραση της διακρανιακής διέγερσης συνεχούς ρεύματος στα προμηκικά και κινητικά συμπτώματα, επιμέρους νευροψυχολογικούς τομείς όπως την ταχύτητα επεξεργασίας, τη λεκτική μνήμη και τη μνήμη επεισοδίων, τις επιτελικές όψεις του λόγου (λεκτική ροή: ικανότητα προσπέλασης και ανάσυρσης πληροφοριών από τη λεξιλογική μνήμη), καθώς και στις καθημερινές δραστηριότητες των ασθενών με Προϊούσα Υπερπυρηνική Παράλυση. Το δε θεραπευτικό όφελος φαίνεται να διαρκεί και μετά το πέρας της νευροτροποποιητικής παρέμβασης.

Λέξεις ευρετηρίου: Προϊούσα υπερπυρηνική παράλυση, διακρανιακή διέγερση συνεχούς ρεύματος (tDCS), κινητική λειτουργία, νοητικές λειτουργίες.

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