Transcranial Direct Current Stimulation Associated with Visual and Auditory Cueing during Gait Training: A Case Study with a Parkinson's Disease Patient

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***Abstract*— Parkinson's Disease (PD) is a neurodegenerative disorder that leads to motor dysfunctions and restricts walking independence. Approaches such as transcranial direct current stimulation (tDCS) and cueing gait are potential rehabilitation strategies that have proven efficient in improving motor function in individuals with PD in preliminary and separate studies. This case study with a single PD patient explores the feasibility and potential effects of combining anodal tDCS (a-tDCS) with visual and auditory cues during 15 gait training sessions. The patient was assessed before the first intervention and after completing all training weeks regarding kinematic parameters of gait, neuronal activation, muscle strength, and functional skills. Results showed a beneficial impact in significantly increasing the participant's speed, stride length, step length, and muscle strength. Furthermore, the decrease in beta brain activity and increase in the delta were associated with a reduction in the effects of the disease, improved motor performance, and shorter functional task times. This study suggests the a-tDCS strategy with double cueing gait can lead to therapeutic potential in relieving the disease's motor symptoms.**

I. INTRODUCTION

According to the World Health Organization (WHO), Parkinson's disease (PD) is the second most common neurodegenerative system disorder that currently affects 7 billion people in the world (1 in 100 people) and is expected to reach 12 million by 2030 [1]. Adults over 60 are mainly affected by the disease, and their motor control is limited due to the destruction of dopaminergic neurons in the brain basal ganglia [2], [3]. The decreased dopamine levels specifically cause tremors, muscle stiffness, and postural instability, leading to a characterized foot-dragging, short steps, and low balance, velocity, and coordination during the gait [4].

Pharmacological treatments and physical therapy represent the standard strategies to treat and decrease the progression of this neurodegenerative disease [5]. Although Levodopa remains the most effective drug against Parkinson's disease, its benefit has proven to be less stable and tends to fluctuate in its advanced stages [6]. Therefore, when conventional therapy fails, surgical interventions (e.g., pallidotomy and deep brain stimulation) are the last therapeutic option to relieve some Parkinson's symptoms. However, these techniques are generally limited due to their high cost, a small, well-defined patient population, and the risk of complications during the procedure [7].

Transcranial direct current stimulation (tDCS) is a brain stimulation technique that delivers a low-intensity current to the scalp, typically over 5 and 30 minutes. The tDCS technique enhances the specific brain activity by neuromodulation of neuronal excitability [8]. Notably, in pathologies like PD, the anodal tDCS (a-tDCS) aims to increase the cortical activity of the motor regions in the brain to improve gait through neurons' depolarization [8], [9]. Based on previous works, a-tDCS to the primary motor cortex (M1) induces immediate brain aftereffects resulting in reduced freezing of gait and enhancements in motor function, skill, and strength tasks of PD patients [10], [11].

Individual physical therapy programs with motor training effectively treat PD gait disturbances. Currently, promising reports have described the success of these techniques combined with sensory cues (i.e., visual, auditory, somatosensory stimuli, and attention-enhancement strategies) for gait treatment [12]. On the one hand, visual cues with floor markers regulate the stride length. They have been demonstrated to be effective in progressively increasing the velocity during the walk of PD patients [12]. On the other hand, auditory cues with rhythmic beat frequencies aim to enhance the deficient internal rhythm, which has also shown improved gait characteristics (i.e., velocity, timing, and cadence of gait) and the relief of freezing episodes [13].

Based on the above, long-term findings suggest that both tDCS physical rehabilitation and cueing therapy-induced improvements in PD patients' gait are independent treatments. However, it is reasonable to assume that the effects of these combined techniques may further strengthen functional benefits beyond the commonly analyzed gait pattern [14]. Therefore, the present case study explores the potential a-tDCS-driven improvements with visual and auditory stimulus strategies during 15 gait training sessions. Specifically, the report intends to compare, on a preliminary basis, the effects on lower-limb motor functioning and the variations at the kinematic, electroencephalographic, muscular, and functional levels according to pre and post-treatment recordings of a single patient. To our knowledge, it is the first long-term case study evaluating the feasibility of two combined cueing techniques during gait training with tDCS [15].

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II. METHODOLOGY

A. Patient Report

This controlled study involved a 63-year-old female diagnosed with PD in 2011 and with Hoehn and Yahr (H&Y) stage II. The patient's clinical report describes the use of coherent and fluent language, in addition to a good mood and excellent sleep quality. In terms of gait, the patient can walk independently without assistance technology but with an evident asymmetry during walking. Therefore, the gait cycle has bilateral affectations of the spatiotemporal parameters (cadence, velocity, stance phase, stride length, and stride length). Further, typically presents an absence of arm swing in the right upper limb with cogwheel stiffness and a fixed semi-flexed elbow position. Current treatment includes a consistent medical routine with levodopa (300 mg daily dose), pramipexole, trihexyphenidyl, fluoxetine, and domperidone. The participant was selected using the following inclusion and exclusion criteria:

- *Inclusion Criteria:* A patient with Parkinson's disease between 40 and 80 years of age with a confirmed diagnosis of stages I-III according to the Hoehn and Yahr scale. According to their clinical history, the participant must demonstrate partial independence to mobilize and not suffer any cognitive impairment. Additionally, they must actively receive (levodopa dosage geq 300 mg per day) a stable medical regimen for at least three weeks before study entry.
- *Exclusion Criteria:* According to the experimental setup and the system features, the candidate was rigorously excluded from the study if they presented other neurological disease, seizures, visual disorders, unstable medication, substance abuse, metallic implants, history of deep brain stimulation, head trauma, pregnancy status, damaged skin or recent scars, evident inability to walk 10 meters, or a severe level of depression or anxiety conferring on the clinical report.

The study was performed under a specific protocol approved by the local Research Ethics Committee of the *Corporación de Rehabilitación Club de Leones Cruz del Sur* (Punta Arenas, Chile). It was carefully conducted below the Declaration of Helsinki as an ethical principle of human research. The patient gave her written informed consent and approval to publish the results before voluntarily participating in the experiment.

B. Experimental Procedure

The experimental design of this study consisted of 15 sessions over five weeks (three sessions per week with a minimum interval of 48 h between sessions) [16]. The interventions had approximately 25 minutes of gait exercise combined with specific cues (i.e., visual and auditory) and anodal tDCS with 'on' state medication. This period was divided into four active training blocks of 5 minutes interspersed with 1-minute blocks of breathing exercises without current stimulation.

Before the initial active gait training, hemodynamic tests (i.e., oxygen saturation, blood pressure, heart rate, and respiratory rate) were carefully performed to identify physiological activity and prevent complications. All therapy sessions were conducted at the Movement Analysis Laboratory of the *Corporación de Rehabilitación Club de Leones Cruz del Sur* (Punta Arenas, Chile). [1].

C. tDCS Intervention

The anodal tDCS was administrated with a Starstim tES 8-channel stimulator (Neuroelectrics, Spain) employing two 35 cm^2 surface electrodes (anode and cathode) soaked in saline solution [16], [17]. Following the international 10-20 system, the anode conductor was placed in the primary motor cortex (Cz), and the cathodic electrode was placed on the right hemisphere frontal cortex (Fp2) [10], [11], [14]. The simulated electric field distribution with SimNIBS 3.2 for a healthy brain (Figure 1) was elementary in the cathode laterality selection to modulate the prefrontal areas and balance cortical activity [18]. The right hemisphere despite having a lower focality, generates a stronger magnitude of the electric field and a notable electric current dispersion compared to the left hemisphere. Under these conditions, the stimulation criteria do not exceed the dosage limit of 0.06 mA/cm^2 [19] and go above the minimum threshold of 0.017 mA/cm^2 for active cortical modulation [20]. Finally, the system configuration was completed with a current intensity of 1.5 mA (0.04 mA/cm^2) since stimulation intensities higher than 1 mA have been reported to be more beneficial in enhancing performance in PD with 15-second up and down ramp periods [21].

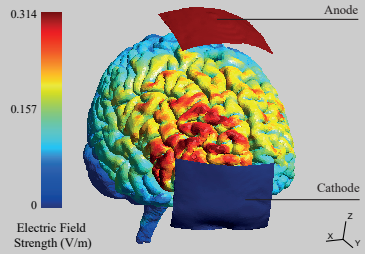

Fig. 1. SimNIBS electrode montage and a-tDCS simulation of the electric field distribution.

The 10-20 system provided by the Neoprene Headcap (Neuroelectric, Spain) ensured consistency of electrode positioning throughout all sessions. This placement was further corroborated with the patient's cranial anatomy to confirm the Cz reference electrode was always positioned at the central vertex.

During tDCS, most people typically present a slight tingling, prickling, warmth sense, and even redness around electrode placement. Although these sensations are temporary and not painful, they can be extremely uncomfortable [19]. Hence, a 3-session adaptation protocol was performed in which the galvanic current intensity was gradually increased

[1]Data is available here

until reaching 1.5 mA on a stable basis. The patient rested during this procedure while the specialist evaluated skin tolerance and comfort. Concluding each session and after removing the electrodes, the patient's skin was moisturized with *La Roche-Posay Toleriane Ultra Fluide* to prevent the irritation caused by the tDCS.

D. Visual and Auditory Cueing Training

During stimulation, the patient performed gait training guided by external visual and auditory cues. On the one hand, visual signals consisted of floor bands (50 cm long and 5 cm wide) placed perpendicularly along a 10 m long walkway, according to the method of Costa-Ribeiro et al. [16]. The distance between the strips was established at 59 cm for all sessions, according to the standardized reference data by age range of the Rehabilitation Center (see Figure 2). On the other hand, auditory cues include rhythmic beats starting at 100 bpm and increasing by 5% every three sessions until reach a maximum of 120 bpm. This way, the patient was instructed to synchronize her cadence to the beat and walk over each floor marker during the tDCS stimulation.

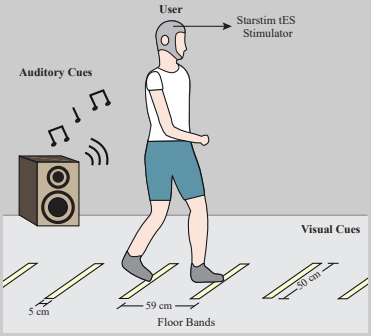

Fig. 2. Experimental system setup with visual and auditory cueing during gait training and a-tDCS stimulation.

E. Outcomes Measurements

Fourth, clinical and functional assessments were performed before and after completing all training weeks, as follows:

- *Gait Kinematic Analysis:* The user kinematic was acquired using ten-cameras VICON (Oxford Metrics, UK) with a sample rate of 100 Hz. This data was tracked and cinematically analyzed with the Nexus (Oxford Metrics, UK) and the Polygon software (Oxford Metrics, Oxford, UK), rendering to the PluginGait biomechanical model [22]. Accordingly, spatiotemporal parameters were obtained from ten free-walking trajectories (i.e., without any stimulation or cueing). The above-included cadence, speed, support phase, stride length, step length, step width, and the *Gait Deviation Index (GDI)*. This last indicates normal gait based on global kinematic variables [23].
- *Electroencephalography (EEG):* Brain electrical activity signals were acquired with a 500 Hz frequency rate using the Enobio 20 (Neuroelectrics, Spain) sensor and the NIC2 software (Neuroelectrics, Spain). Specifically, data were recorded on C3 and C4 channels (according to the 10-20 distribution) related to the sensorimotor functions of the left and right hemispheres, respectively. Data were obtained during 5-minute closed eyes, open eyes, and gait. During the first two conditions, the subject was asked to remain seated still to record the EEG resting state, while in gait, the patient was instructed to perform natural walk exercises. The signal pre-processing included bandpass filtering from 1 to 50 Hz, notch filtering, and an analysis in terms of the Power Spectral Density (PSD) and absolute power of the delta (1-3 Hz), theta (4-7 Hz), alpha (8-12 Hz), and beta (13-30 Hz) frequency bands. The PSD was obtained based on Welch's method with segmentation of the data into a 1-second window with 50% overlap. Furthermore, some signals required a head motion correction to compensate for the movement during walking. The foregoing was carried out with the different functionalities offered by the EEGLAB software [24] and Matlab R2021a version (The MathWorks, Inc., Natick, Massachusetts, United States).
- *Muscle Strength:* Isokinetic muscle strength was measured in the patient's lower limb with the Commander Echo Console Dynamometer (JTech Medical, United States). During this evaluation, voluntary contraction in the hip (flexion, extension, and abduction), knee (flexion and extension), and ankle (plantarflexion and dorsiflexion) muscle groups are performed.
- *Functional Tests:* The standardized timed up-and-go (TUG) test assessed functional mobility, speed, and bradykinesia. The test measures the time for the patient to get up from a chair, walk 3 meters, turn around, and sit back. In this case, the average period in seconds from three trials is the TUG score to reduce variability due to the participant's motor status and obtain a more representative measure. Similarly, the 360° turning test measures the time required to make a 360° turn to both sides to assess the participant's stability.

F. Statistical Analysis

This repeated-measures design study analyzes the effect on the power distribution of two EEG series segmented by frequency bands. The normality distribution of each data set was verified using the Shapiro–Wilk test. Subsequently, the T-Student test assessed the statistical changes ($p < 0.05$) between the two related baseline samples and after the last training session. This part was included for each combination of frequency bands (i.e., delta, theta, alpha, and beta) of each channel (i.e., C3 and C4) for the three different conditions (i.e., eyes-closed, eyes-open, and gait). Finally, the Benjamini-Hochberg multiple comparisons correction method was employed to adjust the p-values obtained and avoid inflating the false-positive rate over a 0.05 significance level ($p < 0.05$). All statistical analyses were performed operating the software SPSS (Version 23.0) (IBM-SPSS Inc, Armonk, New York, NY, United States).

TABLE I

SPATIAL-TEMPORAL PARAMETERS AND GAIT DEVIATION INDEX OF BASELINE AND POST-STIMULATIONS

	Baseline		Post-stimulation		Difference (%)	
	Left	Right	Left	Right	Left	Right
Cadence (steps/min)	103.38	112.73	102.40	100.19	-0.94	-11.12
Speed (m/s)	0.74	0.76	1.06	1.05	**43.24**	**38.16**
Support phase (% cycle)	66.49	66.63	61.36	61.27	-7.71	-8.04
Stride length (m)	0.84	0.88	1.28	1.28	**52.38**	**45.45**
Step length (m)	0.50	0.36	0.67	0.59	**34.00**	**63.88**
Step width (m)	0.10	0.10	0.08	0.07	-20.00	-30.00
GDI	82.35	86.66	87.85	83.71	4.25	-3.40

TABLE II

MUSCULAR STRENGTH OF BASELINE AND POST-STIMULATIONS CONDITION

	Baseline (KgF)		Post-stimulations (KgF)		Difference (%)	
	Left	Right	Left	Right	Left	Right
Hip Flexion	6.4	6.8	8.8	8.6	**35.5**	**26.5**
Hip Extension	3.6	5.2	5.2	4.5	**44.4**	-13.5
Hip Abduction	9.3	5.9	11.6	8.6	**24.7**	**45.8**
Knee Flexion	6.6	4.8	6.6	5.4	0.0	12.5
Knee Extension	8.8	10.7	10.4	9.3	**18.2**	-13.1
Ankle Dorsiflexion	4.5	4.8	6.8	8.4	**51.1**	**75.0**
Ankle Plantiflexion	8.4	7.7	10.9	10.9	**29.8**	**41.5**

III. RESULTS

The patient completed the proposed procedure with a satisfactory response and without any adverse effects. The results of the motion analysis laboratory in the baseline and the last post-stimulation period were compared to identify the effects of the experimental approach. Table I shows the spatiotemporal and GDI results obtained from the lower limb joint kinematics.

Regarding kinematic analysis, the patient exhibited increased gait speed, stride length, step length, and left GDI. However, three of the seven gait parameters presented a decrease: cadence, support phase, and passage width. As observed, all changes, except for the GDI, are associated with both limbs. However, the speed and stride length improvements are more positively associated with the left lower limb, which is the extremity contralateral to the stimulated hemisphere.

On the other hand, Figure 3 presents the PSD results for channels C3 and C4 in the diverse states. A bar graph describes the absolute power for the delta, theta, alpha, and beta bands. Generally, it is possible to observe a modulation of the signal power. Likewise, significant differences in beta for most of the signals and delta for the gait training conditions are obtained. These results are robust and show significant pre- and post-intervention differences that are not attributable to chance, even after adjusting for multiple comparisons.

In terms of the dynamometry results, Table II presents muscular strength for flexion and extension movements of the hip, knee, and ankle. Mainly, decreasing results, close to 13%, were observed only for right hip flexion and right knee flexion. At the same time, the other variables in the same limb revealed significant muscle strength increases exceeding 12% and even reaching a 75% marked improvement in the right ankle dorsiflexion. After stimulation, all flexion and extension movements showed remarkable increases in the left limb. Only left knee flexion did not show any change.

Finally, patient performance in the functional tests is presented in Table III for both TUG and 360° turning trials. In this case, the patient's performance improved for both tests after stimulation, mainly for the 360° turning test.

The data supporting the findings of this study are publicly available on Figshare, with DOI identifier: `10.6084/m9.figshare.25998565`.

TABLE III

FUNCTIONAL TESTS DURATION OF BASELINE AND POST-STIMULATIONS CONDITIONS.

	Baseline (s)		Post-stimulations (s)		Difference (%)	
TUG	8.32 ± 0.65 $\sigma = 0.53$		7.79 ± 0.62 $\sigma = 0.51$		6.37	
360° Turning Test	**Left**	**Right**	**Left**	**Right**	**Left**	**Right**
	3.25	3.04	2.48	2.01	23.69	33.88

IV. DISCUSSION

The findings of this case study indicated that the intervention with a-tDCS combined with visual-auditory cueing training effectively improved motor performance remarkably during the patient's gait. Compared with the baseline, the proposed strategy exhibited considerable changes in three spatiotemporal measurements for both limbs: speed, stride length, and step length. Gait fluidity and speed are affected by decreased cadence (steps per minute) and increased stride length (distance travelled per step). This way, walking faster at a lower cadence means that the stride length has increased more than the cadence has decreased. Experiments like the one conducted by Costa-Ribeiro et al. [16] only stated gait speed significant improvement guided with visual cues after tDCS stimulus. In that report, despite using higher current intensity (i.e., 2mA during 13 min), the differences might be related to a stimulation performed before and not during the gait training. In contrast, Lee et al. [14], who considered tDCS and visual cueing with simultaneous training, only reported increased cadence after 20 sessions with 2mA current intensity. As seen, effects depend on each study's methodology and cue modality. However, it has been shown that gait parameters are enhanced more consistently with auditory cues than with visual cues [25]–[27]. This is reflected

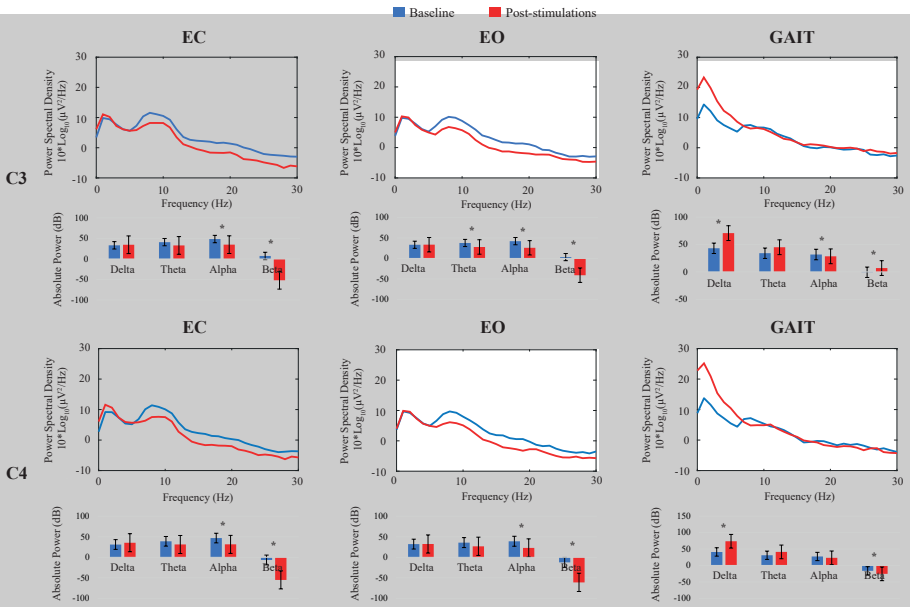

Fig. 3. PSD and Absolute Power Results for the delta, theta, alpha, and beta bands of channels C3 and C4 during the eyes-closed (EC), eyes-open (EO), and gait conditions. The asterisk in the bar graphs shows significant differences between the data sets ($p < 0.05$).

in this study, where there is a more significant number of improved gait variables when the strategy is combined than when evaluated individually with visual stimuli.

At the same time, after a-tDCS stimulation, the power spectral density indicated significant modulation of cerebral activity for all conditions. Based on previous works, increased beta activity in the motor cortex during rest and movement is directly correlated to PD motor impairment, rigidity, and bradykinesia [28], [29]. In the case of the present study, the sensorimotor area registered significant decreases for the beta band in both post-stimulus resting states. However, during the gait, the principal reduction of activity was mainly observed over the right hemisphere, that is, the stimulated half. These results at the cerebral level are related to those exposed in the kinematic analysis of gait, where most of the increases after stimulation favoured the limb contralateral to the stimulated side (i.e., speed, stride length, and GDI). The beta-band decrease positively confirms the strategy's feasibility for treating the disease with similar results to those found in complex procedures like deep brain stimulation [29], [30]. Indeed, the combination of interventions is the one that generates these benefits because although massive profits have been provided in preliminary studies with a-tDCS in M1, there are still contradictory outcomes concerning methodological variability among intervention strategies [31].

On the other hand, it is essential to point out an activity increase of the delta band confined in the left and right hemispheres during the motor task but absent at rest conditions (i.e., open eyes and closed eyes conditions). These changes in brain activity provide valuable information on how the intervention modulates attention, sensory response and movement-related brain activity, which could contribute to improved gait performance. According to Combrisson et al., higher delta amplitude in the motor cortex is observed during movement planning and execution [32]. Furthermore, evidence suggests the delta band as the basis of the kinematic control of the lower limbs through walk [33]. In this case, the significant increase in the delta band may be reasonably related to the improvement of continuous gait development, where PD patients often present slow movements [34]. Thus, the patient's executive function (i.e., planning, goal setting, fluency, and cognitive skill) undoubtedly benefited from the combined tDCS and visual-auditory guided gait training. Accordingly, the proposed technique amply proves to effectively initiate and maintain motor control during gait by facilitating attentional allocation.

Likewise, beneficial effects on strength performance after a-tDCS sessions were observed for most muscle groups involving the lower limb. Muscle weakness is a characteristic symptom of PD present on the more affected limb and has a significant effect on mobility [35]. In the particular case of the participant in this study, the muscle groups most affected were left hip extension and left ankle dorsiflexion, which, after stimulation, increased by 44.4% and 51.1%, respectively. The increase in contraction forces could explain the increased walk speed previously shown, where propulsion and body weight support could have been improved, allowing longer and more efficient steps. The sum of these benefits, together with the improvements in cognitive skills for motor control, impacted movement efficiency and synchronization with evident improvements in neuromuscular coordination. Besides, it reflects the enhanced ability of the central nervous system to drive the muscular structure [36].

Finally, in terms of functional activity, the gait therapy protocol seems to produce a favourable effect on the motor

performances of both limbs, which undoubtedly increased after the current stimulation. The reduced times detected in the TUG and 360° turning test results are related to an enhancement in functional mobility and speed and improved stability. These results relate not exclusively to the outcomes previously described but also to the patient and clinicians' perspective, who claimed to see a much more fluid, coordinated, and symmetrical gait with a decrease in the right upper limb fixed elbow position. Although the results were satisfactory, it is necessary to carry out this consistent study with a larger patient sample to validate its functionality.

V. CONCLUSIONS

This report investigated the effects of a unique case of study in a-tDCS stimulation combined with visual and auditory cueing during gait training. The study showed improvement in kinematic, muscular, and functional abilities. Moreover, the PD patient exhibited a significant decrease in beta-band related to a diminution in PD symptoms, and the marked increase in delta-band activity indicated the improvement of cognitive abilities for lower limb motor control. Thus, the controlled trial reported in this document seems to impact motor training positively, reflecting, according to the literature review, improvements over independent use of a-tDCS only or cues only. However, extensive clinical trials with a larger and controlled sample and the analysis of the signals' evolution during the sessions are still required to detect possible patterns associated with the enhancement that confirm the benefits of this strategy on neurorehabilitation. Furthermore, it is essential to include measurement parameters beyond the spatial-temporal ones to validate these types of techniques' complete spectrum of effects.

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