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The Effects of Transcranial Direct Current Stimulation on Performance and Recovery Sleep during Acute sleep Deprivation

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Abstract

Background: Previous studies have claimed that transcranial direct current stimulation (tDCS) on the left dorsolateral prefrontal cortex (dlPFC) improves cognition in patients, but few studies that have evaluated the effects of tDCS on cognition improvement during sleep deprivation. To determine whether tDCS (anodal on the left DLPFC and cathodal on the right DLPFC at 2mA current for 30 minutes) can be an effective fatigue countermeasure.

Methods: Seven participants and 8 participants underwent active or sham tDCS on the time participants' cognition declined, respectively. All participants completed the psychomotor vigilance task, the trail making test A and B, the digit cancellation test, the stroop color word test, the brief visuospatial memory test-revised and a procedural game every two hours during the sleep deprivation and after recovery sleep.

Results: The active tDCS had beneficial effects on attention, memory, executive function, processing speed, and the ability to inhibit cognitive interference, as well as improvements of subjective drowsiness and fatigue during sleep deprivation. The lasting effect of single tDCS on cognition during sleep deprivation can extend to more than 2 hours. All participants after tDCS gained no disturbed recovery sleep and recovered to baseline cognitive level after the recovery sleep.

Conclusions: The study indicated that tDCS is an effective fatigue countermeasure during sleep deprivation, and doesn't disturb the recovery sleep and performance postrecovery sleep.

Background

Sleep deprivation from extended duty hours is a common complaint in many occupations, especially in military action. These extended periods of wakefulness can lead to serious decrements in mood and mental performances, and increase the risk of accidents. Sleep deprivation can result in feelings of fatigue, loss of vigor, sleepiness, confusion, increased reaction time, decreased accuracy and decreased attention. Williamson et al.[1] found that after 17 h of continued wakefulness, participants had performance equivalent to individuals with a blood alcohol concentration of 0.05%, which is considered illegal to drive a car in most countries. Unfortunately, many occupations require shifts lasting even longer than this; therefore, it is necessary to investigate possible fatigue countermeasures.

Transcranial direct current stimulation (tDCS) is a method to noninvasively stimulate the brain. In this procedure, weak and direct current (1–2 mA) is applied through electrodes that are placed on the scalp to induce alterations in cortical activity and excitability. Anodal stimulation produces a net increase in neuron excitability in the area of stimulation while cathodal stimulation causes a net decrease in excitability. The brain region of interest varies by task; if a researcher is interested in improving fine motor control they will attach electrodes above the motor cortex[2]; if they are interested in improving working memory, sustained attention[3] and mood regulation[4], they will attach electrodes above the dorsolateral prefrontal cortex (DLPFC). Based on previous research, tDCS of the DLPFC can modulate attention[5], arousal, decrease excessive daytime sleepiness, and counter fatigue[6–8]. We hypothesize that tDCS can

be an effective fatigue countermeasure to improve attention, vigilance, memory, processing speeding, and executive function during sleep deprivation. The aims of the study were to determine whether tDCS (anodal on the left DLPFC and cathodal on right DLPFC) can be an effective fatigue countermeasure to improve cognition during sleep deprivation; to determine whether tDCS has an after effect on subsequence recovery sleep and cognition postrecovery sleep.

Methods And Materials

Subjects

Participants were recruited by means of advertisements. Participants completed Pittsburgh Sleep Quality Index, Zung Self-Rating Depression Scale, Zung Self-Rating Anxiety Scale, Insomnia Severity Index, and Stop-Bang Sleep Apnea Questionnaire to exclude the obvious sleep disorders and mood disorders about one week before sleep deprivation. To exclude the short sleepers, long sleepers and chronic insufficient sleep syndrome,participants were required to complete sleep log and to wear an actigraph to document at least 6 hours sleep per night. The trial was approved by the Tangdu Hospital ethics committee. All the participants provided written informed consent and were compensated for their time but were disqualified if they met any of the exclusion criteria or gave up by any reasons of themselves.

Procedures

All participants were required to wake up at 6:00 am and arrive to the lab before 7:00 am on the day of sleep deprivation. Participants underwent blood pressure, pulse rate, respiratory rate, and temperature test every hour from 8:00 am. Participants completed the Psychomotor vigilance task (PVT)[9], the Trail making test A and B (TMT-A, TMT-B)[10], the digit Cancellation test (DCT)[11], the Stroop color and word test A and B (SCWT-A and SCWT-B)[12], the Brief visuospatial memory test-revised (BVMT-R)[13], the Fatigue visual analog scale, the Stanford Sleepiness Scale (SSS), and the Karolinska Sleepiness Scale (KSS) every two hours. They were required to play electrical games to keep their concentration on screen during the gaps between every two hours tests. Coffee, cigarettes, and alcohol were forbidden during the study.

The declined reaction time of PVT at least 30 ms from the previous ones or 5 lapses were used as the primary parameters to determine the time to deliver tDCS. TDCS (2 mA, 30 min) was delivered by a direct current stimulator (neuroConn, Germany), connected to two electrodes, one on the scalp over the left DLPFC (F3 in 10–20 EEG system, anode) and the other above the right DLPFC (F4 in 10–20 EEG system, cathode). Stimulating electrodes were thick (0.3 cm) square (35 cm^2) pieces of saline-soaked synthetic sponge. For safety, multistage monitoring of the output current and electrode/tissue impedance was included. The device automatically shuts off if the impedance becomes greater than 50 kΩ to prevent electric shocks or burns. A constant current of 2 mA over each stimulation electrode for 30 min was applied in a 15 s fade-in/fade-out design to decrease potential skin sensations. For sham stimulation, the current turned off automatically after 15 s fade-in/fade-out. Researchers companied with the participants to remind them to keep alert to do the tests, and decided the time to deliver tDCS. All participants and

researchers were blind to the electrical tests. Researchers input the random numbers to the tDCS machine according to subsequence of participants needed to be delivered tDCS. As the active tDCS and sham tDCS may cause different electrical senses, the researchers were factually not blind after the tDCS performed.

After tDCS treatment, participants continued to perform all the same tests procedures as before until completion of the 10:00 am session tests. According to the PVT, if participants could not recovery, they were arranged to sleep with the monitoring of polysomnograph (PSG) to the time they wanted to get up, or they continued to do the tests until the PVT declined sharply. After participants got up, they performed the last session of tests.

Sleep Examination

PSG (Philips) were performed and analyzed according to The AASM Manual for the Scoring of Sleep and Associated Events 2.5 version (AASM 2.5).

Cognitive tests

Personal computer (PC) -PVT 2.0[9] which was documented to comparable to PVT-192 was used to assess the effects of sleep deprivation on human neurobehavioral performance.

TMT A and B [10] provide information on visual search, scanning, processing speed, mental flexibility, and executive functions. We used the computer version of TMT of which the location of numbers and letters are random each time. TMT-A requires an individual to draw lines sequentially connecting 25 encircled numbers distributed on the screen by mouse. Task requirements are similar for TMT-B except the person must alternate between numbers and letters (e.g., 1, A, 2, B, 3, C, etc.). The score on each part represents the amount of time required to complete the task.

DCT is used to assess attention deficits [11, 14]. DCT was once a paper and pencil test. We programmed it to computer version according to 1992 version[11], that is the 1-digit target matrix acted as a buffer-trial, and test-scores turned out from the 2- and 3-digits targets matrices. The PC-DCT, devised for this study on the basis of the discriminant powers of each matrix among different time of sleep deprivation, provided three variations of the procedures: 1) the mouse is instead of pencil, the screen instead of paper, 2) digits have to be crossed out are random in each tests, 3) digits have to be crossed out within different time-limits, 10 s/matrix, 20 s/matrix, 30 s/matrix, and 45 s/matrix to assess attention, vigilance, memory, processing speeding, and executive function. As 10 s/matrix is too short and 45 s/matrix is too long to evaluate the sensitivity of performance, we just analyzed the 20 s/matrix, 30 s/matrix scores.

SCWT is widely used to multiple cognitive functions, such as the ability to inhibit cognitive interference, attention, processing speed, cognitive flexibility, and working memory[12]. E-Prime 2.0 software was used to perform SCWT. SCWT-A was to choose the color of the ink of the word, while SCWT-B test was to choose the color of reading the word. Each test has 72 random color-word items, in which 36 are color-word in incongruous condition, 36 in congruous condition. Every item color-word shows on the screen for

2000 ms, the 250 ms black screen duration to next item of color-word. When red is chosen, participants are required to click the keyboard D as fast and correctly as they can. Similarly, green click F, yellow click J, blue click K.

BVMT-R is a measure of visual learning and memory[13]. Simply speaking, a visual display of six simple figures randomly arranged in a 2 × 3 matrix on paper is shown to participants for three consecutive 10-second trials. After each trial, participants are to draw as many designs as accurately as they can and in the correct location. The scores should consider the accuracy of both the shape and location.

Analysis

Because treatment conditions started at different time session, the session occurring before the treatment was the last time point at which all participants were treated the same. The last session before treatment was treated as baseline. It was compared the change from the last session before treatment to the first session after treatment to help determine an transient effect of stimulation, and the change from the last session before treatment to the second session after treatment to help determine a 'after term' effect of stimulation. It was compared the change from the session at 10:00 am on the first day to the session after recovery sleep to determine recovery effect. Difference between active and sham groups were assessed at baseline and changes using student t-test for normally distributed continuous variables, and Mann –Whitney U-tests for non-normal continuous variables. These analyses were performed by SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). The level of significance was selected at $p < 0.05$.

Results

The study was one part of study which studied the effect of tDCS on cognition, recruited 57 health male, average age 23.61 ± 1.62 years (range 21–27 years). Twenty participants were underwent this part of study, in which 8 participants were delivered with 2 mA, 30 min tDCS on F3 anode F4 cathode (active group), 12 participants were in the sham tDCS group (sham group). Seven participants in active group and 8 in the ham group were analyzed (Fig. 1). All participants had PVT mean reaction time declined within 18 to 28 hours extended wakefulness. There were no statistically difference in the extended wakefulness time to performing tDCS ($p = 0.773$) between active group (21.4 h ± 1.57 h) and sham group (20.75h ± 3.20 h). The t-tests exposed no difference of minor lapses (500 ms-1000 ms) of PVT ($p = 0.826$), major lapses (> = 1000 ms) of PVT ($p = 0.318$), anticipations of PVT ($p = 0.356$), mean reaction time of PVT ($p = 0.324$), TMT A time ($p = 0.354$), TMT B time ($p = 0.065$), mean DCT-scores achieved for 2-digits targets matrix within the time limit of 20 s ($p = 0.225$) and 30 s ($p = 0.543$), mean DCT-scores achieved for 3-digits targets matrix within the time limit of 20 s ($p = 0.789$) and 30 s ($p = 0.385$), BVMT scores ($p = 0.524$), the fatigue scores ($p = 0.070$), and the SSS scores ($p = 0.056$) between the active group and sham group in the session before the tDCS treatment. The t-tests exposed a significant difference of mean reaction time of SCWT-A (sham 840.43 ± 168.81 ms, F3 + F4- 1072.04 ± 175.52 ms, $p = 0.028$), mean reaction time of SCWT-B (sham 825.65 ± 207.98 ms, F3 + F4- 1012.36 ± 75.37 ms, $p = 0.042$), KSS (sham 4.63 ± 1.69, F3 + F4- 6.57 ± 1.72, $p = 0.046$) between the active group and sham group in the session before the tDCS treatment. (Table 1 and Fig. 2–6)

Table 1
Performance of the last session before tDCS

	Sham			Active			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	9.88	±	4.94	9.29	±	5.25	0.826
PVT Major Lapses (n)	0.88	±	1.36	2.00	±	2.71	0.318
PVT Anticipations (n)	0.00	±	0.00	0.14	±	0.38	0.356
PVT Mean RT (ms)	361.08	±	28.99	397.52	±	96.20	0.324
TMT-A time (s)	72.00	±	26.22	84.29	±	22.76	0.354
TMT-B time(s)	86.88	±	17.18	116.43	±	33.45	0.065
DCT scores 2–20 s	14.32	±	3.60	11.95	±	3.58	0.225
DCT scores 3–20 s	16.36	±	2.37	14.27	±	8.36	0.543
DCT scores 2–30 s	18.04	±	1.29	17.81	±	1.98	0.789
DCT scores 3–30 s	22.33	±	4.12	19.89	±	6.28	0.385
SCWT-A Mean RT (ms)	840.43	±	168.81	1072.04	±	175.52	0.028*
SCWT-B Mean RT (ms)	825.65	±	207.98	1012.36	±	75.37	0.042*
BVMT scores	29.43	±	5.53	27.29	±	6.63	0.524
Fatigue	4.25	±	2.05	6.43	±	2.23	0.070
KSS	4.63	±	1.69	6.57	±	1.72	0.046*
SSS	3.63	±	1.41	4.86	±	0.69	0.056

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, tDCS: transcranial direct current stimulation, TMT-A: Trail making test A, TMT-B: Trail making testB, SSS: Stanford Sleepiness Scale

Transient Effect of tDCS

The t-tests exposed a significantly better outcome of major lapses (≥ 1000 ms) of PVT (p = 0.003), mean reaction time of PVT (p = 0.019), mean DCT-scores achieved for 2-digits targets matrix within the time limit of 20 s (p = 0.025), mean DCT-scores achieved for 3-digits targets matrix within the time limit of 30 s

(p = 0.008), mean reaction time of SCWT-A (p = 0.002), the fatigue scores (p = 0.032), the KSS scores (p = 0.011) and the SSS scores (p = 0.014), between the active group and sham group in the change from the last session before the treatment to the first session after treatment. Compared with sham group, the change from the last session before the tDCS treatment to the first session after the treatment in active group were better tendency, but there were no statistically significant difference in minor lapses (500 ms-1000 ms) of PVT (p = 0.170), anticipations of PVT (p = 0.356), TMT A time (p = 0.320), TMT B time (p = 0.257), mean DCT-scores achieved for 2-digits targets matrix within the time limit of 20 s (p = 0.025) and 30 s(p = 0.355), mean reaction time of SCWT-B (p = 0.463) and BVMT scores (p = 0.804). (Table 2 and Fig. 2–6)

Table 2
Performance change from last session before tDCS to the first session after tDCS

	Sham			Active			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	0.63	±	7.27	-3.43	±	2.23	0.170
PVT Major Lapses (n)	0.38	±	0.52	-1.14	±	1.07	0.003*
PVT Anticipations (n)	0.25	±	0.46	0.43	±	0.79	0.595
PVT Mean RT (ms)	8.26	±	47.72	-58.63	±	48.51	0.019*
TMT-A time (s)	-1.25	±	19.91	-15.86	±	33.95	0.320
TMT-B time(s)	9.25	±	20.23	-9.86	±	40.29	0.257
DCT scores 2–20 s	-0.97	±	3.17	4.38	±	4.96	0.025*
DCT scores 3–20 s	0.38	±	2.97	3.95	±	9.13	0.355
DCT scores 2–30 s	-0.42	±	1.99	-1.41	±	7.09	0.708
DCT scores 3–30 s	-0.70	±	2.76	5.27	±	4.48	0.008*
SCWT-A Mean RT (ms)	61.99	±	88.32	-129.63	±	94.91	0.002*
SCWT-B Mean RT (ms)	26.04	±	111.97	-41.00	±	220.95	0.463
BVMT scores	0.00	±	4.04	0.71	±	6.26	0.804
Fatigue	0.38	±	1.51	-1.29	±	1.11	0.032*
KSS	0.50	±	0.53	-1.14	±	1.21	0.011*
SSS	0.25	±	0.71	-1.00	±	1.00	0.014*

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test

scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, RT: reaction time, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, tDCS: transcranial direct current stimulation, TMT-A: Trail making test A, TMT-B: Trail making test B, SSS: Stanford Sleepiness Scale

After-effects of tDCS

There were significant difference of the change from the last session before the treatment to the second session after the tDCS treatment in TMT B time ($p = 0.013$), fatigue ($p = 0.012$), KSS ($p = 0.031$) and SSS ($p = 0.006$) between the active group and sham group. Compared with sham group, the change from the last session before the tDCS treatment to the second session after the treatment in active group had the tendency to be better, but no statistically significant difference in minor lapses (500 ms-1000 ms) of PVT ($p = 0.690$),major lapses ($\geq$ 1000 ms) of PVT ($p = 0.555$), anticipations of PVT ($p = 0.098$), mean reaction time of PVT ($p = 0.340$), TMT A time ($p = 0.395$), mean DCT-scores achieved for 2-digits targets matrix within the time limit of 20 s ($p = 0.346$) and 30 s ($p = 0.349$), 3-digits targets matrix within the time limit of 20 s ($p = 0.804$) and 30 s ($p = 0.661$), mean reaction time of SCWT-A ($p = 0.086$), and mean reaction time of SCWT-B ($p = 0.080$), and BVMT scores ($p = 0.321$). (Table 3 and Fig. 2–6)

Table 3
Performance change from last time before tDCS to 2 hours later after tDCS

	Sham			Active			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	6.63	±	8.37	4.43	±	12.35	0.690
PVT Major Lapses (n)	3.00	±	4.72	1.29	±	6.24	0.555
PVT Anticipations (n)	0.25	±	0.46	-0.14	±	0.38	0.098
PVT Mean RT (ms)	119.58	±	150.26	33.35	±	186.99	0.340
TMT-A time (s)	5.25	±	22.80	-4.43	±	19.29	0.395
TMT-B time(s)	29.50	±	19.82	-19.86	±	43.52	0.013*
DCT scores 2–20 s	-0.99	±	3.91	1.03	±	4.09	0.346
DCT scores 3–20 s	-0.66	±	3.23	-1.61	±	10.07	0.804
DCT scores 2–30 s	0.21	±	1.47	-2.94	±	3.54	0.349
DCT scores 3–30 s	-0.46	±	4.88	-1.60	±	5.04	0.661
SCWT-A Mean RT (ms)	37.51	±	122.74	-119.27	±	192.13	0.086
SCWT-B Mean RT (ms)	29.71	±	165.23	-104.01	±	90.56	0.080
BVMT scores	-3.29	±	5.77	0.60	±	7.16	0.321
Fatigue	1.75	±	1.58	-0.43	±	1.27	0.012*
KSS	1.63	±	1.41	-0.71	±	2.29	0.031*
SSS	1.25	±	0.71	-0.29	±	1.11	0.006*

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, RT: reaction time, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, tDCS: transcranial direct current stimulation, TMT-A: Trail making test A, TMT-B: Trail making test B, SSS: Stanford Sleepiness Scale

Postrecovery sleep effects of tDCS

There were no difference found in minor lapses (500 ms-1000 ms) of PVT (p = 0.393), major lapses (≥ 1000 ms) of PVT (p = 0.926), anticipations of PVT (p = 0.926), mean reaction time of PVT (p = 0.680), TMT A time (p = 0.878), TMT B time (p = 0.335), mean DCT-scores achieved for 2-digits targets matrix within the time limit of 20 s (p = 0.634) and 30 s (p = 0.795), mean DCT-scores achieved for 3-digits targets matrix within the time limit of 30 s (p = 0.356), BVMT scores (p = 0.603), the fatigue scores (p = 0.620), KSS(p = 0.328) and the SSS scores (p = 0.508) between the active group and sham group in the session after recovery sleep. Only mean DCT-scores achieved for 3-digits targets matrix within the time limit of 20 s (p = 0.017) was found significantly better in the active group in the session after recovery sleep (Table 4). There were no difference found for all tests between the change of tests post-sleep after sleep deprivation from 10 o'clock tests between the active group and sham group (Table 5). Compared with 10 o'clock session, all tests after recovery of sleep deprivation had better trend, in which PVT anticipations (p = 0.005), mean DCT-scores achieved for 3-digits targets matrix within the time limit of 20 s (p = 0.005), mean reaction time of SCWT-A (p = 0.026), SCWT-B (p = 0.009) and fatigue were significantly different. (Table 6,and Fig. 2–6)

Table 4

Performance postrecovery sleep

	Sham			Active			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	1.38	±	2.20	2.71	±	3.59	0.393
PVT Major Lapses (n)	0.13	±	0.35	0.14	±	0.38	0.926
PVT Anticipations (n)	0.13	±	0.35	0.14	±	0.38	0.926
PVT Mean RT (ms)	275.88	±	28.16	284.77	±	51.80	0.680
TMT-A time (s)	55.25	±	8.76	56.29	±	16.21	0.878
TMT-B time(s)	76.88	±	24.35	91.57	±	32.45	0.335
DCT scores 2–20 s	16.57	±	2.29	15.87	±	3.22	0.634
DCT scores 3–20 s	15.83	±	3.23	21.46	±	4.68	0.017*
DCT scores 2–30 s	18.88	±	1.61	19.11	±	1.85	0.795
DCT scores 3–30 s	25.17	±	2.48	26.46	±	2.75	0.356
SCWT-A Mean RT (ms)	741.03	±	81.73	783.24	±	109.25	0.408
SCWT-B Mean RT (ms)	740.42	±	111.34	719.10	±	113.36	0.720
BVMT scores	30.25	±	3.73	31.14	±	2.54	0.603
Fatigue	1.00	±	1.53	1.43	±	1.62	0.620
KSS	1.43	±	1.27	2.14	±	1.35	0.328
SSS	1.43	±	0.79	1.86	±	1.46	0.508

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, RT: reaction time, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, TMT-A: Trail making test A, TMT-B: Trail making test B, SSS: Stanford Sleepiness Scale

Table 5

Performance change from 10 o'clock session on the first day to the session after recovery sleep

	Sham			Active			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	-1.25	±	2.49	0.43	±	4.76	0.398
PVT Major Lapses (n)	0.00	±	0.53	-0.29	±	0.95	0.478
PVT Anticipations (n)	0.13	±	0.35	0.00	±	0.00	0.351
PVT Mean RT (ms)	-16.98	±	32.85	-10.06	±	49.70	0.753
TMT-A time (s)	-19.25	±	26.51	-3.00	±	21.06	0.241
TMT-B time(s)	-17.13	±	26.69	1.67	±	23.08	0.193
DCT scores 2–20 s	2.86	±	4.74	1.20	±	3.31	0.480
DCT scores 3–20 s	1.75	±	3.76	2.25	±	4.34	0.821
DCT scores 2–30 s	1.12	±	2.50	1.44	±	3.27	0.838
DCT scores 3–30 s	2.22	±	2.70	3.42	±	4.95	0.572
SCWT-A Mean RT (ms)	-138.20	±	142.79	-64.04	±	125.62	0.308
SCWT-B Mean RT (ms)	-41.77	±	114.95	-42.87	±	86.43	0.984
BVMT scores	3.00	±	5.66	3.00	±	4.32	1.000
Fatigue	0.25	±	1.39	0.71	±	1.50	0.544
KSS	-0.50	±	1.31	0.43	±	1.62	0.241
SSS	-0.25	±	1.04	0.71	±	1.50	0.166

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, RT: reaction time, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, TMT-A: Trail making test A, TMT-B: Trail making test B, SSS: Stanford Sleepiness Scale

Table 6
Performance between 10 o'clock on the first day and post recovery sleep

	10:00 session			Postrecovery sleep session			p
	Mean	±	SD	Mean	±	SD	
PVT Minor Lapses (n)	2.47	±	2.03	2.00	±	2.90	0.764
PVT Major Lapses (n)	0.27	±	0.59	0.13	±	0.35	0.515
PVT Anticipations (n)	0.07	±	0.26	0.13	±	0.35	0.005*
PVT Mean RT (ms)	293.78	±	23.78	280.03	±	39.59	0.374
TMT-A time (s)	68.93	±	24.55	55.73	±	12.30	0.445
TMT-B time(s)	93.57	±	20.95	83.73	±	28.38	0.068
DCT scores 2–20 s	14.34	±	2.62	16.25	±	2.68	0.389
DCT scores 3–20 s	16.60	±	5.09	18.46	±	4.80	0.005*
DCT scores 2–30 s	17.67	±	2.00	18.99	±	1.67	0.790
DCT scores 3–30 s	23.38	±	4.04	25.77	±	2.60	0.129
SCWT-A Mean RT (ms)	864.32	±	165.38	760.73	±	94.50	0.026*
SCWT-B Mean RT (ms)	772.76	±	125.07	730.47	±	108.75	0.009*
BVMT scores	28.14	±	4.67	30.67	±	3.15	0.447
Fatigue	0.67	±	0.72	1.21	±	1.53	0.034*
KSS	1.73	±	0.80	1.79	±	1.31	0.282
SSS	1.33	±	0.49	1.64	±	1.15	0.836

BVMT-R: the Brief visuospatial memory test-revised, DCT scores 2-20s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s, DCT scores 3-20s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s, DCT scores 2-30s: Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s, DCT scores 3-30s: Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s, Fatigue: Fatigue visual analog scale, KSS: Karolinska Sleepiness Scale, PVT: Psychomotor vigilance task, RT: reaction time, SCWT-A: Stroop color and word test A, SCWT-B: Stroop color and word test B, TMT-A: Trail making test A, TMT-B: Trail making test B, SSS: Stanford Sleepiness Scale

Sleep effect of tDCS

There were no significant difference of recovery sleep architecture such as sleep latency (SL) (p = 0.596), N2 latency (p = 0.757), N3 latency (p = 0.343), rapid eye movement sleep (REM) latency (p = 0.126), time

in bed (TIB) (p = 0.849), total sleep time (TST) (p = 0.849), N1 sleep percent (p = 0.999), N2 sleep percent (p = 0.565), N3 sleep percent (p = 0.240), REM sleep percent (p = 0.188), arousal index (p = 0.591), wake after sleep onset (WASO) (p = 0.822) and sleep efficiency (p = 0.889) between the active group and sham group. All participants had shorted sleep latency (sham group vs active group: 1.50 ± 1.71 min, vs 1.89 ± 0.81 min), N2 latency (sham group vs active group: 2.56 ± 2.16 min, 2.93 ± 2.32 min), N3 latency (sham group vs active group: 16.56 ± 20.23 min, 8.79 ± 5.15 min), REM latency (sham group vs active group: 58.88 ± 27.60 min, 81.67 ± 22.77 min), and increased N3 percent (sham group vs active group: 37.86 ± 9.59 min, 45.89 ± 15.37 min). (Table 7)

Table 7
The effect of tDCS on the recovery sleep

	Sham			F3 + F4-			p
	(Mean	±	SD)	(Mean	±	SD)	
Sleep Latency (min)	1.50	±	1.71	1.89	±	0.81	0.596
N2 Latency (min)	2.56	±	2.16	2.93	±	2.32	0.757
N3 Latency (min)	16.56	±	20.23	8.79	±	5.15	0.343
REM Latency (min)	58.88	±	27.60	81.67	±	22.77	0.126
TIB (min)	277.63	±	218.71	259.01	±	134.77	0.849
TST (min)	265.88	±	211.25	247.86	±	132.92	0.849
REM time (min)	48.38	±	48.98	31.79	±	25.18	0.435
N1 Time (min)	12.06	±	10.71	10.43	±	6.54	0.732
N2 Time (min)	119.25	±	122.79	107.93	±	80.27	0.839
N3 Time (min)	86.19	±	35.88	97.71	±	33.37	0.533
R (%TST)	15.66	±	6.78	10.56	±	7.46	0.188
N1 (%TST)	4.69	±	1.83	4.69	±	2.10	0.999
N2 (%TST)	41.78	±	7.41	38.87	±	11.47	0.565
N3 (%TST)	37.86	±	9.59	45.89	±	15.37	0.240
Arousal index (n/h)	6.70	±	2.70	5.76	±	3.90	0.591
WASO (min)	10.25	±	9.43	9.27	±	6.53	0.822
Sleep Efficiency (%)	95.28	±	2.63	95.07	±	2.91	0.889

TIB: time in bed, TST: total sleep time, REM: rapid eye movement, WASO: wake after sleep onset

Discussion

This study examined the effects of anodal tDCS applied to the left DLPFC and cathode tDCS to the right DLPFC 2 mA 30 min on attention, the ability to inhibit cognitive interference, memory, processing speeding, and executive function in an induced state of fatigue caused by sleep deprivation. Our results suggested that tDCS not only had a better transient effect on attention, the ability to inhibit cognitive interference, mental flexibility, processing speed, and working memory than sham group, but it also had after-effects on visual search, scanning, processing speed, mental flexibility and executive functions that remain at least 2 h when compared to sham group. The duration of lasting after-effects is dependent on stimulation duration and number of treatments[15]. Our data suggest that single 30 min of stimulation produces behavioral after effects lasting at least 2 h. Previous study reported 30 min of stimulation produces behavioral after effects lasting at least 6h[7]. The improvement in cognitive performance with tDCS was accompanied by lower subjective ratings for fatigue and drowsiness. Thus, not only did the participants with tDCS (anodal on left DLPFC and cathode on the right DLPFC 2 mA 30 min) perform better, but they also felt less tired and sleepy than their counterparts given sham tDCS interventions. This was accordance with previous study [7]. The differences of study include the location of tDCS electrodes, the time of tDCS treatment, and the methods to evaluate the cognition. McinTire et al. (2014) put the anodal tDCS electrode to the left DLPFC and cathode on the right bicep which means the place of cortex excitability and the direction of electric current are different from our study which may cause different changes of cognition domain by different evaluation methods. MciTire et al.(2014) applied the tDCS at 4:00 am which meant some participants were already in a state of notable fatigue with cognition declined,while other individuals were still in good condition which could increase the time of tDCS after effect if sample size is too small.

Besides, compared with the tests of 10 o’clock session, at which cognition was thought as the best of the day, the postrecovery sleep performance recovered to or showed better than presleep deprivation levels in both tDCS and sham groups, which was similar to administration of caffeine, dextroamphetamine, and modafinil[16]. This is the first study compared the postrecovery sleep effect on cognitive performance of tDCS improvement during extended wakefulness,which indicated that recovery sleep is still the best fatigue countermeasure.

The study evaluated the effects with tDCS on recovery sleep after sleep deprivation. Our results showed that tDCS with anodal on the left DLPFC and cathode on the right DLPFC 2 mA 30 min didn’t increase sleep latency and arousal after sleep deprivation. Participants in active tDCS group as well as in sham group had shortened sleep, N2, N3 and REM latency, increased N3 percentage, similar TST, arousal index, wake after sleep onset and sleep efficiency. The change of sleep architecture was contributed to acute sleep deprivation, but not tDCS. Neither did tDCS disturb postrecovery sleep. This is the first study compared the effect of tDCS on cognitive performance and recovery sleep during extended wakefulness. Previous study showed that caffeine and modafinil are wakefulness-promoting stimulants that have been approved by many countries as fatigue countermeasure drugs[17]. However, previous studies also documented that caffeine[18] could disturb daytime recovery sleep after sleep deprivation such that there

was increased WASO, SL, duration and number of awakenings, reduced SWS, TST, and SE. Modafinil after total sleep deprivation diminished slow wave sleep as well as rapid eye movement sleep and prevented the sleep rebound[19]. The study documented that tDCS with anodal on left DLPFC and cathode on the right DLPFC 2 mA 30 min improved the cognition during sleep deprivation and didn't disturb recovery sleep which is the best method to recovery performance after sleep deprivation; therefore it would not worse the postrecovery sleep performance.

Several limitations should be considered. Firstly, small sample sizes of the study would affect the reliability of the results because it leads to a higher variability, which may lead to bias. In future study, we need more samples to verify the results. Secondly, participants couldn't treat the tests as seriously as real work situation. Even with the surveillance of study personnel, there were obviously abnormal tests which caused them to been excluded to analyze and decreased the sample sizes. Thirdly, only male were included in the study, who were not sensitive to the tDCS intervention[20]. Fourthly, the study used the decrease of PVT mean reaction time as the standardization to delivery tDCS, which caused some sample didn't had enough time to observe the after effect of tDCS.

Conclusions

Our findings suggested that anode tDCS applied to the left DLPC and cathode tDCS to the right DLPC 2 mA for 30 min had beneficial effects on attention, the ability to inhibit cognitive interference, memory, processing speeding, and executive function during the beginning periods of sleep-deprivation induced fatigue. Additionally, the tDCS-induced performance benefits were coupled with improvements in subjective drowsiness and fatigue. The lasting effect of single tDCS on cognition during sleep deprivation can extend to more than 2 h. This is the first data to suggest that tDCS may have no disadvantages on recovery sleep after sleep deprivation and cognition can soon get recovery to baseline level after the recovery sleep. Given these initial promising findings, we conclude that tDCS should be further examined as an intervention for fatigue and sleep.

Abbreviations

BVMT-R
Brief visuospatial memory test-revised
DCT scores 2-20s
Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 20 s
DCT scores 3-20s
Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 20 s
DCT scores 2-30s
Digit cancellation test scores achieved for 2-digits targets matrix within the time limit of 30 s
DCT scores 3-30s
Digit cancellation test scores achieved for 3-digits targets matrix within the time limit of 30 s
DLPFC
Dorsolateral prefrontal cortex

Fatigue
Fatigue visual analog scale
KSS
Karolinska Sleepiness Scale
PC
Personal computer
PSG
Polysomnography
PVT
Psychomotor vigilance task
SCWT-A
Stroop color and word test A
SCWT-B
Stroop color and word test B
REM
Rapid eye movement
SL
Sleep latency
SSS
Stanford Sleepiness Scale
tDCS
Transcranial direct current stimulation
TIB
Time in bed
TMT-A
Trail making test A
TMT-B
Trail making test B
TST
Total sleep time
WASO
Wake after sleep onset

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by Independent Ethics Committee of Institution for National Drug Clinical Trial, Tangdu Hospital, Fourth Military Medical

University (the reference number 2018-01-1). Informed consent was obtained from all individual participants included in this study.

Consent to publish

Not applicable.

Availability of data and materials

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

Competing interests

None of the authors have potential conflicts of interest to be disclosed

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Authors' Contributions

JXC: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing

XZ: Data curation; Investigation; Methodology; Resources

JQ: Data curation; Investigation; Methodology; Software; Validation; Writing - review & editing

YJ: Data curation; Investigation; Formal analysis

JR: Data curation; Investigation; Validation; Visualization; Writing - review & editing

SS: Data curation; Investigation; Validation; Writing - review & editing

RW: Software

CS: Conceptualization; Funding acquisition; Project administration; Resources; Supervision; Writing - original draft; Writing - review & editing

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Figures

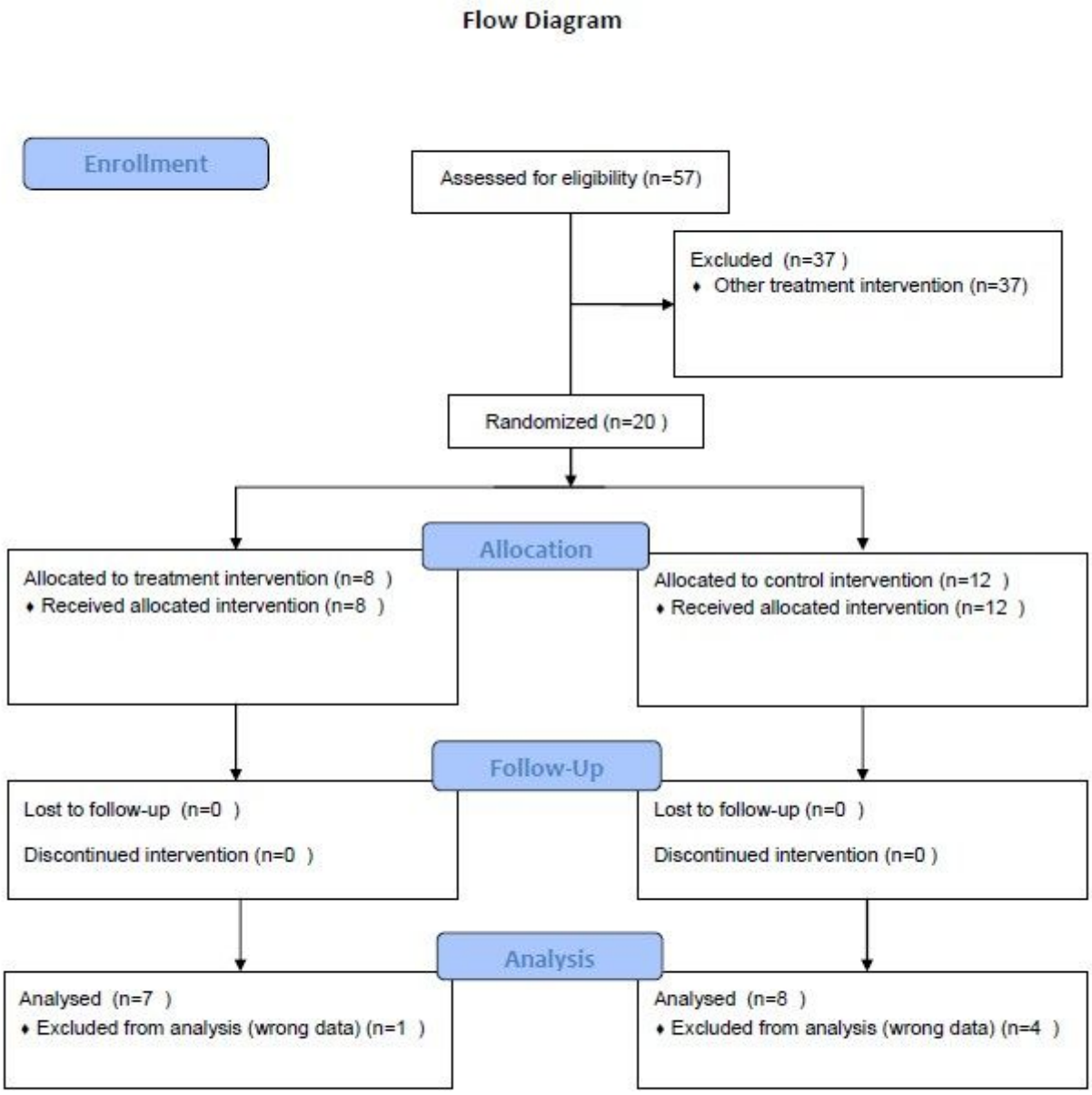

Figure 1

Flow Diagram

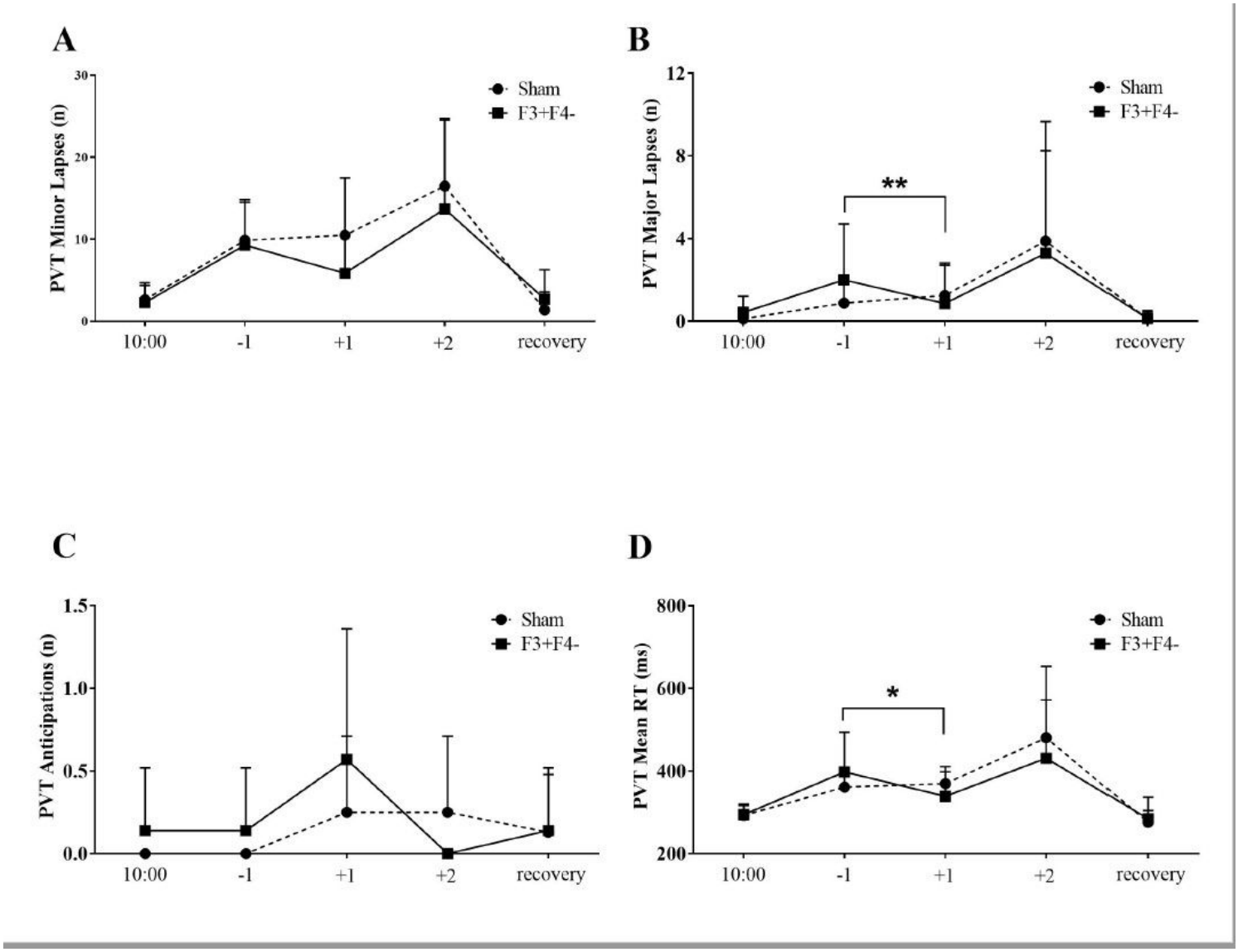

Figure 2

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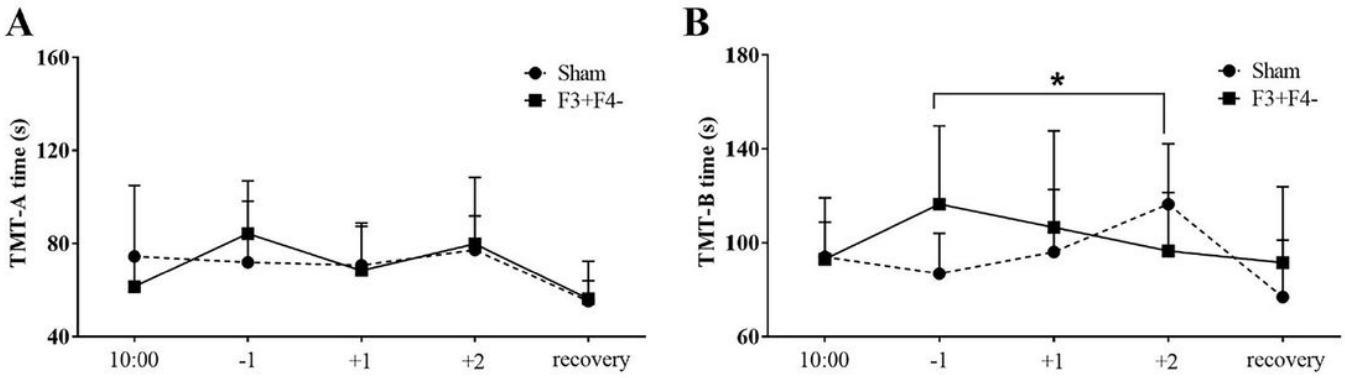

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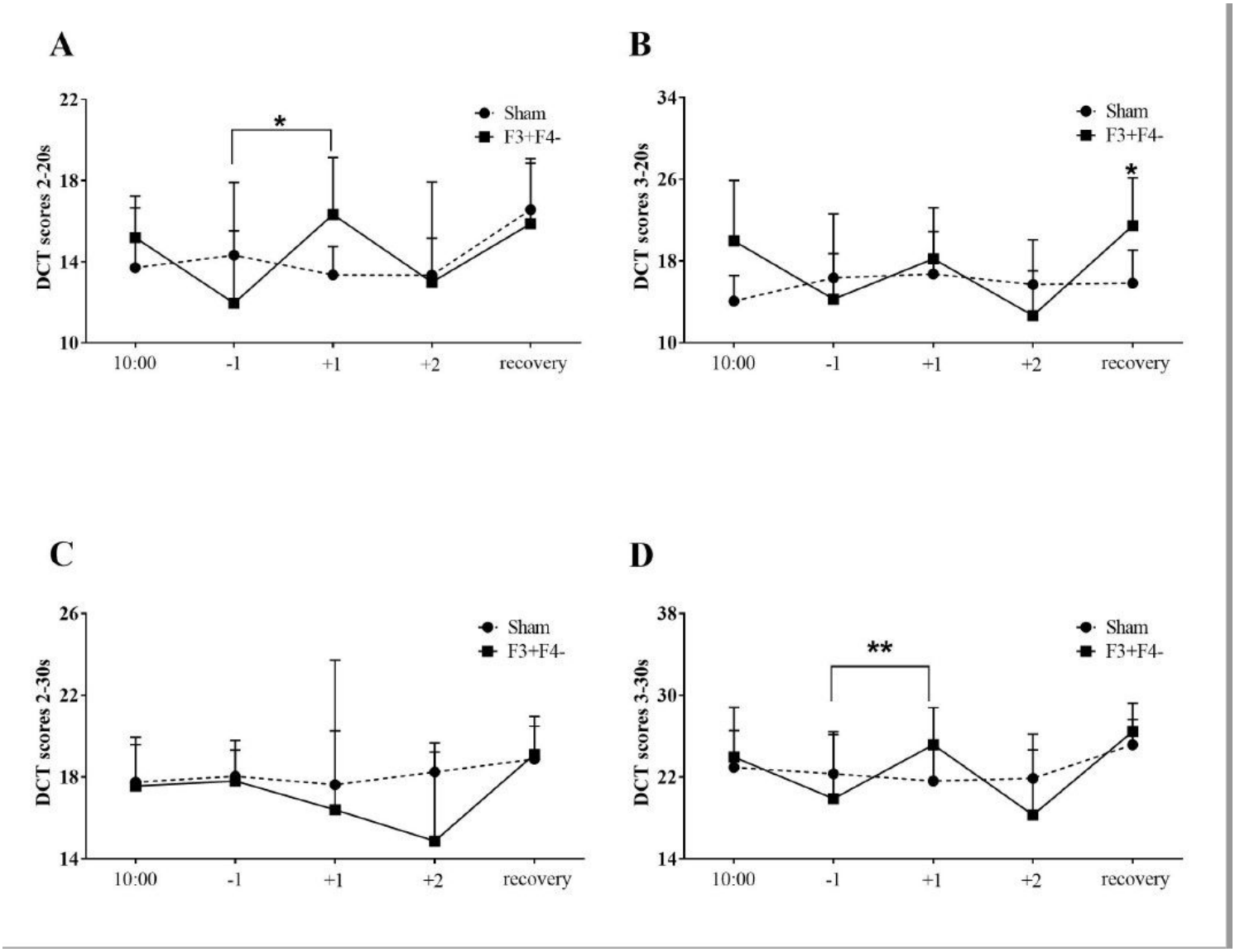

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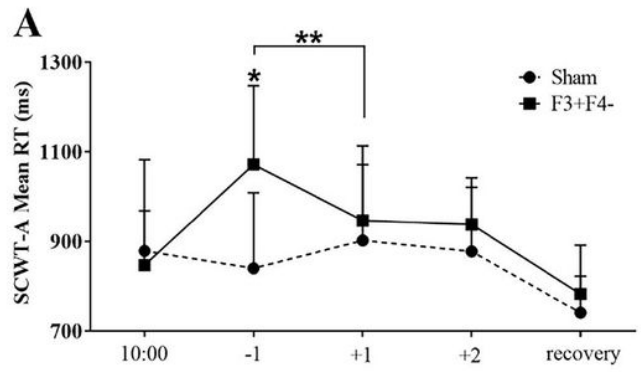

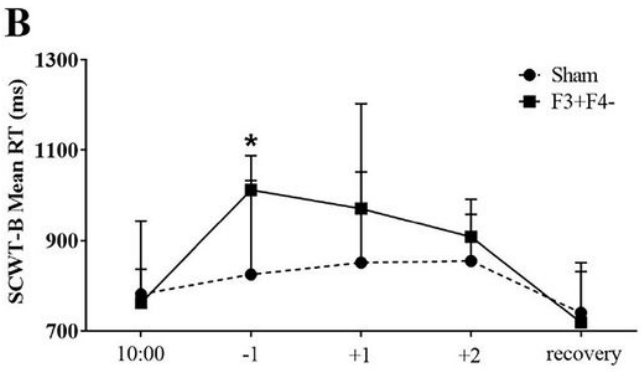

Figure 5

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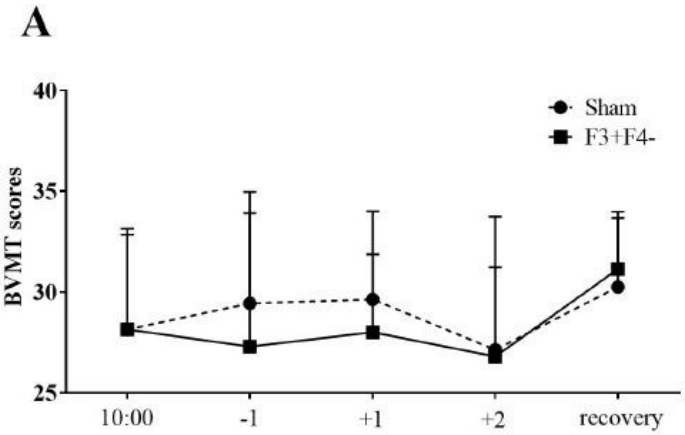

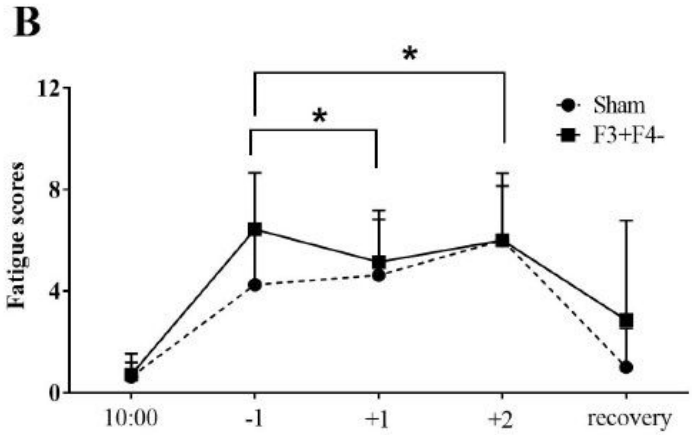

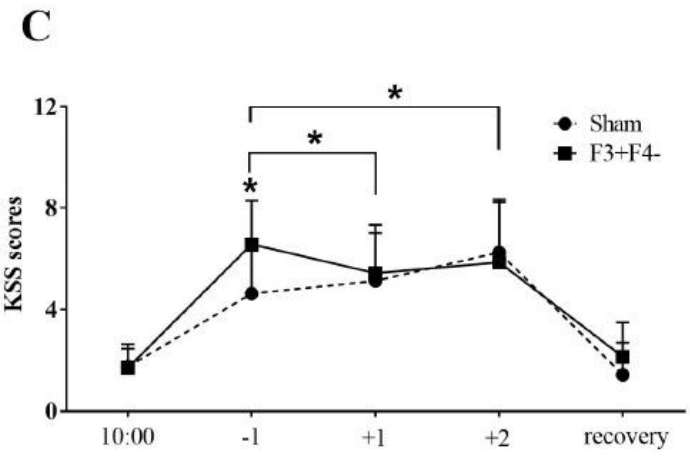

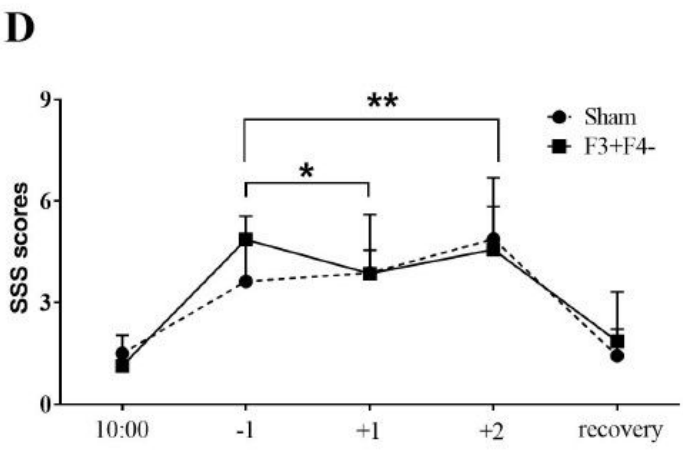

Figure 6

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