



ORIGINAL ARTICLE

WILEY

A pilot study on efficacy and tolerability of cognitive behavioral therapy (CBT-FD) for Japanese patients with focal dystonia

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Funding information

Intramural Research, Grant/Award Number: 27-4, 30-4; Neurological and Psychiatric Disorders of NCNP

[Correction added on 29 November 2019, after first online publication: The acknowledgement section has been corrected. Funding information were added.]

Abstract

Background: Abnormal involuntary movement disorders such as dystonia are likely to be affected by a person's psychological state. Nevertheless, reports of the literature describing investigations of psychological interventions to dystonic patients are scarce. Patients with focal dystonia (FD) are left to confront various psychosocial difficulties. Ioannou and colleagues proposed a holistic approach to seek mechanisms of the basal ganglia associated with athletic performance from the perspective of neuro-psycho-motor-cognitive perspective. This viewpoint endorses that treatment is not as simple as being solitary: Rather, it must incorporate physical, psychological, and social aspects. Empirical intervention studies using psychotherapy are urgently necessary.

Aim: The purpose of this study was to examine the efficacy and tolerability of cognitive behavioral therapy (CBT: hereinafter, CBT-FD) in mental health and dystonia symptoms of patients with FD. This report is the first study of Japanese patients with FD followed up for one year after CBT-FD intervention.

Methods: We administered 8 sessions of CBT-FD to 15 patients without history of mental disorders who had focal dystonia and a score of 14 or higher on the Beck Inventory-II. We evaluated the effectiveness and tolerability of CBT-FD.

Results: Significant improvements were found in many scales. Most improvements were sustained for one year. Improvement of dysfunction occurred independently of a decrease in depression and anxiety levels.

Conclusions: Results of this study suggest that CBT-FD is effective for improving patient depression, anxiety, disability, pain, and quality of life including relation with the environment. We verified that CBT-FD contributes safely to holistic recovery.

KEYWORDS

CBT-FD, cognitive behavior therapy, focal dystonia, holistic approach

1 | INTRODUCTION

Focal dystonia (FD) affects sites in the upper half region of the head, the lower region of the head, the neck, the larynx, the trunk,

the upper limbs, and the lower limbs.^{1,2} Actually, FD is assumed to stem from an organic lesion. It is probably a disorder of motor circuits in the basal ganglia, thalamus, cerebral cortex, brain stem, and cerebellum.³⁻⁵

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The first recommended treatment option^{1,6} is botulinum toxin therapy, with effects lasting about 3 months. For Japanese patients with cervical dystonia, the remission rate of one year or longer is reportedly 32.4%.⁷ Oral treatment with drugs such as clonazepam and trihexyphenidyl hydrochloride has been used,² but they entail side effects such as drowsiness, weakness, and dry mouth, and have only limited effectiveness. In recent years, stereotactic brain surgery has also been performed. In fact, FD might be painful⁶; stress is involved in attenuation of therapeutic effects.⁸ When selecting treatment, consideration should be given not only to treatment effectiveness but also to the effectiveness/tolerability ratio, invasiveness, cost, and other factors together with the difficulty of diagnosing mild cases and the challenges posed by treatment. Any or all might result in unproductive or discontinued treatment.

Psychological research related to FD has revealed that 50% of patients with cervical dystonia have high anxiety and that 62% have depression.⁹ Musicians' dystonia (MD), a syndrome of FD, develops at the peak of a performer's career^{10,11}; 62% of affected professional musicians subsequently choose to abandon their careers.¹² Anxiety, as a factor exacerbating the deterioration of MD along with the possible influence of perfectionism,^{13,14} interacts with triggering external factors to discourage performers.¹³ The salient concern of MD is not a psychological reaction but a possibly different effect from those of other FD pathophysiologically,¹³ such as the possibility that psychological characteristics interacting with psychological influence might reflect two maladaptive processes mediated through different circuits of the cortical basal ganglia and ganglion-thalamic circuits. Many such hypotheses have been postulated.¹⁵ It is noteworthy that Brandfonbrener and colleagues¹⁶ have reported that sympathy alone is inadequate as an aid to musicians who are adversely affected by FD. Moreover, sympathy often engenders strong feelings of frustration.

Therefore, patients with FD are left to confront various psychosocial difficulties. Ioannou and colleagues proposed a holistic approach to seek mechanisms of the basal ganglia associated with athletic performance from the perspective of neuro-psycho-motor-cognitive.¹⁵ This viewpoint endorses that treatment is not as simple as being solitary: Rather, it must incorporate physical, psychological, and social aspects. The "motor loop" is also related to the psychological state. Empirical intervention studies using psychotherapy are urgently necessary. This report is the first of a study of Japanese patients with FD followed up for one year after cognitive behavioral therapy (CBT: hereinafter, CBT-FD) intervention.

2 | EVOLUTION AND APPLICATION OF CBT FOR PATIENTS WITH FD

Developed from evidence obtained from cognitive therapy, CBT is a structured short-term psychotherapy.¹⁷ Currently in Japan, it is posted in guidelines in the field of psychiatry and general medical care.^{18,19} In the field of neurological medicine, reports have described intervention studies of depression in Parkinson's disease.²⁰

For FD, one CBT intervention trial conducted for a limited number of patients has been reported, with results suggesting that group therapy accommodating CBT for nine patients with cervical dystonia was useful for improving depression, anxiety, and adaptation.²¹

3 | METHODS

3.1 | Patients

In this study, conducted during November 2015-March 2018, 15 patients with FD agreed to participate. Each had 14 or more points on the Beck Depression Inventory-Second Edition (BDI-II) but had no history of mental illnesses. Each had completed eight CBT-FD sessions by the end of July 2018. Patient characteristics are presented in Table 1.

Given a preliminary nature of this study, no formal sample size calculation was performed although this study is expected to serve as a pilot work in accordance with a suggestion by Moore et al.²²

3.2 | Ethical considerations

This research was conducted with the approval of the Ethics Committee of the National Center of Neurology and Psychiatry, Japan (approval number, A2014-095; approval date, October 17, 2014). Explanations were given using documents in all cases. Written consent was obtained from each participant. The CBT-FD and the evaluation were done by two clinical psychologists who had completed CBT and semi-structured contact (GRID HAM-D) training for the Hamilton Depression Rating Scale and who had an FD clinical career. The safe and appropriate practice of CBT-FD was secured through supervision by a Master Therapist, a cognitive behavior therapist.

3.3 | CBT program developed for patients with FD

3.3.1 | Overview of cognitive behavioral therapy

Cognitive behavioral therapy (CBT) is a structured and problem-focused psychotherapy which helps people understand and overcome a wide range of emotional and physical difficulties. CBT considers problems emerge from interactions between thought, emotion, behavior, and physical processes. CBT takes a problem-focused and skill-based approach which aims to improve distressing physical and emotional symptoms, re-evaluate unhelpful thoughts, and encourage helpful behavioral reactions.

3.3.2 | Understanding and intervention of cognitive behavioral therapy specific to focal dystonia

Already, CBT has been shown to be effective in treating nonpsychotic conditions such as chronic pain. In recent years, in the field of neurology, it has been shown to be effective in depression with anxiety in Parkinson's disease patients and FD patients. And furthermore, when searching for empirical studies in the field of neurology,

TABLE 1 Patient data

	n	Mean of age	Mean of disease duration	Mean of age onset	Therapeutic experience	
					Botulinum neurotoxin	Continuation of oral medication
Overall	15	42.6 ± 15.7	6.1 ± 3.3	36.5 ± 14.1	4	8
Sex						
Male	11	43.5 ± 15.6	5.9 ± 3.2	37.6 ± 13.9	2	5
Female	4	40.3 ± 18.4	6.5 ± 3.9	33.8 ± 16.3	2	3
By mechanism of pathogenesis						
Musicians' dystonia	6	42.8 ± 16.6	6.5 ± 3.3	36.3 ± 15.1	0	2
Non-musicians' dystonia	9	42.4 ± 16.1	5.8 ± 3.4	36.7 ± 14.3	4	6
By body distribution						
Musicians' dystonia						
Embouchure	3	45.7 ± 20.5	7.0 ± 2.6	38.7 ± 20.6	0	1
Upper limb	3	40.0 ± 15.7	6.0 ± 4.4	34.0 ± 11.4	0	1
Non-musicians' dystonia						
Head under half range	4	39.8 ± 8.0	4.8 ± 2.6	35.0 ± 7.8	2	3
Cervical	1	63.0	12.0	51.0	1	1
Upper limb	4	40.0 ± 21.7	5.3 ± 3.1	34.8 ± 20.2	1	2

Note: Botulinum neurotoxin: Administration was stopped before 3 mo over intake interview for CBT.

Continuation of oral medication: Oral medication continued to be prescribed for them without change.

there is an RCT whose primary evaluation is PD depression. However, empirical research CBT for FD is an issue for the future and has not yet been conducted in Japan. Therefore, depression was the primary evaluation for this study. Based on these facts, this study selected cognitive behavioral therapy as one of the noninvasive treatments. The purpose of this study was to test whether CBT is efficacy and tolerability not only for depression and anxiety in patients with FD, but also for dystonia-related disability and pain. We decided to implement cognitive behavioral therapy with a focus on understanding the relationship between cognitive/behavior/emotion and physical condition, because based on findings revealed in previous studies such as tension and integrity in MD patients and obsessive-compulsive tendency in patients with spastic torticollis, and based on preliminary our research and knowledge gained from clinical practice that attention focused on FD symptoms, the development or heightening of depression and anxiety after dystonia onset, and independence and spontaneity in treatment. In this way, we have developed a CBT-FD program consisting of eight sessions that follow the basic principles of CBT, based on preliminary studies, previous studies, and clinical findings. The CBT-FD program includes pre-assessment, co-treatment relationship building, psychoeducation on FD and CBT, self-monitoring, breathing and relaxation, cognitive reconstruction, and behavioral activation incorporating exposure therapy.

3.4 | Treatment

Injection of clostridium botulinum toxin therapy was discontinued for 3 months or more before participation in CBT-FD. Internal medicine prescriptions were continued without changes before CBT-FD.

Of 15 participants, 4 (26.7%) had received treatment with botulinum injection before participating in CBT-FD, 8 (66.7%) continued internal medicine prescriptions, and 4 were untreated (26.7%).

3.5 | Psychological and physical assessments

The evaluation period was from November 2015 to the end of March 2018. For evaluation of depression severity after intervention, the BDI-II²³ was used as the primary scale for intake and for the follow-up sessions (3 months, 6 months, 12 months after intervention). Additionally, GRID HAM-D²⁴ and Anxiety and Depression Scale (HADS—depression)^{25,26} were used for the evaluation of depression severity. The State-Trait Anxiety Inventory—Form JYZ (STAI status/trait)²⁷ and HADS anxiety^{25,26} were used to evaluate anxiety severity. The MOS 36-Item Short-Form Health Survey (SF-36v2)²⁸ and World Health Organization Quality of Life 26 (WHOQOL 26)²⁹ were used to evaluate quality of life (QOL). To evaluate dystonia symptoms, the Toronto Western Spasmodic Torticollis Rating Scale's disability score and pain score (below, it is described as disability/pain.)³⁰ were applied to the affected body parts (the above is shown as Table S1). In sessions 1-7, only HADS was used.

3.6 | Execution of CBT

The flow of implementation of CBT-FD is portrayed in Figure 1.

3.7 | Statistical analyses

The affected body parts of FD were classified in accordance with "Dystonia clinical practice guideline 2018."² Data aggregation and

FIGURE 1 Follow-up of CBT and numbers of participants. The contents of CBT-FD session 1 to session 8 and the follow-up session, the number of participants, the reason for non-participation, and the number of non-participant were shown. In this study, 15 patients with FD who met the criteria were enrolled and all completed 8 sessions. Three months after the intervention, 1 person was unable to attend because of work and 2 persons showed no participation. Six months after the intervention, 1 person was less than 6 mo after the intervention and two persons did not participate. Twelve months after the intervention, 3 persons were less than 12 mo after the intervention, and 2 persons did not participate

12 mo after intervention • Assessment • Discussion of issues and task	n = 10	Ongoing subjects: n = 3 Not participating: n = 2
↑		
6 mo after intervention • Assessment • Discussion of issues and task	n = 12	Ongoing subject: n = 1 Not participating: n = 2
↑		
3 mo after intervention • Assessment • Discussion of issues and task	n = 12	Not going for work: n = 1 Not participating: n = 2
↑		
Session 8 • Assessment: HADS scale • Program: Looking back and toward the future.	n = 15	Full participation
↑		
Session 7 • Assessment: HADS scale • Program: Behavior activation.	n = 15	Full participation
↑		
Session 6 • Assessment: HADS scale • Program: Cognitive reconstruction②.	n = 15	Full participation
↑		
Session 5 • Assessment: HADS scale • Program: Cognitive reconstruction①.	n = 15	Full participation
↑		
Session 4 • Assessment: HADS scale • Program: Depression and anxiety.	n = 15	Full participation
↑		
Session 3 • Assessment: HADS scale • Program: Relationship between emotion and body.	n = 15	Full participation
↑		
Session 2 • Assessment: HADS scale • Program: To observe the mind. Types and meanings of emotions. • Goal setting	n = 15	Full participation
↑		
Session 1 • Assessment: HADS scale • Program: Introduction. • Self-monitoring	n = 15	Full participation
↑		
Intake assessment • Assessment • Initial interview	n = 15	Full participation

analysis were conducted at the National Center Hospital, National Center of Neurology and Psychiatry, Japan. Pearson's correlation coefficients were calculated using software (SPSS ver. 23; SPSS Inc) to assess the correlation between disability/pain and BDI-II, HAM-D, HADS, and STAI. Mixed effect models were applied to the change from baseline for disability/pain and BDI-II, HAM-D, HADS, and STAI. The subject was specified as the random effect. The time point (3 months, 6 months, and 12 months after intervention) was specified as the fixed effect. The mixed effect models including time point, MD/non-MD, and time point by MD/non-MD interaction as fixed effects were also applied; *F* tests for the fixed effects were used in this model. In the mixed effect model analyses, inference on the least square mean for each time point and time point by MD/non-MD interaction was conducted. Analysis of HADS depression/anxiety at 8 points from intake to session 7

was done in the same way. Analyses based on the mixed effect models were conducted with software (SAS ver. 9.4; SAS Institute Japan Inc).

4 | RESULTS

In this study, 15 patients with FD who met the criteria were enrolled and all completed 8 sessions. Three months after the intervention, 1 person was unable to attend because of work and 2 persons showed no participation. Six months after the intervention, 1 person was less than 6 months after the intervention and two persons did not participate. Twelve months after the intervention, 3 persons were less than 12 months after the intervention, and 2 persons did not participate.

Significant improvement was found in many of the scales. Many of such improvements were sustained for one year. No significant correlation was found between disability/pain and depression or anxiety. At 8 points up to session 7 with intake as the baseline, the presence or absence of significant overall improvement obtained as a result of *t* tests using the null hypothesis that the least mean square value is 0, as described below. The depression score improved significantly from session 4 through session 7 ($P = .012$, $P = .035$, $P = .024$, $P = .000$). The anxiety scores improved significantly from session 2 through session 7 ($P = .028$, $P = .044$, $P = .001$, $P = .002$, $P = .002$, $P = .000$). Furthermore, no correlation was found between disability and BDI-II ($P = .236$), disability and HAM-D ($P = .382$), disability and HADS depression ($P = .327$) or anxiety ($P = .347$), STAI trait ($P = .474$), pain and BDI-II ($P = .880$), pain and HAM-D ($P = .627$), pain and HADS depression ($P = .683$) or anxiety ($P = .195$), and pain and STAI trait ($P = .700$).

The total and the overall scale transition by onset mechanism (MD or non-MD) are presented in Table S2. In addition, Tables 2 and 3 show the significant difference between the least mean square value and the amount of change, divided into overall and disease pathogenesis.

Further, depression measures slightly different content at each scale (eg, reflecting physical and cognitive problems). Regarding the evaluation period, BDI-II asks about the past 2 weeks, and HADS and HAM-D ask about the past week. And environmental factors in the meantime are reflected in the value of depression and anxiety. Of course, due to these various factors, the score and significance differ depending on the point being evaluated.

5 | DISCUSSION

The results of this study suggest that CBT-FD is effective for improving patient depression, anxiety, and quality of life including disability, pain, and relations with the environment. Moreover, results verified that CBT-FD contributes safely to holistic recovery. Improvement of dysfunction and pain occurred irrespective of a decrease in depression and anxiety, which stands in sharp contrast to the stance that FD is solely psychogenic.¹³ Actually, CBT is established through a stable therapeutic alliance between patients and therapists and is established by patients themselves tackling the task.¹⁷ Therefore, CBT-FD is expected to have helped to elicit the patient's potential.

One important consideration is that the decline in the HADS score partially supports the results reported by Sandhu et al.²¹ However, the present study was effective irrespective of the site of onset or occupation. With respect to the transition of HADS scores from baseline to session 7, depression decreased from the middle of the sessions. Furthermore, anxiety declined steadily from session 2. Some up and down fluctuations were apparent in the score, but the tendency was observed to improve smoothly once the descent started. This tendency differs from that found for mental disorders such as depression and anxiety disorder. Actually, CBT is useful for

depression and anxiety in FD, as it is with other neurological diseases.²¹ Quality of life improved, but the environment and other considerations improved irrespective of the occupational level and characteristic anxiety. During the 6-12 months following intervention, one participant changed residence. Also, one participant's family composition changed. However, no other participant exhibited a clear environmental change intake to 12 months after the intervention. For this reason, the environmental perception and social interaction of the participant changed,¹³ showing improvement. These improvements were thought to enhance the therapeutic effect⁸ and to improve relationships with medical staff.

From the viewpoint of the mechanism of pathogenesis, compared to MD, widely diverse improvements were achieved with non-MD in terms of trait anxiety. Amplification of improvement and deterioration was large in functional disorder, but the improvement trend continued 3 months after the intervention. Nevertheless, gradual improvement was found in trait anxiety, with moderate improvement and deteriorating waves in disability with MD. All patients with MD from this study continued performance activities during study participation. Therefore, the psychological condition and quality of life were in a state of being prone to stimulation from the perspectives of performance, physical condition, and environmental conditions. Under the present circumstances, under which more than 60% of MDs might abandon their careers,¹³ many participants participated in research at a time when they were distraught about future music activities, but no one ceased employment while participating in this study. Results show that, in almost identical cases, some participants' symptoms were remarkably improved; others were not. However, in both types of cases, thinking ability and self-determination ability were revitalized. Because recovery of one's mental and physical condition can also serve as a basis for rehabilitation of musicians with MD, creating professional specialization programs, numbers of sessions, follow-up intervals, etc, are necessary. Because of CBT-FD, symptoms and physical and mental conditions did not worsen in any single case, which suggests that the CBT-FD program is well tolerated when performed carefully. Further, all patients with MD were botulinum untreated patients. They never wanted botulinum treatment because of concerns that it would be difficult to perform performance activities if botulinum treatment was too effective. However, when treated with botulinum, it was considered useful to evaluate whether the subject's disability was further alleviated or the effect of CBT-FD was further increased, and was considered a future research question.

This study has important limitations that participants were few, no control group was set, and bias deriving from open trials must be considered. Future studies must examine larger numbers of participants, use random assignment trials, and conduct more detailed research to support wider generalization of the results.

In conclusion, results of this study suggest that CBT-FD is effective for improving patient depression, anxiety, and quality of life including disability, pain, and relations with the environment. Moreover, CBT-FD contributes effectively to holistic recovery. Improvement in disability was achieved independently of anxiety and depression

TABLE 2 Inference results for least square means at respective times

Outcome	Time	Estimate	SE	Lower CL	Upper CL	t value	P value	
(a)								
BDI-II	After intervention	-9.20	2.01	-13.52	-4.88	-4.57	.000	***
	3 mo after intervention	-5.84	1.70	-9.90	-1.78	-3.44	.012	*
	6 mo after intervention	-8.71	2.37	-14.06	-3.35	-3.67	.005	**
	12 mo after intervention	-12.97	2.88	-19.83	-6.11	-4.50	.003	**
HAM-D	After intervention	-6.20	1.02	-8.39	-4.01	-6.08	.000	***
	3 mo after intervention	-5.01	0.85	-6.86	-3.15	-5.90	.000	***
	6 mo after intervention	-6.38	0.76	-8.02	-4.73	-8.35	.000	***
	12 mo after intervention	-5.51	1.39	-8.56	-2.46	-3.96	.002	***
HADS_depression	After intervention	-3.80	0.81	-5.54	-2.06	-4.68	.000	***
	3 mo after intervention	-3.68	0.96	-5.78	-1.58	-3.84	.002	**
	6 mo after intervention	-3.94	1.16	-6.47	-1.41	-3.39	.005	**
	12 mo after intervention	-4.31	1.31	-7.20	-1.41	-3.29	.008	**
HADS_anxiety	After intervention	-4.20	0.70	-5.70	-2.70	-6.01	.000	***
	3 mo after intervention	-3.62	1.14	-6.16	-1.07	-3.17	.010	**
	6 mo after intervention	-2.68	1.00	-4.84	-0.51	-2.69	.019	*
	12 mo after intervention	-4.58	1.08	-6.96	-2.19	-4.23	.001	**
STAI_state anxiety	After intervention	-8.53	2.19	-13.24	-3.83	-3.89	.002	**
	3 mo after intervention	-4.02	2.82	-10.12	2.09	-1.42	.179	ns
	6 mo after intervention	-5.83	2.82	-11.93	0.27	-2.07	.059	ns
	12 mo after intervention	-11.23	2.91	-17.53	-4.94	-3.86	.002	**
STAI_trait anxiety	After intervention	-10.87	3.15	-17.62	-4.11	-3.45	.004	**
	3 mo after intervention	-7.60	2.58	-13.18	-2.01	-2.94	.012	*
	6 mo after intervention	-8.91	2.67	-14.63	-3.19	-3.33	.005	**
	12 mo after intervention	-15.62	3.58	-23.64	-7.61	-4.36	.002	**
SF36v2_Physical Function	After intervention	6.67	1.80	2.80	10.54	3.70	.002	**
	3 mo after intervention	6.51	1.67	2.93	10.10	3.91	.002	**
	6 mo after intervention	5.28	2.59	-0.28	10.85	2.04	.061	ns
	12 mo after intervention	5.23	2.68	-0.65	11.10	1.95	.076	ns
SF36v2_Role Physical	After intervention	15.83	5.38	4.29	27.38	2.94	.011	*
	3 mo after intervention	12.44	5.88	-0.53	25.40	2.11	.058	ns
	6 mo after intervention	16.40	6.22	2.70	30.10	2.64	.023	*
	12 mo after intervention	12.35	8.83	-7.35	32.06	1.40	.192	ns
SF36v2_Role Emotional	After intervention	9.72	6.35	-3.89	23.34	1.53	.148	ns
	3 mo after intervention	11.49	6.15	-2.08	25.07	1.87	.089	ns
	6 mo after intervention	17.55	7.58	1.15	33.95	2.31	.038	*
	12 mo after intervention	13.38	8.43	-5.34	32.10	1.59	.143	ns
(b)								
SF36v2_Social Functioning	After intervention	10.83	5.57	-1.12	22.78	1.94	.072	ns
	3 mo after intervention	9.59	5.47	-2.45	21.63	1.75	.107	ns
	6 mo after intervention	7.24	4.82	-3.37	17.84	1.50	.161	ns
	12 mo after intervention	26.80	10.31	3.49	50.12	2.60	.029	*
SF36v2_Mental Health	After intervention	19.47	4.87	9.01	29.92	3.99	.001	**
	3 mo after intervention	10.49	6.79	-4.44	25.42	1.54	.150	ns
	6 mo after intervention	12.91	6.18	-0.42	26.24	2.09	.057	ns
	12 mo after intervention	24.46	7.84	7.41	41.51	3.12	.009	**
SF36v2_Bodily Pain	After intervention	5.07	6.27	-8.39	18.52	0.81	.433	ns
	3 mo after intervention	7.10	6.20	-6.64	20.83	1.14	.278	ns
	6 mo after intervention	0.66	7.27	-15.29	16.61	0.09	.930	ns
	12 mo after intervention	2.62	6.82	-12.38	17.63	0.39	.708	ns

(Continues)

TABLE 2 (Continued)

Outcome	Time	Estimate	SE	Lower CL	Upper CL	t value	P value	
SF36v2_Vitality	After intervention	15.42	5.24	4.17	26.66	2.94	.011	*
	3 mo after intervention	12.50	6.34	-2.01	27.01	1.97	.083	ns
	6 mo after intervention	12.28	4.52	2.39	22.17	2.72	.019	*
	12 mo after intervention	16.87	4.81	6.07	27.67	3.51	.006	**
SF36v2_General Health Perceptions	After intervention	18.00	4.31	8.76	27.24	4.18	.001	**
	3 mo after intervention	13.58	4.18	4.54	22.63	3.25	.006	**
	6 mo after intervention	11.86	5.63	-0.23	23.95	2.11	.054	ns
	12 mo after intervention	15.48	6.22	1.23	29.74	2.49	.037	*
WHOQOL26_Overall Mean	After intervention	0.40	0.16	0.07	0.73	2.57	.022	*
	3 mo after intervention	0.39	0.22	-0.09	0.87	1.74	.103	ns
	6 mo after intervention	0.14	0.23	-0.35	0.64	0.62	.545	ns
	12 mo after intervention	0.17	0.29	-0.46	0.81	0.61	.557	ns
WHOQOL26_Physical Area	After intervention	0.59	0.11	0.36	0.83	5.38	.000	***
	3 mo after intervention	0.43	0.13	0.16	0.70	3.44	.004	**
	6 mo after intervention	0.51	0.19	0.10	0.92	2.71	.018	*
	12 mo after intervention	0.80	0.20	0.37	1.23	3.99	.002	**
WHOQOL26_Mental Area	After intervention	0.60	0.18	0.21	0.99	3.30	.005	**
	3 mo after intervention	0.39	0.22	-0.10	0.87	1.76	.109	ns
	6 mo after intervention	0.58	0.22	0.10	1.06	2.64	.021	*
	12 mo after intervention	0.54	0.23	0.03	1.05	2.38	.039	*
WHOQOL26_Social Area	After intervention	0.16	0.19	-0.25	0.56	0.82	.425	ns
	3 mo after intervention	0.30	0.12	0.04	0.56	2.46	.028	*
	6 mo after intervention	0.31	0.13	0.03	0.60	2.40	.032	*
	12 mo after intervention	0.28	0.14	-0.02	0.59	2.01	.067	ns
(c)								
WHOQOL26_Environment	After intervention	0.29	0.08	0.13	0.45	3.85	.002	**
	3 mo after intervention	0.18	0.10	-0.04	0.40	1.80	.101	ns
	6 mo after intervention	0.38	0.12	0.11	0.64	3.12	.009	**
	12 mo after intervention	0.46	0.12	0.20	0.73	3.81	.002	**
WHOQOL26_Mean Value of QOL	After intervention	0.44	0.10	0.22	0.65	4.40	.001	**
	3 mo after intervention	0.32	0.10	0.10	0.55	3.11	.009	**
	6 mo after intervention	0.39	0.14	0.10	0.69	2.89	.012	*
	12 mo after intervention	0.56	0.14	0.25	0.87	3.92	.002	**
Disability	After intervention	-2.60	0.67	-4.05	-1.15	-3.85	.002	**
	3 mo after intervention	-0.28	0.42	-1.22	0.66	-0.66	.521	ns
	6 mo after intervention	-3.14	0.64	-4.56	-1.72	-4.94	.001	**
	12 mo after intervention	-3.07	0.70	-4.65	-1.49	-4.38	.002	**
Pain	After intervention	-2.12	1.12	-4.49	0.26	-1.89	.077	ns
	3 mo after intervention	-1.13	1.24	-3.78	1.52	-0.91	.378	ns
	6 mo after intervention	-2.19	1.33	-5.06	0.67	-1.65	.123	ns
	12 mo after intervention	-3.62	1.73	-7.39	0.15	-2.09	.058	ns

Note: Estimate: point estimate of least square means.

SE: standard error of least square means.

Lower: minimum lower limit of the 95% confidence interval.

Upper: maximum upper limit of the 95% confidence interval.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

TABLE 3 Least square means of musicians' dystonia and non-musicians' dystonia (each level of interaction)

Outcome	Time	Estimate		SE		Lower		Upper		t value		P value		
		MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	
(a)														
BDI-II	After intervention	-6.33	-11.11	3.14	2.56	-13.11	-16.65	0.45	-5.58	-2.02	-4.34	.065	ns	**
	3 mo after intervention	-4.17	-7.09	2.31	2.59	-10.6	-13.35	2.26	-0.84	-1.81	-2.74	.146	ns	*
	6 mo after intervention	-6.5	-9.83	3.89	3.46	-15.93	-17.91	2.93	-1.75	-1.67	-2.84	.144	ns	*
	12 mo after intervention	-10.17	-16.21	3.29	4.62	-19.38	-27.28	-0.95	-5.14	-3.09	-3.51	.038	*	.011
HAM-D	After intervention	-5	-7	1.62	1.32	-8.49	-9.85	-1.51	-4.15	-3.09	-5.3	.009	**	0
	3 mo after intervention	-5.33	-4.3	1.18	1.22	-7.96	-6.96	-2.71	-1.63	-4.51	-3.51	.001	**	.004
	6 mo after intervention	-5.33	-7.18	1.13	1.02	-7.82	-9.4	-2.85	-4.97	-4.72	-7.01	.001	**	0
	12 mo after intervention	-4.33	-6.03	1.95	2.14	-8.74	-10.72	0.07	-1.35	-2.22	-2.82	.053	ns	.016
HADS_depres- sion	After intervention	-3.5	-4	1.33	1.08	-6.37	-6.34	-0.63	-1.66	-2.64	-3.69	.021	*	.003
	3 mo after intervention	-3.17	-4.45	1.35	1.39	-6.22	-7.49	-0.11	-1.41	-2.35	-3.21	.044	*	.008
	6 mo after intervention	-3.5	-4.29	1.79	1.64	-7.52	-7.89	0.52	-0.7	-1.96	-2.62	.08	ns	.023
	12 mo after intervention	-3.83	-5.37	1.95	2.11	-8.3	-10.07	0.63	-0.67	-1.96	-2.54	.084	ns	.029
HADS_anxiety	After intervention	-3.83	-4.44	1.14	0.93	-6.29	-6.45	-1.37	-2.44	-3.37	-4.78	.005	**	0
	3 mo after intervention	-4.33	-2.23	1.88	1.76	-8.68	-6.15	0.01	1.69	-2.31	-1.27	.05	*	.234
	6 mo after intervention	-2.5	-2.57	1.67	1.43	-6.23	-5.71	1.23	0.58	-1.5	-1.8	.165	ns	.1
	12 mo after intervention	-4.17	-4.92	1.57	1.7	-7.85	-8.69	-0.48	-1.16	-2.65	-2.89	.032	*	.015
STAI_state anxiety	After intervention	-12.17	-6.11	3.35	2.74	-19.41	-12.03	-4.92	-0.19	-3.63	-2.23	.003	**	.044
	3 mo after intervention	-6	-2.8	4.17	4.01	-15.2	-11.42	3.2	5.83	-1.44	-0.7	.179	ns	.497
	6 mo after intervention	-6.5	-6.14	4.29	3.8	-15.89	-14.32	2.89	2.05	-1.52	-1.61	.156	ns	.13
	12 mo after intervention	-10.33	-13.93	3.98	4.04	-19.09	-22.59	-1.57	-5.26	-2.6	-3.44	.025	*	.004
STAI_trait anxiety	After intervention	-12.5	-12.5	5.13	4.19	-23.59	-18.83	-1.41	-0.72	-2.44	-2.33	.03	*	.036
	3 mo after intervention	-8.83	-8.83	3.91	3.76	-17.48	-14.75	-0.19	1.49	-2.26	-1.77	.046	*	.101
	6 mo after intervention	-10.17	-10.17	4.23	3.69	-19.36	-15.95	-0.97	-0.14	-2.4	-2.18	.033	*	.047
	12 mo after intervention	-13	-13	4.39	5.67	-23.13	-33.62	-2.87	-7.94	-2.96	-3.67	.018	*	.005
SF36v2_ Physical Function	After intervention	6.67	6.67	2.96	2.42	0.27	1.45	13.06	11.89	2.25	2.76	.042	*	.016
	3 mo after intervention	6.67	6.24	2.63	2.33	0.9	1.23	12.43	11.25	2.54	2.68	.027	*	.018
	6 mo after intervention	5	5.57	4.2	3.54	-4.15	-2.06	14.15	13.21	1.19	1.58	.257	ns	.139
	12 mo after intervention	5.83	4.07	3.95	4.1	-3.12	-4.93	14.78	13.07	1.48	0.99	.174	ns	.342
SF36v2_Role Physical	After intervention	20.83	12.5	8.65	7.06	2.15	-2.75	39.52	27.75	2.41	1.77	.032	*	.1
	3 mo after intervention	14.58	9.48	8.18	8.85	-3.78	-10.07	32.95	29.03	1.78	1.07	.107	ns	.308
	6 mo after intervention	15.63	17.66	9.08	9.26	-4.76	-2.92	36.01	38.24	1.72	1.91	.118	ns	.085
	12 mo after intervention	14.58	15.92	12.34	11.86	-13.56	-10.17	42.73	42.01	1.18	1.34	.269	ns	.206

(Continues)

TABLE 3 (Continued)

Outcome	Time	Estimate		SE		Lower		Upper		t value		P value	
		MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD
SF36v2_Role Emotional	After intervention	8.33	10.65	10.4	8.49	-14.14	-7.7	30.81	29	0.8	1.25	.437	ns
	3 mo after intervention	9.72	13.48	8.8	9.81	-10.31	-8.33	29.76	35.29	1.11	1.37	.299	ns
	6 mo after intervention	18.06	16.67	11.53	10.91	-7.38	-7.01	43.49	40.36	1.57	1.53	.146	ns
	12 mo after intervention	6.94	25.92	10.02	11.14	-16.27	1.31	30.16	50.53	0.69	2.33	.508	*
(b)													
SF36v2_Social Functioning	After intervention	12.5	9.72	9.12	7.45	-7.21	-6.37	32.21	25.82	1.37	1.31	.194	ns
	3 mo after intervention	12.5	4.04	8	8.62	-5.62	-15.24	30.62	23.31	1.56	0.47	.153	ns
	6 mo after intervention	10.42	3.95	6.88	7.1	-4.91	-11.86	25.74	19.75	1.51	0.56	.161	ns
	12 mo after intervention	18.75	52.4	14.65	19.8	-28.3	0.51	65.8	104.29	1.28	2.65	.292	*
SF36v2_Mental Health	After intervention	11.67	24.67	7.49	6.12	-4.52	11.45	27.86	37.89	1.56	4.03	.144	**
	3 mo after intervention	11.67	7.47	9.47	10.38	-9.51	-15.46	32.85	30.4	1.23	0.72	.247	ns
	6 mo after intervention	6.67	17.24	9.15	8.76	-13.43	-1.79	26.77	36.28	0.73	1.97	.481	ns
	12 mo after intervention	15.83	29.92	11.34	11.82	-9.7	4.2	41.37	55.64	1.4	2.53	.195	*
SF36v2_Bodily Pain	After intervention	2	7.11	10.24	8.36	-20.11	-10.94	24.11	25.17	0.2	0.85	.848	ns
	3 mo after intervention	3.5	7.19	8.44	8.99	-15.45	-12.52	22.45	26.9	0.41	0.8	.688	ns
	6 mo after intervention	-3.17	4.31	10.68	10.8	-27.03	-19.6	20.69	28.22	-0.3	0.4	.773	ns
	12 mo after intervention	-8.67	19.46	8.03	8.08	-26.83	1.93	9.5	36.99	-1.08	2.41	.309	*
SF36v2_Vitality	After intervention	11.46	18.06	8.48	6.93	-6.87	3.09	29.79	33.02	1.35	2.61	.2	*
	3 mo after intervention	14.58	7.71	9.31	9.32	-7.36	-13.34	36.53	28.76	1.57	0.83	.161	ns
	6 mo after intervention	11.46	12.22	6.92	6.7	-4.27	-2.6	27.18	27.04	1.66	1.82	.133	ns
	12 mo after intervention	12.46	24.81	5.71	7.48	-0.7	7.97	25.62	41.65	2.18	3.31	.061	**
SF36v2_General Health Perceptions	After intervention	13.67	20.89	6.9	5.63	-1.23	8.72	28.57	33.05	1.98	3.71	.069	**
	3 mo after intervention	10	16.22	6.39	5.94	-4.14	3.36	24.14	29.08	1.56	2.73	.147	*
	6 mo after intervention	11.67	10.75	8.67	8.04	-7.28	-6.57	30.62	28.07	1.35	1.34	.204	ns
	12 mo after intervention	7	22.66	8.49	8.95	-12.93	2.47	26.93	42.85	0.82	2.53	.436	*
WHOQOL26_Overall Mean	After intervention	0.33	0.44	0.25	0.21	-0.22	0	0.88	0.89	1.31	2.14	.213	ns
	3 mo after intervention	0.33	0.45	0.34	0.32	-0.42	-0.24	1.08	1.14	0.98	1.4	.349	ns
	6 mo after intervention	0.42	-0.18	0.33	0.31	-0.31	-0.86	1.14	0.5	1.26	-0.58	.233	ns
	12 mo after intervention	0.5	-0.21	0.39	0.43	-0.37	-1.16	1.37	0.74	1.29	-0.49	.229	ns
WHOQOL26_Physical Area	After intervention	0.52	0.63	0.18	0.15	0.14	0.32	0.91	0.95	2.94	4.36	.012	**
	3 mo after intervention	0.4	0.44	0.19	0.19	-0.02	0.03	0.83	0.85	2.14	2.34	.058	*
	6 mo after intervention	0.52	0.46	0.3	0.27	-0.13	-0.12	1.18	1.04	1.76	1.71	.106	ns
	12 mo after intervention	0.62	0.98	0.29	0.28	-0.03	0.38	1.27	1.58	2.12	3.5	.059	**

(Continues)

TABLE 3 (Continued)

Outcome	Time	Estimate		SE		Lower		Upper		t value		P value	
		MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD	MD	Non_MD
WHOQOL26_Mental Area	After intervention	0.69	0.54	0.3	0.24	0.05	0.01	1.33	1.06	2.34	2.22	.036	*
	3 mo after intervention	0.53	0.26	0.34	0.31	-0.24	-0.42	1.29	0.95	1.57	0.86	.152	ns
	6 mo after intervention	0.78	0.4	0.35	0.31	0.01	-0.27	1.55	1.07	2.24	1.3	.048	*
	12 mo after intervention	0.58	0.59	0.32	0.39	-0.16	-0.29	1.33	1.47	1.85	1.53	.107	ns
WHOQOL26_Social Area	After intervention	0.17	0.15	0.31	0.25	-0.5	-0.4	0.84	0.7	0.54	0.58	.601	ns
	3 mo after intervention	0.22	0.38	0.18	0.16	-0.17	0.02	0.62	0.73	1.24	2.29	.241	ns
	6 mo after intervention	0.22	0.42	0.2	0.17	-0.21	0.05	0.66	0.78	1.12	2.44	.285	ns
	12 mo after intervention	0.11	0.56	0.17	0.17	-0.27	0.2	0.49	0.92	0.65	3.37	.532	ns
(c)													
WHOQOL26_Environment	After intervention	0.33	0.26	0.12	0.1	0.07	0.05	0.6	0.48	2.7	2.62	.018	*
	3 mo after intervention	0.31	0.02	0.12	0.14	0.04	-0.3	0.59	0.34	2.56	0.11	.03	*
	6 mo after intervention	0.46	0.31	0.18	0.18	0.06	-0.08	0.86	0.7	2.56	1.74	.028	*
	12 mo after intervention	0.44	0.55	0.17	0.19	0.07	0.15	0.81	0.95	2.62	2.96	.025	*
WHOQOL26_Mean Value of QOL	After intervention	0.45	0.43	0.16	0.13	0.1	0.14	0.8	0.71	2.76	3.22	.016	*
	3 mo after intervention	0.38	0.26	0.15	0.16	0.03	-0.08	0.72	0.6	2.46	1.65	.035	*
	6 mo after intervention	0.52	0.26	0.22	0.19	0.04	-0.15	1	0.67	2.38	1.36	.036	*
	12 mo after intervention	0.49	0.67	0.19	0.22	0.05	0.18	0.92	1.16	2.52	2.98	.032	*
Disability	After intervention	-1.67	-3.22	1.06	0.86	-3.95	-5.08	0.61	-1.36	-1.58	-3.74	.138	ns
	3 mo after intervention	-0.67	0.21	0.53	0.55	-1.89	-1.01	0.56	1.43	-1.25	0.38	.246	ns
	6 mo after intervention	-2	-4.05	0.91	0.85	-4.09	-5.93	0.09	-2.17	-2.19	-4.77	.058	ns
	12 mo after intervention	-1.83	-3.91	1.08	1.09	-4.53	-6.46	0.87	-1.37	-1.7	-3.6	.145	ns
Pain	After intervention	0	-3.53	1.66	1.35	-3.53	-6.41	3.53	-0.64	0	-2.61	ns	*
	3 mo after intervention	0	-1.43	1.88	1.73	-4.07	-5.1	4.07	2.24	0	-0.83	1	ns
	6 mo after intervention	0	-3.87	1.86	1.76	-4.1	-7.64	4.1	-0.09	0	-2.2	1	ns
	12 mo after intervention	0	-7.44	1.91	2.04	-4.3	-11.91	4.3	-2.97	0	-3.66	1	ns

Note: Estimate: point estimate of least square means; SE: standard error of least square means.

Lower: minimum lower limit of the 95% confidence interval.

Upper: maximum upper limit of the 95% confidence interval.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

status, which suggests the need for a change in approach to the psychogenicity of FD. Because of its high efficacy and tolerability, CBT-FD can be a link in the chain to providing a holistic approach to treating FD patients. We regard the promotion of psychological clinical research in FD as necessary for future development.

ACKNOWLEDGMENTS

The authors express gratitude for participants in this study. We express their heartfelt gratitude to Professor Takefumi Suzuki, Department of Neuropsychiatric Medical Ethics, Yamanashi University School of Medicine, gave many instructions as a teaching teacher. And we gratitude and condolences to Dr. Miho Murata who is the Former director of National Center of Neurology and Psychiatry Hospital and Former visiting professor at the Yamanashi University. This study was funded by the Intramural Research Grant (27-4, 30-4) for Neurological and Psychiatric Disorders of NCNP.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Kobayashi K, Sakamoto T, Maruo K, et al. A pilot study on efficacy and tolerability of cognitive behavioral therapy (CBT-FD) for Japanese patients with focal dystonia. *Neurol Clin Neurosci*. 2020;8:16-27. <https://doi.org/10.1111/ncn3.12344>