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Pilot Investigation of the Effects of Laughter Therapy on Mood, Stress, and Self-Efficacy in People with Multiple Sclerosis and Other Central Nervous System Disorders

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BACKGROUND

- Group exercises may provide benefits for mood disorders in MS and other neurological conditions
- Laughter therapy (LT, similar to laughter yoga) combines laughter with breathing and body exercises in a class setting. LT may give health benefits through strengthening of breathing muscles, improving mood, and relieving pain and stress.
- After pilot testing a group-based LT class for one year, we conducted the first prospective open-label trial of LT in patients with central nervous system (CNS) disorders, including MS.

OBJECTIVES

To assess the effects of an 8-week LT program on depression and anxiety as measured by the PHQ-9 and GAD-7, and on other wellness measures in a CNS disorder population.

METHODS

- Open-label, uncontrolled trial with pre and post testing of a cohort including people with MS (PWMS) and other CNS disorders (N=24).
- Timeline: 1) Screening/randomization 2) Laughter therapy (start < 90 days post screening) 8 week intervention 3) Post-treatment follow-up 8 weeks post-intervention.
- Outcomes: Questionnaires administered at baseline, end of treatment (Week 8) and at 8-week follow-up (Week 16). Co-primary outcomes were PHQ-9 and GAD-7 at 8 weeks. Additional outcomes were General Self-Efficacy Scale (GSE), Breathlessness Questionnaire (BQ), Modified Fatigue Impact 5-item Scale (MFIS-5), and Perceived Stress Scale (PSS-10). Disability measured by the Mental Disabilities Rating Scale (MDRS) and Physical Disabilities Rating Scale (PDRS).
- Analyses were conducted with per-protocol analysis.

Table 1. Eligibility criteria

Inclusion criteria	Exclusion criteria
• Diagnosis based on medical record review of one of the following neurological diseases: Alzheimer's disease, amyotrophic lateral sclerosis, brain injury, Huntington's Disease, multiple sclerosis, Parkinson's Disease, post-stroke, spinal cord injury. • Age > 18 • Medically stable for at least 2 months • Not participating in Laughter therapy for 30 days prior to screening	• Females who are pregnant • Unstable medical condition • Severe cognitive deficits • Severe abdominal pain, chest pain or back pain • Abdominal, chest or back surgery within 90 days • Psychosis or severe mental illness • Untreated hernia • Persistent cough • Advanced hemorrhoids • Epilepsy • Uncontrolled Hypertension – SBP >170 or DBP >105

INTERVENTION

- Participants received 8 weekly classes of LT in groups of 8-12.
- 60-minute classes were led by a certified LT instructor with over 5 years of experience.
- The classes involved 10 or more activities involving laughter. Examples included play-acting (mixing a cocktail of laughter, making an "evil laugh") and combining simulated laughter with arm or body movements. All activities done seated. Activities were interspersed with conversation aimed toward maintaining a peaceful, positive attitude. *See Figure 1 and 2.*

Figure 1. LT group activity. The instructor, 2nd from left, leading a laughter exercise intermixed with round-table conversation.

Figure 2. Group laughter, including upper limb activity, stretching and deep breathing.

RESULTS

Informed consents were signed by 30 subjects. Protocol adherence criteria (at least 4 sessions attended) were met by 14 subjects. The other 16 subjects terminated early or did not attend any sessions.

- **Baseline Demographics and Subject Characteristics**
  See Table 1.1 for all subjects and in Table 1.2 for per-protocol subjects.
- **Outcomes**
  - The descriptive statistics for co-primary efficacy endpoints and secondary efficacy endpoints are presented in Table 2.1 and Table 3.1 respectively. Statistical analyses are shown in Tables 3.1 and 3.2, respectively.
  - For PHQ-9, there were non-significant improvements at Week 8 and Week 16.
  - For GAD-7, there was no change at either endpoint.
  - For MFIS, a near significant reduction was found at Week 8 (-1.71, p = 0.056). This did not carry-over at Week 16.
  - For PSS, a non-significant reduction at Week 8 became significant at Week 16.
  - For Patient Global Impression, there was a significant change (improvement) at Week 16 vs baseline and between Week 16 and Week 8.
- **Adverse Events (AEs)**
  One moderate AE that was possibly related to treatment was recorded: elevated blood pressure in a patient with Parkinson's Disease.

Table 1.1. Baseline Demographics and Subject Characteristics All Subjects

		Total (N=30)
Age	N	30
	Mean (SD)	63.17 (10.64)
	Median	63
	Min, Max	45, 92
Gender	N	30
	F	21 (70%)
	M	9 (30%)
Diagnosis	N	30
	ALS	1 (3.3%)
	Alzheimer	1 (3.3%)
	HD	1 (3.3%)
	MS	17 (56.7%)
	PD	7 (23.3%)
	Spinal Cord Injury	2 (6.7%)
	Stroke	1 (3.3%)
Mental Disability Rating Scale (MDRS)	N	19
	None (0)	4 (21.1%)
	Mild (1)	10 (52.6%)
	Moderate (2)	5 (26.3%)
Physical Disability Rating Scale (PDRS)	N	21
	None (0)	2 (9.5%)
	Mild (1)	7 (33.3%)
	Moderate (2)	6 (28.6%)
	Severe (3)	6 (28.6%)

Table 1.2. Baseline Demographics and Subject Characteristics Per-Protocol Subjects

		Total (N=14)
Age	N	14
	Mean (SD)	62.29 (7.95)
	Median	60
	Min, Max	53, 76
Gender	N	14
	F	10 (71.4%)
	M	4 (28.6%)
Diagnosis	N	14
	ALS	1 (7.1%)
	HD	1 (7.1%)
	MS	8 (57.1%)
	PD	3 (21.4%)
	Spinal Cord Injury	1 (7.1%)
Mental Disability Rating Scale (MDRS)	N	14
	None (0)	4 (28.6%)
	Mild (1)	7 (50%)
	Moderate (2)	3 (21.4%)
Physical Disability Rating Scale (PDRS)	N	14
	None (0)	2 (14.3%)
	Mild (1)	4 (28.6%)
	Moderate (2)	5 (35.7%)
	Severe (3)	3 (21.4%)

Table 2.1. Summary of Co-Primary Efficacy Measures Per-Protocol Subjects

		Baseline (N=14)	Week 8 (N=14)	Week 16 (N=14)
PHQ-9	N	14	14	14
	Mean (SD)	6.5 (4.01)	4.93 (3.1)	6.07 (4.27)
	Median	6	5.5	6.5
	Min, Max	0, 13	0, 11	0, 16
GAD-7	N	14	14	14
	Mean (SD)	2.79 (4.08)	2.79 (3.21)	3.64 (3.82)
	Median	1.5	1	2.5
	Min, Max	0, 14	0, 9	0, 13

Table 2.2. Analysis of Co-Primary Efficacy Measures Per-Protocol Subjects

	Comparison	N	Mean Difference (95% CI)	p-value
PHQ-9	Week 8 vs. Baseline	14	-1.57 (-3.72, 0.57)	0.138
	Week 16 vs. Baseline	14	-0.43 (-2.84, 1.99)	0.708
	Week 16 vs. Week 8	14	1.14 (-0.96, 3.24)	0.26
GAD-7	Week 8 vs. Baseline	14	0 (-1.69, 1.69)	1
	Week 16 vs. Baseline	14	0.86 (-1.31, 3.03)	0.409
	Week 16 vs. Week 8	14	0.86 (-1.38, 3.1)	0.423

Table 3.1. Summary of Secondary Efficacy Measures Per-Protocol Subjects

		Baseline (N=14)	Week 8 (N=14)	Week 16 (N=14)
General Efficacy Scale (GSE)	N	14	14	14
	Mean (SD)	30.5 (6.21)	32.79 (4.74)	32.29 (5.09)
	Median	31	32.5	32
	Min, Max	14, 38	25, 39	21, 40
Breathless Questionnaire (BQ)	N	14	14	14
	Mean (SD)	2.14 (2.8)	2.14 (2.82)	2.5 (3.03)
	Median	1.5	1.5	0.5
	Min, Max	0, 10	0, 9	0, 8
Modified Fatigue Impact Scale-5 Item (MFIS-5)	N	14	14	14
	Mean (SD)	9.86 (3.86)	8.14 (4.33)	10.57 (4.5)
	Median	10.5	8.5	11
	Min, Max	1, 14	0, 13	0, 18
Perceived Stress Scale (PSS-10)	N	14	14	14
	Mean (SD)	16.29 (5.55)	13.71 (6.23)	13.36 (7.41)
	Median	17	11.5	14.5
	Min, Max	5, 26	7, 28	3, 26
Geriatric Depression Scale	N	14	14	13
	Mean (SD)	4.14 (4.05)	4 (3.26)	2.62 (2.33)
	Median	3.5	3.5	2
	Min, Max	0, 14	0, 11	0, 7
Patient Global Impression	N	14	14	14
	Mean (SD)	3.43 (1.34)	4.07 (0.83)	4.57 (0.51)
	Median	3.5	4	5
	Min, Max	0, 5	2, 5	4, 5

Table 3.2. Analysis of Secondary Efficacy Measures Per-Protocol Subjects

	Comparison	N	Mean Difference (95% CI)	p-value
General Efficacy Scale (GSE)	Week 8 vs. Baseline	14	2.29 (-0.82, 5.39)	0.136
	Week 16 vs. Baseline	14	1.79 (-1.98, 5.56)	0.325
	Week 16 vs. Week 8	14	-0.5 (-3.5, 2.5)	0.725
Breathless Questionnaire (BQ)	Week 8 vs. Baseline	14	0 (-2.23, 2.23)	1
	Week 16 vs. Baseline	14	0.36 (-1.1, 1.82)	0.606
	Week 16 vs. Week 8	14	0.36 (-1.76, 2.48)	0.722
Modified Fatigue Impact Scale-5 Item (MFIS-5)	Week 8 vs. Baseline	14	-1.71 (-3.49, 0.06)	0.057
	Week 16 vs. Baseline	14	0.71 (-1.19, 2.61)	0.431
	Week 16 vs. Week 8	14	2.43 (-0.06, 4.92)	0.055
Perceived Stress Scale (PSS-10)	Week 8 vs. Baseline	14	-2.57 (-5.63, 0.49)	0.093
	Week 16 vs. Baseline	14	-2.93 (-5.78, -0.08)	0.045
	Week 16 vs. Week 8	14	-0.36 (-2.81, 2.1)	0.758
Geriatric Depression Scale	Week 8 vs. Baseline	14	-0.14 (-1.54, 1.25)	0.828
	Week 16 vs. Baseline	13	-0.77 (-1.88, 0.34)	0.156
	Week 16 vs. Week 8	13	-0.85 (-1.97, 0.28)	0.128
Patient Global Impression	Week 8 vs. Baseline	14	0.64 (-0.13, 1.41)	0.095
	Week 16 vs. Baseline	14	1.14 (0.4, 1.89)	0.006
	Week 16 vs. Week 8	14	0.5 (0.06, 0.94)	0.029

DISCUSSION

- This population was not selected for either anxiety or depression and no significant change was found on either of these primary outcomes.
- Significant improvements were found on patient global impression and on perceived stress and a near significant reduction was found for fatigue. This suggests that LT may improve some aspects of well-being in neurological populations.
- The drop-out rate was >50%, and about equal amongst patients with and without MS. Most participants who dropped out never attended a single LT session. This may have been due to long screening period (up to 90 days) and limited enthusiasm. Dropouts also occurred after one or more sessions, sometimes due to patients feeling that the LT class was too hard or made them feel "out of their comfort zone."
- Participant comments indicated that for some participants, LT improved their outlook, while others lost interest.
- LT was well-tolerated amongst those who attended.

Limitations

This was an uncontrolled, open-label trial. Subject numbers were small, including a minority with non-MS disorders of the CNS.

Conclusions

This pilot study found that laughter therapy did not alter mood, but yielded improvements on some aspects of well-being amongst PWMS and other CNS conditions. Drop-outs were greater than seen with more conventional exercise classes in a neurological population. LT may be well-tolerated and applicable for a variety of neurological patients, including those with severe disability. Further work is needed to identify the proper "dosing" and administration of laughter therapy, including varying the content, duration, frequency and setting of LT classes.

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