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Empathy-based supportive treatment in amyotrophic lateral sclerosis: A pragmatic study

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ABSTRACT

Scarce literature has been dedicated to the psychological treatment of amyotrophic lateral sclerosis (ALS). However, there have been some encouraging findings, such as in hypnosis-based studies, which revealed patient improvements in anxiety, depression and quality of life (QoL). We replicated such a design of a pragmatic study on empathy-based supportive counseling treatment in four weekly domiciliary sessions. Twenty-one people with ALS (pALS) consecutively attending the Motor Neuron Disease Center of Padova University were recruited to the study; in total, 21 pALS who did not undergo any kind of psychological treatment served as the control group. In the treatment group, depression, anxiety and QoL (measured respectively with the HADS-D, HADS-A and ALSSQOL-R) were assessed at pre- and post-treatment levels and at 3- and 6-month follow-ups. Statistical mixed-model regression analyses revealed that in the treated group, perceived conditions of anxiety, depression and QoL were significantly stable compared to worsening in the control patients. Interestingly, there were improvements in the QoL domains "Interaction", "Emotion" and "Physical" at the 6-month follow-up. Overall, even if not directly comparable, our current results on support-based counseling, though interesting, seem not to reach the efficacy of a hypnosis-based study in which the observed dimensions were significantly improved with respect to the baseline. The implications of our results from a psychodynamic perspective are highlighted.

Amyotrophic lateral sclerosis (ALS) is a degenerative, rare motor neuron disease mainly affecting the voluntary motor system, characterized by increasing weakness, spasticity and dysarthric speech; cognitive impairment from mild to severe can occur in nearly 50% of cases (Phukan, Pender, & Hardiman, 2007). The ALS crude annual incidence rate in the general European population is 2.16 per 100,000 person years (Logroscino et al., 2010), but a recent odds ratio projection shows that the number of ALS cases across the globe will increase 69% by 2040 (Arthur et al., 2016). Death usually comes within 3–5 years of disease onset from respiratory failure. Prognosis can be extended up to a decade in a locked-in state when patients elect to undergo long-term mechanical ventilation (Vianello et al., 2011). ALS imposes a huge burden on patients' caregivers, leading to extreme distress and burnout (Cipolletta & Amicucci, 2015; Cipolletta, Gammino, Francescon, & Palmieri, 2018; Pagnini et al., 2010).

Despite the gravity of its symptoms, ALS is currently characterized by poor public awareness, and it lacks a timely diagnosis (Chen et al., 2015). Worse, there is currently no effective cure for ALS (Chen et al., 2015; Wrubel, Acree, Goodman, & Folkman, 2009).

From a psychological perspective, the opinion of many authors, including ours, is that such a relentless syndrome implies -even more than common terminal disease- intense reactions to facing one's own death. People with ALS (pALS) must indeed watch their own body slowly die before their mind. In the day-to-day ALS experience, moreover, progressive body paralysis erodes patients' personal autonomy and their own freedom in many dimensions of existence (de Wit et al., 2018).

As for unconscious reactions to such a condition, peculiar defense mechanisms, such as denial (Caputo, 2019; Cipolletta, Gammino, & Palmieri, 2017; Ferro, Riefolo, Nesci, & Mazza, 1987) and splitting (Caputo, 2019; Sakellariou, Boniface, & Brown, 2013), are used by patients in an effort not to be overwhelmed by this emotional tsunami. Patients may also ignore the relevance of the physical, psychological or social aspects of life affected by ALS. This primary defense process, denial, is commonly described in severe medically ill patients as a reaction to the loss of somatic functions, experienced as a secondary object-loss from a psychodynamic perspective (Freyberger & Freyberger, 1994). From a neuroimaging perspective, indeed, the emotional processing of negative valance information seems impaired in pALS (Palmieri et al., 2010).

Splitting mechanisms separate the self from internal object representations unconsciously perceived as threatening (Lichtenberg & Slap, 1973). Namely, Caputo (2019) and Sakellariou et al. (2013) highlight the remarkable presence of such a mechanism in pALS, used to maintain a good self-image as separated from self-image made vulnerable by disease and jeopardized by an incumbent evil.

Explicit psychological reactions to such a condition imply resentment, hate, emotional lability (Palmieri et al., 2009) and suicidal ideation (Palmieri et al., 2010), but also hope (Oster & Pagnini, 2012), and these reactions have been commonly described together with the degradation of empathic traits (Pick, Kleinbub, Mannarini, & Palmieri, 2019). Overall, however, in terms of prevalence, the most reported psychopathological features of ALS are anxiety (values of around 30% up to 70%) and depression (values of around 40% up to 70%; Kurt, Nijboer, Matuz, & Kübler, 2007; Taylor, Wicks, Leigh, & Goldstein, 2010; Wicks et al., 2007).

Finally, perceived quality of life (QoL) among people with ALS is obviously dramatically impaired and, interestingly, not necessarily associated with measures of strength and physical function (Cipolletta et al., 2017; Palmieri et al., 2010).

Although psychotherapy and psychological interventions are suggested as strategies for reducing patient depression and anxiety, coping with the fear of death and improving wellbeing and QoL (Pagnini et al., 2010), there is still a paucity of literature on the efficacy of psychological treatments, and guidelines for their administration are completely lacking (Cerutti et al., 2017). In detail, research on the efficacy of psychological intervention is limited and inconsistent, despite its potential importance, and scientific concern in this direction has been raised (Pagnini, Simmons, Corbo, & Molinari, 2012).

Gould et al. (2015) and Walklet, Muse, Meyrick, and Moss (2016), in their systematic reviews of psychotherapy, pharmacotherapy and psychosocial interventions in the domain of neuromuscular disorders, found only five studies on the psychological treatment of pALS until 2016, and, to the best of our knowledge, no new empirical contributions have been

published since then. The above-mentioned studies are briefly listed in the following paragraph.

Our pilot study in 2012 (Palmieri et al., 2012) demonstrated the feasibility and efficacy of an Ericksonian hypnosis-based intervention on anxiety, depression and QoL in pALS. In a following study (Kleinbub et al., 2015), we replicated this previous research (Palmieri et al., 2012) using a hypnosis-based intervention on a larger sample of pALS, and we longitudinally monitored their anxiety, depression and QoL scores, with strongly encouraging results: patients' anxiety symptoms improved to statistically significant levels immediately post treatment, and this improvement persisted 3 and 6 months after treatment completion. Depression levels also improved immediately post-treatment, but returned to pre-treatment levels at 3 months; the global QoL scores showed a similar trend. Moreover, it is worth noting that an improvement in perceived secondary physical symptomatology immediately after treatment was observed, and a significantly slower functionality loss was found when comparing our treated group to an ALS control group.

Averill and colleagues in 2013 proposed a structured emotional disclosure intervention, showing that the treatment could improve psychological wellbeing in pALS having difficulty expressing their emotions. A few years later, a contribution from Aoun, Chochinov, and Kristjanson (2015) reported that pALS were highly satisfied with brief so-called dignity therapy conceived to alleviate distress in life-limiting illnesses, although they showed no improvement in anxiety, depression or QoL. In 2016, Díaz and colleagues found that adopting the principles of cognitive behavioral therapy in counseling interventions was effective in reducing both anxiety and depression in pALS. More recently, Pagnini et al. (2017) reported a beneficial improvement in QoL, depression and anxiety symptoms and interaction with people in the environment as a result of their randomized control trial of an ALS-specific meditation training for a large sample of pALS.

Although the efficacy of supportive counseling has been proven in many medical conditions, mainly depressive and anxiety symptoms in patients with terminal disease (Manne et al., 2017; Ream, Richardson, & Alexander-Dann, 2006), there are no studies investigating such an intervention in pALS.

From a psychodynamic perspective, as well, supportive counseling could be particularly indicated for severe medically ill patients, as it is considered an eligible treatment to cope with typical defense mechanism processes, such as denial and splitting, which can sometimes become too rigid (Freyberger & Freyberger, 1994; Kleinbub et al., 2015; Palmieri et al., 2010), as happens in other severe physical illnesses (Cramer, 2015), impeding one's ability to accept the unacceptable. Denial, for instance, can be an adaptive strategy in the first phases of the disease to cope with the overwhelming burden of prognosis, but it could become dysfunctional and pathological if it assumes a persistent and frozen posture, thus limiting bargaining and acceptance of the fatal diagnosis (Zimmermann, 2004). Analogously, beyond an immediate protective effect, the splitting mechanism becomes maladaptive, leading to various phenomena of a body–mind disconnection (Caputo, 2019; Sakellariou et al., 2013).

Finally, supportive counseling is typically characterized by a psychoeducational nature as well, and it is useful in demanding diseases, such as ALS, which implies everyday life difficulties in simple tasks, as well, due to progressive muscular weakness.

Considering these premises, the goal of the present study is to propose a supportive counseling treatment for ALS patients that aims to reduce anxiety and depression and to boost various QoL domains.

Thanks to the encouraging results we found in our previous studies on Ericksonian hypnosis-based treatment, we chose person-centered approach inspired to Rogerian theory (Rogers, 1942, 1951) for supportive counseling interventions proposed for patients because of the number of commonalities with Ericksonian hypnosis (Larkin, 2007). These include enhancement of the power to make personal choices, self-defined health-promoting goals, the promotion of awareness of one's own feelings and thoughts and emphasis on the individual's uniqueness.

The present study was structured to compare two specific psychological interventions to reduce suffering and improve wellbeing in pALS, namely Rogerian supportive counseling and hypnosis-based intervention. Briefly, we replicated a previous design that featured four weekly domiciliary sessions and the same questionnaires for depression (Hospital Anxiety and Depression Scale [HADS]-D), anxiety (HADS-A) and QoL (Amyotrophic Lateral Sclerosis-Specific Quality of Life [ALSSQOL-R]), which are considered gold standard measures to evaluate depression, anxiety and QoL in ALS (Pagnini, Manzoni, Tagliaferri, & Gibbons, 2015). No measures of denial and splitting levels in participants were collected; in fact, despite our reflection on supportive counseling indications for pALS in terms of their typical defense mechanisms, there are no satisfying self-report measures for the assessment of such unconscious reactions (Davidson & MacGregor, 1998). HADS-D, HADS-A and ALSSQOL-R scores were employed as dependent variables measured at baseline, at the end of treatment and at 3- and 6-month follow-ups.

Methods

Participants

All participants volunteered and were recruited consecutively via the Motor Neuron Disease Center at Padova University Hospital. Patients diagnosed with probable or confirmed sporadic ALS according to the revised El Escorial criteria (Brooks, Miller, Swash, & Munsat, 2000) were included. Patients with significant neuropsychological impairments (as described in the guidelines of the European Federation of Neurological Societies task force on the diagnosis and management of ALS; Andersen et al., 2012) or concomitant psychiatric or neurological disorders, as well as those using high-dose psychoactive medication, were excluded. Among 40 patients showing interest in the treatment, 21 were considered eligible according to the above-mentioned inclusion and exclusion criteria and underwent supportive counseling treatment. Using the same inclusion criteria, all 15 eligible and interested patients for which treatment was not possible due to logistic reasons were recruited as controls.

Given the rarity of the disease and the lack of comparable data in the literature, the sample size for the study could not be estimated a priori through a power analysis. Instead, we recruited all Motor Neuron Disease Center patients matching our inclusion criteria starting from March 2012. All follow-ups ended by June 2018.

None of the patients involved in the study received any further psychological assistance during the period of observation. This pragmatic trial thus collected data on two groups of

pALS: a group given supportive counseling (n = 21) and a group of untreated controls (n = 15).

In the treatment group, one patient dropped out after 2 months due to a drastic deterioration in his physical condition, and another two dropped out before the 6-month follow-up for the same reason. Three patients in this group died before the 6-month follow-up. All available data were used for all participants. In total, 51 pALS were thus considered in the analysis, among whom 36 were from the current trial and 15 from the previous hypnosis study. Demographic data for all considered pALS are presented in Table 1. All patients were informed of the study's purpose and methods and signed to give their written informed consent to the study protocol, which was approved by the Ethical Committee of the University of Padova and conducted in accordance with the principles of the Declaration Of Helsinki, as revised in 1983. Due to ethical concerns related to the short survival expectancy of pALS, the psychological interventions were started as soon as funding and institutional permission became available. For this reason, the trial was only retrospectively registered and is deposited in the ISRCTN registry with registration number ISRCTN11845385 (doi: 10.1186/ISRCTN11845385).

Procedures

Our supportive counseling group was sampled following pragmatic study principles (Patsopoulos, 2011). All patients underwent a complete neurological examination and an exhaustive neuropsychological assessment about 2 weeks before the first supportive counseling session (or the administration of the first questionnaires to the control group) to exclude pALS with cognitive impairment. We also conducted a preliminary psychological interview to collect motivational and autobiographical details. The supportive counseling intervention consisted of four weekly domiciliary sessions lasting 60 minutes each and was conducted by a psychologist with specific expertise in ALS psychological reactions and management. A second psychologist administered two questionnaires, one on anxiety and depression (HADS) (Zigmond & Snaith, 1983) and another on QoL (the ALSSQOL-Revised [ALSSQOL-R]) (Pagnini & Simmons, 2010; Simmons et al., 2006) at baseline, after completing the treatment and 3 and 6 months after the treatment. The second psychologist took no part in the treatment sessions. The experimental design

Table 1. Clinical characteristics of ALS patients and controls.

	Support			Control			Hypnosis		
	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD
Age (years)	65.5	65.35	8.84	65.0	65.8	8.38	54	55.33	8.72
Months since diagnosis	7.5	8.4	7.62	13	22.27	19.85	11	14.79	11.05
ALSFRS-r*	37	34.48	8.37	41	38.8	7.28	38	33.13	9.88
Gender:	n			n			n		
Female	8			3			8		
Male	13			12			7		
Onset of ALS:									
Bulbar	5			1			4		
Spinal	16			14			11		

*Functional impairments owing to ALS were assessed using the ALS Functional Rating Scale – Revised (ALS-FRS-R; Cedarbaum et al., 1999), which represents the gold standard to evaluate physical decline caused by the disease. Based on activities of daily living, this scale consists of 12 items, each scored from 0 (no movement) to 4 (normal function), encompassing assessment of bulbar, upper-extremity, lower-extremity, and respiratory functions.

and procedure (e.g. number of sessions, length) of this study on supportive counseling treatment replicate those of our previous hypnosis-based intervention on pALS (Kleinbub et al., 2015; Palmieri et al., 2012), as well as the employed assessment measures and the inclusion/exclusion criteria.

The pALS serving as the control group completed the same questionnaires at baseline and at 3 and 6 months without receiving any treatment. Their post-treatment data could not be collected because while the 3-month measures were acquired in the context of the routine hospital examination, the post-treatment assessment was collected via domiciliary visits for the treated patients, and this was unfeasible for most control participants due to logistics.

Supportive counseling treatment

The supportive counseling treatment was inspired by Rogers's person-centered approach (Rogers, 1942, 1951) using the therapist's unconditional positive regard, patient acceptance and genuine empathy as the main tools to help them achieve their potential. In this theoretical framework, in which an individual's potential can be expressed despite the disease, the aims of our supportive counseling were to facilitate patients' active and aware coping with negative thoughts and emotions associated with the physical progression of the disease and to help them accept their feelings and share them with family and friends, eventually counting on their empathic reactions and support. While treatment of each patient followed these principles, given the high influence of individual patients' characteristics on the development of empathic closeness, its delivery was individually tailored from a patient-centered perspective. Although interventions were individually shaped, the general conception of the supportive treatment was to follow three orders of the denial mechanism in terminal diseases (i.e. in the first period after diagnosis, it is used by patients to defend themselves from the initial evidence of the illness; in the second phase, denial is more related to disease implications in everyday life and the loss of vitality; third-order denial involves the effort to cope with the idea of one's own death), as described by Weisman (1972). Great attention to splitting mechanisms was also paid by the counselor. Psychoeducational aspects (e.g. information about noninvasive ventilation vs long-term mechanical ventilation, neurological roots of the emotional lability caused by the disease or national legislation on the will to live) were included in the intervention sessions and tailored to the patients' needs.

Measures

Anxiety and depression

The HADS (Zigmond & Snaith, 1983) is a widely-used, reliable (Bjelland, Dahl, Haug, & Neckelmann, 2002) self-report measure of anxiety and depression. It consists of two subscales with seven items each, which are scored from 0 to 3: the HADS-A assesses anxiety and the HADS-D depression. Among a variety of generic depression scales used in pALS, the content of the HADS items seems less prone to distortions due to the somatic impairments caused by ALS (Pagnini et al., 2015). A specific version of the HADS for motor neuron diseases has also been developed, and its quantitative efficacy was confirmed using Rasch analysis in a study by Gibbons et al. (2011), who proposed the revised scoring method and cutoffs used in the present study.

Quality of life

The ALSSQOL-R (Pagnini & Simmons, 2010; Simmons et al., 2006) was used to assess different dimensions of health-related QoL. It is a 46-item disease-specific questionnaire that uses a Likert scale from 0 to 10, where 0 is the least desirable situation and 10 the most desirable. It consists of six subscales: Negative Emotion, Interaction with People and the Environment, Intimacy, Religiosity, Physical Symptoms and Bulbar Function. The total score, including all the items, was used in our analyses. The ALSSQOL-R was chosen because it provides insight into the psychological aspects, spirituality and social issues associated with the disease (Simmons et al., 2006).

Data analysis

Linear mixed regression models were used to study the interaction between treatment *type* and *time*. Two different analyses were applied because no post-treatment data were available for the untreated controls. A first analysis was run considering the baseline and post-treatment time points in the two intervention groups (supportive counseling and hypnosis) to investigate and compare the pre- and post-treatment effects. A second analysis compared the long-term effects of the two interventions on the control group, considering the data collected at baseline and the 3-month and 6-month follow-ups. No ancillary analyses were performed.

For each analysis, a separate model was fitted for each of the following dependent variables: HADS-A, HADS-D and ALSSQOL-R total scores. Each model used *time* and *treatment* and their interaction as fixed factors and *subject-id* as a random factor to assess adequately the repeated-measure nature of the data. To test the effect of interaction, each model was compared against an identical one without the interaction term using likelihood ratio tests (LRTs). To control for the familywise error rate of our three main outcomes, we used a Bonferroni corrected *alpha* level of 0.0167. For secondary data exploration, a second analysis was also repeated for each of the ALSSQOL-R subscales using an uncorrected alpha level. All analyses were performed with the R statistical software, version 3.3.1 (R Core Team, 2018). All models were fitted using the lme4 package (Bates, Mächler, Bolker, & Walker, 2014). The conditional R_GLMM2 of the models were computed with the MuMIn package (Barton, 2009) and used to calculate Cohen's F^2 for the interaction terms.

Results

We investigated the long-term performance of supportive counseling compared with untreated controls, examining the data at baseline and at two follow-ups of 3 and 6 months after treatment completion. The results (see Figure 1) showed that the patients in the counseling group presented higher HADS-D and HADS-A scores at both baseline and 3 months. These scores remained constant at the 6-month follow-up, whereas patients in the control group reported a stark deterioration. The *group × time* interaction in the regression analyses did not reach significant level on the HADS scores, though.

ALSSQOL-R total scores, instead, showed a constant improvement in the counseling group, albeit of a moderate magnitude, whereas in the control group, the scores declined at the 3- and 6-month follow-ups. Regression analyses confirmed this observation, reporting a significant *group × time* interaction [$\chi^2(2) = 8.802$, $p = .012$] with a small effect size ($F^2 = 0.099$).
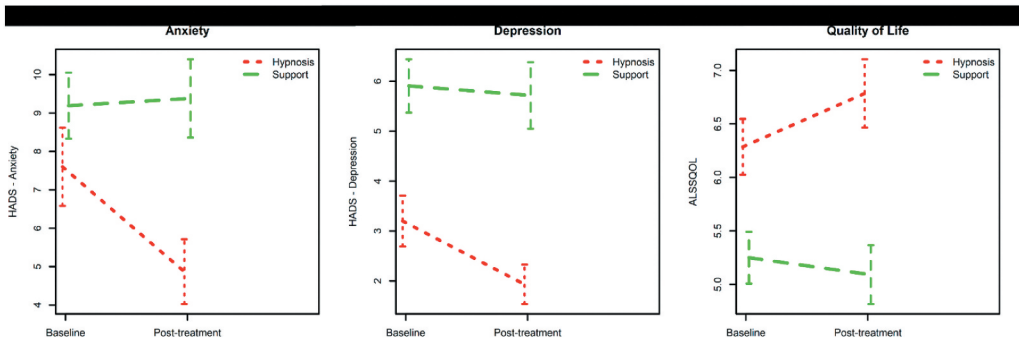
Figure 1. Pre-post treatment comparison.
The three panels show the average change after the two types of treatment (supportive counseling and hypnosis) from the baseline to the post-treatment assessment in the three main outcome measures: anxiety, depression and global QoL. The error bars represent the standard error of the mean.
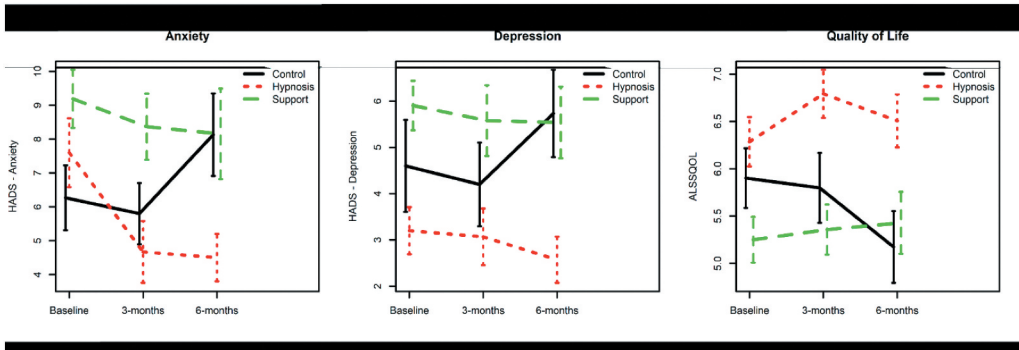
Figure 2. Longitudinal comparison.
The three panels represent the *treatment* x *time* interactions of supportive counseling, hypnosis and no treatment at the baseline, and at the 3- and 6-month follow-ups for the three main outcome measures: anxiety, depression and global QoL. The error bars represent the standard error of the mean.

The trends of the various ALSSQOL-R subscales are shown in Figure 2. All regression parameters are reported in Table 2.

Discussion

Our pragmatic study aimed to assess the efficacy of empathy-based supportive counseling on pALS. The literature on psychological interventions in ALS has produced fascinating but scarce and hardly comparable results (Aoun et al., 2015; Averill, Kasarskis, & Segerstrom, 2013; Díaz et al., 2016; Kleinbub et al., 2015; Pagnini et al., 2017; Palmieri et al., 2012; for reviews on this topic, see Gould et al., 2015; Walklet et al., 2016). These few studies differed in terms of their psychological intervention approaches, methods and measures used to assess pALS' wellbeing. Because our previous hypnosis-based intervention showed interesting results in terms of anxiety, depression, QoL and physical symptoms (Kleinbub et al., 2015; Palmieri et al., 2012), we replicated the same experimental design in our pragmatic study

Table 2. Baseline to post-treatment regression analysis.

		Estimate	SE	t	Random SD (residual)	Interaction factor LRT	Interaction factor F2
HADS-A	Intercept	7.6	1.045	7.274	3.20 (2.47)	$\chi^2(1) = 5.95$	0.151
	Time	−2.733	0.903	−3.026		$p = .015$*	††
	Hypnosis	1.59	1.368	1.163			
	Time X hypnosis	2.924	1.183	2.472			
HADS-D	Intercept	3.2	0.621	5.152	2.10 (1.18)	$\chi^2(2) = 3.68$	0.078
	Time	−1.267	0.43	−2.948		$p = .055$	†
	Hypnosis	2.705	0.813	3.326			
	Time X hypnosis	1.076	0.563	1.913			
ALSSQoL-R Total	Intercept	6.286	0.301	20.907	1.06 (0.48)	$\chi^2(2) = 7.71$	0.205
	Time	0.499	0.176	2.829		$p = .005$*	††
	Hypnosis	−1.037	0.394	−2.633			
	Time X hypnosis	−0.658	0.231	−2.85			

* $p < 0.0167$; † $F^2 \geq 0.02$, †† $F^2 \geq 0.15$, and ††† $F^2 \geq 0.35$ represent small, medium, and large effect sizes, respectively (Cohen, 1988).

based on empathy-based supportive counseling. Our findings did not show clear significant effect of supportive counseling in patients when comparing pre- and post-treatment levels in all variables considered, i.e. depression, anxiety and QoL as evaluated according to the HADS-D, HADS-A and ALSSQOL-R. However, it is worth noting that interesting findings arose and they reached significant levels, comparing trajectories of patients and controls. First, treated patients showed generally stable scores in all measure outcomes, contrary to the control group, which reported a stark deterioration in all assessed domains. In our clinical opinion, the tendency to maintain stability in psychological symptoms is considered a quite satisfying outcome in such a devastating, progressive disease. Surprisingly, the supportive counseling group's QoL scores gradually improved some months after the end of treatment, reaching a statistically significant difference compared to non-treated controls at the 6-month follow-up. Namely, ALSSQOL-R subscales tended to show a gradual improvement up to the 6-month follow-up in the scores of the "Interaction", "Emotion" and "Physical" domains, compared to the clear decrease in these subscales in the control group.

The reason QoL gradually improved over time, becoming significantly better at the 6-month follow-up, is complex to identify. Many variables implicated in the treatment could converge in this result. On the one hand, the most immediate explanation might be that such an improvement is a long-term consequence of psychoeducational elements included in supportive counseling.

This kind of treatment, on the other hand, traditionally operates to manage defense mechanisms, as they are conceived as a resource for coping with the most challenging life events. As mentioned in theoretical premises, in pALS, defenses should sometimes be reinforced, but other times must be softened to avoid jeopardizing the patient's acceptance of their declining physical condition.

Particular attention should be devoted to improving the ALSSQOL-R subscale dedicated to physical impairment. Such an improvement should be interpreted only in light of defense mechanisms. Consistently, with object relations theory (Schattner & Shahar, 2011), indeed, ALS, as well as all terminal diseases, may represent a relentless object loss – the body – that must be recognized, accepted and worked through (D'Alberton, Nardi, & Zucchini, 2012). Consequently, as mentioned above, the individual may resort to denial and splitting mechanisms, which, if too rigid, could interrupt mind–body integration, thus implying

perceptions of the body as a "separate object" that can succumb to the disease without jeopardizing the self, which can remain safe. The adoption of these unconscious responses could be explained as a strategy to cope with the perceived body–mind disconnection, because "the patient lives a progressive destructuration of his body image which has been integrated during the early stages of the development of the self" (Ferro et al., 1987, p. 315).

In our opinion, the reason the "Physical" symptoms subscale of the ALSSQOL-R showed a greater improvement with respect to the other QoL subscales is identifiable in the above mentioned arguments: the capacity to repair internal objects and rely on psychic resources to reframe one's condition should have been favored by supportive counseling treatment (Schattner, Shahar, & Abu-Shakra, 2008; Shahar & Lerman, 2013). This would allow for the integration with previously mentioned denied or split patients' body representation.

Analogous results were found in our previous studies on hypnosis-based treatment for pALS (Kleinbub et al., 2015; Palmieri et al., 2012), in which a significant anxiety reduction and QoL improvement, as well as a discrete improvement in depression (which anyhow failed to reach statistical significance), were prompted when comparing patients' pre- and post-treatment levels. Moreover, hypnosis continued to reduce anxiety and improve QoL at both the 3- and 6-month follow-ups, while the supportive counseling group showed a significant improvement only at 6 months and only for QoL.

In other words, although we are referring to two different studies, but with the same experimental design, hypnosis seems more effective than supportive counseling in maintaining or further ameliorating the anxiety and QoL levels recorded immediately after the treatment.

Overall, the apparent difference in the efficacies of the two treatments could relate to their distinctive features with respect to the specificities of ALS. Indeed, despite the many commonalities of these two approaches (Larkin, 2007), some relevant theoretical and pragmatic distinctions could have influenced our efficacy results.

On the theoretical side, hypnosis directly focuses on unconscious associations between previous unique biographical patterns and perceptions and novel ones, operating via a specific mechanism capable of bypassing them, much more so than counseling, which mainly operates at the conscious level, or changing the individual's ego defenses, which is crucial in ALS, at the unconscious level (Erickson & Rossi, 1976).

On the pragmatic side, better results obtained by hypnosis-based treatment could be explained by its two advantages over supportive counseling for pALS. First, it can be administered without any intense verbal exchange between patient and therapist. Interactive conversation is often difficult due to the gradual bulbar impairment caused by the disease, and it ultimately becomes almost impossible as the patient evolves toward a locked-in state (Kurt et al., 2007). Second, hypnosis has a well-established ability to induce muscle relaxation (for a review, see Brugnoli, 2016). Muscle relaxation is another feature of hypnosis that could be crucial in treating pALS, who can suffer from muscle pain, cramps and fasciculation (Chiò, Mora, & Lauria, 2017).

Generally, we have proposed both psychodynamic and pragmatic theoretical motivations that could explain such a remarkable difference between empathy-based support treatment and hypnosis-based treatment. However, it is relevant to consider that while hypnosis-based treatment shows promise in becoming a possible eligible treatment for ALS, the difference in training for hypnosis compared to supportive counseling is significant and highly unbalanced in terms of the complexity and time necessary to become a hypnosis expert

operator. These elements should be evaluated when drawing the expected guidelines for psychological intervention in ALS.

Our results and related interpretations should be considered also from a broader psychological perspective which can impose some caveats. For instance, although depression, anxiety and QoL, as well as individual personality and physical impairments, are closely connected in a dynamic and mutually causative way in pALS (Cipolletta et al., 2017), individual characteristics that may have contributed to the treatment outcomes have not been specifically investigated, as the small size of our groups limited this kind of analysis. Moreover, although symptomatological questionnaires (HADS-A, HADS-D and ALSSQOL-R) are composed by closed-ended questions, a tiny bias could be prompted by the fact that the psychologist who administered questionnaires was not blind to the patients' group condition.

From methodological perspective, sample size should be increased, and the role of gender in the outcome score should be considered, as it has been yet demonstrated as crucial in cognitive impairment in ALS on the one hand (Palmieri et al., 2015) and in perceived psychotherapy results on the other (Lebow, 1983). Another methodological limitation is that the three groups demonstrated significant baseline differences in demographic variables and levels of depression, anxiety and QoL due to the pragmatic recruitment study design and the rare nature of this disease. Thus, we cannot exclude the possibility that some patients were more receptive to treatment due to having an improved baseline condition.

Despite these limitations, our findings, showing that a supportive counseling intervention was efficacious in promoting pALS' wellbeing, albeit not as much as hypnosis-based treatment, represent a contribution to the identification of an appropriate psychological treatment for pALS. There are numerous urgent reasons for pursuing this crucially important goal, including the fact that the mortality risk in pALS is strongly and negatively influenced by distress, psychopathological symptoms and poor QoL (Johnston et al., 1999; Krampe et al., 2008; McDonald, Wiedenfeld, Hillel, Carpenter, & Walter, 1994; Pizzimenti, Aragona, Onesti, & Inghilleri, 2013), whereas positive life attitudes reportedly contribute to extending life expectancy in pALS (Krampe et al., 2008; Pagnini, Phillips, Bosma, Reece, & Langer, 2015). Namely, future studies shall continue the investigation of potential ways to help patients connect with their affective and somatic dimensions. One such approach, for instance, could be exploring the synchronization of physiological activity (Kleinbub et al., 2020) between pALS and psychologists, a recent development that has been reported efficacious in assessing the quality of the therapeutic relationship (Cipolletta et al., 2018; Kleinbub et al., 2019) and has been proposed as a potential aid in clinical practice (Gennaro, Kleinbub, Mannarini, Salvatore, & Palmieri, 2019). Further studies are warranted in such a direction.

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