

# A survey on self-assessed well-being in a cohort of chronic locked-in syndrome patients: happy majority, miserable minority



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## ABSTRACT

**Objectives:** Locked-in syndrome (LIS) consists of anarthria and quadriplegia while consciousness is preserved. Classically, vertical eye movements or blinking allow coded communication. Given appropriate medical care, patients can survive for decades. We studied the self-reported quality of life in chronic LIS patients.

**Design:** 168 LIS members of the French Association for LIS were invited to answer a questionnaire on medical history, current status and end-of-life issues. They self-assessed their global subjective well-being with the Anamnestic Comparative Self-Assessment (ACSA) scale, whose +5 and –5 anchors were their memories of the best period in their life before LIS and their worst period ever, respectively.

**Results:** 91 patients (54%) responded and 26 were excluded because of missing data on quality of life. 47 patients professed happiness (median ACSA +3) and 18 unhappiness (median ACSA –4). Variables associated with unhappiness included anxiety and dissatisfaction with mobility in the community, recreational activities and recovery of speech production. A longer time in LIS was correlated with happiness. 58% declared they did not wish to be resuscitated in case of cardiac arrest and 7% expressed a wish for euthanasia.

**Conclusions:** Our data stress the need for extra palliative efforts directed at mobility and recreational activities in LIS and the importance of anxiolytic therapy. Recently affected LIS patients who wish to die should be assured that there is a high chance they will regain a happy meaningful life. End-of-life decisions, including euthanasia, should not be avoided, but a moratorium to allow a steady state to be reached should be proposed.

## INTRODUCTION

Locked-in syndrome (LIS) is defined by quadriplegia (or quadriparesis) and aphonia (or severe hypophonia) with a primary mode of communication by eye movements or

## ARTICLE SUMMARY

### Article focus

- To describe chronic locked-in patients' subjective well-being and identify factors that are associated with high or low overall subjective well-being.
- To evaluate the degree to which locked-in patients are able to return to a normal life.
- To assess the views of locked-in patients on end-of-life issues.

### Key messages

- Although most chronic locked-in patients self-report severe restrictions in community reintegration, the majority profess good subjective well-being, in line with the notion that patients with severe disabilities may report a good quality of life despite being socially isolated or having major difficulties in activities of daily living.
- 28% of our locked-in patients declared unhappiness. Variables associated with unhappiness were dissatisfaction with mobility in the community, with recreational activities and with capacity to face up to life events. Shorter time in locked-in, anxiety and non-recovery of speech production were also associated with unhappiness.
- The principal clinical conditions for requests for euthanasia or physician-assisted death to be legally valid are unbearable suffering and irreversibility of the situation; however, irreversibility cannot be ascertained until the patient's subjective well-being has reached a steady state, which may take up to a year.

blinking.<sup>1</sup> Most often LIS is caused by an acute (vascular) anterior pontine brainstem lesion. The syndrome can be subdivided on the basis of motor disability<sup>2</sup>: 'classic' LIS is characterised by quadriplegia and aphonia with coded communication by vertical eye movement or blinking; 'incomplete' LIS patients have remnants of voluntary motion other than vertical eye movement; and 'total' LIS is defined by complete immobility,

## Article summary

## Article focus

## Strengths and limitations of this study

- This study is the largest survey of chronic locked-in syndrome patients ever performed and assesses the patients' own self-assessed quality of life, general well-being and end-of-life wishes. The clinical and ethical implications are evident and important for the medical community at large.
- We also identify variables associated with unhappiness that can be improved and permit evidence-based policy changes in the management of these challenging and vulnerable patients.
- Our study had a low response rate and may be subject to selection bias, and the results might therefore not be representative of chronic LIS patients in general since all participants were members of a patient association (ie, Association of Locked-in Syndrome, ALIS), indicating a stable condition and possibly a degree of social integration. Nonetheless, as discussed in the article, quality of life research has many methodological pitfalls, especially in this low-incidence pathology with limited and difficult communication.

including all eye movements. Once a patient is medically stabilised in LIS, the 10-year survival is more than 80%.<sup>3</sup> With intensive rehabilitation,<sup>4</sup> many classic LIS patients may evolve to incomplete LIS, with voluntary control of the head, fingers or foot and sometimes recovery of speech production.<sup>5</sup> Nearly all chronic LIS patients remain dependent on others for activities of daily living. Physicians and caregivers may tend to consider that LIS patients will die anyway<sup>3</sup> or would prefer to die if they knew what the clinicians (think they) know.<sup>6</sup> On the other hand, it is known that people with severe persistent disability tend to self-report good subjective well-being (SWB)—the 'disability paradox'.<sup>7</sup> A previous study assessing the quality of life (QoL) in 15 LIS patients showed that they reported normal mental and personal general health despite maximal restriction in physical activities.<sup>8</sup> The objective of this study is to describe chronic LIS patients' SWB and their views on end-of-life issues, and to identify factors that are associated with high or low overall SWB.

## METHODS

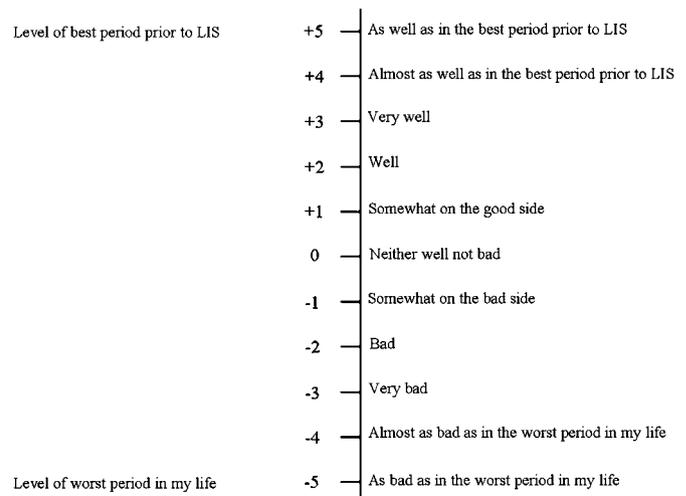
## Participants and procedures

In collaboration with the French association for LIS (ALIS; <http://alis-asso.fr/>), a non-profit association created in 1997 to help LIS patients and their families, 168 patients who were members of LIS were invited (in January 2008) by letter to fill in a structured questionnaire, aided by the patient's proxy. The questionnaire included items about socio-demographic (age, gender, educational level, place and condition of living, religiosity, net monthly household income), clinical (aetiology and duration of LIS, level of speech production and motor recovery) and QoL and SWB variables. We used the French postal version of the Reintegration to Normal Living Index (RNLI),<sup>9–12</sup> which evaluates the

degree to which a patient has been able to return to a normal life. The RNLI is an 11-item scale that covers areas such as participation in recreational and social activities and movement within the community, and how comfortable the individual is in his or her role in the family and with other relationships. Given the specific constraint of eye-coded communication in the surveyed LIS patients, instead of the visual analogue scale<sup>11</sup> a 4-point Likert scale was used as described elsewhere,<sup>13</sup> where a value of 1 was assigned to 'no', 2 to 'rather no', 3 to 'rather yes' and 4 to 'yes'. The scores were normalised to 100, with a score of 100 indicating that the participants were fully satisfied, scores of 60–99 indicating mild to moderate restrictions in self-perceived community reintegration, and scores less than 60 indicating severe restrictions in self-perceived community reintegration, as previously reported.<sup>14</sup> Overall SWB was rated by means of the Anamnestic Comparative Self-Assessment (ACSA)<sup>15</sup> scale, whose biographical +5 and –5 scale anchors were the patients' memories of the best period in their life before LIS and their worst period ever (figure 1). Participants were also asked about the presence of depressive symptoms (yes, no), pain and anxiety (none, moderate, extreme) and end-of-life issues: suicidal thoughts (never, occasionally, often), resuscitation in case of cardiac arrest (yes, no) and euthanasia (envisaged, never envisaged). Completion of the anonymous questionnaire was voluntary and taken as consent for participation in the survey. The study was approved by the ethics committee of the Faculty of Medicine of the University of Liège.

## Statistical analysis

Data were analysed using Stata 10.0 (Stata, 2007, Stata Statistical Software, TX, USA). The normality distribution of continuous variables was assessed using Shapiro–Wilk tests. For the descriptive analyses, we used subject counts and percentages for categories, calculating mean±SD or median with IQR for continuous



**Figure 1** Anamnestic Comparative Self-Assessment scale. LIS, locked-in syndrome.

variables. Only questions with a response rate above 70% were deemed representative of the population and considered for further analyses. ACSA ratings were divided into happy (ratings 0 to 5) and unhappy (ratings -1 to -5). Univariate associations between the dependent variable happy/unhappy and the RNLI and end-of-life questions co-variables were assessed using the Student t test, Wilcoxon or  $\chi^2$  tests as appropriate. Multivariable backward stepwise logistic regression was used to assess the associations between happiness status and the significant covariates selected by the univariate analysis. Analyses were performed using casewise deletion. Differences were considered as significant at  $p < 0.05$ .

## RESULTS

A total of 168 LIS patients were invited to fill in the structured questionnaire. Seventy seven patients did not reply (46%). Among the 91 LIS patients who replied, 26 responses (29%) had missing RNLI and/or ACSA data and were excluded: five subjects gave ACSA ratings but failed to answer RNLI questions and 21 failed to report ACSA ratings. The included sample hence consisted of 65 patients (figure 2). LIS patients who failed to report QoL and/or SWB ( $n=26$ ) were less educated ( $p=0.009$ ) and had more physical pain ( $p=0.009$ ) compared to LIS patients included in the QoL and SWB study sample ( $n=65$ ). Other socio-demographic, physical and functional variables including age, duration in LIS, living at home or with a partner, income, recovery of speech production or limb mobility were not different between QoL/SWB non-respondents and respondents (table 1). The socio-demographic characteristics of the 65 LIS patients included in our sample are shown in table 2. All had chronic LIS (>1 year after the insult; median 8 years, range 1–28 years) following a brainstem vascular accident. The majority lived at home (64%), had a spouse or partner (64%) and were religious (70%). About half (55%) had recovered some speech and 70% had recovered some limb mobility.

Overall SWB, as measured by the ACSA scale, permitted the two subpopulations to be disentangled: 72% of LIS patients declared happiness (ACSA rating  $\geq 0$ , median +3) and 28% unhappiness (ACSA rating  $< 0$ , median -4) (figure 3). As assessed by the RNLI, 51% of the sampled LIS patients reported severe restrictions

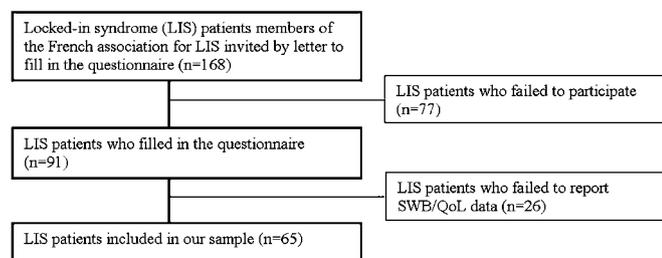
and 49% reported mild to moderate restrictions in self-perceived overall community reintegration. Most (82%) were comfortable with personal relationships, but only 21% were engaged most of the day in activities which they considered important. Only a minority were dissatisfied with their participation in recreational (12%) or social (40%) activities.

The happy and unhappy groups did not differ regarding socio-demographic, physical and functional variables including religion, living at home or with a partner, income, education, physical care and feeling comfortable in the company of others (table 2). Depression, suicidal ideas, consideration or wish for euthanasia and the wish not to be resuscitated in case of cardiac arrest were significantly more frequent in the unhappy group. Variables associated with unhappiness were dissatisfaction with mobility in the community, with recreational activities and with the capacity to deal with life events. Shorter time in LIS, anxiety and non-recovery of speech production were also associated with unhappiness. Only half of the respondents stating happiness wished to be resuscitated in case of cardiac arrest and this rate was as low as 14% among the unhappy respondents ( $p=0.011$ ) (table 2). Multivariate logistic regression showed that the variables associated with happiness were time spent in LIS ( $p=0.007$ ), absence of anxiety ( $p=0.032$ ) and recovery of speech production ( $p=0.013$ ) (table 3).

## DISCUSSION

It is important to stress that our study may be subject to selection bias given that only 91 of 168 invited patients participated in the study (54%). The patients who did not return the questionnaire may be those with the lowest QoL. Therefore, our results might not be representative of chronic LIS patients in general. All participants were members of a patient association (ie, the French Association of LIS), indicating a stable condition and possibly a degree of social integration.<sup>16</sup> Given the dependence of LIS participants on the help of a caregiver for communication of the survey answers, a dependency relationship, social desirability<sup>17</sup> or 'self-presentation'<sup>18, 19</sup> may also have biased some responses, despite a written recommendation not to allow helpers influence responses. Patients with a lower educational level and more pain were under-represented among those answering the QoL questions. This might also have resulted in overestimation of QoL rates in our LIS patients as low educational level<sup>6, 20</sup> and presence of pain are inversely associated with satisfaction with QoL.<sup>21–23</sup> In sum, some methodological constraints may have biased the SWB ratings of our patients and most biases were likely to result in overestimations of SWB.

A recurrent problem in QoL research<sup>19</sup> is the possible relativity bias or response shift, by which, for example, patients with severe chronic conditions tend to assess their QoL relative to peers or given the circumstances. This problem tends to invalidate comparisons of SWB



**Figure 2** Participation. LIS, locked-in syndrome; QoL, quality of life; SWB, subjective well-being.

**Table 1** Socio-demographic and disease characteristics of LIS respondents versus non-respondents to the RNLI and ACSA

	LIS patients included in our sample (N=65)	LIS patients who failed to report RNLI/ACSA (N=26)	p Value
Mean age±SD (years)	49±11	52±12	0.46
Male gender	43/63 (68%)	16/26 (61%)	0.72
Mean duration in LIS (years), median (IQR)	8 (5–10)	7 (4–9)	0.60
Educational level: university or college (vs high school or lower)	25/56 (45%)	3/21 (14%)	0.009
Net monthly household income ≥€2500 (vs <€2500)	20/53 (38%)	5/24 (21%)	0.13
Place of living: home (vs institution)	38/59 (64%)	18/26 (69%)	0.65
Living with spouse or partner (vs single)	36/56 (64%)	15/25 (60%)	0.93
Religious (vs non-religious)	40/57 (70%)	21/26 (81%)	0.3
Recovery of speech production			0.99
None	26/58 (45%)	11/23 (48%)	
Words	11/58 (19%)	5/23 (22%)	
Sentences	21/58 (36%)	7/23 (30%)	
Recovery of some limb mobility	39/56 (70%)	14/23 (61%)	0.59
Suicidal thoughts			0.56
Never	40/59 (68%)	16/20 (80%)	
Occasionally	14/59 (24%)	3/20 (15%)	
Often	5/59 (8%)	1/20 (5%)	
Anxiety			0.47
No	20/61 (33%)	8/22 (36%)	
Moderate	33/61 (54%)	9/22 (41%)	
Extreme	8/61 (13%)	5/22 (23%)	
Pain			0.009
None	32/59 (54%)	4/21 (19%)	
Moderate	25/59 (42%)	14/21 (67%)	
Extreme	2/59 (4%)	3/21 (14%)	
Euthanasia			0.22
Envisaged	31/59 (53%)	6/19 (32%)	
Never envisaged	28/59 (47%)	13/19 (68%)	
Depression			0.66
Yes	8/60 (13%)	3/17 (18%)	
No	56/60 (87%)	14/17 (82%)	

ACSA, Anamnestic Comparative Self-Assessment Scale; LIS, locked-in syndrome; RNLI, Reintegration to Normal Living Index.

between groups.<sup>24</sup> Such relativity biases may result in rather similar responses across objectively very dissimilar disease groups, and even between healthy and diseased people,<sup>25</sup> including those with spinal cord injury.<sup>26</sup> We have therefore chosen to employ the ACSA scale, a self-anchored scale whose upper limit here was the memory of the best period in the patient's life experience before their LIS state. A strength of the ACSA methodology is that by virtue of its biographical references, it affords a practical compromise between the hedonic and the eudaimonic philosophies of QoL, allowing the respondent to choose between the two perspectives, or to take both into account.<sup>27</sup> This internal standard of the ACSA reduces the likelihood of peer relativity or 'under-the-circumstances' responses.<sup>28</sup> However, the retrospective anchoring of the ACSA scale also has a drawback. Paraplegic patients may recall their past as happier than do controls, a phenomenon called the 'nostalgia effect'.<sup>29</sup> If this applies in LIS, it would have tended to depress the ratings of current SWB with the ACSA. This said, some authors have played down relativity biases, arguing that

'given the circumstances' responses of disabled people must be taken at face value and that there is no such thing as a disability paradox.<sup>30</sup>

Given these limitations, our results show that most chronic LIS patients self-report severe restrictions in community reintegration, in line with previous studies in paraplegia following spinal cord injury.<sup>16, 31</sup> Nevertheless, the majority of our sample profess 'good' SWB. This is in line with the notion that patients with severe disabilities may report a good QoL despite being socially isolated or having major difficulties in activities of daily living.<sup>7, 32</sup> That some LIS patients self-report happiness may suggest that they have succeeded in adapting to their condition of extreme physical disability. According to Cummins' theory of SWB, their homeostatic resources may have overcome even the formidable challenge of LIS.<sup>33</sup> Our results hence underscore the strength of homeostatic processes of adaptation to chronic (often definitive) extreme disability.

The 'happy' subgroup of LIS survivors may indeed be those capable of high flexibility and plasticity who have

**Table 2** LIS patients' socio-demographic, disease characteristics, quality of life and end-of-life data in unhappy (ACSA ratings <0) versus happy (ACSA ≥0) respondents

	All patients (N=65)	Unhappy (ACSA <0) (N=18)	Happy (ACSA ≥0) (N=47)	p Value
Mean age±SD (years)	49±11	50±10	49±12	0.571
Male gender	43/63 (68%)	12/18 (67%)	31/45 (69%)	0.864
Mean duration in LIS* (years), median (IQR)	8 (5–10)	7 (3–8)	9 (5–13)	0.005
Educational level: university or college (vs high school or lower)	25/56 (45%)	5/16 (31%)	20/40 (50%)	0.197
Net monthly income ≥€2500 (vs <€2500)	20/53 (38%)	4/13 (30%)	16/40 (40%)	0.547
Place of living: home (vs institution)	38/59 (64%)	9/17 (53%)	29/42 (69%)	0.247
Living with spouse or partner (vs single)	36/56 (64%)	9/16 (56%)	27/40 (67%)	0.431
Religious (vs non-religious)	40/57 (70%)	13/16 (81%)	27/41 (66%)	0.240
Recovery of speech production*				
None	26/58 (45%)	10/16 (63%)	16/42 (38%)	0.049
Words	11/58 (19%)	4/16 (25%)	7/42 (17%)	
Sentences	21/58 (36%)	2/16 (12%)	19/42 (45%)	
Recovery of some limb mobility	39/56 (70%)	10/17 (59%)	29/39 (74%)	0.252
Reintegration to Normal Living Index items				
I move around my living quarters as I feel necessary				
Yes	23/60 (38%)	6/17 (35%)	17/43 (40%)	0.453
Rather yes	13/60 (22%)	2/17 (12%)	11/43 (26%)	
Rather no	10/60 (17%)	3/17 (18%)	7/43 (16%)	
No	14/60 (23%)	6/17 (35%)	8/43 (18%)	
I move around my community as I feel necessary*				
Yes	6/59 (10%)	0/18 (0%)	6/41 (15%)	0.042
Rather yes	16/59 (27%)	4/18 (22%)	12/41 (29%)	
Rather no	14/59 (24%)	3/18 (17%)	11/41 (27%)	
No	23/59 (39%)	11/18 (61%)	12/41 (29%)	
I am able to take trips out of town as I feel necessary				
Yes	17/57 (30%)	3/17 (18%)	14/40 (35%)	0.298
Rather yes	13/57 (23%)	3/17 (18%)	10/40 (25%)	
Rather no	7/57 (12%)	2/17 (11%)	5/40 (13%)	
No	20/57 (35%)	9/17 (53%)	11/40 (27%)	
I am comfortable with how my self-care needs (dressing, feeding, toileting, bathing) are met				
Yes	36/59 (61%)	10/18 (56%)	26/41 (64%)	0.292
Rather yes	16/59 (27%)	4/18 (22%)	12/41 (29%)	
Rather no	3/59 (5%)	1/18 (6%)	2/41 (5%)	
No	4/59 (7%)	3/18 (16%)	1/41 (2%)	
I spend most of my days occupied in work activity that is necessary or important to me				
Yes	8/60 (13%)	1/18 (5%)	7/42 (17%)	0.390
Rather yes	5/60 (8%)	2/18 (12%)	3/42 (7%)	
Rather no	7/60 (12%)	1/18 (5%)	6/42 (14%)	
No	40/60 (67%)	14/18 (78%)	26/42 (62%)	
I am able to participate in recreational activities (hobbies, crafts, sports, reading, television, games, computers, etc) as I want to*				
Yes	35/61 (57%)	8/18 (44%)	27/43 (63%)	0.028
Rather yes	18/61 (31%)	4/18 (22%)	14/43 (33%)	
Rather no	2/61 (3%)	1/18 (6%)	1/43 (2%)	
No	6/61 (9%)	5/18 (28%)	1/43 (2%)	
I participate in social activities with family, friends and/or business acquaintances as is necessary or desirable to me				
Yes	22/60 (37%)	5/18 (28%)	17/42 (40%)	0.113
Rather yes	14/60 (23%)	4/18 (2%)	10/42 (24%)	
Rather no	9/60 (15%)	1/18 (6%)	8/42 (19%)	
No	15/60 (25%)	8/18 (44%)	7/42 (17%)	
I assume a role in my family which meets my needs and those of my family members				
Yes	25/59 (42%)	8/18 (44%)	17/41 (41%)	0.396
Rather yes	21/59 (36%)	4/18 (22%)	17/41 (41%)	
Rather no	5/59 (8%)	2/18 (12%)	3/41 (8%)	
No	8/59 (14%)	4/18 (22%)	4/41 (10%)	

Continued

Table 2 Continued

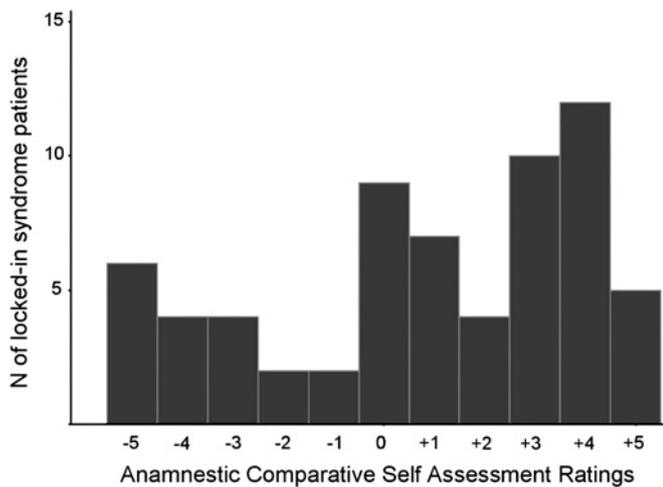
	All patients (N=65)	Unhappy (ACSA <0) (N=18)	Happy (ACSA ≥0) (N=47)	p Value
In general I am comfortable with my personal relationships				
Yes	32/61 (52%)	9/18 (50%)	23/43 (53%)	0.884
Rather yes	18/61 (30%)	5/18 (28%)	13/43 (30%)	
Rather no	4/61 (7%)	1/18 (5%)	3/43 (7%)	
No	7/61 (11%)	3/18 (17%)	4/43 (10%)	
In general I am comfortable with myself when I am in the company of others				
Yes	27/60 (45%)	7/18 (39%)	20/42 (48%)	0.293
Rather yes	19/60 (31%)	4/18 (22%)	15/42 (36%)	
Rather no	7/60 (12%)	3/18 (17%)	4/42 (9%)	
No	7/60 (12%)	4/18 (22%)	3/42 (7%)	
I feel that I can deal with life events as they happen*				
Yes	20/60 (33%)	6/18 (33%)	14/42 (33%)	0.022
Rather yes	18/60 (30%)	3/18 (17%)	15/42 (36%)	
Rather no	12/60 (20%)	2/18 (11%)	10/42 (24%)	
No	10/60 (17%)	7/18 (39%)	3/42 (7%)	
Depression, anxiety and pain				
Depression*				
Yes	8/60 (13%)	5/18 (28%)	3/42 (7%)	0.040
No	52/60 (87%)	13/18 (72%)	39/42 (93%)	
Anxiety*				
No	20/61 (33%)	5/18 (28%)	15/43 (35%)	0.015
Moderate	33/61 (54%)	7/18 (39%)	26/43 (60%)	
Extreme	8/61 (13%)	6/18 (33%)	2/43 (5%)	
Pain				
No	32/59 (54%)	10/18 (56%)	22/41 (54%)	0.071
Moderate	25/59 (43%)	6/18 (33%)	19/41 (46%)	
Extreme	2/59 (3%)	2/18 (11%)	0/41 (0%)	
End-of-life issues				
Resuscitation in case of cardiac arrest*				
Yes	23/55 (42%)	2/14 (14%)	21/41 (51%)	0.011
No	32/55 (58%)	12/14 (86%)	20/41 (49%)	
Euthanasia*				
Envisaged	31/59 (53%)	12/16 (75%)	19/43 (44%)	0.032
Never envisaged	28/59 (47%)	4/16 (25%)	24/43 (56%)	
Suicidal thoughts*				
Never	40/59 (68%)	9/17 (54%)	31/42 (74%)	0.040
Occasionally	14/59 (24%)	4/17 (23%)	10/42 (24%)	
Often	5/59 (8%)	4/17 (23%)	1/42 (2%)	

\*Significant variables identified by the univariate analyses comparing unhappy versus happy with related p values. ACSA, Anamnestic Comparative Self-Assessment Scale; LIS, locked-in syndrome.

fully succeeded in recalibrating, reprioritising and reorienting their needs and values, whereas the low raters cope poorly because they cannot shed the needs and values from their previous life. Because such an adaptation process is lengthy, this hypothesis is consistent with the observed positive association of SWB with duration of time in LIS, corroborating previous studies on QoL in spinal cord injury patients.<sup>31 34</sup> However, the direction of causality might be otherwise if unhappiness and its correlates, by whatever mechanisms, reduce survival. Unhappy patients may be more susceptible to complications, these may be treated less vigorously and more end-of-life decisions may be made. The association between a long time in LIS and happiness would then be an effect of selection by attrition.

The second finding is that some LIS patients self-report a state of unhappiness. Depression, suicidal

ideas and a wish not to be resuscitated were associated with unhappiness, but are most probably co-variables of unhappiness rather than causal factors. The identified predictors of SWB in LIS differed somewhat from those previously reported in traumatic brain or spinal cord injury.<sup>35 36</sup> Living conditions appear less determining for SWB than in spinal cord injury, possibly because in LIS expectations are lower. In our LIS patients, partner relationships were also not correlated with SWB, unlike in traumatic spinal cord or brain injury<sup>37 38</sup> or in patients with multiple sclerosis.<sup>39</sup> Importantly, a shorter time spent in LIS, anxiety and no recovery of speech production were found to be possible predictors of unhappiness. Yet, the studied variables and objective characteristics explained only 38% of the variance of overall SWB. Maybe this was because some potentially important variables such as



**Figure 3** Distribution of Anamnestic Comparative Self-Assessment ratings in locked-in syndrome.

personality traits could not be explored in our study. Other variables associated with unhappiness that can potentially be remediated, included dissatisfaction with mobility in the community and with recreational activities, in line with previous studies on QoL in spinal cord injury, multiple sclerosis, cerebral palsy and stroke.<sup>40 41</sup>

For clinical practice, our data show that, whatever the physical devastation and mental distress of LIS patients during the acute stage of the condition, optimal life-sustaining care and revalidation can have major long-term benefit. Maybe, since low satisfaction with mobility and recreational activities were here associated with poor SWB, extra palliative efforts directed at these problems could be helpful. Also more vigorous treatment of anxiety may be valuable. Finally, our results also bear on existential and ethical issues.<sup>42</sup> Because they are cognitively intact,<sup>43</sup> LIS patients are competent to make decisions on whether to continue life in LIS or to ask for withholding or withdrawal of treatment or for physician-assisted death.<sup>44</sup> That half of the respondents professing happiness do not wish to be resuscitated in case of cardiac arrest complicates the interpretation of their statement of happiness. As for current wish for euthanasia, expressed by only four of the 59 subjects (7%) responding to this question, it must be taken into account that, unlike in Belgium, the Netherlands, Luxemburg, Oregon, Washington and Montana, euthanasia and physician-assisted suicide are not legally

permitted in France, where the study was carried out. What do our data suggest regarding the practice of euthanasia or physician-assisted suicide? The principal clinical conditions for requests for physician-assisted death to be legally valid are 'unbearable' suffering and irreversibility of the situation. Whereas the first condition may apply in some LIS patients, irreversibility cannot be ascertained until, after rehabilitation, their SWB has reached a steady state, which may take as long as a year.<sup>3</sup> This is particularly true in view of expected medical progress such as by, for example, brain-computer interfaces (ie, modes of communication in which commands or messages are emitted directly by the brain without needing motor or verbal mediation).<sup>45 46</sup> We suggest that patients recently struck by LIS should be informed that, given proper care, they have a considerable chance of regaining a happy life. In our view, shortening-of-life requests by LIS patients are valid only when the patients have been given a chance to attain a steady state of SWB. Anderson *et al* reported suicidal thoughts in four out of seven LIS patients with long-term survival, but all patients nevertheless wanted life-sustaining treatment.<sup>47</sup> Acute or subacute LIS patients' requests for early death should be received with sympathy, but our data suggest that a moratorium should be proposed.<sup>48 49</sup>

Taking into account the possible methodological challenges and limitations of QoL research, especially when dealing with LIS patients, our data show that a non-negligible group of chronic LIS survivors self-report a meaningful life and their demands for euthanasia are surprisingly infrequent. It is important to stress the discussed possible biases in our study. The observed results may hence not be representative of chronic LIS patients in general. It should also be noted that given the dependence of LIS participants on the help of a caregiver for communication of their answers, social desirability might have confounded patients' responses. Nevertheless, in our view, these results are important as healthy individuals and medical professionals might assume that the comfort of a LIS patient is so limited that it is not worth living.<sup>8</sup> Such discrepancies in valuation of disability states between the healthy and those affected raise questions about the validity of utility measures based on valuation of disease states by panels of healthy people using, for example, standard gamble or time trade-off.<sup>50</sup> Underestimation of patients' self-reported QoL by caregivers and family has previously

**Table 3** Significant associations between happiness status and variables identified by the univariate analyses (marked by an asterisk in table 2)

	Odds ratio	SE	Z score	p> z	95% CI
Duration in LIS*	1.5	0.2	2.71	0.007	1.1 to 2.0
Speech production	20.47	24.87	2.48	0.013	1.89 to 221.45
Anxiety	0.19	0.15	-2.14	0.032	0.04 to 0.87

\*Odds ratio per year in LIS. LIS, locked-in syndrome.

also been reported for amyotrophic lateral sclerosis patients.<sup>6 51 52</sup> More research is needed to investigate the factors influencing the success or failure of adaptation to LIS. Also, longitudinal studies of LIS patients should throw light on the reversibility of high or low SWB and on when happiness is a consequence or a causal factor of long survival in LIS.

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## REFERENCES

- American Congress of Rehabilitation Medicine. Recommendations for use of uniform nomenclature pertinent to patients with severe alterations of consciousness. *Arch Phys Med Rehabil* 1995;76:205–9.
- Bauer G, Gerstenbrand F, Rumpel E. Varieties of the locked-in syndrome. *J Neurol* 1979;221:77–91.
- Doble JE, Haig AJ, Anderson C, et al. Impairment, activity, participation, life satisfaction, and survival in persons with locked-in syndrome for over a decade: follow-up on a previously reported cohort. *J Head Trauma Rehabil* 2003;18:435–44.
- Casanova E, Lazzari RE, Lotta S, et al. Locked-in syndrome: improvement in the prognosis after an early intensive multidisciplinary rehabilitation. *Arch Phys Med Rehabil* 2003;84:862–7.
- Leon-Carrion J, van Eeckhout P, Dominguez-Morales Mdel R. The locked-in syndrome: a syndrome looking for a therapy. *Brain Inj* 2002;16:555–69.
- Lule D, Zickler C, Hacker S, et al. Life can be worth living in locked-in syndrome. *Prog Brain Res* 2009;177:339–51.
- Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. *Soc Sci Med* 1999;48:977–88.
- Laureys S, Pellas F, Van Eeckhout P, et al. The locked-in syndrome: what is it like to be conscious but paralyzed and voiceless? *Prog Brain Res* 2005;150:495–511.
- Wood-Dauphinee S, Williams JI. Reintegration to Normal Living as a proxy to quality of life. *J Chronic Dis* 1987;40:491–502.
- Daneski K, Coshall C, Tilling K, et al. Reliability and validity of a postal version of the Reintegration to Normal Living Index, modified for use with stroke patients. *Clin Rehabil* 2003;17:835–9.
- Wood-Dauphinee SL, Opzoomer MA, Williams JI, et al. Assessment of global function: The Reintegration to Normal Living Index. *Arch Phys Med Rehabil* 1988;69:583–90.
- Stark SL, Edwards DF, Hollingsworth H, et al. Validation of the Reintegration to Normal Living Index in a population of community-dwelling people with mobility limitations. *Arch Phys Med Rehabil* 2005;86:344–5.
- Pang MY, Eng JJ, Miller WC. Determinants of satisfaction with community reintegration in older adults with chronic stroke: role of balance self-efficacy. *Phys Ther* 2007;87:282–91.
- Carter BS, Buckley D, Ferraro R, et al. Factors associated with reintegration to normal living after subarachnoid hemorrhage. *Neurosurgery* 2000;46:1326–33; discussion 1333–24.
- Bernheim JL. How to get serious answers to the serious question: “How have you been?”: subjective quality of life (QOL) as an individual experiential emergent construct. *Bioethics* 1999;13:272–87.
- May LA, Warren S. Measuring quality of life of persons with spinal cord injury: external and structural validity. *Spinal Cord* 2002;40:341–50.
- Sprangers MA, Schwartz CE. Integrating response shift into health-related quality of life research: a theoretical model. *Soc Sci Med* 1999;48:1507–15.
- Westerman MJ, The AM, Sprangers MA, et al. Small-cell lung cancer patients are just ‘a little bit’ tired: response shift and self-presentation in the measurement of fatigue. *Qual Life Res* 2007;16:853–61.
- Westerman MJ, Hak T, Sprangers MA, et al. Listen to their answers! Response behaviour in the measurement of physical and role functioning. *Qual Life Res* 2008;17:549–58.
- Bodur H, Ataman S, Rezvani A, et al. Quality of life and related variables in patients with ankylosing spondylitis. *Qual Life Res*. Published Online First: 27 October 2010. doi:10.1007/s11136-010-9771-9.
- Berges IM, Ottenbacher KJ, Kuo YF, et al. Satisfaction with quality of life poststroke: effect of sex differences in pain response. *Arch Phys Med Rehabil* 2007;88:413–17.
- Skevington SM. Investigating the relationship between pain and discomfort and quality of life, using the WHOQOL. *Pain* 1998;76:395–406.
- Donnelly C, Eng JJ. Pain following spinal cord injury: the impact on community reintegration. *Spinal Cord* 2005;43:278–82.
- Schwartz CE, Andresen EM, Nosek MA, et al. Response shift theory: important implications for measuring quality of life in people with disability. *Arch Phys Med Rehabil* 2007;88:529–36.
- de Haes JC, de Ruiter JH, Tempelaar R, et al. The distinction between affect and cognition in the quality of life of cancer patients—sensitivity and stability. *Qual Life Res* 1992;1:315–22.
- Chwalisz K, Diener E, Gallagher D. Autonomic arousal feedback and emotional experience: evidence from the spinal cord injured. *J Pers Soc Psychol* 1988;54:820–8.
- Ryan RM, Deci EL. On happiness and human potentials: a review of research on hedonic and eudaimonic well-being. *Annu Rev Psychol* 2001;52:141–66.
- Bernheim JL, Theuns P, Mazaheri M, et al. The potential of anamnestic comparative self-assessment (ACSA) to reduce bias in the measurement of subjective well-being. *Journal of Happiness Studies* 2006;7:227–50.
- Brickman P, Coates D, Janoff-Bulman R. Lottery winners and accident victims: is happiness relative? *J Pers Soc Psychol* 1978;36:917–27.
- Goering S. ‘You say you’re happy, but...’: contested quality of life judgments in bioethics and disability studies. *Journal of Bioethical Inquiry* 2008;5:125–35.
- Tonack M, Hitzig SL, Craven BC, et al. Predicting life satisfaction after spinal cord injury in a Canadian sample. *Spinal Cord* 2008;46:380–5.
- Post MW, de Witte LP, van Asbeck FW, et al. Predictors of health status and life satisfaction in spinal cord injury. *Arch Phys Med Rehabil* 1998;79:395–401.
- Cummins R. Normative life satisfaction: measurement issues and a homeostatic model. *Soc Indic Res* 2003;64:225–56.
- Calmels P, Bethoux F, Roche G, et al. [Evaluation of the handicap and the quality of life in spinal cord injuries: study in a population of 58 patients living at home] (In French). *Ann Readapt Med Phys* 2003;46:233–40.
- Steadman-Pare D, Colantonio A, Ratcliff G, et al. Factors associated with perceived quality of life many years after traumatic brain injury. *J Head Trauma Rehabil* 2001;16:330–42.
- Hammell KW. Exploring quality of life following high spinal cord injury: a review and critique. *Spinal Cord* 2004;42:491–502.
- Kreuter M, Sullivan M, Dahllöf AG, et al. Partner relationships, functioning, mood and global quality of life in persons with spinal cord injury and traumatic brain injury. *Spinal Cord* 1998;36:252–61.
- Hicken BL, Putzke JD, Novack T, et al. Life satisfaction following spinal cord and traumatic brain injury: a comparative study. *J Rehabil Res Dev* 2002;39:359–65.
- Williams RM, Turner AP, Hatzakis M Jr, et al. Prevalence and correlates of depression among veterans with multiple sclerosis. *Neurology* 2005;64:75–80.
- Crawford A, Hollingsworth HH, Morgan K, et al. People with mobility impairments: Physical activity and quality of participation. *Disabil Health J* 2008;1:7–13.
- Johansson U, Hogberg H, Bernspang B. Participation in everyday occupations in a late phase of recovery after brain injury. *Scand J Occup Ther* 2007;14:116–25.
- Fins JJ. Clinical pragmatism and the care of brain damaged patients: toward a palliative neuroethics for disorders of consciousness. *Prog Brain Res* 2005;150:565–82.
- Schnakers C, Majerus S, Goldman S, et al. Cognitive function in the locked-in syndrome. *J Neurol* 2008;255:323–30.

44. Bernat JL. *Ethical Issues in Neurology*. 2nd edn. Boston: Butterworth Heinemann, 2002.
45. Kubler A, Neumann N. Brain-computer interfaces - the key for the conscious brain locked into a paralyzed body. *Prog Brain Res* 2005;150:513–25.
46. Smart CM, Giacino JT, Cullen T, *et al*. A case of locked-in syndrome complicated by central deafness. *Nat Clin Pract Neurol* 2008;4:448–53.
47. Anderson C, Dillon C, Burns R. Life-sustaining treatment and locked-in syndrome. *Lancet* 1993;342:867–8.
48. Patterson DR, Miller-Perrin C, McCormick TR, *et al*. When life support is questioned early in the care of patients with cervical-level quadriplegia. *N Engl J Med* 1993;328:506–9.
49. Anderson JF, Augoustakis LV, Holmes RJ, *et al*. End-of-life decision-making in individuals with Locked-in syndrome in the acute period after brainstem stroke. *Intern Med J* 2010;40:61–5.
50. Arnold D, Girling A, Stevens A, *et al*. Comparison of direct and indirect methods of estimating health state utilities for resource allocation: review and empirical analysis. *BMJ* 2009;339:1–8.
51. Bach JR, Tilton MC. Life satisfaction and well-being measures in ventilator assisted individuals with traumatic tetraplegia. *Arch Phys Med Rehabil* 1994;75:626–32.
52. Trail M, Nelson ND, Van JN, *et al*. A study comparing patients with amyotrophic lateral sclerosis and their caregivers on measures of quality of life, depression, and their attitudes toward treatment options. *J Neurol Sci* 2003;209:79–85.