



Spirituality and quality of life in epilepsy and other chronic neurological disorders



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ABSTRACT

Purpose: The patients with neurological disorders often report a different quality of life (QoL), which is in part explained by clinical–pathological or psychosocial variables. This study evaluated spirituality in patients with chronic brain pathologies, aiming to clarify its specificity and position to a multidimensional model of QoL.

Methods: A hundred and ninety-nine adult patients with epilepsy (E) (n = 88), mild cognitive impairment (MCI) (n = 32), ischemic vascular disorders (n = 29), tumors (n = 28), or multiple sclerosis (MS) (n = 22), and 66 healthy subjects were assessed using the World Health Organization Quality of Life (WHOQoL) 100, Spiritual, Religious and Personal Beliefs (SRPB), Beck Depression Inventory (BDI), and State–Trait Anxiety Inventory (STAI) for the QoL, spirituality, depression, and anxiety. The Multiple Ability Self-Report Questionnaire (MASQ) and neuropsychological tests evaluated the cognitive functions.

Results: Factor analysis of the SRPB, STAI, and BDI scores yielded four factors: Personal Meaning, Inner Freedom, Awe and Openness, and Mood. Quality of life and spirituality were very similar between the patient groups. In comparison with the controls, all of the patients showed worse QoL, spirituality, mood, and lexical-memory abilities, and the patients with MCI and brain vascular disorders (BVD) also revealed worse cognitive impairments. Trait anxiety, self-rated health, age, and the SRPB Inner independence and Hope and optimism facets predicted the patients' WHOQoL 100 total score; the spiritual, affective, and socioeconomic variables predicted many QoL domains, but diagnosis only affected the Physical domain. Anxiety, self-rated health, Hope and optimism, and Personal beliefs predicted the controls' WHOQoL 100 total score.

Conclusions: Spirituality, as marked by the meaning of self, inner independence, and transcendence, is distinct from mood. It cooperates, together with the affective states, to determine the QoL of the patients with chronic brain pathologies whereas diagnosis has a limited impact. These findings support a multidimensional cross-disease model for the QoL in neurological disorders.

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1. Introduction

The conception of the quality of life (QoL) has been refined during the last decades, evolving from a performance-related construct [1] towards a multidimensional, subjective, and dynamic model including mood, social relations and environment [2–10]. This is in line with a definition of health that involves completeness (nothing is missing from the person), proper function (all is working efficiently), and well-being, not only freedom from diseases [11]. According to the biomedical model, the QoL encompasses disease-related dimensions [5,6,10]. For

a person-oriented model, the QoL relies on individual features such as personality, strategies of coping, self-efficacy, self-esteem, locus of control, and affective states [2,12–14]. Calman [2] considered the QoL as “the correspondence between hopes, expectations, ideals, and actual experiences” while others considered the “sense of well-being derived from a person's current experience of life as a whole” or “human values, the ability to manage own life, and the satisfaction of own necessities” [3,4]. Many studies of disease-related QoL in neurological patients focused on the effects of drugs, surgery, or symptomatology, but a scrutiny of recent literature only reveals few multidimensional approaches to the QoL [15–19]. Moreover, the clinical–pathological and psychosocial variables incompletely explain the variability of the QoL in medical conditions [20–22], suggesting a causative role for unexplored factors.

Spirituality has been defined as the complex of unique qualities of a person, giving direction to the existence and meaning to

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human experiences [23], the potentiality of the self [24], the dimensions of life which precedes and gives cohesiveness to all of the others [25], the connection with other people [26], the transcendence or ability to surpass contingent aspects of life and health [27], and the thing which gives meaning, motivation, energy, and direction to a person's behavior [28]. The World Health Organization [29] indicated that spirituality includes transcendence, connectedness, purpose, and values (e.g., faith, forgiveness, gratitude, sense of belonging, love) that may be shared by people with different ethnic, cultural, and religious background. Spiritual well-being was referred to as "a high level of faith, hope, and commitment in relation to a well-defined worldview or belief system that provides a sense of meaning and purpose to existence in general and that offers an ethical path to personal fulfillment which includes connectedness with self, others, and a higher power or larger reality" [30]. Spirituality is free and unorganized and encompasses cross-cultural human aspects whereas religiosity expresses the degree of participation to beliefs and practices of an organized religion in a sociocultural context [27].

In people with cancer [31,32], Human Immunodeficiency Virus (HIV) diseases [32], heart diseases [33], limb amputation, or spinal cord injuries [34], spiritual involvement significantly improved the QoL. In rehabilitation settings, it also significantly predicted the QoL [35]. Positive spiritual experiences may enhance the inner resources of patients with tumor [28], pulmonary [9], psychiatric [36], or cardiac diseases [37], but, in other cases, they gave no benefits for health [38], mental well-being [37], or symptom control [39].

In patients with chronic brain pathologies, spirituality has received inconsistent attention. Previous studies of epilepsy (E) reported on the use of spiritual healing for treating seizures [40], the connection between seizures and mystical states [41–46], hyperreligiosity and mystic attraction in interictal states [44], interictal religious experiences [47,48], and the personality of patients with temporal lobe epilepsy (TLE) characterized by religiosity, philosophical interests, and sense of personal destiny [49–52]. On the contrary, few investigations assessed the relation of spirituality to the QoL [53–55]. Spirituality was also assessed in patients with dementia as a life-limiting condition candidate to palliative care [56], while, in patients with vascular dementia, it was considered a positive lifestyle component favoring clinical improvement [57]. In patients with mild cognitive impairment (MCI), spirituality was rarely evaluated [58]. In patients with multiple sclerosis (MS), spirituality was evaluated in the context of chronic medical conditions [20], but it was rarely assessed for the QoL [59]. As for brain tumors (BTs), some studies included spirituality in the overall QoL [6,8] while others approached single inner facets [60]. A study comparing different neurological disorders revealed a significant influence of spirituality on the QoL, suggesting that these aspects may be independent of diagnosis [22].

In brief, many patients with chronic brain pathologies experience physical, cognitive, and emotional disabilities and face a chronic condition with uncertain prognosis, which in part explain the variability of their QoL. This study evaluated spirituality in patients with chronic brain pathologies, aiming to further clarify its features and effects on the QoL. Given that the impact of a chronic condition may surpass the effects of specific diagnosis, we focused on the type and duration of disease in patients with different pathologies (E, MS, BT, MCI, ischemic vasculopathy). As some variables, not necessarily related to the disease, such as age, schooling, number of family members, and income, may cooperate to determine the QoL, we compared the patients with healthy subjects, therefore using generic QoL measurements. Specific objectives of this study were the following: a) to clarify the main components of spirituality and their distinction from affectivity, b) to compare spirituality between patients with brain damage and healthy subjects, and c) to determine the impact of spirituality on their QoL.

2. Methods

2.1. Participants

Consenting patients with E, MCI, brain vascular disorders (BVD), BT, or MS, a chronic course, and disease duration longer than a year were evaluated from January 2008 to April 2011. Healthy subjects recruited from among the hospital staff, and visitors were controls.

2.2. Inventories

The World Health Organization Quality of Life (WHOQoL) 100 and WHO Spiritual, Religious and Personal Beliefs (SRPB) [9] inventories were used to assess QoL and spirituality, respectively, because they are not disease-specific, have adequate psychometric properties, and were validated in different sociocultural contexts [9]. The SRPB comprehends 15 facets that include different numbers of questions; each answer is rated on a 5-point Likert scale where 1 indicates low, negative perceptions and 5 indicates high, positive perceptions. Fifteen facet scores are calculated as the mean of the item scores within each facet (Table 2). The WHOQoL 100 scale [9] consists of 25 facets each including four items. The facets are grouped into seven domains that contain different facets: Overall QoL (a facet), Physical (pain and discomfort, energy and fatigue, sleep and rest), Psychological (positive feelings, thinking, learning, memory and concentration, self-esteem, bodily image and appearance, negative feelings), Level of independence (and mobility, activities of daily living, dependence on medication or treatments, work capacity), Social relationships (personal relationships, social support, sexual activity), Environment (physical safety and security, home environment, financial resources, health and social care – accessibility and quality, opportunities for acquiring new information and skills, participation in and opportunities for recreation/leisure activities, physical environment – pollution/noise/traffic/climate, transport), and Influence of beliefs on life (one facet). The individual items are rated on a 5-point Likert scale where 1 indicates low, negative perceptions and 5 indicates high, positive perceptions. The following scores were computed: 1) the total WHOQoL 100 score: sum of all item scores and 2) the domain scores: the mean of the facet scores (i.e., the mean of item scores within the facet) within the domain multiplied by four (range: 4–20), except for the Overall QoL and Influence of beliefs on life.

The Beck Depression Inventory (BDI) [61] provides a total score (0–36) proportional to the level of depression. The State-Trait Anxiety Inventory (STAI) 1 and 2 [62] gives two scores (20–80) that are proportional to the level of actual or habitual anxiety. The Multiple Ability Self-Report Questionnaire (MASQ) [63,64] assesses the subjective perception of cognitive failures; 38 questions investigate language, visuospatial functions, verbal and visual memory, and attention/concentration; one to five points are attributed to each answer depending on the frequency of the difficulties (almost always, often, sometimes, very seldom, almost never), with a total score that is proportional to the severity of the difficulties (38–190).

2.3. Neuropsychological tests

Standardized tests were used to assess selective attention, visuomotor coordination, set shifting, abstract reasoning, verbal initiative and fluency on phonemic or semantic cues, visual perception, constructive praxis, and verbal and visuospatial immediate and long-term memory. Higher test scores indicate better performances except for the Trail making test that requires to count the number of seconds needed to complete a trail [53,64].

2.4. Statistical analysis

Factor analysis examined the distribution of the SRPB, BDI, and STAI scores. Each score was attributed to a factor if the eigenvalue was > 1,

and the factor loading was >0.4 . Another factor analysis assessed the neuropsychological test scores. Multivariate analysis of variance (MANOVA) and tests of between-subjects effects compared the WHOQoL 100 total score and domain scores of the patients and controls. Given a possible impact of demographic aspects on vulnerability, we extended data analysis including age, years of schooling, number of family members, and income level as the covariates. According to Bonferroni correction for eight variables, significance was set as $p < 0.006$. Separate MANOVA compared the SRPB factors and facets ($p \leq 0.05$ and ≤ 0.003 , for three and 15 comparisons, respectively), and BDI and STAI scores. Separate one-way analysis of variance (ANOVA) assessed the MASQ and neuropsychological test scores ($p \leq 0.05$) and demographic and clinical features. Hierarchical regression analysis examined the predictors of the WHOQoL 100 scores; serial blocks included the demographic (age, gender, years of schooling, marital status, number of family members, work, financial level), clinical (diagnosis, disease duration), affective (anxiety, depression, perceived cognitive functions, and self-rated health expressed by a WHOQoL 100-item not included in the QoL scores), neuropsychological, religion-related (religiosity, the belonging to a religious community, creed, and personal beliefs expressed by SRPB items), and spiritual variables. We extended data analysis in order to explore if brain damage (as expressed by type of disease, disease duration, and cognitive impairment) may affect spirituality.

3. Results

3.1. Participants

Table 1 summarizes the participants' features. Two hundred and thirty-seven patients were invited to participate to the study, and 199 patients with E ($n = 88$), MCI ($n = 32$), BVD ($n = 29$), BT ($n = 28$), or MS ($n = 22$) and disease duration ranging from one to 25 years were evaluated. Thirty-eight patients (four with E, 10 with MCI, 10 with BVD, eight with BT, and six with MS) declined to participate

because of clinical worsening, problems with transportation, or lack of interest in the topic. The patients with E were affected by TLE ($n = 48$), or frontal lobe epilepsy (FLE) ($n = 18$), or idiopathic generalized tonic-clonic epilepsy (IGE) ($n = 22$); 14 patients with TLE, five with FLE, and five with IGE had drug-resistant seizures. The patients with MCI were affected by memory impairments associated with other cognitive disturbances in 15 cases. The patients with BVD showed multiple ischemic lesions in the white matter, different cognitive impairments, and mild motor-sensorial defects, reporting a minor stroke in 13 cases. The patients with BT were affected by anaplastic astrocytoma ($n = 19$) and oligodendroglioma. Multiple sclerosis was primarily progressive with partial gait and balance impairment in all of the cases. The patients with BT and MS had very mild cognitive disturbances. Twenty-eight patients required inconstant help to fill in the questionnaire, which was given by a neurologist or neuropsychologist. The patient groups had different disease duration [$F(4,194) = 7.36$, $p < 0.001$] owing to longer duration in the patients with E and MS in comparison with the patients with MCI, BVD, and BT. The patients with E and MS were younger, and the patients with MCI and BVD were older than 66 healthy controls; the patients with E and the patients with MS were also younger than the patients with MCI, BVD, and BT [$F(5,259) = 31.72$, $p < 0.001$]. The patients with BVD had received fewer years of schooling than the controls [$F(5,259) = 3.14$, $p = 0.009$]. Self-rated health (as expressed by a WHOQoL 100-item: very bad, bad, middle, good, or very good) was worse in all patients in comparison with the controls and in the patients with BVD compared with the patients with MCI and BT [$F(5,259) = 17.73$, $p < 0.001$]. The patients with MCI had fewer family members than controls and other patients [$F(5,259) = 3.30$, $p = 0.007$]. Paid workers and retired workers were more numerous than housewives, unemployed, and students in all of the groups ($\chi^2 = 99.05$, $p < 0.001$). High income was more frequent in the controls while middle income was prevalent within the patients (WHOQoL 100-item: low, low/middle, middle, or high income; $\chi^2 = 33.42$, $p = 0.004$). The patient and control groups were similar in

Table 1
Sociodemographic, clinical, and religious aspects.

	All patients (n = 199)	Epilepsy (n = 88)	MCI (n = 32)	BVD (n = 29)	BT (n = 28)	MS (n = 22)	Controls (n = 66)
F/M	107/92	57/31	17/15	12/17	15/13	6/16	38/28
Age	47.92 ± 17.00	37.92 ± 13.49	67.28 ± 7.77	60.72 ± 11.97	47.11 ± 15.95	39.00 ± 9.29	49 ± 15.06
Schooling	11.95 ± 3.81	12.59 ± 3.38	10.94 ± 4.10	10.31 ± 3.81	12.32 ± 4.33	12.59 ± 3.71	12.95 ± 3.62
Marital status							
Single	66	39	4	6	8	9	8
Married	111	38	25	20	18	10	52
Cohabitant	6	3	0	1	1	1	2
Separated	7	4	0	1	1	1	1
Divorced	4	1	1	1	0	1	2
Widower	5	3	2	0	0	0	1
Work							
Payed worker	98	52	6	8	15	14	42
House worker	15	10	2	2	0	1	6
Retired	48	8	23	11	7	2	12
Student	18	8	0	5	5	0	4
Unemployed	9	4	0	2	0	3	1
Searching the first work	6	5	0	0	0	1	0
Other	5	1	1	1	1	1	1
Income							
Low	38	19	6	4	4	5	2
Middle	104	47	15	14	16	12	24
High	57	22	11	11	8	5	40
Number of family members	2.78 ± 0.98	2.85 ± 1.07	2.22 ± 0.91	2.69 ± 1.04	3.00 ± 0.98	3.14 ± 0.89	2.95 ± 0.93
Religiosity	2.79 ± 0.99	2.91 ± 1.04	2.69 ± 0.96	2.69 ± 1.07	2.93 ± 0.77	2.73 ± 1.12	3.05 ± 0.99
Religious community	2.36 ± 1.11	2.34 ± 1.08	2.34 ± 1.03	2.21 ± 1.17	2.39 ± 1.03	2.50 ± 1.30	2.83 ± 1.09
Creed	3.02 ± 1.06	3.16 ± 1.08	2.97 ± 1.03	2.90 ± 1.14	2.96 ± 0.88	3.09 ± 1.15	3.53 ± 0.91
Personal beliefs	3.24 ± 1.02	3.21 ± 0.95	3.22 ± 1.07	3.14 ± 1.12	3.46 ± 0.96	3.18 ± 1.00	3.62 ± 0.79
Self-rated health	2.98 ± 0.79	2.98 ± 0.66	3.19 ± 0.73	2.55 ± 0.82	3.32 ± 0.77	2.86 ± 0.99	3.82 ± 0.55
Disease duration	6.94 ± 4.74	8.42 ± 4.46	5.13 ± 3.07	5.45 ± 4.64	4.57 ± 3.93	8.68 ± 6.24	-

MCI, mild cognitive impairment. BVD, brain vascular disorders. BT, brain tumor. MS, multiple sclerosis.

terms of religiosity (none, poor, enough, high, or very high), belonging to a religious community, type of religious community, creed, personal beliefs, gender, and marital status.

3.2. Factor analysis

In the whole participants group, the SRPB, STAI1, STAI2, and BDI scores yielded four factors (Mood, Personal Meaning, Inner Freedom, Awe and Openness), (Table 2). The neuropsychological test scores yielded two factors (Executive, Lexical-memory), (Table 3).

3.3. QoL

Group membership significantly affected the WHOQoL 100 scores [Pillai's value = 0.38, $F = 2.65$, $p < 0.001$]. Subsequent tests of between-subjects effects revealed significant differences for the Overall [$F(5) = 5.11$, $p < 0.001$], Physical [$F(5) = 5.88$, $p < 0.001$], and Level of independence [$F(5) = 7.53$, $p < 0.001$] domain scores and not significant differences for the total [$F(5) = 3.12$, $p = 0.009$], Influence of beliefs in life [$F(5) = 2.64$, $p = 0.024$], and Psychological domain scores [$F(5) = 2.24$, $p = 0.05$]. In comparison with controls, the patients with E ($p = 0.001$), BVD ($p = 0.005$), and BT ($p = 0.003$) had a lower Overall QoL, the patients with BVD ($p < 0.001$) and BT ($p = 0.037$) had lower Physical scores, and the patients with E ($p < 0.001$), BVD ($p < 0.001$), BT ($p = 0.004$), and MS ($p = 0.003$) had a lower Level of independence. Furthermore, the patients with BVD had lower total scores ($p = 0.005$), the patients with MCI had lower Influence of beliefs in life scores ($p = 0.017$), and the patients with BVD had lower Psychological ($p = 0.036$) scores than controls. The patients with BVD also reported a worse Physical domain in comparison with the patients with E ($p = 0.001$) and MCI ($p = 0.009$), (Table 4).

The MANOVA with age, years of schooling, number of family members, and income level as the covariates, confirmed the results, revealing a significant influence of age [Pillai's value = 0.07, $F = 2.40$, $p = 0.016$] and group [Pillai's value = 0.34, $F = 2.29$, $p < 0.001$]. Age had a significant impact on Social relationships [$F(1) = 8.81$, $p = 0.003$] while group affected the total WHOQoL 100 [$F(5) = 2.18$, $p = 0.057$] and the Overall QoL [$F(5) = 4.42$, $p = 0.001$], Physical [$F(5) = 4.82$, $p < 0.001$], and Level of independence domain scores [$F(5) = 6.35$, $p < 0.001$].

Explorative analyses of the WHOQoL 100 facets showed between-group differences in pain and discomfort [$F(5) = 3.77$, $p = 0.003$;

Table 2

Factor analysis of the Spiritual, Religious and Personal Beliefs, State-Trait Anxiety Inventory, and Beck Depression Inventory scores.

SRPB facets	Personal Meaning	Mood	Inner Freedom	Awe and Openness
Spiritual connectedness	0.83			
Meaning of life	0.62			
Wholeness and integration	0.58			
Spiritual strength	0.73			
Faith	0.86			
Love	0.81			
Inner peace		0.65		
Hope and optimism		0.61		
BDI		-0.78		
STAI1		-0.86		
STAI2		-0.86		
Forgiveness			0.77	
Ethical rules			0.81	
Inner independence			0.63	
Death and dying				-0.43
Awe				0.64
Kindness to others				0.75
Acceptation				0.45
Total explained variance = 65.40%	22.24%	20.26%	12.63%	10.26%

SRPB, Spiritual, Religious and Personal Beliefs. STAI, State-Trait Anxiety Inventory. BDI, Beck Depression Inventory.

Table 3

Factor analysis of the neuropsychological test scores.

	Executive	Lexical-memory
Raven's progressive matrices	0.64	
Attentive matrices	0.79	
Trail making test A	-0.84	
Trail making test B	-0.75	
Token test	0.62	
Street's completion test	0.52	
Rey's complex figure copying	0.80	
Corsi's blocks span		0.59
Digit span		0.76
Phonemic fluency		0.76
Semantic fluency		0.79
Short story		0.74
Rey's complex figure delayed reproduction		0.69
Total explained variance = 65.83%	32.50%	33.33%

worse in the patients with BVD in comparison with controls], energy and fatigue [$F(5) = 8.03$, $p < 0.001$; lower in the patients with BVD, BT, and MS in comparison with controls], sleep and rest [$F(5) = 2.64$, $p = 0.024$; worse in the patients with BVD in comparison with controls], positive feelings [$F(5) = 2.70$, $p = 0.021$; lower in the patients with BVD in comparison with controls], thinking, learning, memory, and concentration [$F(5) = 3.99$, $p = 0.002$; lower in the patients with BVD and MCI in comparison with controls], mobility [$F(5) = 2.52$, $p = 0.03$; lower in the patients with MS in comparison with controls], activities of daily living [$F(5) = 6.58$, $p < 0.001$; lower in the patients with BVD, BT, and MS in comparison with controls], dependence on medication or treatments [$F(5) = 20.83$, $p < 0.001$; greater in the patients with E, BVD, BT, and MS in comparison with controls and in the patients with E and BVD in comparison with patients with MCI], work capacity [$F(5) = 5.32$, $p < 0.001$; reduced in the patients with MCI and BVD in comparison with controls], physical environment [$F(5) = 2.82$, $p = 0.017$; worse in the patients with E than in patients with MCI], and transportation [$F(5) = 2.87$, $p = 0.015$; less efficient in the patients with E in comparison with controls].

3.4. Spirituality

The spiritual factors (Pillai's value = 0.10, $F = 1.67$, $p = 0.05$) and SRPB facets (Pillai's value = 0.38, $F = 1.37$, $p = 0.02$) were different between the patient and control groups. The patients with BVD showed a lower Inner Freedom factor in comparison with the controls and patients with E [$F(5) = 2.28$, $p = 0.048$] and a lower Inner independence facet [$F(5) = 3.48$, $p = 0.005$; post hoc test: $p = 0.003$] in comparison with the controls (Table 5).

3.5. Mood

The group had a significant global influence on the BDI and STAI scores [Pillai's value = 0.13, $F = 2.36$, $p = 0.003$], with significant between-subject effects for the BDI [$F(5) = 3.65$, $p = 0.003$] and STAI2 [$F(5) = 2.92$, $p = 0.01$]. In comparison with controls, the patients with E ($p = 0.027$), BVD ($p = 0.023$), and BT ($p = 0.015$) had higher BDI scores, and the patients with E had higher STAI2 scores ($p = 0.035$), with no differences between the patients (Table 5).

3.6. Perceived cognitive functions and neuropsychological performances

All of the controls completed the MASQ (Table 5), while 40 of them only performed the neuropsychological tests. Therefore, the MASQ and neuropsychological factor scores were analyzed by means of separate one-way ANOVAs. There were significant differences for the MASQ [$F(5,259) = 7.40$, $p < 0.001$] and Executive [$F(5,233) = 8.25$, $p < 0.001$] and Lexical-memory factors [$F(5,233) = 27.03$, $p < 0.001$]. In comparison with the controls, the patients with MCI and BVD ($p < 0.001$) reported

Table 4
Mean WHOQoL 100 scores.

	All patients	Epilepsy	MCI	BVD	BT	MS	Controls
Total score	346.84 ± 57	351.20 ± 59	347.50 ± 56	328.93 ± 63	344.61 ± 59	352.09 ± 55	372.82 ± 38
Overall QoL	3.29 ± 0.73	3.27 ± 0.65	3.49 ± 0.56	3.20 ± 0.85	3.17 ± 0.91	3.36 ± 0.72	3.69 ± 0.60
Physical	13.69 ± 2.7	14.95 ± 1.94	14.41 ± 2.49	12.19 ± 3.18	13.16 ± 2.98	13.78 ± 2.76	14.95 ± 1.94
Psychological	13.32 ± 2.6	13.46 ± 2.37	13.25 ± 2.15	12.59 ± 3.38	13.37 ± 2.46	13.93 ± 2.64	14.27 ± 2.05
Level of independence	13.72 ± 3	14.02 ± 2.56	14.48 ± 2.46	12.86 ± 3.31	13.75 ± 3.36	13.51 ± 3.40	16.03 ± 1.72
Social relationships	14.03 ± 2.6	14.38 ± 2.47	13.61 ± 1.94	13.56 ± 3.14	14.41 ± 2.85	14.19 ± 2.78	14.47 ± 2.12
Environment	14.13 ± 2.2	14.44 ± 2.20	13.87 ± 2.01	13.80 ± 2.50	14.13 ± 2.23	14.44 ± 1.94	14.71 ± 1.79
Influence of beliefs on life	3.58 ± 0.84	3.71 ± 0.83	3.30 ± 0.92	3.50 ± 0.70	3.55 ± 1.01	3.84 ± 0.76	3.84 ± 0.69

WHOQoL, World Health Organization Quality of Life. SRPB, Spiritual, Religious and Personal Beliefs. MCI, mild cognitive impairment. BVD, brain vascular disorders. BT, brain tumor. MS, multiple sclerosis.

worse cognitive difficulties and lower Executive scores ($p < 0.001$). In comparison with the patients with E, the patients with BVD also reported more serious cognitive difficulties ($p = 0.029$), and the patients with BVD ($p = 0.001$) and MCI ($p < 0.001$) showed lower Executive scores; the patients with MCI also showed lower Executive scores than the patients with MS ($p = 0.025$). All patients revealed impaired Lexical-memory ($p < 0.001$).

3.7. QoL predictors

3.7.1. Neurological patients

Chronological age explained 2%, two affective variables (trait anxiety: 41%; self-rated health: 7%) explained 48%, and a religion-related variable (personal beliefs) explained 2% of the variance of the WHOQoL 100 total score. The SRPB facets (Hope and optimism, 28%; Inner independence, 11%; Awe and Openness, 3%; Inner peace, 1%; Spiritual connectedness, 1%) explained 44% of this score whereas diagnosis, disease duration, and the neuropsychological factors showed no effects. Cumulative regression analysis entering the significant variables revealed that 56% of the WHOQoL total score was predicted by trait anxiety (41%), self-rated health (7%), Inner independence (4%), Hope and optimism (3%), and chronological age (1%), (Table 6).

The Overall QoL (44%) was predicted by Trait anxiety, self-rated health, Completeness, Kindness to others, and state anxiety, the Physical domain (39%) by Trait anxiety, self-rated health, diagnosis, Inner independence, and schooling, the Psychological domain (61%) by trait anxiety, Hope and optimism, self-rated health, depression, and Completeness, the Level of Independence (43%) by depression, self-rated

health, marital status, Inner independence, and number of family members, the Social relationships (39%) by trait anxiety, age, Acceptation, Awe, marital status, and religious community, and the Environment domain (47%) by trait anxiety, Acceptation, self-rated health, Inner peace, Inner independence, income level, and Kindness to others (Table 7).

3.7.2. Healthy subjects

Three affective variables (trait anxiety: 42%, self-rated health: 11%, state anxiety: 4%) explained 57% of the variance of the WHOQoL 100 total score while the personal beliefs and SRPB facets (Hope and optimism: 32%, Inner peace: 5%) explained 14% and 37%, respectively, and the demographic and neuropsychological variables showed no effects. Cumulative regression analysis revealed that 65% of the WHOQoL 100 total score related to trait anxiety (42%), self-rated health (11%), Hope and optimism (9%), and personal beliefs (3%) (Table 8).

3.8. Spirituality predictors

The Personal Meaning, Inner Freedom, or Awe and Openness factors did not relate to diagnosis, disease duration, or Executive and Lexical-memory factors.

4. Discussion

The QoL, an important endpoint of disease outcome, is partially determined by clinical-pathological and psychological variables. This study evaluated spirituality in patients with chronic brain pathologies, aiming to clarify its specificity and impact on the QoL. Given that variables unrelated to the disease could affect the QoL, we compared the

Table 5
Mean scores of the Spiritual, Religious and Personal Beliefs facets, Beck Depression Inventory, State-Trait Anxiety Inventory, and Multiple Ability Self-report Questionnaire.

	All patients	Epilepsy	MCI	BVD	BT	MS	Controls
Spiritual connectedness	2.49 ± 1.10	2.15 ± 1.11	2.57 ± 1.00	2.56 ± 1.10	2.62 ± 1.08	2.55 ± 1.25	3.04 ± 1.15
Meaning of life	3.30 ± 0.90	3.27 ± 0.77	3.15 ± 0.91	3.34 ± 0.87	3.30 ± 0.86	3.44 ± 1.12	3.65 ± 0.80
Awe	3.51 ± 0.88	3.51 ± 0.73	3.28 ± 0.87	3.45 ± 1.04	3.81 ± 0.91	3.54 ± 0.85	3.79 ± 0.76
Wholeness and integration	3.22 ± 0.78	3.25 ± 0.73	3.19 ± 0.87	3.20 ± 0.84	3.08 ± 0.70	3.38 ± 0.80	3.57 ± 0.53
Spiritual strength	2.73 ± 0.92	2.60 ± 0.96	3.00 ± 0.75	2.72 ± 0.90	2.52 ± 0.82	2.82 ± 1.21	3.07 ± 0.79
Inner peace	2.96 ± 0.91	2.84 ± 0.88	2.89 ± 0.91	3.03 ± 1.08	2.91 ± 0.90	3.15 ± 0.81	3.12 ± 0.74
Hope and optimism	3.05 ± 0.89	2.96 ± 0.85	2.96 ± 0.81	2.84 ± 1.06	2.90 ± 0.80	3.60 ± 0.97	3.24 ± 0.75
Faith	2.67 ± 1.05	2.72 ± 1.10	2.69 ± 0.98	2.56 ± 0.94	2.66 ± 1.03	2.72 ± 1.21	3.00 ± 1.01
Love	3.12 ± 0.89	3.16 ± 0.88	3.06 ± 0.89	2.97 ± 0.95	3.19 ± 0.91	3.22 ± 0.85	3.50 ± 0.83
Kindness to others	3.46 ± 0.78	3.53 ± 0.70	3.44 ± 0.68	3.43 ± 0.94	3.31 ± 0.83	3.59 ± 0.77	3.71 ± 0.52
Death and dying	3.06 ± 1.15	3.06 ± 1.23	3.09 ± 1.14	2.99 ± 1.22	2.79 ± 0.97	3.40 ± 1.22	3.02 ± 1.01
Acceptation	3.15 ± 0.66	3.23 ± 0.65	3.14 ± 0.77	3.05 ± 0.72	3.09 ± 0.69	3.27 ± 0.50	3.37 ± 0.52
Forgiveness	3.25 ± 0.52	3.21 ± 0.69	3.33 ± 0.48	3.08 ± 0.59	3.15 ± 0.33	3.50 ± 0.54	3.25 ± 0.40
Ethical rules	3.65 ± 0.5	3.68 ± 0.64	3.78 ± 0.37	3.48 ± 0.47	3.61 ± 0.46	3.71 ± 0.56	3.79 ± 0.37
Inner independence	3.45 ± 0.57	3.44 ± 0.64	3.58 ± 0.52	3.15 ± 0.66	3.45 ± 0.58	3.64 ± 0.49	3.64 ± 0.49
Beck Depression Inventory	7.18 ± 6.18	6.75 ± 5.76	6.56 ± 5.77	7.83 ± 6.53	8.04 ± 5.28	6.73 ± 7.58	3.95 ± 3.22
State-Trait Anxiety Inventory							
State anxiety	41.93 ± 11.94	42.93 ± 12.44	38.91 ± 10.77	45.07 ± 14.40	44.93 ± 11.65	37.82 ± 10.44	39.44 ± 11.68
Trait anxiety	42.58 ± 11.14	44.33 ± 11.50	39.94 ± 11.64	45.14 ± 11.83	43.75 ± 10.74	39.77 ± 9.99	38.86 ± 9.67
Multiple Ability Self-report Questionnaire	88.20 ± 24.43	82.82 ± 24.59	95.75 ± 23.20	98.93 ± 30.05	84.46 ± 22.23	79.02 ± 22.08	71.77 ± 21.83

MCI, mild cognitive impairment. BVD, brain vascular disorders. BT, brain tumor. MS, multiple sclerosis.

Table 6
The predictors of the WHOQoL 100 total score in neurological patients.

Blocks	Predictors	Adjusted R ² – Standardized β	F – p
I. Demographic	Chronological age	0.02 – –0.15	4.71, 0.03
II. Disease-related	–	–	–
III. Health-related	Trait anxiety	0.41 – –0.56	139.57, <0.001
	Self-rated health	0.48 – 0.28	93.46, <0.001
IV. Religion-related	Personal beliefs	0.02 – 0.16	5.43, 0.02
V. SRPB facets	Hope and optimism	0.28 – 0.53	49.51, <0.001
	Inner independence	0.39 – 0.36	45.52, <0.001
	Awe and Openness	0.42 – 0.19	44.53, <0.001
	Inner peace	0.43 – 0.16	44.11, <0.001
	Spiritual connectedness	0.44 – –0.13	43.67, <0.001
Cumulative regression	Trait anxiety	0.41 – –0.56	139.57, <0.001
	Health-related health	0.48 – 0.28	93.46, <0.001
	Inner independence	0.52 – 0.22	72.44, <0.001
	Hope and optimism	0.55 – 0.20	60.47, <0.001
	Chronological age	0.56 – –0.13	51.45, <0.001

WHOQoL, World Health Organization Quality of Life. SRPB, Spiritual, Religious and Personal Beliefs.

patient groups with healthy subjects, therefore using generic measurements. The patients reported significantly lower spirituality and QoL in comparison with the healthy subjects, in the absence of particular differences between the patient groups. Spirituality, as marked by sense of meaning, inner freedom, and transcendence, cooperated to predict the QoL.

In accord with theoretical definitions [9,22,23,27] and previous studies in patients with different neurological disorders [22], factor analysis distinguished spirituality and mood. Personal Meaning included the human values, meaning of self, and personal resources, Inner Freedom contained some personal aspects that help to face life challenges and difficulties, and Awe and Openness expressed the capacity

to transcend health problems, highlighting the positive aspects of nature, life, and people. These factors resemble Plato's *daimon* (The Myth of Er) that contains a person's identity and Jung's suggestion that we mean something in virtue of the essence we incarnate. Moreover, these factors contained no religion-related items, supporting a distinction between spirituality and religiosity [9]. Depression, anxiety, Inner peace, and Hope and optimism composed Mood's negative and positive aspects.

The spiritual factors and facets were very similar in patients with different neurological disorders and, in comparison with the controls and patients with E, the patients with BVD only revealed lower Inner Freedom maybe because of mental rigidity. A combination of similar

Table 7
The predictors of the WHOQoL 100 domains.

Domains	Predictors	Adjusted R ² – Standardized β	Explained variance (%)	F*
Overall quality of life	Trait anxiety	0.32 – –0.49	32	93.56
	Self-rated health	0.38 – 0.27	6	62.04
	Completeness	0.42 – 0.21	4	47.72
	Kindness to others	0.43 – –0.14	1	38.20
	State anxiety	0.44 – –0.19	1	32.24
Physical	Trait anxiety	0.24 – –0.41	24	63.80
	Self-rated health	0.32 – 0.30	8	47.73
	Diagnosis	0.37 – –0.21	5	38.49
	Inner independence	0.38 – 0.15	1	31.11
	Schooling	0.39 – 0.13	1	26.30
Psychological	Trait anxiety	0.50 – –0.53	50	193.75
	Hope and optimism	0.57 – 0.33	7	131.74
	Self-rated health	0.59 – 0.15	2	94.61
	Depression	0.60 – –0.17	1	74.59
	Completeness	0.61 – 0.12	1	61.99
Level of independence	Depression	0.25 – –0.40	25	67.24
	Self-rated health	0.38 – 0.38	13	61.81
	Marital status	0.41 – 0.16	3	45.95
	Inner independence	0.42 – 0.15	1	37.10
	Number of family members	0.43 – 0.11	1	30.95
Social relationships	Trait anxiety	0.24 – –0.50	24	61.76
	Chronological age	0.30 – –0.26	6	43.54
	Acceptation	0.34 – 0.23	4	35.28
	Awe and Openness	0.37 – 0.17	3	29.20
	Marital status	0.38 – 0.12	1	24.58
Environment	Religious community	0.39 – 0.12	1	21.69
	Trait anxiety	0.31 – –0.44	31	87.38
	Acceptation	0.37 – 0.28	6	58.34
	Self-rated health	0.40 – 0.20	3	44.45
	Inner peace	0.43 – 0.22	3	37.41
	Inner independence	0.44 – 0.14	1	31.73
	Income level	0.45 – 0.12	1	27.89
	State anxiety	0.46 – –0.18	1	25.11
Kindness to others	0.47 – –0.12	1	25.75	

WHOQoL, World Health Organization Quality of Life.

* $p < 0.001$.

Table 8
The predictors of the WHOQoL 100 total score in healthy subjects.

Blocks	Predictors	Adjusted R ² – Standardized β	F – p
I. Demographic	–	–	–
III. Health-related	Trait anxiety	0.42 – –0.53	48.10 – <0.001
	Self-rated health	0.53 – 0.36	37.69 – <0.001
	State anxiety	0.57 – –0.30	29.60 – <0–001
IV. Religion-related	Personal beliefs	0.17 – 0.39	11.21 – 0.001
V. SRPB facets	Hope and optimism	0.32 – 0.38	30.98 – <0.001
	Inner peace	0.37 – 0.31	19.68 – <0.001
Cumulative regression	Trait anxiety	0.42 – –0.53	48.07
	Health-related health	0.53 – 0.36	37.69
	Hope and optimism	0.62 – 0.34	36.33
	Personal Beliefs	0.65 – 0.20	31.06

WHOQoL, World Health Organization Quality of Life. SRPB, Spiritual, Religious and Personal Beliefs.

spiritual facets in patients with different brain pathologies may be a consequence of a damage to temporofrontolimbic areas involved in insight, self-awareness, or semantic memory [48,50,51,54]. However, the spiritual factors were not related to disease severity and E, which may comprehend ictal and interictal mystical or spiritual experiences [45,46], was not associated with abnormal spiritual expressions. It is possible that an underestimated spirituality is a consequence of a chronic stressful condition that absorbs energy and creativity. Nevertheless, the spiritual facets, such as Inner independence, Completeness, Kindness to others, Acceptation, and Awe and Openness, cooperated to the prediction of the patients' QoL to a greater extent than to the QoL of the healthy subjects. These effects were also wider than that reported in a general population where spirituality only affected Overall QoL [65]. It may be argued that a person's inner resources become important in serious life conditions and positive spiritual experiences and values may favor a patient's well-being. Indeed, Baker [27] claimed that spirituality may help to understand the events of life, to make sense of them, to realize the integrity of one's own life, and to perceive a good QoL in front of the adversities. Bussing et al. [20] reported that spiritual coping can provide a way for reinterpreting personal life events and looking for disease's meaning. In neurological patients, positive spiritual facets may reinforce coping towards disability and enhance the sense of self and the internal locus of control, favoring compliance to clinical exams and therapies [66]. All this suggests that individual spiritual resources or weaknesses may help to explain the differences of the QoL of patients with very similar impairments [53,67,68].

Worth noting, the patient groups reported a very similar QoL except for the Physical domain that was better in the patients with E and MCI in comparison with the patients with BVD, which is may be due to motor disturbances. These neurological disorders are long-standing, cannot benefit of curative treatment or have few therapeutic options, and have uncertain prognosis, which may supersede specific disease-related features and explain the lack of differences in the QoL. In keeping with these findings, the patient groups also reported similar levels of anxiety and depression and showed impaired lexical-memory capacities, which may favor a negative appraisal of one's own QoL. In comparison with the controls, all of the patient groups reported a lower Level of independence, and the patients with BVD, E, and BT were also impaired in diverse domains; the patients with E, BT, and BVD were more depressed, and the patients with E were also more anxious while the patients with BVD and MCI also reported more cognitive failures and executive impairments. These findings confirm the impact of chronic brain pathologies on affective balance and cognitive functions [15–19,22,69].

In addition to spirituality, trait anxiety explained 41% of the variance of the WHOQoL 100 total score, and it was a major predictor for many QoL domains. Depression and self-rated health also cooperated to predict the QoL domains, underlining the impact of mood and functional aspects on the QoL of neurological patients [70].

The present study also revealed an influence of socioeconomic aspects (marital status, number of family members, age, belonging to a religious community, financial level) on the patients' QoL but not on the QoL of the healthy subjects, suggesting that brain pathology itself may represent a risk for socioeconomic problems. In this framework, diagnosis only showed an impact on the Physical domain, and disease duration had no effects. Such a multidimensional approach to the QoL highlights, in patients with chronic brain pathologies, the greater importance of the personal sphere and socioeconomic aspects in comparison with disease-related variables. The position of spirituality in this scenery enhances the role played by inner resources and weaknesses in reinforcing or worsening the QoL.

Present findings should take into account some limitations. The study only included some brain pathologies and different numbers of patients. Therefore, the results cannot be generalized to all neurological conditions. The WHOQoL 100 is a generic inventory that allows to compare patients and healthy subjects, but it cannot determine specific disease-related aspects.

5. Conclusions

Spirituality, as marked by the meaning of self, inner independence, and transcendence, is distinct from mood. It cooperates, together with the affective states and socioeconomic aspects, to determine the QoL of the patients with chronic brain pathologies whereas diagnosis has a limited impact. These findings support a multidimensional cross-disease model for the QoL in neurology. Further studies are needed to clarify the neural correlates of spirituality in diverse neurological conditions and to disentangle the interrelationships between the determinants of the QoL. Longitudinal studies and studies assessing the efficacy of interventions aiming to improve patients' QoL focusing on psychological and spiritual dimensions can also play a major role in this endeavor.

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Declaration of interest

The authors declare no conflicts of interests.

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References

- [1] Coscarelli Shag C, Heinrich RL, Ganz P. Karnofsky performance status revised: reliability, validity, and guidelines. *J Clin Oncol* 1984;2:187–93.
- [2] Calman KC. Quality of life in cancer patients – an hypothesis. *J Med Ethics* 1984;10:124–8.
- [3] Ferrans C, Powers M. Quality of life index: development and psychometric properties. *Adv Nurs Sci* 1985;8:15–24.
- [4] Grant MM, Padilla GV, Ferrell BR, Rhiner M. Assessment of quality of life with a single instrument. *Semin Oncol Nurs* 1990;6:260–70.
- [5] Schipper H. Guidelines and caveats for quality of life measurement in clinical practice research. *Oncology* 1990;4:51–7.
- [6] Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. *J Clin Oncol* 1993;11:570–9.
- [7] Testa MA, Simonson DC. Assessment of quality of life outcomes. *N Engl J Med* 1996;334:835–40.

- [8] Osoba D, Brada M, Prados MD, Yung WKA. Effect of disease burden on health-related quality of life in patients with malignant gliomas. *Neuro Oncol* 2000;2: 221–8.
- [9] World Health Organization Quality of Life Group. What quality of life? World Health Organization quality of life assessment. *World Health Forum* 1996;17: 354–6.
- [10] Moore PM, Baker GA. The neuropsychological and emotional consequences of living with intractable epilepsy: implications for clinical management. *Seizure* 2002;11: 224–30.
- [11] Zachariae B, Bech P. Quality of life concept. *Ugeskr Laeger* 2008;170:821–5.
- [12] Salander P, Bergenheim T, Henriksson R. The creation of protection and hope in patients with malignant brain tumors. *Soc Sci Med* 1996;42:985–96.
- [13] Newton HB, Malkin MG. Ethical issues in neuro-oncology. *Semin Neurol* 1997;17: 219–26.
- [14] Suurmeijer TP, Reuvekang MF, Aldenkamp BP. Social functioning, psychological functioning, and quality of life in epilepsy. *Epilepsia* 2001;42:1160–8.
- [15] Leong TI, Weiland TJ, Jelinek GA, Simpson S, Brown CR, Neate SL, et al. Longitudinal associations of the healthy lifestyle index score with quality of life in people with multiple sclerosis: a prospective cohort study. *Front Neurol* 2018;9:874.
- [16] Muncie SEP, Perrier L, Shin S, Adhietty C, Pitzul K, Nelson MLA, et al. Impact of quality improvement strategies on the quality of life of individuals post-stroke: a systematic review. *Disabil Rehabil* Nov 2018;1–7.
- [17] Pan-Weisz TM, Kryza-Lacombe M, Burkeen J, Hattangadi-Gluth J, Malcarne VL, McDonald CR. Patient-reported health-related quality of life outcomes in supportive-care interventions for adults with brain tumors: a systematic review. *Psychooncology* 2019;28:11–21.
- [18] Stites SD, Harkins K, Rubright JD, Karlawish J. Relationships between cognitive complaints and quality of life in older adults with mild cognitive impairment, mild Alzheimer disease dementia, and normal cognition. *Alzheimer Dis Assoc Disord* 2018;32:276–83.
- [19] Cano-López I, Hampel KG, Garcés M, Villanueva V, González-Bono E. Quality of life in drug-resistant epilepsy: relationships with negative affectivity, memory, somatic symptoms and social support. *J Psychosom Res* 2018;114:31–7.
- [20] Bussing A, Ostermann T, Matthiessen PF. Role of religion and spirituality in medical patients: confirmatory results with the spREUK questionnaire. *Health Qual Life Outcomes* 2005;3(10). <https://doi.org/10.1186/1477-7525-3-10>.
- [21] Gramstad A, Iversen E, Rngelsen BA. The impact of affectivity disposition, self-efficacy and locus of control on psychosocial adjustment in patients with epilepsy. *Epilepsy Res* 2001;46:53–61. <https://doi.org/10.1155/2015/756849>.
- [22] Giovagnoli AR, Martins da Silva A, Riva A, Cornelio F. On the personal facets of quality of life in chronic neurological disorders. *Behav Neurol* 2009;21:155–63.
- [23] Mueller PS, Plevak DJ, Rummans TA. Religious involvement, spirituality, and medicine: implications for clinical practice. *Mayo Clin Proc* 2001;76:1125–35. <https://doi.org/10.4065/76.12.1225>.
- [24] Fry A. Spirituality, communication and mental health nursing: the tacit interdiction. *Aust N Z J Ment Health Nurs* 1998;7:25–32.
- [25] Payne SA. Coping with palliative chemotherapy. *J Adv Nurs* 1990;15(6):652–8.
- [26] Dawson PJ. A reply to Goddard's 'Spirituality as integrative energy'...Nancy Goddard's (1995) paper 'spirituality as integrative energy' in the journal of advance nursing. *J Adv Nurs* 1997;25:282–9.
- [27] Baker DC. Studies of inner life: the impact of spirituality on quality of life. *Qual Life Res* 2003;12:51–7.
- [28] Ellison CW. Spiritual well-being: conceptualization and measurement. *J Psychol Theol* 1983;11:330–40.
- [29] Schalock RL, Brown I, Brown R, Cummins RA, Felce D, Matikka L, et al. Conceptualization, measurement, and application of quality of life for persons with intellectual disabilities: report of an international panel of experts. *Ment Retard* 2002;40: 457–70.
- [30] Hawks S. Spiritual health: definition and theory. *Wellness Perspect* 1994;10:3–13.
- [31] Cotton SP, Levine EG, Fitzpatrick CM, Dold KH, Targ E. Exploring the relationships among spiritual well-being, quality of life, and psychological adjustment in women with breast cancer. *Psychooncology* 1999;8:429–38.
- [32] Brady MJ, Peterman AII, Fitchell G, Mo M, Cella D. A case for including spirituality in quality of life measurement in oncology. *Psychooncology* 1999;8:417–28.
- [33] Matthews DA, Larson DB, Barry CP. The Faith factor: an annotated bibliography of clinical research on spiritual subjects. vol. 1. National Institute for Healthcare Research: Rockville, Md; 1993.
- [34] Riley BB, Perna R, Tate DG, Forchheimer M, Anderson C, Luera G. Types of spiritual well-being among persons with chronic illnesses: their relation to various forms of quality of life. *Arch Phys Med Rehabil* 1998;79:258–64.
- [35] Tate DG, Forchheimer M. Quality of life, life satisfaction, and spirituality. *Am J Phys Med Rehabil* 2002;31:400–10.
- [36] Sodergren SC, Hyland ME, Crawford A, Partridge MR. Positivity in illness: a self-delusion or existential growth? *Br J Health Psychol* 2004;9:163–74. <https://doi.org/10.1348/135910704773891023>.
- [37] Ai AL, Bolling SF. The use of complementary and alternative therapies among middle-aged and older cardiac patients. *Am J Med Qual* 2002;17:21–7. <https://doi.org/10.1177/106286060201700105>.
- [38] Tsuang MT, Williams WM, Simpson JC, Lyons MJ. Pilot study of spirituality and mental health in twins. *Am J Psychiatry* 2002;159:486–8. <https://doi.org/10.1176/appi.ajp.159.3.486>.
- [39] Sloan RP, Bagiella E. Claims about religious involvement and health outcomes. *Ann Behav Med* 2002;24:14–21. https://doi.org/10.1207/S15324796ABM2401_03.
- [40] Cohen MH. Regulation, religious experience, and epilepsy: a lens on complementary therapies. *Epilepsy Behav* 2003;4:602–6.
- [41] Dewhurst K, Beard AW. Sudden religious conversions in temporal lobe epilepsy. *Br J Psychiatry* 1970;117:497–507.
- [42] Persinger MA. Religious and mystical experiences as artifacts of temporal lobe function: a general hypothesis. *Percept Mot Skills* 1983;57:1255–62.
- [43] Saver JL, Robin J. The neural substrates of religious experience. *J Neuropsychiatry Clin Neurosci* 1997;9:498–510.
- [44] Hansen BA, Brodtkorb E. Partial epilepsy with "ecstatic" seizures. *Epilepsy Behav* 2003;4:667–73.
- [45] Dolgoff-Kaspar R, Ettinger AB, Golub SA, Perrine K, Harden C, Croll SD. Numinous-like auras and spirituality in persons with partial seizures. *Epilepsia* 2011;52:640–4.
- [46] Dong L, Zhou X. An uncommon automatism with religious connotation—prostration in a case of right temporal lobe epilepsy. *Seizure* 2016;35:33–5.
- [47] Devinski O. Psychiatric comorbidity in patients with epilepsy: implications for diagnosis and treatment. *Epilepsy Behav* 2003(Suppl. 4):S2–S10.
- [48] Devinsky O, Lai G. Spirituality and religion in epilepsy. *Epilepsy Behav* 2008;12:636–43.
- [49] Bear D. Temporal lobe epilepsy: a syndrome of temporo-limbic hyperconnection. *Cortex* 1979;15:357–84.
- [50] Trimble M, Freeman A. An investigation of religiosity and the Gastaut-Geschwind syndrome in patients with temporal lobe epilepsy. *Epilepsy Behav* 2006;9:407–14.
- [51] Geschwind N. Personality changes in temporal lobe epilepsy. *Epilepsy Behav* 2009; 15:425–33.
- [52] Devinsky J, Schachter S. Norman Geschwind's contribution to the understanding of behavioral changes in temporal lobe epilepsy: the February 1974 lecture. *Epilepsy Behav* 2009;15:417–24.
- [53] Giovagnoli AR, Meneses RF, Martins da Silva A. The contribution of spirituality to quality of life in focal epilepsy. *Epilepsy Behav* 2006;9:133–9. <https://doi.org/10.1016/j.yebeh.2006.04.002>.
- [54] Lee S-A, Ryu HU, Choi E-J, Koa M-A, Jeon J-Y, Han S-H, et al. Associations between religiosity and anxiety, depressive symptoms, and well-being in Korean adults living with epilepsy. *Epilepsy Behav* 2017;75:246–51.
- [55] Lin C-Y, Saffari M, Koenig HG, Pakpour AH. Effects of religiosity and religious coping on medication adherence and quality of life among people with epilepsy. *Epilepsy Behav* 2018;78:45–51.
- [56] Mast KR, Salama M, Silverman GK, Arnold RM. End-of-life content in treatment guidelines for life-limiting diseases. *J Palliat Med* 2004;7:754–73.
- [57] Coulson I, Strang V, Marino R, Minichiello V. Knowledge and lifestyle behaviours of healthy older adults related to modifying the onset of vascular dementia. *Arch Gerontol Geriatr* 2004;39:43–58.
- [58] Dos Santos SB, Rocha GP, Fernandez LL, de Padua AC, Reppold CT. Association of lower spiritual well-being, social support, self-esteem, subjective well-being, optimism and hope scores with mild cognitive impairment and mild dementia. *Front Psychol* 2018;9:371.
- [59] Nsamenang SA, Hirsch JK, Topciu R, Goodman AD, Duberstein PR. The interrelations between spiritual well-being, pain interference and depressive symptoms in patients with multiple sclerosis. *J Behav Med* 2016;39:355–63.
- [60] Giovagnoli AR, Silvani A, Colombo E, Boiardi A. Facets and determinants of quality of life in recurrent high-grade glioma patients. *JNNP* 2005;76:562–8. <https://doi.org/10.1136/jnnp.2004.036186>.
- [61] Beck AT, Steer RA, Brown GH. Manual of the Beck Depression Inventory. 2nd ed. San Antonio, TX: Psychological Corporation; 1996.
- [62] Spielberger CD. Inventario per l'ansia di stato e di tratto. Nuova versione italiana dello S.T.A.I. Forma Y. Firenze: Organizzazioni Speciali; 1989.
- [63] Seidenberg M, Haltiner A, Taylor MA, Hermann BB, Wyler A. Development and validation of a Multiple Ability Self-Report Questionnaire. *J Clin Exp Neuropsychol* 1994;16:93–104.
- [64] Giovagnoli AR. Awareness, overestimation, and underestimation of cognitive functions in epilepsy. *Epilepsy Behav* 2013;26:75–80. <https://doi.org/10.1016/j.yebeh.2012.11.001>.
- [65] Patrick DL, Kinne S, Engelberg RA, Pearlman RA. Functional status and perceived quality of life in adults with and without chronic conditions. *J Clin Epidemiol* 2000; 53:779–85.
- [66] World Health Organization SRPB Group. A cross-cultural study of spirituality, religion, and personal beliefs as components of quality of life. *Soc Sci Med* 2006;62: 1486–97. <https://doi.org/10.1016/j.socscimed.2005.08.001>.
- [67] Tedman S, Thornton E, Baker G. Development of a scale to measure core beliefs and perceived self-efficacy in adults with epilepsy. *Seizure* 1995;4:221–31.
- [68] Norderson A, Engstrom B, Norberg A. Self-reported quality of life for patients with progressive neurological disease. *Qual Life Res* 1998;7:257–66.
- [69] Giovagnoli AR, Erbetta A, Reati F, Bugiani O. Differential neuropsychological patterns in frontotemporal dementia and Alzheimer's disease in a study of diagnostic concordance. *Neuropsychologia* 2008;46:1495–504. <https://doi.org/10.1016/j.neuropsychologia.2007.12.023>.
- [70] Kanner AM, Barry JJ. The impact of mood disorders in neurological diseases: should neurologists be concerned? *Epilepsy Behav* 2003;4:53–S13.