Cognitive function and quality of life in multiple sclerosis patients

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This is a study on the longitudinal evaluation of cognitive functions in multiple sclerosis (MS) patients and their quality of life (QoL). The study follow-up lasted for 3 years and the evaluation was performed every 9 months for four times altogether. We present data on the first and second session, when we evaluated the frontal component of cognitive functions, behavioural memory and quality of life. We administered the Luria Frontal Lobe Syndrome test (LFLS), the Rivermead Behavioural Memory Test (RBMT), the State-Trait Anxiety Inventory (STAI), the Beck Depression Inventory (BDI), SF-36 for QoL evaluation. The frontal component of cognitive functions and behavioural memory involvement is related to a worsening of QoL, in particular in the Physical Functioning and the Mental Health of SF-36. *Journal of NeuroVirology* (2000) **6,** S186–S190.

Introduction

Over the last few years there has been a growing interest in the development of accurate and reproducible methodologies aimed at evaluating QoL. Interest in the 'Quality of Life' construct seems to be the logical consequence of the definition of health articulated by the WHO, according to which health is defined within a multidimensional scope that includes the description of the physical, psychological and social conditions of individuals and populations. Within the scope of the multicenter trial promoted by the Mental Health Division of the WHO, aimed at developing and perfecting a tool for the evaluation of QoL, to be implemented on an international scale (WHO Quality of Life Instrument), QoL has been defined as: 'the perception that the individuals have their own position in life in the context of the culture and the value system in which they live, and in relation to their objectives, their expectations, their standards and their concerns' (WHO-QOL Group,1994).

This growing interest on the part of the scholars towards QoL has also characterised the scientific community dealing with multiple sclerosis. As a matter of fact, it is now 5 years since the Consortium of Multiple Sclerosis Center articulated the minimal criteria for setting up the clinical trials according to a health model which takes into account the individual dimensions of QoL (Consortium of MS Center, 1994).

The need to measure QoL also arises from the fact that traditional evaluation instruments of the patient's functional status have hitherto displayed substantial limits. In particular, the EDSS has proven to be a scarcely analytical instrument with regard to the single functional areas, overly influenced by the relative weight of the integrity of the neuro-motor function and too little by that of the neuro-psychic apparatus. This appears even more evident if we consider, in terms of treatment with Interferon Beta, that the cognitive apparatus seems to be one of the main mediators of the improvement in the patient's QoL (Rao,1997).

In spite of such considerations, it can be noted that the studies aimed at evaluating the QoL of MS patients are very few and far between. In the by now classic study by Rudick in 1992 it was demonstrated that MS has a greater impact on quality of life compared to chronic intestinal illnesses and rheumatoid arthritis (Rudick *et al*, 1992). Other works that have taken into consideration the QoL in MS patients have highlighted that, amongst other things that from a clinical standpoint the impact of MS on QoL cannot be predicted solely on the grounds of

the degree of severity and the duration of the disease (Aschoff and Braitinger 1986; Lawson *et al*, 1985; Wineman and Schwetz 1995; Stiufbergen 1995; Vickrey *et al*, 1995; Robnett and Gliner, 1995; Muthny *et al*, 1992; Gulick *et al*, 1993; Muthny, 1992).

As regards the relationship between cognitive deficits and QoL in MS, Rao *et al*, have compared two groups of non-hospitalized patients perfectly homogeneous for degree of physical disability, one with cognitive deficits and the other without. The patients with cognitive deficits were most frequently jobless, with a lesser overall amount of social contact, a prevalence of major sexual dysfunctions and with greater difficulties in domestic routines (Rao *et al*, 1992). However, in contrast, Halligan did not confirm such a relationship (Halligan *et al*, 1988).

The evaluation of the relationship between cognitive functions and QoL is the objective of a 3-year long longitudinal study. This study comprises four evaluation sessions, one every 9 months and overall involved 80 patients affected by MS. Of these 40 are followed up at the Multiple Sclerosis Center of the City of Bologna A.U.S.L., 20 at the outpatients' surgery of the Neurological Clinic of the University of Parma (Prof D Visintini), and 20 at the MS outpatients' surgery of the Neurological Clinic of the University of Ancona (Dr G Giuliani).

In this paper we report the data relating to the first evaluation session on the patients from the MS Center of Bologna.

Considering that the prevalent current interpretation concerning the cognitive disorder of MS is that of an impairment in executive functions (Beatty *et al*, 1989; Peyser and Poser, 1986; and, more recently, Brassington and Marsh, 1998), we decided to evaluate the frontal component of the cognitive functions, while as regards the evaluation of QoL, we decided to utilise the SF-36 questionnaire. In order to take into account the weight of the patients' motivation factor on their cognitive performance, we evaluated their emotional status at the moment of the test administration.

Results

The scores obtained by the patients at the SF-36, already transformed into 0–100 scale, are displayed in Table 1. A comment upon those data will be made subsequently in the Discussion. In Table 2 are reported the data relating to the significant correlations between the various SF-36 scales and the cognitive tests. In particular, the following appear to be significantly correlated: the score at Luria's test for the frontal lobe syndromes positively with the score at the Beck Depression Inventory, and negatively with the scores for physical function and life satisfaction. The score at the Rivermead

Behavioural Memory Test is inversely and significantly correlated with the score of the scale relating to the role limitation due to emotional problems. Moreover, the Beck Depression Inventory score turned out to be significantly positively correlated with the frontal functionality score, with a score at the STAI anxiety trait, with the number of exacerbation relating to the previous year; the BDI score itself is significantly inversely correlated with the STAI score anxiety state, with the physical functionality score, with the role limitations scale due to physical impairments, with the role limitations due to emotional problems, with the overall score of the quality of life, with life satisfaction and, lastly, of course, with the score relating to mental health in general.

Discussion

As concerns the significance of the above-mentioned data, it is interesting to note that the patients, before a perception of relative well-being in regard to physical performance (PF=81.74), nevertheless feel that the same physical status somehow limits their routine everyday tasks (RP=45.29), such as walking for distances of varying lengths, or generally carrying out activities with a physical commitment of differing intensity. The greater degree of fatigue among MS patients can account for such a contradiction. The measures relating to the other SF-36 scales have scores that are lower than those of the Italian normative group (Apolone

Table 1 SF-36 scores transformed into 0-100 scale

Physical functioning	(PF)	81.74 ± 19.48
Role physical	(RP)	45.29 ± 36.39
Body pain	(BP)	71.53 ± 25.22
General health	(GH)	48.44 ± 24.25
Vitality	(VIT)	50.29 ± 20.96
Social functioning	(SF)	64.50 ± 23.35
Emotional role	(ER)	55.18 ± 34.02
Mental health	(MH)	62.53 ± 19.27

Table 2 Correlation matrix of the results

LNNB (frontal)
    BDI   0.3400 *P*=0.04
    PF   −0.4341 *P*=0.012

RMBT (results profile)
    RE   −0.4015 *P*=0.0028

BDI
    MH   −0.7197 *P*=0.000   RP −0.7068 *P*=0.000
    STAI1 −0. 6635 *P*=0.000
    PF   −0.7867 *P*=0.000   SF −0.4294 *P*=0.018
    N. exacerbation 0.4304   *P*=0.009   STAI2 0.7398 *P*=0.000
    RE   −0.6543 *P*=0.000
    LNNB 0.3400 *P*=0.04

and Mosconi, 1998). In other words, the QoL of the MS patients with a degree of disability up to 3.5 emerges as being definitely affected by a diminished perception of well-being in all the single dimensions of the construct, in the face of a good physical functionality, that is. This aspect, moreover, constitutes a further critical argumentation in regard to the efficacy of the Kurtzke scale in analytically detecting the different functional limitations. As regards the possible relationship between QoL and the cognitive functionality of the patients, the data show the following: the influence of a possible impairment in the ('ecological') behavioural memory on the perception of role limitations due to emotional problems, the influence of a possible frontal dysfunction (executive function) on the general sense of life satisfaction and, not surprisingly, on the patient's depressive state. Furthermore, what emerges is that the patient's emotional state (ansio-depressive) influences important dimensions of the QoL represented by physical functionality, the perception of the limitations deriving from this, from the social functioning, from the sense of psychological impotence. Moreover, the evaluation confirms the common observation, deriving from the clinical experience, that a worsening of the depressive status is predicted by the increase in the number of exacerbation in the previous year.

In conclusion, although this study suffers from a substantial drawback, as represented by the relatively low number of patients, (but it should be remembered that it is a longitudinal study), it highlights an overall picture of the patient relatively free from disabilities (EDSS up to 3.5), in which are interwoven within a network of reciprocal influences the subjective perception of the state of health and personal well-being and satisfaction, cognitive functionality and the motivational state, as well as the physical condition itself.

Once again, by highlighting the complexity of the clinical manifestation of multiple sclerosis, what is quite apparent is the need for an interdisciplinary approach towards the patient affected by this disease, one which duly takes into account the patient's cognitive-affective status along with the current clinical parameters.

Materials and methods

Patients

The MS group of patients consists of *n*=40 subjects followed up at the Multiple Sclerosis Center of Bologna, all with a definite diagnosis of MS according to the international criteria of Poser (Poser *et al*, 1983). The inclusion criteria are represented, besides the certain diagnosis of MS, by an age between 20 and 50 years, by EDSS lower than or equal to 3.5, by the remittent-recalcitrant form of the disease. The exclusion criteria are represented by the presence of a positive psychia-

tric clinical history, by the presence of language impairments, the presence of visual dysfunctions, the presence of dysfunctions of dominant upper limb, by the presence of any other disabling pathologies. The sexual composition of the sample is represented by 30 per cent males (*n*=12) and by 70 per cent females (*n*=28). The mean age of the patients is 38.67 years with s.d.=±7.44 (Table 3).

Within the scope of the assessment the following characteristics are noted which, however, do not constitute exclusion or inclusion criteria for the study: number of exacerbation during the year prior to the evaluation, age of disease onset, any treatment cycles for neuro-motor re-education performed in concomitance with the study.

Tests and questionnaires

The tests and questionnaires administered to the patients are the following.

Short Form-36 (SF-36) (Ware, 1993) This is a questionnaire for the evaluation of the quality of life, consisting of 36 items. It represents the concise form of a larger questionnaire developed within the scope of the Medical Outcomes Study MOS (Ware and Sherbourn, 1992; McHorney *et al*, 1993, 1994). This questionnaire has two important fundamental characteristics: (a) it highlights accurately and profoundly the patient's point of view in the treatment process; (b) the administration time is relatively short. The 36 items that make up the questionnaire are grouped in Likert-like 8 scales, as follows: physical functionality, role limitations due to problems of a physical nature, social functionality, limitations due to emotional problems, general mental health, physical pain, vitality, general perception of health. The sum of the scores obtained in the items in each scale constitutes the raw mark. By means of a specific algorithm (which takes account of the raw mark, the lowest raw mark and the range of the raw marks of the individual scales), the raw mark of the individual scales is transformed

Table 3 Description of the MS patient sample

N=40
  Males=12 (30%) Females=28 (70%)
  Mean age 38.67±7.44

Inclusion criteria
  Certain diagnosis of MS according to the international criteria of Poser
  Minimum age 20 years–maximum age 50 years
  EDSS lower than or equal to 3.5
  Form of the disease: remittent-recalcitrant (R-R)

Exclusion criteria
  Patients with negative psychiatric anamnesis
  Patients with language dysfunctions
  Patients with visual dysfunctions
  Patients with dysfunctions of the dominant upper limb
  Patients with other disabling pahtologies

into a score ranging between 0 (total absence of health) and 100 (status of complete well-being). The overall time allowed for filling out the questionnaire ranges between 20 and 40 min.

Luria's Frontal Lobe Syndromes (LFLS) Test This is represented by a group of items drawn from the Luria-Nebraska Neuropsychological Battery (LNNB) and validated by Malloy and colleagues (Malloy *et al*, 1985) by means of the evaluation of the capacity of such items in discriminating, in a group of patients, those with right and left frontal lesions from those with right and left posterior lesions. The evaluation consists of ten tests to assess the optical-spatial organization of movement, three tests drawn from the rhythm scale, two tests to evaluate the visual function, seven tests to evaluate the understanding of language, two calculation tests, five memory tests and four tests relating to intellectual processes. The overall time for test administration was about 20 min.

Rivermead Behavioural Memory Test (RBMT) (Wilson *et al*, 1985) This measures the behavioural memory. It evaluates the mnemic function understood in its 'ecological' sense. Indeed, the tests are conceived of in such a way as to simulate the everyday use of memory with particular attention to the spontaneous re-evocation and the cued re-evocation. the results are expressed in a screening score and in a standard results profile.

Beck Depression Inventory (BDI) (Beck *et al*, 1961) This is a scale made up of 21 items, each one investigating a particular aspect of the depressive state. As is known, that questionnaire was developed to assess the depressive disorders with a view to predisposing a therapeutic intervention within the scope of the cognitive depression model (Beck, 1976; Beck *et al*, 1979). In particular, the focus of the questionnaire is directed towards the cognitive structure which in

the depressed patient is oriented towards a pessimistic vision of the self and the reality surrounding him/her. For this reason such a scale appears to be particularly suited to the evaluation of cognitive, affective and behavioural dysfunctions in MS (Sullivan *et al*, 1995; Rodin and Voshart, 1994; Bishop *et al*, 1993). Indeed, the content of the individual items is not correlated to the somatic symptoms of depression, which often overlap with the organic symptoms of the disease, but, as already said, with the cognitive aspects of the very same depression.

State-Trait Anxiety Inventory (STAI) (Spielberger *et al*, 1970) This measures anxiety both as a state (20 items) and as a stable character trait (20 items). Such a distinction between state variables and trait variables regards those characteristics of the personality that express a stable organization of attitudes and temperament (traits), as opposed to those traits that are influenced by contingent events and are thus limited to a certain time-interval. It is particularly suitable for the diagnosis of anxiety disorders in non-psychiatric patients. The answers are organized in a Likert-like scale with four levels. The score ranges from a minimum of 20 to a maximum of 80.

Procedure

The administration of the above-described test came about in two sessions. During the first session the STAI, BDI and the LFLS tests were administered. At the end of the first session a copy of the SF-36 that the patient fills in at home and returns during the second session was given. During the latter the RBMT was administered and the STAI was re-administered.

For the statistical elaboration the mean, the standard deviation and the calculation of the linear correlation coefficient was worked out.

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