Research Paper Medical Science

Happiness in Interferon-beta-1a (Rebif) Treated Multiple Sclerosis Patients: a European survey.

Yoram Barak, MD, MHA	The Sheba Medical Center Multiple Sclerosis Center and the Tel-Aviv University Sackler School of Medicine, Israel.
Karol Jastrzebski, MD, PhD	Department of Neurology and Epileptology Teaching Hospital, Lodz, Poland.
Vesna Brinar, MD, PhD	Polyclinic for Neurology and Internal Medicine "Cortex", Zagreb, Croatia
Csilla Rozsa	MD Ferenc Delpesti Hospital, Budapest, Hungary
Anat Achiron, MD, PhD	The Sheba Medical Center Multiple Sclerosis Center and the Tel-Aviv University Sackler School of Medicine, Israel

ABSTRACT

Objective: Happy persons are healthier and demonstrate enhanced immune function. Multiple sclerosis (MS) adversely affects wellbeing and happiness. Increasing happiness in MS patients may promote immunity and adherence. We compared happiness and personal growth between MS patients and healthy volunteers across different countries in Europe.

Methods: The Satisfaction with Life Scale (SLS; reflecting happiness) and the Personal Growth Initiative Scale (PGIS) were endorsed by RRMS patients and matched healthy subjects. All patients had been treated for at least 6 months with Rebif.

Results: In all, 302 participants were enrolled; 188 MS patients from Israel, Hungary, Croatia, Poland and the Czech Republic were enrolled with 114 healthy controls. Mean patients' age was 45 + 0.3 and 45.2 + 0.4 years for controls. Female to male ratio was 2:1 in both groups. Mean disease duration was 6.9 + 5.4 years. Mean EDSS score was 2.5 + 2.3. Patients were treated with Rebif for a mean of 3.2 + 2.4 years. Happiness and personal growth scores were similar for MS patients and controls. Only in the Czech Republic happiness and personal growth were lower in MS patients. In all countries, Rebif treated patients had a mean happiness score higher than "neutral." There were no significant differences in happiness scores between countries. Personal growth differed significantly between countries.

Conclusion: Happiness scores were similar between MS patients and controls across five European countries. Early treatment may enable patients to achieve a sense of control over the disease process reflected in these positive psychology variables.

Significant Outcomes: happiness levels were assessed in MS patients across 5 countries in Europe for the first time. Treated MS patients can have highly significant satisfaction with life. Personal growth may be more sensitive to cultural and sociodemographic influences.

Limitations: sample size in each country is modest, all patients were treated by a single drug and religious, health beliefs and other sociocultural issues were not investigated.

KEYWORDS multiple sclerosis, survey, happiness, interferon.

INTRODUCTION

Happiness is associated with multiple positive outcomes in interpersonal, economic and health related life spheres. Happy people are more successful primarily because positive affect engenders success (1). Happiness is also associated with better health and heralds numerous successful health related outcomes, as well as lifestyle behaviors paralleling success. Several studies report that longevity and functional health are increased by positive self-perception and that more positive self-perception is associated with enhancement of cognitive and behavioral outcomes. Recent years have witnessed increased interest in the relationship between positive psychological well-being and physical health. A review of 35 studies investigating mortality in initially healthy populations and 35 studies of disease populations was undertaken by Chida and Steptoe (2). The meta-analyses showed that positive psychological well-being was associated with reduced mortality in both the healthy population and the disease population. Both positive affect, including happiness and positive trait-like dispositions, including life satisfaction were associated with reduced mortality (2). Happiness is thus a crucial mediator in maintaining well-being and health.

Brain disorders represent a considerable social and economic burden in Europe. Data collected by the World Health Organization (WHO) suggest that brain diseases are responsible for 35% of Europe's total disease burden. Multiple sclerosis (MS) is a chronic progressive disabling disorder. It is the primary cause of nontraumatic disability in young adults. Recently it has been estimated that there are nearly 400,000 MS patients in Europe (3). As MS is the commonest disabling neurological condition afflicting young adults it carries a high social burden (4). In MS depressed mood and lower satisfaction with life are frequently reported both at disease onset and when disability accumulates. In a chronic life-long disease such as MS the ability to cope overtime and to persist with positive personal growth may be mediated through positive affect and particularly happiness (5). We have demonstrated that amongst Rebif treated MS patients in Israel happiness and personal growth are preserved. As positive psychology outcomes are in part culture bound it is important to expand these initial findings beyond a single country (6).

Aims of the study: the present study aimed to evaluate happiness and personal growth in relapsing-remitting MS (RRMS) patients treated with interferon-beta-1a (Rebif) across 5 countries in Europe in comparison with age and gender matched healthy subjects.

MATERIALS and METHODS

The Satisfaction with Life Scale (SLS) (7,8) and the Personal Growth Initiative Scale (PGIS) (9) were endorsed by RRMS patients and matched healthy subjects. In addition, the Hospital Depression and Anxiety Scale) (HADS) (10) was scored by all participants in order to rule out clinically significant depression or anxiety. All scales were endorsed in the participants' language. Permission to use the translated and validated versions was obtained from the scales developers (11).

The SLS was developed and validated as a scale to measure global life satisfaction by Diener and colleagues (7). The SLS is shown to have favorable psychometric properties, including high internal consistency and high temporal reliability. The SLS is suited for use as a screening tool for large-scale surveys with a wide range of age groups and applications. In addition, the high convergence of self- and peer-reported measures of subjective wellbeing and life satisfaction provide strong evidence that it is a relatively global and stable phenomenon, not simply a momentary judgment based on fleeting influences. The SLS consists of five items that are rated on a Likert scale from 1 = Strongly agree to 7 = Strongly disagree. Item scores are summed to obtain a total SLS score. Higher scores reflect more satisfaction with life.

The PGIS is a self-report instrument reflecting a person's active and intentional involvement in self changing and developing (9). The PGIS was shown to be positively related to psychological well-being and hope with high reliability and validity (12). The PGIS consists of nine items that are rated on a Likert scale from 1 = Strongly Disagree to 6 = Strongly Agree. Item scores are summed to obtain a total PGI score. Higher scores are related to improved personal growth.

In each of the participating countries at least 20 patients and 10 matched controls were recruited. Countries participating in this project were: Israel, Hungary, Croatia, Poland and the Czech Republic.

Clinical and demographic variables were extracted from the patients' medical files. All patients enrolled were treated for at least 6 months with Rebif, (either Rebif or Rebif New formulation). All patients underwent qualitative assessment of their level of disability utilizing the Expanded Disability Status Scale (EDSS). In brief, the scale combines grades of impairment within 8 functional systems and an overall Disability Status Scale that has steps from 0 (normal) to 10 (death due to MS), (13).

The study was approved by all the relevant local IRB committee.

Endpoints of the study

Primary endpoint:

To assess differences between Rebif treated MS patients and healthy volunteers regarding happiness and personal growth.

Secondaryendpoint:

To assess any correlation between patients' demographic or clinical data and positive psychology outcomes.

Statistical Methods

All measured variables and derived parameters were tabulated by descriptive statistics. The following statistical methods were used in the analysis of the data:

T-test was applied for testing the statistical significance of the differences in happiness scores between MS patients and the control group.

Pearson correlation was applied for testing the internal correlation between the happiness scores. Pearson correlation was applied for testing the correlation between the happiness scores and age. T-test was applied for testing the statistical significance of the differences in happiness scores between males and females.

All tests applied were two-tailed, and p value of 5% or less was considered statistically significant.

The data was analyzed using the SAS® 9.1 software package (SAS Institute, Cary, North Carolina).

RESULTS

The present survey succeeded in enrolling patients and controls from the following countries: Israel, Hungary, Croatia, Poland and the Czech Republic.

In all, 302 participants were enrolled; 188 MS patients as well as 114 healthy controls. Mean age for the patients was 45 $\pm$ 0.3 years compared to 45.2 $\pm$ 0.4 years for the controls. The female to male ratio was 2:1 in both groups. Mean disease duration was 6.9 $\pm$ 5.4 years. Mean EDSS score was 2.5 $\pm$ 2.3. Patients were treated with Rebif for a mean of 3.2 $\pm$ 2.4 years. There were no gender differences in mean scores of the SLS or PGIS and thus analyses included both women and men for each country.

Mean happiness and personal growth scores were similar for MS patients and controls. When subsuming all participants and all controls in two main groups as "patients" versus "controls" there were no significant between-groups differences in mean SLS or PGIS scores. Only in the Czech Republic happiness and personal growth were decreased in MS patients compared to controls. In all countries, Rebif treated patients had a mean happiness score higher than "neutral." There were no significant differences in mean happiness scores between countries. On the other hand, personal growth differed significantly between all countries studied [p (for distribution) = 0.003].

See Table 1 for details of scale means and statistical differences.

One of the important outcomes we investigated is the trans-cultural differences in happiness and personal growth. Although SLS mean scores ranged from 19.4 in Poland to 27.2 in the Czech Republic the differences between all 5 participating countries were not statistically significant. PGIS mean scores ranged from 30.6 to 45.9 and there was a significant between-countries difference (p=0.003).

Disease and treatment variables were analyzed to decipher their influence on happiness and personal growth. The correlation between happiness levels as reflected by SLS score and three clinical variables: EDSS score, disease duration and treatment duration was tested. The only significant correlation (r= - 0.27, p= 0.03) was found between EDSS score and happiness. This was a negative correlation, implying that with disease progression and more severe disability happiness levels of MS patients' decrease. However, the explanation for these findings may be more complex. Neither disease duration nor treatment duration was significantly correlated to happiness scores – although the direction of correlation (similar to EDSS) was negative for treatment duration and positive for disease duration. Possibly, more severe cases of MS treated for longer periods of time are adversely affected in the domains of positive psychology.

DISCUSSION

The association between disability and happiness is complex. One of the hypotheses in the field, the so-called "happiness paradox", states that disabled individuals could maintain reasonable levels of quality of life and even happiness. Studies

comparing health-related quality of life in patients with chronic diseases to that of normal individuals are essential to build an objective benchmark of their impact on well-being perceptions of affected individuals. Some researchers have pointed to the fact that many individuals with chronic health conditions apparently recovered their levels of welfare, constituting what has been called happiness, well-being or quality of life paradox (14). One of the most important challenges in resolving the happiness paradox is the comparison of happiness levels among individuals with various chronic health conditions and with the normal population.

Existing literature.
Results from the few studies comparing MS patients to healthy individuals are conflicting (15,16). Results of a recent study show that MS patients present lower levels of quality of life in comparison to healthy controls, arguing against the happiness paradox hypothesis. Preservation of quality of life levels against certain levels of disability may be restricted to a group of patients (17). However, these authors have not quantified happiness directly nor did they correct for treatment, cultural or disease duration effects.

Happiness has been little studied as an endpoint in individual neurological diseases, either in therapeutic trials or in studies investigating the impact and pathology of disease. Monitoring and improving happiness and well-being in patients with neurological diseases is, however, a critical component of successful treatment to improve outcomes (6). To the best of our knowledge the only study to quantify happiness and personal growth in MS patients was completed by our group – however – it focused only on one center in Israel (18).

Main findings. In the present survey we focused on evaluating happiness and personal growth in five countries in Europe. Happiness scores were similar between patients and controls across these five countries in Europe. The exception to these encouraging findings was the disparity between MS patients lowered happiness scores (compared with controls) in the Czech Republic. We need to further investigate country-specific variables that may have contributed to this disparity. Nevertheless, in all countries participating in the present survey MS patients mean and median happiness scores were higher than the "neutral" score of the rating scale used. This is in line with our previous publication on happiness amongst Israeli MS patients. In that sense, the expansion of the Israeli findings to different countries and cultures warrants a cautionary generalized statement.

Strengths and limitations. To the best of our knowledge this is the first attempt to systematically study happiness and personal growth in MS patients from different countries. The use of well validated and accepted rating scales is one of our studies strengths. Clearly defined criteria were employed. However, sample size is modest and depression or anxiety were not corrected for if not of clinical significance.

Implications. We can tentatively suggest that identifying unhappy MS patients and teaching them to increase their happiness levels may be feasible, cost-effective and will enhance adherence to DMD treatment.

Authors contributions: All authors (YB, KJ, VB, CR AA) formulated the research questions and designed the study as well as writing the article. KJ, VB and CS carried out the study, collected the data and analyzed the data. YB and AA helped in collecting the data. YB and AA supervised the data collection and with KJ, VB and CR wrote the paper.

Acknowledgements: None.

Financial support: this work was supported by an unrestricted educational grant from Merck-Serono and by the Czech Ministry of Education (research program MSM 0021620849)

Ethical standards: the authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Table 1
Satisfaction with Life and Personal Growth

Site Variable	Czech Republic		Israel		Hungary		Croatia		Poland	
Status	HC (N=15)	MS (N=21)	HC (N=34)	MS (N=65)	HC (N=28)	MS (N=58)	HC (N=26)	MS (N=21)	HC (N=11)	MS (N=23)
Mean SLS score (±SD)	27.2 4.2	20.6 5.6	24.4 5.8	24.5 6.9	25.6 5.9	22.8 6.4	23.8 6.4	25.6 4.8	19.4 5.5	22.2 5.9
Mean PGIS score (±SD)	45.9 5.2	34.0 8.6	40.9 4.6	40.6 10.7	44.5 6.1	43.9 6.3	38.7 8.7	37.8 7.5	30.6 4.4	38.6 8.8
P (diff)	P=0.005		NS		NS		NS		NS	

Legend:
HC = healthy controls
MS = multiple sclerosis patients
P (diff) = difference between HC and MS scores for each country
NS = not significant
SLS = satisfaction with life scale
PGIS = personal growth inventory score

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