

Impact of Earthquake on Multiple Sclerosis Attacks

Depremi Multipl Skleroz Ataklarına Etkisi

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ABSTRACT

Objective: The association between stressful life events and subsequent multiple sclerosis (MS) attacks has been frequently reported with conflicting results. In this study, we investigated the impact of a common stressor on MS attacks. **Methods:** We prospectively evaluated the attack and disability status of 48 consecutive relapsing remitting (RRMS) or secondary progressive MS (SPMS) patients (Group 1) exposed to 1999 Izmit earthquake in comparison to 34 consecutive MS patients (Group 2) with similar demographic and clinical features and living outside the earthquake zone.

Results: An increased proportion of patients had relapses in Group 1 within the 3month period after earthquake with no difference in EDSS in a 1year followup period. Furthermore, Group 1 patients with attacks exhibited significantly increased numbers of relapses in a 1year followup period compared to Group 1 patients without attacks and Group 2 patients with or without attacks. Alternatively, the average annual attack rates in Group 1 patients without attacks were significantly reduced. Logistic regression analysis revealed the exposure to earthquake as a predictor of MS attacks. There was no statistically significant association between MS attacks and occurrence of posttraumatic stress disorder.

Conclusion: Our results suggest that stress has opposing effects on MS attacks in different patients. (*Archives of Neuropsychiatry 2010; 47: 324-7*)

Key words: Multiple sclerosis, earthquake, attack, stress

ÖZET

Amaç: Stresli yaşam olayları ile onları izleyen multipl skleroz (MS) atakları arasındaki ilişki üzerine birbiriyle çelişen pek çok yazı vardır. Bu çalışmada, genel bir stres kaynağının MS atakları üzerine etkisini araştırdık.

Yöntemler: 1999 İzmit depremine maruz kalan 48 ardışık relapsing remitting (RRMS) veya sekonder progresif (SPMS) MS hastasının (Grup 1) atak ve özürüllük durumları, benzer demografik ve klinik özelliklere sahip ve deprem bölgesinin dışında yaşayan 34 ardışık MS hastasının (Grup 2) prospektif olarak karşılaştırıldı.

Bulgular: Depremden sonraki 3 aylık dönem içinde, daha fazla sayıda Grup 1 hastasında atak gözlemlendi. Ancak bu hastaların 1 yıllık takiplerinde EDSS skorları değişmedi. Ayrıca, 1 yıllık izlem süresi içinde, ataklı Grup 1 olguları, atakları olmayan Grup 1 ve ataklı veya ataksız Grup 2 olgularına kıyasla, daha fazla sayıda atak geçirdi. Ataksız Grup 1 hastalarının ortalama yıllık atak sayıları belirgin derecede düşüktü. Lojistik regresyon analizi, depreme maruz kalmamanın, bir MS atağı prediktörü olduğunu gösterdi. MS atakları ile posttravmatik stres bozukluğu gelişimi arasında istatistiksel olarak anlamlı bir ilişki yoktu.

Sonuç: Sonuçlarımız stresin, farklı hastalarda, MS atakları üzerinde birbirine zıt etkileri olduğunu göstermektedir. (*Nöropsikiyatri Arşivi 2010; 47: 324-7*)

Anahtar kelimeler: Multipl skleroz, deprem, atak, stres

Introduction

Since the very beginning of multiple sclerosis (MS) research, association between stressful life events and MS attacks has aroused interest. However, the results of the studies investigating this association have been somewhat conflicting-some conferring an attack-triggering role to stress,

whereas others do not. Stress might have been exerting differing effects on attacks, presumably due to variations in stress type, severity, duration, and individual physical and psychological features of the patients making the causal interpretation difficult (1-7).

A previous report examining MS patients exposed to a common stressor and thus, avoiding stress variability, has shown

that a series of common stressor events alleviate MS and decrease the number of attacks (8). In another attempt to untangle the stress-attack association, we evaluated a group of MS patients who were prospectively followed after being exposed to a single and short but severe stressor, an earthquake. To our knowledge, this is the first report on the impact of an earthquake on the clinical course of MS.

Methods

Patients

The 1999 Marmara (Izmit) earthquake was approximately a 7.4 magnitude earthquake that struck northwestern Turkey on August 17, 1999, lasting for about 45 seconds and killing over 17.000 people. Consecutive 82 definite relapsing-remitting (RRMS, n=55) or secondary progressive MS (SPMS, n=27) patients, who attended our clinic for a routine prescheduled visit within the 3-month period following the earthquake were enrolled. All visits had been scheduled before the earthquake and all included patients met the McDonald diagnostic criteria. In the same region, another earthquake with a magnitude of 7.2 occurred 3 months after the Izmit earthquake. To avoid the interference of this earthquake, the patient enrollment period was limited to 3 months. The patients were divided into two groups: those living in (Group 1, n=48) or outside (Group 2, n=34) the earthquake zone during the earthquake. Group 1 and 2 patients were further divided into two subgroups based on experiencing at least one MS attack in the 3-month period following the earthquake (with attacks) or not (without attacks). The rate of patients attending the scheduled visits in all groups was over 95% and was statistically identical.

Neurological Evaluation

An attack was considered a worsening of previous symptoms or appearance of new ones lasting more than 24 hours in the absence of fever or other possible factors. The decision of an attack for each patient was made depending on patient's medical

history and a thorough neurological examination. Disability scores were determined using the Kurtzke Expanded Disability Status Scale (EDSS). The patients were followed every 3 months for 1 year after the earthquake and, in each visit, were further examined and questioned for an attack. The attack numbers and EDSS scores at the end of the 1-year follow-up period were recorded.

Psychiatric Evaluation

Group 1 patients were examined by a psychiatrist, who was unaware of the attack status of the patients, using the post-traumatic stress disorder (PTSD) scale and the impact of event scale (IES) (9). To avoid the impact of acute trauma, this evaluation was performed at least one month after the earthquake. PTSD diagnosis was considered when the patients' status fulfilled all or all except the first of PTSD criteria. In IES evaluation, the patients were not only evaluated by their numerical scores but also by the severity of the scores classified as mild, moderate and severe. Since this evaluation aimed at investigating the influence of earthquake on MS attacks, Group 2 patients living outside the earthquake zone did not undergo psychiatric evaluation.

Statistical Analysis

Student's t-test (two groups) or ANOVA (multiple groups) were used for parametric comparisons and the Mann-Whitney U (two groups), the Kruskal-Wallis (multiple groups) or Fisher's exact test methods were used for non-parametric comparisons. Moreover, relation of attack occurrence after the earthquake to other variables (exposure to earthquake, gender, age during the earthquake, duration of MS, MS type and EDSS score during the earthquake) was assessed by logistic regression analysis.

Results

The demographic and clinical features of the patients are listed in Table 1. Before the earthquake, there was no statistically

Table 1. Demographic and clinical features of the patients

	Group 1 (EQZ)	Group 2 (OEQZ)	p value
Gender (F/M)	48 (32/12)	34 (20/14)	NS
Average age of onset±SE	26.8±1.3	24.8±1.2	NS
Multiple sclerosis type	33 RRMS 15 SPMS	22 RRMS 12 SPMS	NS
Median duration of disease	74 months	83 months	NS
Median follow-up time	47 months	42 months	NS
EDSS before EQ±SE	3.09±0.3	3.01±0.4	NS
EDSS one year after EQ±SE	3.32±0.3	3.21±0.3	NS
Number of patients with attacks 3 months after EQ	23	8	
Number of patients without attacks 3 months after EQ	25	26	p<0.05
Number of attacks/year before EQ ± SE	0.83±0.1	0.63±0.1	NS
Number of attacks/year after EQ ± SE	0.66±0.1	0.42±0.1	NS
Number of attacks in 3 months after EQ ± SE	0.23±0.04	0.09±0.03	p<0.05
Number of attacks in 4-12 months after EQ ± SE	0.43±0.08	0.32±0.08	NS

EQZ: earthquake zone; OEQZ: outside the earthquake zone; F: female; M: male; NS: not significant; SE: standard error; EQ: earthquake; RRMS: relapsing remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis

significant difference between demographic and clinical features of Group 1 and 2 patients (Table 1).

Frequency of MS attacks and disability scores in the aftermath of the earthquake: Within the 3-month period following the earthquake, significantly more Group 1 patients exhibited attacks (23 of 48 patients, 17 women, 6 men) than Group 2 patients (8 of 34 patients, 5 women, 3 men) ($p<0.05$), suggesting that a severe and short-lasting stressor might facilitate MS attacks. Although RRMS patients were more likely (23/55; 41.8%) to experience attacks than SPMS patients (8/27; 29.6%), this difference was not statistically significant. Number of attacks in the first 3 months was significantly higher in Group 1 ($p<0.05$), whereas this difference subsided in the following 4-12 months period (Table 1).

After the earthquake: Group 1 patients with MS attacks had significantly higher annual number of attacks (1.06 ± 0.1) than Group 1 patients without attacks (0.21 ± 0.1) and Group II patients with (0.54 ± 0.1) or without attacks (0.37 ± 0.1) ($p<0.05$), while the annual attack rates before the earthquake were statistically not different (Table 2). Notably, Group 1 patients without attacks developed significantly fewer attacks (0.21 ± 0.1) than the other 3 groups after the earthquake (indicated by** in Table 2). Likewise, when pre- and post-earthquake attack frequencies were compared, Group 1 patients without attacks (0.68 ± 0.1 vs. 0.21 ± 0.1) had a significantly reduced MS attack frequency ($p<0.05$,

indicated by* in Table 2). There were no significant differences between the annual pre- and post-earthquake attack frequencies of the other groups.

In contrast with attack numbers, Group 1 and 2 patients with or without attacks demonstrated comparable EDSS scores. Also, pre- and post-earthquake EDSS scores were comparable for each group (Tables 1 and 2). The logistic regression analysis showed that the only variable associated with attack occurrence was exposure to the earthquake. In other words, MS patients exposed to earthquake ($p=0.007$, odds ratio=4.348, 95% confidence interval=1.489-12.692) were more likely to develop MS attacks.

Psychiatric Evaluation of Group I Patients

Fifteen Group I patients fulfilled all of the PTSD scale criteria and 5 fulfilled all but the first one (total of 20 patients with PTSD; 13 women, 7 men). Only 11 (8 women, 3 men) PTSD patients developed attacks. PTSD rates of patients with and without attacks were not significantly different (Table III). On the other hand, social dysfunction subcategory of PTSD scale was observed in 26 patients, and 15 of these patients had developed attacks ($p=0.04$). Although both PTSD scale and IES scores were higher in patients with attacks as compared to patients without attacks, these differences did not attain statistical significance (Table 3). Similarly, PTSD scale and IES scores of patients

Table 2. Comparison of disability scores and attack numbers of Group 1 and 2 patients with or without attacks

	Group 1 (EQZ)		Group 2 (OEQZ)		p value
	With attacks (n=23)	Without attacks (n=25)	With attacks (n=8)	Without attacks (n=26)	
Number of attacks/year before EQ \pm SE	0.98 \pm 0.1	0.68 \pm 0.1	0.74 \pm 0.3	0.58 \pm 0.1	NS
Number of attacks/year after EQ \pm SE	1.06 \pm 0.1	0.21 \pm 0.1*	0.54 \pm 0.1	0.37 \pm 0.1	$p<0.05^{**}$
EDSS before EQ \pm SE	2.58 \pm 0.4	3.50 \pm 0.5	3.25 \pm 0.7	2.90 \pm 0.4	NS
EDSS one year after EQ \pm SE	3.33 \pm 0.4	3.76 \pm 0.5	3.60 \pm 0.7	3.19 \pm 0.4	NS

EQZ: earthquake zone; OEQZ: outside the earthquake zone; NS: not significant; SE: standard error; EQ: earthquake

*Significant difference ($p<0.05$) in before and after earthquake comparison (0.68 vs 0.21 by Student's t-test)

**Significant difference ($p<0.05$) between Group 1 and Group 2 patients with or without attacks (1.06 vs 0.21 vs 0.54 vs 0.37 by ANOVA)

Table 3. Post-traumatic stress disorder (PTSD) scale and impact of event scale (IES) results of Group 1 patients

	Patients with attacks (n=23)	Patients without attacks (n=25)	p value
PTSD (+)	11	9	NS
Social dysfunctioning (+)	15	11	$p<0.05$
mild	5	2	NS
moderate-severe	10	9	NS
Symptom severity score \pm SE	16.8 \pm 13.5	11.5 \pm 10.4	NS
Symptom severity rating			
mild	6	10	NS
moderate-severe	12	12	
IES intrusion score \pm SE	11.8 \pm 9.25	9.8 \pm 6.8	NS
IES avoidance score \pm SE	15.2 \pm 9.5	10.4 \pm 9.4	NS
Total IES score \pm SE	26.5 \pm 16.4	20.2 \pm 14.6	NS

NS: not significant, SE: standard error

with attacks requiring or not requiring steroid treatment were comparable. The patients with or without PTSD were also similar by means of age of MS onset, gender, EDSS scores and attack numbers.

Discussion

The studies on the influence of stress on MS attack frequency have so far given conflicting results. This might be basically due to the fact that diverse types and durations of stress have been studied in different studies. Previous reports on MS and stress association have focused on either acute or chronic non-life threatening stressful situations (e.g. a parent's death, financial problems) or long-lasting life threatening stress (e.g. exposure to missile attacks for a few weeks). Even the studies on the same type of stress might yield opposing results depending on the methodology and patient inclusion criteria employed. For instance, as a long-term stressor, living under the threat of missile attacks has been reported to either decrease or increase the risk for MS attacks (2,8). These discrepancies are probably due to influence of various moderators between stress and MS activity, such as MS type, nature of the stressor, patient's individual biological, social and psychological features (5,6).

Our results suggest that as a short-lasting life threatening stressor, earthquake significantly increases the number of attacks in the short term. Moreover, exposure to the earthquake does not appear to alter the disability scores of MS patients, which might be explained by relatively short follow-up times in our study. Also, MS attacks induced by a short common stressor might not have a severe and debilitating character. Our results also failed to show a clear and robust association between increased MS attacks due to stress and PTSD development. In the long term, MS patients might show two distinct types of responses to the brief severe stress induced by the earthquake. Patients with relatively more active disease and more frequent attacks appear to display increased MS attacks. On the contrary, the earthquake as a stressor is more likely to reduce the frequency of the attacks in patients with a slightly more benign disease course and relatively lower attack numbers. Therefore, the attack rates and severity of the disease before exposure to a stressor might determine the frequency of MS attacks in the aftermath of the stress-inducing event.

Pathogenic factors behind this duality are obscure and can only be speculated. Group I patients without attacks might have higher levels of cognitive or behavioral coping (5) or might have been exposed to a more severe stress, as moderate stress has been associated with increased MS attack risk, and severe stress has been related to decreased disease activity (5). Variable attack frequencies in response to stress might also be associated with different patients' diverse hypothalamic-pituitary-adrenal axis mediated cortisol or IFN- γ responses, both of which have been shown to be affected by stress conditions and accordingly to increase or decrease the MS severity (10,11). Other factors influencing this discrepancy need to be further elucidated.

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