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Life Events in the Year Preceding the Onset of Narcolepsy

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Summary: A multifactorial etiology for narcolepsy has been postulated, stressing the importance of environmental factors in the clinical onset of the condition. Our study evaluated the occurrence of stressful life events in the year preceding the onset of narcolepsy. Fifty narcoleptic and 50 control subjects completed a life event questionnaire (the Schedule of Recent Experiences). The proportion of narcoleptic subjects reporting the presence of life events in the year preceding the onset of narcolepsy was significantly greater than the proportion of control subjects reporting life events in the corresponding year. Moreover the weight of life events was increased in narcoleptic subjects in comparison with controls. In conclusion life events seem to be increased in narcoleptic subjects in the year preceding the onset of their condition. However a number of other factors could not be taken into consideration, which limits the full significance of these data. **Key Words:** Narcolepsy—Environmental factors—Life events.

Narcolepsy is a neurological condition related to a dysfunction of brainstem sleep–wake mechanisms and is expressed as a tetrad of four major symptoms: excessive daytime sleepiness with irresistible episodes of sleep, cataplexy, sleep paralysis and hypnagogic hallucinations. Genetic factors are important in its pathogenesis. Different series have been reported with a varying percentage of probands having one or several family members affected (1–7). There is an extraordinary association with the human leukocyte antigen (HLA) haplotype DR2 DQ1 (8–10). Yet in a family with a narcoleptic proband and several members carrying the haplotype, only a few develop narcolepsy. In addition, studies in monozygotic twins have shown an important percentage of discordance for the disease (11,12). Thus the role of environmental factors is most likely important in the occurrence of narcolepsy.

Different precipitant factors, such as a sudden abrupt change of the sleep–wake schedule, psychological stress, infectious disease, operation, anesthetic, head injury and pregnancy, have been described preceding the onset of narcolepsy (13–15). Except for two studies of streptococcal antibodies in narcolepsy (16,17), however, no systematic study has investigated any of these environmental factors.

Considering the large number of subjects reporting psychological stress at the onset of narcolepsy, we thought it interesting to look at life events previous to the appearance of symptoms in a group of narcoleptic subjects. Studies of life events have been of considerable use in researching the association between stressful life events and illnesses (18–22) and a number of questionnaires have been developed (23–25). Despite some limitations and criticisms (26,27) we decided to use this methodology.

METHODS

Fifty narcoleptic subjects (32 men and 18 women, median age 45 years, range 14–73) with two sleep onset rapid eye movement (REM) episodes or more on the multiple sleep latency test, all DR2 DQ1 positive, were included in the study. A control group consisting of 50 individuals matched for sex, age and socioprofessional level was used. Among the available questionnaires we chose the Schedule of Recent Experiences (23), a 40-item questionnaire pertaining to major areas of significance in the social structure (including family constellation, marriage, occupation, economics, group relationship, education, recreation and health) of the subject. All subjects were interviewed by the same investigator (C.O.) either in person or by telephone. Nar-

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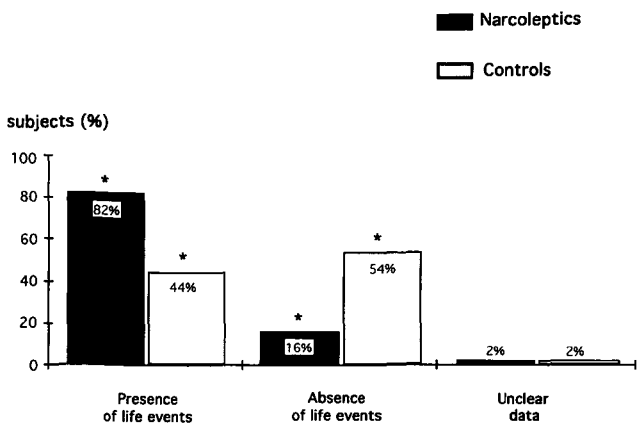

FIG. 1. Incidence of life events in the year preceding the onset of excessive daytime sleepiness.

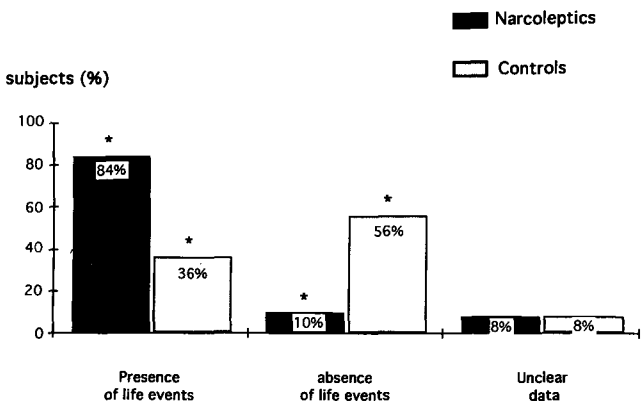

FIG. 2. Incidence of life events in the year preceding the onset of cataplexy.

coleptic subjects were questioned about the existence of life events in the year preceding the onset of excessive daytime sleepiness and cataplexy, and controls were questioned about the existence of life events in the corresponding year in which the matched narcoleptic subjects developed the disease.

We were also interested in evaluating the weight of life events preceding the beginning of excessive daytime sleepiness and cataplexy in narcoleptic subjects and the weight of life events in the corresponding years in control subjects. Thus 50 individuals representative of the French population (INSEE data, 1982) were asked to give a weight to each of the items of the questionnaire on a scale from 1 to 100. Then the total weight of life events reported by narcoleptic subjects was compared to that reported by control subjects.

Statistics

Chi square was used to compare the proportion of narcoleptic subjects with life events in the year preceding the onset of excessive daytime sleepiness and in the year preceding the onset of cataplexy with the proportion of control subjects reporting life events in the corresponding years. Student's *t* test was used to compare the mean of the reported weights of life events in narcoleptic and control subjects.

RESULTS

Eighty-two percent of narcoleptic subjects reported one or several life events in the year preceding the onset of excessive daytime sleepiness. In comparison 44% of the control population referred to the existence of life events in the corresponding year ($\chi_{-} = 15.48$, $p < 0.0001$) (Fig. 1). In the case of cataplexy 84% of narcoleptic individuals referred to the presence of life events, compared to 36% of controls ($\chi_{-} = 24$, $p < 0.0001$) (Fig. 2). Uncertainty about the precise year of the beginning of the symptoms was noted in 2% of cases for excessive daytime sleepiness and 8% for cataplexy. Life events reported by narcoleptic subjects are shown in Table 1, in descending order of frequency.

In addition, the weight of life events reported by narcoleptic subjects was compared with the corresponding weight of life events reported by control subjects (Table 2). The weight of life events reported by narcoleptic subjects in the years preceding the beginning of both excessive daytime sleepiness and cataplexy was significantly higher than the weight of life events reported by control subjects in the corresponding years.

DISCUSSION

One of the main issues in this type of study is the choice of the specialized questionnaire to be used. As already pointed out there are several available questionnaires. The oldest one is the Schedule of Recent Experiences (23). Some difficulties have been indicated with this questionnaire (24,28). Some of the items are worded vaguely, hence the risk that different people do not report on a similar event. Some events of the Schedule of Recent Experiences could actually be thought of as symptoms rather than events (e.g. marital difficulties), which raises the issue of criteria contamination. The range of events being sampled in the Schedule of Recent Experiences is either too restrictive or not appropriate for a given population. The Schedule of Recent Experiences lacks predictive validity. On the other hand this questionnaire has the advantage of having been validated by a great number of studies in the same field (29,30) and includes a relatively com-

TABLE 1. *Life events reported by narcoleptic subjects in the year preceding the onset of excessive daytime sleepiness (s) and cataplexy (c), in descending order of frequency*

Major changes in sleeping habits	34% (s) 26% (c)
Major personal injury or illness	32% (s) 20% (c)
Major changes in the health of a family member	20% (s) 16% (c)
Revision of personal habits	18% (s) 16% (c)
Death of a close family member	14% (s) 14% (c)
Major changes in social relationships	12% (s) 10% (c)
Change of residence	<8%

TABLE 2. *Weight of life events reported by narcoleptics in the year preceding excessive daytime sleepiness and in the year preceding cataplexy and weight of life events reported by controls in the corresponding years*

	Narcoleptics (n = 41)	Controls (n = 22)	p
Year preceding excessive daytime sleepiness	142.34 ± 69.76	87.59 ± 55.64	<0.001
Year preceding cataplexy	132.25 ± 69.09	78.31 ± 40.19	<0.001

prehensive list of events. It is not an exceedingly time-consuming method of data collection and is a practical method of quantification based on adding scores of each event; hence, the choice that we made to use this questionnaire.

The Interview Schedule for Events and Difficulties of Bedford College (24) is based upon the gathering of data by interviewers who have undergone specialized training. The interview has the advantage of including a wider range of circumstances. It is tape-recorded. Although it represents an excellent approach to life events research, the drawback of this strategy is its time-consuming nature: almost half a day may have to be spent with the subject. In addition, personalized training must be accomplished. Finally a large investment in time for interview and rating, and in research costs, is required for proper use of the schedule.

The Interview for Recent Life Events developed by Paykel (25) consists of a semistructured interview, shorter and less detailed than the previous one. Good reliability has been found and this interview should be considered in the future.

Narcoleptic subjects may have a better recollection of life events in the year preceding the onset of their condition, in comparison with controls of the same age, because of the development of clinical symptoms. An improvement of the method would be the use as controls of patients affected with another chronic condition, with a precise onset, such as posttraumatic paraplegia. Even in that case, it may turn out that the life event (e.g. bereavement) would have altered the driving skills, introducing another bias.

A number of subjects, either narcoleptic or control, did not report any life event in the corresponding year, and this may be due to a too restricted range of circumstances.

There is a high frequency of low-weight events compared with high-weight events. This may be related to the generally early age of onset of narcolepsy. It is possible that the weight of life events varies with age and that a so-called low-weight life event has greater impact in young subjects.

A further approach to this subject would be to study a control population matched with the narcoleptic population not only for age, sex and socioprofessional status, but also for the incriminated haplotype HLA DR2 DQ1. Such a study would be extremely difficult to conduct, but it could be the ultimate refinement in the study of the impact of life events on the development of narcolepsy.

In conclusion, our data show a higher proportion of subjects with life events during the year preceding the onset of narcolepsy than in normal controls at the same age. A number of other factors, however, such as the role of the patient's premorbid personality, his coping style, the meaning of the stress to a particular individual and the social support he may have benefited by, were not taken into account. All these factors may be of prime importance.

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