

Correlation of anxiety and depression symptoms in patients with restless legs syndrome: a population based survey

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Background and objectives: Restless legs syndrome (RLS) is an important and common cause of insomnia, and previous studies indicate that psychiatric wellbeing may be impaired among RLS patients. We aimed to investigate the interaction between anxiety/depression and RLS in a population based survey.

Methods: Data were drawn from the Mersin University Neuro-Epidemiology Project, a representative community sample of adults aged over 17 years residing in Mersin (n=3234). Subjects found to be positive for RLS (n=103) were evaluated for symptoms of anxiety and depression using the Hamilton Anxiety and Depression Scales and compared with the same number of contemporaneous control subjects.

Results: Significantly greater anxiety and depression symptoms were observed among patients with RLS than in the control subjects. Our data also seem to provide initial evidence of a correlation between the severity of RLS and of anxiety and depression symptoms ($r=0.21$, $p=0.03$ and $r=0.201$, $p=0.04$ respectively).

Conclusions: Assessment of psychiatric status of RLS patients can be helpful and sometimes necessary to determine additional features and treatment strategies of this bothering condition. Further studies are needed to replicate our findings using longitudinal data.

Restless legs syndrome (RLS) is a common and treatable disorder, which interferes with sleep onset and disturbs sleep. The syndrome is principally characterised by dysesthasias in the lower extremities occurring especially at bedtime, associated with an irresistible urge to move the legs. The minimal diagnostic criteria for RLS established by the International Restless Legs Syndrome Study Group (IRLSSG) are: (a) desire to move the limbs, usually associated with paresthasias/dysesthasias; (b) motor restlessness; (c) symptoms worse or exclusively present at rest (lying or sitting) with at least partial and temporary relief by activity; and (d) symptoms worse in the evening or at night.¹ The underlying aetiology is uncertain, although recent imaging data suggest clinically and functionally impaired central dopaminergic transmission.^{2–5} A number of triggering factors have also been described, including pregnancy, iron deficiency, uraemia, neuropathy, and drugs.^{6–17}

Many patients with RLS are reported to complain of great psychological discomfort due to their disorder;¹⁸ hence, RLS symptoms along with the impairment of sleep may cause distress and lead to psychiatric illness and decreased wellbeing. Although the first study attracting attention to psychiatric comorbidity in patients with RLS was reported more than 30 years ago, little progress has been made since then in attempts to explore this relationship.¹⁹ In one of the two recent epidemiological surveys, the MEMO study, depression was reported to be more common among patients with RLS compared with normal individuals,¹⁰ and Philips *et al* found RLS to be significantly related to diminished general health and mental health based on the two self reported questions included in their study.²⁰ In another recent study, RLS patients demonstrated significantly higher depression and anxiety scores than control subjects and had similar electroencephalography (EEG) changes to patients with major depression.²¹ There are very few studies investigating psychiatric comorbidity, and data on this association are insufficient, including any on the relationship between the magnitude of the symptom burden, the risk of

psychological symptoms, and the therapeutic effects of accurate treatments of RLS on any psychiatric illness accompanying the condition. Therefore, it seemed reasonable to investigate depression and anxiety, which were mostly thought to be associated with RLS, among patients with RLS in a population based survey. Data were collected as a part of the population based Mersin University Neuro-Epidemiology Project (MUNEP), the objective of which was to examine the prevalence and characteristics of RLS and essential tremor in Mersin.

METHODS

The study was conducted in Mersin, an administrative province on the Mediterranean coast of Turkey. The area of the province is 776 000 km². According to the national census in 2000, the adult population of Mersin numbered 962 770, of which 40.3% were resided in the capital city, 29.8% in the other cities, and 20.9% in villages.

A population based, cross sectional, and selective (including samples older than 18 years of age) study was performed. Multi-step, stratified, cluster, and systematic samplings were used.

Estimation of sample size

Previous studies have indicated that RLS symptoms are experienced by 0.1–29% of the population. Assuming a prevalence of 5%, a confidence interval (CI) of 99%, an error of 1% and a population of 962 770, the minimum sample size was calculated to be 3141 persons. After consulting the household identification of the state health centres for a sampling with respect to gender and age group, it was determined that selecting 3500 persons would best represent

Abbreviations: EEG, electroencephalography; HAM-A, Hamilton Rating Scale for Anxiety; HAM-D, Hamilton Rating Scale for Depression; IRLSSG, International Restless Legs Syndrome Study Group; IRLSSGRS, IRLSSG Rating Scale; MUNEP, Mersin University Neuro-Epidemiology Project; RLS, restless legs syndrome

the sample universe. The sample size randomisation was made with the EPI 6 INFO programme. Randomisation was also weighted according to gender, age, and population of each region (capital city, other cities, and villages). The sampling was carried out in five steps as follows: (1) All health centres were classified into three groups: capital city health centres, city health centres and village health centres. According to the number of health centres in each of the three regions, 20 original and 5 additional health centres were randomly selected. (2) With respect to their weighted populations, sample size was determined for each group (capital city, cities, and villages). (3) Each ward of any selected health centre district was considered as a cluster, and clusters included in the study were randomly selected. (4) Sample size for each cluster was determined. (5) Finally, in each cluster representing a ward, residents were selected by systematic sampling method with respect to gender and age group from the household identification of that particular health centre. An additional sample group, 20% of the original, was also determined by the same method. The target study population consisted of 3500 adults from 20 health centres of 151 in the province. This sample represented 0.28% of the entire adult population of Mersin.

Study procedure

The epidemiological survey consisted of face to face, door to door interviews with 3500 adult residents of Mersin. Two neurologists and two neurology residents who are experienced in evaluating RLS, and in using the Hamilton Rating Scale for Anxiety (HAM-A) and Hamilton Rating Scale for Depression (HAM-D), conducted all the interviews. They visited 3500 homes in designated areas in Mersin between July and 26 December 2002. Only one respondent per home was interviewed. Before interviewing each person, written informed consent was obtained. A form including the demographic features consisting of 11 items was administered to each person included in the study. The four minimal criteria suggested by the IRLSSG were used in the assessment for RLS: (a) the desire to move the limbs associated with paresthesias/dysesthesias; (b) motor restlessness; (c) symptoms present exclusively or worse at rest (lying and sitting) with at least partial and temporary relief by activity; and (d) symptoms worse in the evening or at night.¹ Where necessary, the four screening questions were explained in detail to participants. Only those who gave a clear and distinct positive response to all four questions were classified as having RLS at pre-digit level. The interviewers performed neurological examinations in order to distinguish RLS from other disorders that can mimic it (particularly akathisia, polyneuropathy, and radiculopathy) and to determine possible causative or co-morbid conditions where necessary. Respondents who did not report RLS symptoms in the previous month (even if they had experienced the symptoms previously) were excluded. The interview followed a three part questionnaire for participants identified as positive by the screening process. The aim of the structured first part was to determine the characteristics of RLS and the biological and sociodemographic variables that potentially influence it. The second part was comprised of the IRLSSG Rating Scale (IRLSSGRS) and used to assess the severity of RLS.²² The third part, which is the main subject of this paper, consisted of the Turkish version of the HAM-A and HAM-D, and was used to determine the depression and anxiety scores of the RLS patients.²³⁻²⁴ An age and gender matched RLS negative individual from the same health centre district was taken into the control group for each person diagnosed as RLS and given the same questionnaire (except for the 10 questions in the first part and the IRLSSGRS).

The interviewers assessed the agreement of the four screening questions on a subgroup of participants, and an interclass correlation of the IRLSSGRS on a subgroup of patients.

Statistical analysis

All data were coded using the SPSS PC 11.0 data entry program and summarised using frequency and contingency tables for categorical variables, and means and standard deviation for continuous variables. The prevalence of RLS among participants was estimated with descriptive statistics. Comparisons were made between HAM-A and HAM-D scores and anxiety and depression features of patients and control subjects. Additionally, the relation of the results of these two scales with the major demographic features and the biological and sociodemographic variables of patients and control subjects was assessed. The three questions about sleep disorders in the HAM-D and one in the HAM-A were excluded from the comparisons between patients and controls. We used the χ^2 test to test the independence of criteria of classification, and independent *t* test and analysis of variance followed by the Bonferroni test to compare the means. The Mann-Whitney U test was used to compare the mean ranks between the groups and *t* test to compare proportions. *P* values ≤ 0.05 were regarded as statistically significant.

The inter-rater agreement of the Turkish version of four screening questions were assessed by kappa statistics. Intra-class correlation coefficient was calculated for a total score of the IRLSSGRS.

RESULTS

Of the selected 3500 persons, 3234 (designated as "participants") contributed to the study and the rate of participation was calculated to be 92.4%. After at least two attempts, 193 (5.51%) people and their substitutes could not be found at their homes on at least two trials. Five persons (0.14%) who had cerebrovascular disease ($n=2$), dementia ($n=2$), and mental retardation ($n=1$) were unable to respond and were excluded. In addition, 68 persons (1.94%) refused participation, 43 of whom did not want to state a reason for their refusal. The stated reasons for non-participation were denial of having any illness at all ($n=12$), not having time to participate ($n=4$), having their own doctor ($n=4$), lack of belief in the benefit of such studies ($n=2$), embarrassment ($n=2$), and lack of belief in the interviewers' profession ($n=1$). Participants generally did not have difficulties understanding the RLS criteria questions.

Agreement among the four raters for the Turkish versions of each of the four screening questions and of the IRLSSGRS were both found to be nearly perfect (each of the four kappa value was >0.81). The intra-class correlation coefficient was calculated to be 0.92 ($p<0.001$) for the total score of the IRLSSGRS.

Demographic data of the participants

The respondents had a mean age of 40.48 with a standard deviation (SD) of 15.3 years, and were comprised of 1643 (50.7%) women and 1591 (49.3%) men. Of the 3234, 46% were residing in the capital city, 28.4% in other cities and 25.6% in the villages. The average number of years of education of respondents was 6.09 years (SD: 4.1, min: 0, max: 19). Most of the women included in the study were (85.6%) housewives. Among the men, 24.3% were tradesmen, 24.1% manual labourers, 15.1% retired, 13.8% farmers and 9.3% civil servants. All the demographic mean values given above did not differ significantly from that of the mean values obtained in the 2000 national population census of Mersin province.

Patients

Among 3234 respondents who successfully answered the demographic and diagnostic questions, 103 (3.18%) were found to be screen positive according to the diagnostic criteria of the IRLSSG (64 women and 39 men). Two individuals who full-filled the minimal criteria of RLS at the pre-digit level were excluded owing to lumbar radiculopathy ($n = 1$) and diabetic polyneuropathy ($n = 1$) after getting a comprehensive medical history and performing a physical examination. One patient was on serotonin reuptake inhibitor therapy (sertraline) and differential diagnosis of RLS with akathisia was performed after detailed interrogation and examination of this patient, including the questions on the provocative affect of rest and sleep on symptoms, the impact of sensory symptoms, relief of symptoms by activity, and inspection and examination. The diagnosis of RLS in this patient was made by the consensus of two interviewers of the study.

Demographic data of the RLS patients

The mean age of the patients was 43.28 years (SD 15.31, range 18–79). The prevalence of RLS was 3.9% for females and 2.45% for males, and the female to male ratio was 1.6:1. Of the 103 patients, 47 (45.6%) were residing in the capital city, 27 (26.2%) in other cities, and 29 (28.2%) in villages. The mean education of patients in years was 5.57 (SD 3.98). Forty-six patients (44.7%) were current cigarette smokers and 34 (73.94%) of this subgroup smoked more than 10 cigarettes per day. Six patients (5.83%) reported their mean daily alcohol consumption to be more than 10 grammes. None of the patients reported their income level to be “very good” on the five point rating scale. The income status reported by the patients was “good” for 9, “fair” for 48, “bad” for 35 and “very bad” for 4. Six patients did not respond to the relevant question and one was missing. The reported co-morbid illnesses were hypertension ($n = 10$), anaemia ($n = 8$), chronic kidney disease ($n = 7$), depression ($n = 4$), diabetes mellitus ($n = 3$), and migraine ($n = 2$).

Characteristics of RLS

The average age of onset of RLS was 36.11 years (SD 14.08, range 12–75) and the mean duration of complaints was 7.42 years (SD 7.52). RLS was found to be more prevalent among women under the age of 48 years compared with men ($p = 0.003$). Of the 31 patients (30% of all patients) reporting that they had complained to their own physicians about RLS symptoms previously, only one (3.36%) was diagnosed with RLS and had received accurate treatment. The remaining 102 patients were unaware of having RLS. The average score of IRLSSGRS was 22.27 (SD 5.53, range 9–34).

Anxiety and depression scores of RLS patients

The mean (SD) anxiety score of patients was 8.03 (6.02), and depression 9.27 (5.03). HAM-A and HAM-D scores correlated with the total IRLSSGRS score ($r = 0.21$, $p = 0.03$ and $r = 0.201$, $p = 0.04$ respectively). A positive linear correlation was found to exist between the age and anxiety scores of patients ($r = 0.24$, $p = 0.01$), but not between age and depression scores ($r = 0.16$, $p = 0.1$). The anxiety and depression scores were not found to vary with gender, cigarette smoking, income status, or existence of any co-morbid disease.

Control group

The mean age of the control group was 43.1 years (SD 15.22, range 18–78) and the mean (SD) number of years of education was 5.74 (3.58). Thirty-three control subjects (30.1%) were current cigarette smokers and two (1.94%) reported their mean daily alcohol consumption to be more

than 10 grammes. None of the control subjects reported their income level to be “very good” on the five point rating scale. The forcome status reported by the controls was “good” for 11, “fair” for 44, “bad” for 40 and “very bad” for 6. Two persons did not respond to the relevant question. The reported co-morbid illnesses in the control group were hypertension ($n = 14$), anemia ($n = 4$), diabetes mellitus ($n = 2$), and chronic kidney disease ($n = 1$). The mean (SD) anxiety score of control subjects was 5.91 (6.68), and the mean depression score 5.88 (4.99).

Comparison of the patient and control groups

The age, gender, and regional distribution were similar in the patient and control groups, as had been previously determined. The proportion of current cigarette smokers was significantly higher in the patient group compared with control subjects, and individuals who smoked >10 cigarettes per day were more likely to experience RLS ($p = 0.021$ and $p < 0.001$ respectively). RLS patients reported anaemia, chronic kidney disease, depression, and overall co-morbid illnesses more frequently than the controls ($p = 0.01$, $p < 0.001$, $p < 0.001$, and $p = 0.01$ respectively). No significant differences were found between the patient and control groups regarding profession, level of education, alcohol consumption, and income status.

The mean scores on HAM-A and HAM-D of the patients were found to be significantly higher than those of the control subjects ($p < 0.001$ for both variables) (figs 1 and 2). Significant differences ($p < 0.05$) were found in mean item scores for the two groups for anxious mood ($p < 0.001$), tension ($p < 0.001$), insomnia ($p < 0.001$), cognitive functions ($p = 0.04$), depressed mood ($p < 0.001$), and somatic muscular ($p < 0.001$), somatic sensory ($p = 0.027$), cardiovascular ($p = 0.01$), respiratory ($p = 0.001$), genitourinary, ($p = 0.05$) and autonomic symptoms ($p = 0.026$) on HAM-A. No significant differences were found for gastrointestinal symptoms and behaviour at interview, with low scores in both groups.

In addition, significant differences ($p < 0.05$) were found in mean item scores for the two groups for depressed mood ($p < 0.001$), guilt ($p = 0.017$), suicide ($p = 0.07$), initial ($p < 0.001$), middle ($p < 0.001$), and late insomnia ($p < 0.001$), work and interests ($p < 0.001$), agitation

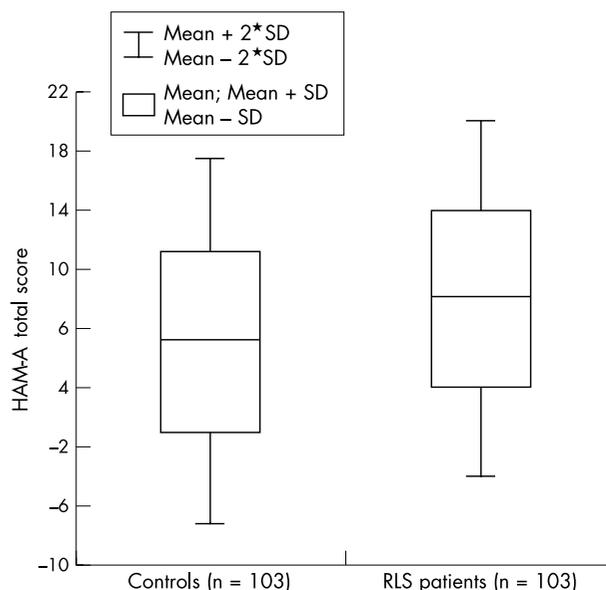


Figure 1 The anxiety scores on HAM-A of RLS patients and controls.

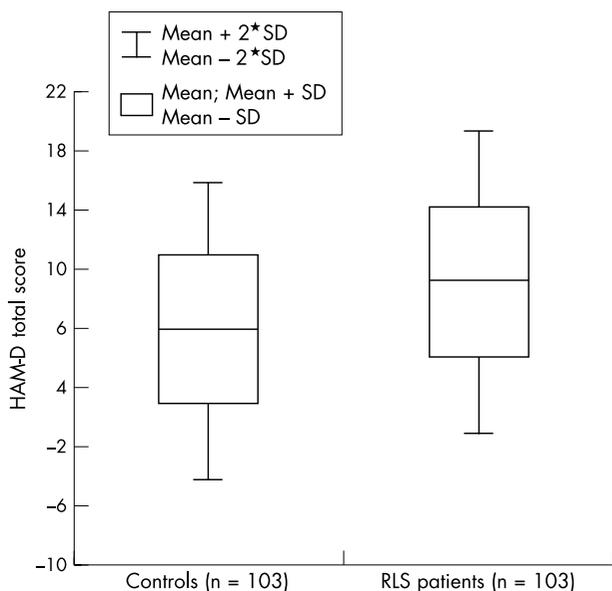


Figure 2 The depression scores on HAM-D of RLS patients and controls.

($p = 0.026$), psychic ($p < 0.001$) or somatic anxiety ($p = 0.038$), gastrointestinal ($p = 0.004$), somatic ($p = 0.003$), or genital symptoms ($p = 0.009$), and hypochondriasis ($p = 0.026$) on HAM-D. No significant differences were shown for psychomotor retardation, loss of weight, and insight.

DISCUSSION

The participation rate was high in our study. A possible explanation for the high rate of participation is the face to face design of our study, rather than by telephone call or letter, and we think that this high participation rate makes our results more reliable.

Our investigation confirmed that the RLS population was more anxious and depressed than the controls. This result is compatible with the only previously reported population based survey on RLS using an anxiety and depression scale and with several hospital based studies on the issue.^{10 19 21} More importantly, we used the IRLSSGRG as a measure of severity and found a clear relationship indicating that HAM-A and HAM-D scores were directly related to increased IRLSSGRS scores. Moreover, having any co-morbid disease with RLS was not found to have a relation with the total scores of HAM-A and HAM-D. Taken together, having RLS was probably the major determining factor for the anxiety and depression scores, with higher scores correlating with more severe RLS.

The strength of our study is that it is population based, and 102 of the 103 RLS positive individuals were unaware of having RLS. In the several previous studies focusing on RLS and co-morbid psychiatric illness, research has been conducted in patients who presented to neurology clinics or patients who participated in clinical trials.^{19 21 26} In these studies, the psychiatric impact of RLS may have been overestimated because the patient samples were not likely to be representative of patients with RLS in the community. Patients who consult physicians are more likely to have more severe RLS and this may influence the anxiety and depression scores.

The severity, persistence, and frequency of RLS symptoms are important for the physician in deciding the patient's need for pharmacotherapy and selection of the accurate drug. The

presence and/or severity of anxiety and depression currently are not routinely assessed in therapeutic trials of RLS. Further studies investigating the effects of levodopa, dopaminergics, and antidepressants on anxious and depressive symptoms among RLS patients are needed to determine the best treatment strategy. Such new studies regarding alterations in anxiety and depression symptoms along with the other scales used to determine the severity of RLS can reflect the therapeutic effect of a drug more clearly, and possibly the existence or otherwise of a demand for specific treatment of anxiety and depression.

In the first study on RLS and comorbid psychiatric disease, Gorman and co-workers found higher scores on depression and psychoasthenia scales in RLS patients when they compared these scores with those of both the general population and psychiatric referrals.¹⁹ Of the 27 RLS patients assessed for psychiatric symptoms, they found 13 to have depression and most of them to be tense. The investigators concluded that depression and tension among their patients was unlikely to be due to their chronic discomfort, because in at least 6 of the 13 patients depression and tension antedated the discomfort in the legs. In contrast, the implication deriving from the results of our study is that mood disorders are more likely to be due to the RLS symptoms, and that the impairment of sleep and chronic sleep deprivation caused by RLS is likely to be the chief cause of daytime symptoms such as sleepiness, depression, and anxiety.

However, we have no available data on the onset of anxiety and depression symptoms, or the relation between the sequence of RLS and anxiety/depression symptoms in our patient group. Hence, we do not find it reasonable to claim definitely that higher anxiety and depression are the consequences of RLS referring to our data. Further studies investigating this association using longitudinal epidemiological data are needed to address the issue of temporality as suggested by Rothdach *et al.*¹⁰ Some other limitations of our study should be carefully considered when interpreting results. Firstly, the HAM-A and HAM-D scales were not designated to measure the level of anxiety and depression among RLS patients, and items related to sleep were excluded before comparing the total scores of patients and controls. This impeded the grouping of patients in one of the four result categories of the scales. The second issue to consider is that we did not measure quality of life, which could be supportive in interpreting the data of anxiety and depression scales. Thirdly, even though there is a clearcut difference between the mean scores of HAM-A and HAM-D of the patient and control groups, the number of smokers was significantly higher in the patient group compared with the controls, and it is possible that this state could at least have contributed to this discrepancy, as anxiety and depression are shown to be more common among cigarette smokers.^{27 28}

This report demonstrates significantly higher anxiety and depression symptoms in RLS patients compared with contemporaneous control subjects, and a correlation of the intensity of these symptoms with the severity of RLS in a population based survey. Thus, we conclude that assessment of psychiatric status of RLS patients can be helpful and sometimes necessary to determine additional features and treatment strategies of this troublesome condition.

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REFERENCES

- 1 **Walters AS**. The International Restless Legs Syndrome Study Group. Toward a better definition of the restless legs syndrome. *Mov Disord* 1995;**10**:634–42.
- 2 **Trenkwalder C**, Hening WA, Walter AS, et al. Circadian rhythm of periodic limb movements and sensory symptoms of restless legs syndrome. *Mov Disord* 1999;**14**:102–10.
- 3 **Turjanski N**, Lees AJ, Brooks DJ. Striatal dopaminergic function in restless legs syndrome: 18F-dopa and 11C-racloripride PET studies. *Neurology* 1999;**52**:932–7.
- 4 **Ruottinen HM**, Partinen M, Hublin C, et al. An FDOPA PET study in patients with periodic limb movement disorder and restless legs syndrome. *Neurology* 2000;**54**:502–4.
- 5 **Wetter TC**, Collado-Seidel V, Pollmacher T, et al. Sleep and periodic movement patterns in drug-free patients with Parkinson's disease and multiple system atrophy. *Sleep* 2000;**23**:361–7.
- 6 **Goodman JD**, Brodie C, Ayida GA. Restless legs syndrome in pregnancy. *BMJ* 1988;**297**:1101–2.
- 7 **McParland P**, Pearce JM. Restless legs syndrome in pregnancy. Case reports. *Clin Exp Obstet Gynecol* 1990;**17**:5–6.
- 8 **Lavigne GJ**, Montplaisir JY. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. *Sleep* 1994;**17**:739–43.
- 9 **Chokroverty S**, Jankovic J. Restless legs syndrome: a disease in search of identity. *Neurology* 1999;**52**:907–10.
- 10 **Rothdach AJ**, Trenkwalder C, Habersack J, et al. Prevalence and risk factors of RLS in an elderly population. *Neurology* 2000;**54**:1064–8.
- 11 **Bahk WM**, Pae CV, Chae JH, et al. Mirtazapine may have the propensity for developing a restless legs syndrome? A case report. *Psychiatry Clin Neurosci* 2002;**58**:209–10.
- 12 **Bonin B**, Vandel P, Kantelip JP. Mirtazapine and restless legs syndrome: a case report. *Therapie* 2000;**55**:655–6.
- 13 **Hargrave R**, Beckley DJ. Restless legs syndrome exacerbated by sertraline. *Psychosomatics* 1998;**39**:177–8.
- 14 **Markkula J**, Lauerma H, Mianserin and restless legs. *Int Clin Psychopharmacol* 1997;**12**:53–8.
- 15 **Sanz-Fuentenebro FJ**, Huidobro A, Tejedas-Rivas A. Restless legs syndrome and paroxetine. *Acta Psychiatr Scand* 1996;**94**:482–4.
- 16 **Bakshi R**. Fluoxetine and restless legs syndrome. *J Neurol Sci* 1996;**142**:151–2.
- 17 **Salin-Pascual RJ**, Galicia-Polo L, Drucker-Colin R. Sleep changes after 4 consecutive days of venlafaxine administration in normal volunteers. *J Clin Psychiatry* 1997;**58**:348–50.
- 18 **Wilson V**. *Sleep thief: restless legs syndrome*. Orange Park, FL: Galaxy Books, 1996.
- 19 **Gorman CA**, Dyck PJ, Pearson JS. Symptoms of restless legs. *Arch Intern Med* 1965;**115**:155–60.
- 20 **Philips B**, Young T, Finn L, et al. Epidemiology of restless legs symptoms in adults. *Arch Intern Med* 2000;**160**:2137–41.
- 21 **Saletu M**, Anderer P, Saletu B, et al. EEG mapping in patients with restless legs syndrome as compared with normal controls. *Psychiatry Res* 2002;**115**:49–61.
- 22 **Hening WA**, Walters AS, Rosen R, et al. Members of the International RLS Study Group. The international RLS study group rating scale: a reliable and valid instrument for assessing severity of the restless legs syndrome. *Neurology* 2001;**56**(Suppl. 3):A4.
- 23 **Akdemir A**, Turkcapar MG, Orsel SD, et al. Reliability and validity of the Turkish version of the Hamilton Depression Rating Scale. *Compr Psychiatry* 2001;**42**:161–5.
- 24 **Yazici MK**, Demir B, Tanriverdi N, et al. Hamilton Anksiyete Degerlendirme Olcegi; Degerlendiriciler Arasi Guvenirlilik ve Gecerlik Calismasi. *Turk Psikiyatri Dergisi* 1998;**9**:114–17.
- 25 **Gorman CA**, Dyck PJ, Pearson JS. Symptoms of restless leg. *Arch Intern Med* 1965;**115**:155–160.
- 26 **Kuny ST**. Psychiatrische Katamnese bei Patienten mit "restless legs." *Schweiz Med Wschr* 1991;**121**:72–6.
- 27 **Amering M**, Bankier B, Berger P, et al. Panic disorder and cigarette smoking behavior. *Compr Psychiatry* 1999;**40**:35–8.
- 28 **Sonntag H**, Wittchen HU, Hofer M, et al. Are social fears and DSM-IV social anxiety disorder associated with smoking and nicotine dependence in adolescents and young adults? *Eur J Psychiatry* 2000;**15**:67–74.