Specific Characteristics of the Pain/Depression Association in the General Population

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Objective: To evaluate how the presence of a chronic painful physical condition (CPPC) lasting 6 months or more influences the frequency and severity of depressive symptoms in subjects with major depressive disorder (MDD). ***Method:*** Random samples of 18,980 subjects aged between 15 and 100 years who were representative of the general population of 5 European countries (the United Kingdom, Germany, Italy, Portugal, and Spain) were interviewed by telephone between 1994 and 1999. Subjects answered a series of questions that allowed positive and differential diagnosis of DSM-IV mental disorders. The questionnaire also included a series of questions about painful physical conditions, medical treatment, consultations, and hospitalizations for medical conditions and a list of diseases. ***Results:*** A total of 4% (95% CI = 3.7% to 4.3%) of the sample had MDD at the time of the interview. Nearly half of subjects with MDD (43.4%) also reported having a CPPC. Compared with MDD subjects without chronic pain, MDD subjects with a CPPC had a longer duration of depressive symptoms (7 months longer) and were more likely to report severe fatigue (OR = 5.4), insomnia nearly every night (OR = 3.3), severe psychomotor retardation (OR = 3.3), weight gain (OR = 2.3), severe difficulty concentrating (OR = 1.7), and severe feelings of sadness or depressed mood (OR = 1.8). ***Conclusion:*** A CPPC was present in nearly half of subjects with MDD. CPPCs increased the severity of physical symptoms of depression (fatigue, insomnia, psychomotor retardation, weight gain). Moreover, CPPCs affected the duration of depressive episodes and their recurrence. Physicians should consider CPPCs as a major factor in the expression and evolution of MDD. They must remember that MDD patients tend to amplify physical symptoms, to the detriment of their depressive symptomatology.

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It is estimated that in 2020, major depressive disorder (MDD) will be the second cause of disability in industrialized countries, exceeded only by ischemic heart disease.[1] Most recent epidemiologic studies have estimated the prevalence of MDD to be between 4% and 6% of the United States and western Europe.[2–7]

Major depressive disorder comprises several physical symptoms: insomnia, hypersomnia, psychomotor agitation or retardation, changes in appetite or weight, and fatigue. These symptoms are often the only reasons evoked by patients with depressive disorders for seeking medical help: according to the results of an international multicenter study,[8] up to 69% of primary care patients identified as having MDD reported only somatic symptoms.

Furthermore, subjects with MDD have a 4 times greater risk of suffering from chronic painful physical conditions (CPPCs) than nondepressed individuals[9] and a greater risk of having long-term medical conditions.[10–12]

A pitfall in nonpsychiatric settings is limiting the treatment to physical symptoms while overlooking other signs of depression. Treating only physical symptoms or only the depressive disorder may adversely affect the course of depression.

This study examined how CPPCs lasting at least 6 months influenced the frequency and severity of depressive symptoms in subjects from the general population with MDD.[9] My colleagues and I postulated that the presence of a CPPC would impact not only on the frequency but also on the severity of depressive symptoms. We also explored the evolution of depressive illness in subjects with a CPPC in terms of chronicity and relapse because of their impact on treatment.

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METHOD

Subjects

This epidemiologic survey was conducted by telephone using representative samples of 5 European countries: the United Kingdom (N = 4972), Germany (N = 4115), Italy (N = 3970), Portugal (N = 1858), and Spain (N = 4065). The target population was noninstitutionalized individuals 15 years or older living in one of these 5 countries. The population represented 205 million inhabitants.

The representative samples were achieved using a 2-stage sampling design: at the first stage, the official census data of each country were used to divide the population according to geographical distribution. Telephone numbers were subsequently randomly selected according to this stratification. In the second stage, a controlled selection method was applied to maintain the representative nature of the sample according to age and gender. The Kish method[13] was used to this end and served to select 1 respondent in the household. If the selected household member refused to be interviewed, the household was dropped and replaced by another.

Subjects had to grant verbal consent before being interviewed. Individuals with insufficient fluency in the national language, with a hearing or speech impairment, or with an illness precluding the feasibility of an interview were excluded.

The overall participation rate was 80.4%, comprising 79.6% in the United Kingdom, 68.1% in Germany, 89.4% in Italy, 83.0% in Portugal, and 87.5% in Spain.

Procedure

Lay investigators performed the interviews using the Sleep-EVAL expert system,[14,15] a computer program designed for use in epidemiologic studies of sleep habits and mental disorders in the general population. Sleep-EVAL is a level 2 non-monotonic expert system endowed with a causal reasoning mode, which means that the system has the capability to formulate diagnostic hypotheses that are validated or rejected through further queries and deductions.

A typical interview covered sociodemographic information, sleep/wake schedule, sleeping habits, psychiatric symptoms, medical treatments, and physical illnesses. Once these data were collected, the system used this information to formulate diagnostic hypotheses of sleep and mental disorders according to classifications in DSM-IV[16] and International Classification of Sleep Disorders.[17] Further questions were asked during this process in order to establish (or discard) a diagnosis. The inference engine (or knowledge processor) performed this dynamic reasoning process. This engine based its differential process on a series of key rules allowing or prohibiting the co-occurrence of 2 (or more) diagnoses. A "neural network" managed any uncertainty in the subject's answers as well as in diagnoses. Once all diagnostic possibilities were exhausted, the system closed the interview.[15] Previous validation studies have demonstrated a good validity of the tool.[18–21]

The duration of interviews ranged from 28 to 150 minutes. Interviews could be completed over the course of 2 or more sessions if the duration exceeded 60 minutes or if requested by the subject. The computer program selected all of the questions and displayed them on the screen. The role of the human interviewer was to pose these questions by telephone to the subject being interviewed. Samples and directives regarding how responses should be recorded were also provided.

Questionnaire on Pain

Several questions were used to obtain data on painful physical conditions. Data were gathered on current treatment for a medical condition, current medication consumption (prescribed or not) and indication, and hospitalizations and reasons for hospitalization in the previous year. Lists of diseases (42 diseases listed) were included, and duration of these diseases was elicited.

A painful physical condition was defined as one that lasted for at least 6 months and had consequences on daily functioning or required the use of a medication.

Questionnaire on Depressive Disorders

The questionnaire assessing depressive disorders was composed of 36 questions assessing the various symptoms of MDD: feeling sad, downcast, or depressive; loss of interest and lack of pleasure in activities formerly considered pleasant; changes in appetite or weight; insomnia or hypersomnia symptoms; psychomotor agitation or retardation; fatigue or loss of energy; feelings of worthlessness or guilt; difficulties in concentration or thinking; difficulties making decisions; and suicidal ideation. Most of the symptoms were measured on an intensity scale (extremely, a lot, moderately, slightly, not at all, does not know).

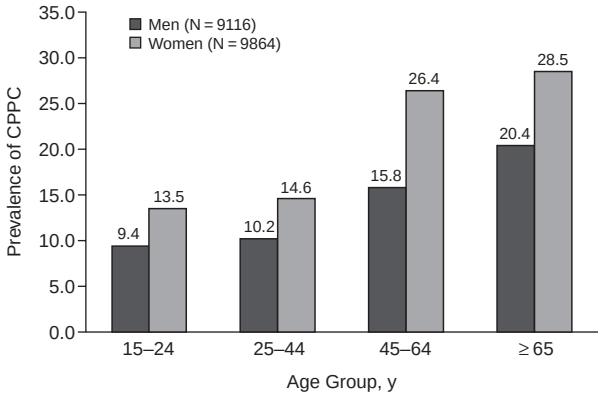
Analyses

The data were weighted to compensate for disparities between the samples and the national census figures for the noninstitutionalized population aged 15 years or over in each of the surveyed countries. Bivariate analyses were performed using the χ^2 test with Yates correction or the Fisher exact test when the number of subjects was smaller than 5. Reported differences were significant at the .05 level or less.

RESULTS

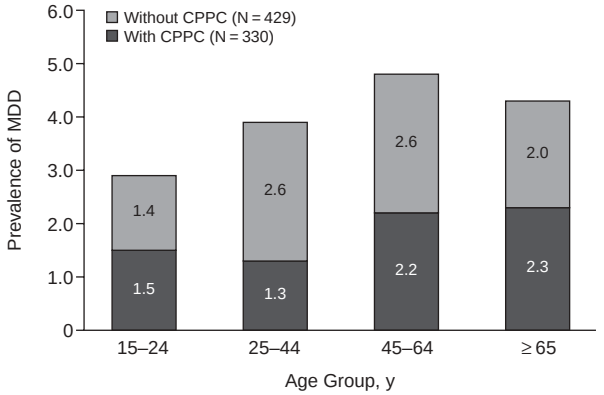
The total sample included 18,980 subjects aged between 15 and 100 years; 52% of the subjects were women.

Figure 1. Prevalence of Chronic Painful Physical Conditions (CPPCs) by Age Group and Gender[a]



[a]p < .0001 between age groups (15- to 24-year-old and 25- to 44-year-old groups vs. 45- to 64-year-old and ≥ 65-year-old groups) and between genders.

Figure 2. Prevalence of Major Depressive Disorder (MDD) by Presence of Chronic Painful Physical Condition (CPPC) and Age Group[a,b]



[a]The total of the 2 CPPC categories equals the total prevalence of MDD for each age group.
[b]p < .001 for the 15- to 24-year-old group vs. the 45- to 64-year-old and ≥ 65-year-old groups.

Prevalence of Chronic Painful Physical Conditions

A total of 17.1% (95% CI = 16.5% to 17.6%) of the subjects reported at least 1 CPPC. The prevalence linearly increased with age and was higher in women than in men (Figure 1). The most frequent CPPCs were headaches (7.6% of the sample), pain in the lower or upper limbs (5.8%), joint/articular disease (3.2%), backaches (3.1%), and gastrointestinal diseases (1.5%).

Prevalence of Major Depressive Disorder

A DSM-IV diagnosis of MDD was found in 4.0% (95% CI = 3.7% to 4.3%) of the sample. The prevalence of MDD was higher in women than in men (4.9% vs. 3.1%; $p < .0001$). The prevalence of MDD was significantly lower in subjects younger than 25 years ($p < .0001$) compared with the other age categories (Figure 2).

As seen in Figure 2, approximately half of all MDD subjects in each age group also had a CPPC. More specifically, 43.4% of subjects with MDD reported at least 1 CPPC compared with 16.1% in the rest of the sample (OR = 4.0 [95% CI = 3.5 to 4.7]; $p < .001$).

Major depressive disorder subjects with a CPPC reported a longer duration of the current depressive episode (31.4 months) than did MDD subjects without a CPPC (24.3 months; Mann-Whitney U: $z = –1.980$, $p < .05$) and were also more likely to have had a past depressive episode than MDD subjects without a CPPC (24.4% vs. 17.4%; $p = .01$).

Frequency and Severity of Depressive Symptoms in Major Depressive Disorder

Table 1 presents the frequency and severity of depressive symptoms in MDD subjects with a CPPC compared with MDD subjects without a CPPC.

A total of 7 symptoms were significantly associated with CPPCs in MDD subjects: feeling sad or depressed, psychomotor agitation and retardation, weight gain, insomnia, fatigue, and impaired concentration. For psycho motor retardation nearly every day, fatigue, and impaired concentration, the significant differences were observed for the category "a lot/extremely"; responses of "moderately" were comparable between the 2 groups. For insomnia, only the category "5 to 7 nights/week" was significant.

The highest odds ratio was observed for severe (a lot/extremely) fatigue nearly every day: MDD subjects with a CPPC were 5 times more likely to report severe fatigue than MDD subjects without a CPPC. The second highest odds ratio was observed for insomnia nearly every night and severe psychomotor retardation; MDD subjects with a CPPC were 3.3 times more likely to report these symptoms than MDD subjects without a CPPC.

The most frequent depressive symptom in MDD subjects with a CPPC was insomnia (3 nights/week or more), followed by feeling sad or depressed (moderately to extremely).

DISCUSSION

This study investigated the relationship between CPPCs and the frequency/severity of depressive symptoms in subjects with MDD in a large sample from 5 European countries. As the results showed, the presence of a CPPC increased the frequency and severity of 7 depressive symptoms: feeling sad or depressed, psychomotor agitation and retardation, weight gain, insomnia, fatigue, and impaired concentration. Five of these were physical symptoms of

Table 1. Frequency and Severity of Depressive Symptoms According to Presence of Chronic Painful Physical Condition (CPPC) in Subjects With Major Depressive Disorder

Symptom	With CPPC (N = 330), %	Without CPPC (N = 429), %	OR (95% CI)
Feeling sad, depressed nearly every day			
Moderately	41.2***	30.7	1.6 (1.2 to 2.1)
A lot/extremely	28.0***	17.9	1.8 (1.3 to 2.5)
Loss of interest in activities nearly every day			
Moderately	28.3	24.8	1.2 (0.9 to 1.7)
A lot/extremely	26.5	21.5	1.3 (0.9 to 1.8)
Psychomotor agitation nearly every day	13.8*	9.2	1.6 (1.0 to 2.5)
Moderately	7.9	5.4	1.5 (0.8 to 2.7)
A lot/extremely	5.9	3.8	1.6 (0.8 to 3.1)
Psychomotor retardation nearly every day			
Moderately	14.1	10.2	1.5 (0.9 to 2.2)
A lot/extremely	7.7***	2.5	3.3 (1.6 to 6.7)
Weight loss	28.9	23.6	1.3 (0.9 to 1.8)
Weight gain	21.3**	10.4	2.3 (1.1 to 5.2)
Insomnia			
3–4 nights/week	43.1	44.4	1.0 (0.7 to 1.3)
5–7 nights/week	31.1***	12.2	3.3 (2.2 to 4.7)
Hypersomnia			
3–4 nights/week	8.2	10.5	0.8 (0.5 to 1.3)
5–7 nights/week	12.8	8.3	1.6 (1.0 to 2.6)
Fatigue nearly every day			
Moderately	17.2	15.5	1.1 (0.8 to 1.7)
A lot/extremely	13.0***	2.7	5.4 (2.8 to 10.5)
Feeling of worthlessness or guilt nearly every day			
Moderately	12.3	7.9	1.6 (1.0 to 2.6)
A lot/extremely	7.4	6.7	1.1 (0.6 to 1.9)
Impaired concentration			
Moderately	16.5	11.9	1.5 (1.0 to 2.2)
A lot/extremely	13.4**	8.4	1.7 (1.1 to 2.7)
Suicidal ideation	44.1	37.3	1.3 (1.0 to 1.8)

*p < .05.
**p < .01.
***p < .001.

depression: psychomotor agitation and retardation, weight gain, insomnia, and fatigue.

Some authors have suggested that depression should be assessed differently in subjects with physical pain.[22–26] This argument is based on the fact that several physical symptoms of depression can be produced by pain rather than by the depressive illness, as is the case for insomnia: difficulties initiating or maintaining sleep are frequently reported by nondepressed patients with chronic pain and are related to pain discomfort. Such is also the case for fatigue, psychomotor agitation, psychomotor retardation, loss of appetite, and difficulties with concentration. Our results clearly showed that subjects with MDD and CPPCs more frequently reported all of these symptoms compared with MDD subjects without a CPPC. One of the precepts of DSM-IV is to discard a symptom when it is clearly and fully accounted for by a physical condition. However, in practice, it is not that simple. It has been reported that most patients with MDD and CPPCs, even those who are severely depressed, tend to attribute their depressive physical symptoms to their painful physical condition.[8,24] Therefore, adopting an approach based solely on the patient's report may lead to an excessively high number of false-negative cases, with the consequence that these patients may not receive appropriate treatment for the ongoing depressive disorder.

To date, there is no clear consensus on how to manage depressive somatic symptoms in the context of painful physical conditions. Some argue that the overlap between pain and depressive symptoms may even compromise the validity of diagnostic questionnaires in that specific population.[27–29] However, there is no convincing empirical evidence that different criteria should be applied to assess depressive disorders in subjects with chronic pain.

Studies that assessed chronic pain and MDD focused mostly on the evaluation of depression in patients with chronic pain or specific pain (for example, low back pain, fibromyalgia, or arthritis).[10–12,30] Frequencies of depressive disorders largely varied depending on the targeted population: for example, in the general population, about 17% of subjects with chronic pain were found to have MDD,[31] while this rate reached up to 64% in pain clinics.[32] The association between depression and pain is very complex. Longitudinal studies have shown that the presence of pain is predictive of new onset of depression but have also shown the reverse situation: depressed individuals were more likely to develop multiple physical symptoms than were nondepressed subjects.[31,33] Our data are cross-sectional; therefore, they offer limited information about the course of pain and depression. We found, however, that depressed mood was present significantly longer—by about 7 months—in subjects who reported a CPPC. Therefore, pain could also contribute to the prolongation of a depressive episode, as reported in clinical studies.[25]

General Comments and Limitations

The point prevalence of MDD was 4% in this representative sample, which is close to results reported by other recent studies using different assessment tools and time frames (for example, the 1-month prevalence of 4.9% reported in the National Comorbidity Survey).[2]

The prevalence of CPPCs found in our study (17.1%) is comparable to those reported in epidemiologic studies assessing chronic pain.[34–37] However, it is lower than the rates reported in studies that addressed both short-term and chronic painful physical conditions and that detailed specific pain sites.[38–40] This was a limitation of the present study: since it was primarily designed to investigate sleep and mental disorders in the general population, the questionnaire did not include extensive investigation of pain sites. The data collected on pain relied on self-reporting. However, since pain is mainly a subjective perception and experience, self-reports of pain are commonly considered

accurate. Studies that have examined the concordance between subjective reports of pain and external measures of pain have found good agreement between the two.[41]

CONCLUSIONS

In summary, this study clearly shows that CPPCs are frequent in subjects with MDD. For subjects with a CPPC, depressive illness is characterized by more frequent and more severe physical symptoms of depression. Consequently, physicians need to consider a diagnosis of MDD in patients consulting for chronic pain, especially if other physical symptoms are present.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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