

# Work-related stress disorders: variability in clinical expression and pitfalls in psychiatric diagnosis

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## KEY WORDS

Occupational stress; stressor-related disorders; mood spectrum

## PAROLE CHIAVE

Stress occupazionale; disturbi stress-correlati; spettro dell'umore

## SUMMARY

**Background:** Putative occupational stress-related psychiatric disorders are Adjustment Disorders (AD) and Post-Traumatic Stress Disorder (PTSD). Mood Disorders (MD) are not excluded but are unlikely to be identified as occupational diseases. The differential diagnosis between AD and MD is not easy and is based on strict categorical criteria. **Objectives:** The aim of this study was to explore differences in personality and mood spectrum symptoms among workers investigated for occupational stress suffering from AD or MD. **Methods:** Sixty-two patients with AD and 43 with MD were recruited and evaluated by means of rating scales for psychosocial occupational risk and work-related stress (WHS, CDL, OSQ), for sleep disturbances (PSQI), for personality disorders (SCID-II) and for mood spectrum symptoms (MOODS-SR). **Results:** The diagnostic groups did not differ for WHS, OSQ and PSQI scores. The duration of exposure to stressful/adversative work situations was significantly higher in the MD group ( $p=0.03$ ). Positive family psychiatric history ( $p=0.005$ ), personality disorders ( $p=0.009$ ) and pathological personality traits ( $p<0.0001$ ) were significantly more frequent in the MD group. The MOODS-SR questionnaire total score ( $p=0.019$ ) and the manic component score ( $p=0.001$ ) but not the depressive score were significantly higher in the MD group. **Conclusions:** The present study suggests that positive family psychiatric history, pathological personality traits and spectrum manic symptoms represent markers of vulnerability and low resilience for workers exposed to occupational stress. These characteristics could weaken the etiological relationship between work-related stress and an initial major depressive episode when it is under investigation as a possible occupational disease.

## RIASSUNTO

«**Disturbi da stress lavoro-correlato: variabilità nell'espressione clinica e criticità della diagnosi psichiatrica.** **Introduzione:** I disturbi psichiatrici associati allo stress lavoro-correlato sono i Disturbi dell'Adattamento (DA) e il Disturbo Post-Traumatico da Stress. I Disturbi dell'Umore (DU) vengono difficilmente riconosciuti come malattie professionali. La diagnosi differenziale fra DA e DU non è agevole e si basa su rigidi criteri categoriali. **Obiettivi:**

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*Lo scopo dello studio è valutare profili di personalità e sintomi di spettro dell'umore in due gruppi di lavoratori esposti a stress occupazionale affetti da DA o DU. **Metodi:** Sessantadue pazienti con DA e 43 con DU sono stati valutati con questionari per il rischio occupazionale e lo stress lavoro-correlato (WHS, CDL, OSQ), per i disturbi del sonno (PSQI), per i disturbi di personalità (SCID-II) e per i sintomi di spettro dell'umore (MOOD-SR). **Risultati:** Non sono emerse differenze significative tra i gruppi nei punteggi delle scale WHS, OSQ e PSQI. La durata dell'esposizione alle situazioni stressanti/avversative sul lavoro è risultata più alta nel gruppo DU ( $p=0,03$ ). La familiarità per disturbi psichiatrici ( $p=0,005$ ), la presenza di disturbi della personalità ( $p=0,009$ ) o di tratti patologici di personalità ( $p<0,0001$ ) sono risultati più frequenti nel gruppo DU. Il punteggio totale del MOOD-SR ( $p=0,0019$ ) e il punteggio della componente maniacale ( $p=0,001$ ) sono risultati più alti nel gruppo DU. **Conclusioni:** La familiarità per disturbi psichiatrici, i tratti patologici di personalità e i sintomi di spettro dell'umore maniacali rappresentano markers di vulnerabilità e bassa resilienza per lavoratori esposti a stress occupazionale e potrebbero indebolire il nesso eziologico fra lo stress lavoro-correlato e un episodio depressivo maggiore nella valutazione della malattia professionale.*

## INTRODUCTION

The concept of work-related stress is described in the context of the European agreement on stress at work (2004) (1), where stress is defined as “a state which is accompanied by physical, psychological or social complaints or dysfunctions and which results from individuals feeling unable to bridge a gap with the requirements or expectations placed on them”. When these demands and expectations are referred to the work environment they may determine a condition of work-related stress. Exposure to chronic work-related stress could lead to psychiatric occupational diseases.

While it is widely accepted that the work environment can affect workers' mental health, there is no general consensus on the question of recognition of work-related mental disorders as occupational diseases in Europe (26). However, from the viewpoint of psychosocial prevention the subject of work-related illnesses is increasingly researched mainly using an epidemiological approach. Most studies on the clinical effects of psychosocial risks are focused on work harassment situations; since bullying at work is characterized by a powerful psychotraumatic effect, it allows a better evaluation of the causal relationship between heterogeneous clinical pictures and work experiences (13, 14, 37, 38). Therefore, clinical investigations could have a key role in better clarifying which mental disorders can be recognized as caused by work organisa-

tion, working conditions, management methods or changes taking place in the companies.

In Italy, the recent list of occupational diseases with mandatory reporting includes the group of “Mental and psychosomatic disorders related to work organization dysfunction” which includes Post-Traumatic Stress Disorder (PTSD) and Adjustment Disorders (AD) (2). Mood Disorders (MD) are not mentioned in the list.

AD are defined as disorders which occur within three months of the onset of one or more objectively identified stressful events and which, once the stressor or its consequences have terminated, do not persist for more than an additional 6 months. They are characterized by heterogeneous emotional or behavioural symptoms belonging to the anxiety area (emotional instability, hypervigilance, inability to relax, sleep disturbances, psychic and somatic anxiety symptoms) or to the depression area, which causes a significant impairment in social, occupational, or other important areas of functioning (6). When these symptoms cause enough distress to require medical attention and further treatment, the defining line which differentiates AD from normal adaptive responses to stressors is exceeded (16). The last version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (6) places AD along with PTSD in the “Trauma- and Stressor-Related Disorders” section. AD are no longer a residual category and can be diagnosed in co-morbidity with other mental disorders (including mood disorders)

if these do not justify the symptoms that the person experiences in response to current stressors (6). Nevertheless, the problem of differential diagnosis between AD and major depressive episodes (especially if mild) or forms of “other specified” depression provided by DSM is still under discussion. The question remains whether AD are reversible and nosologically autonomous “stress-related disorders” or if they represent syndromes just quantitatively minor but qualitatively identical to the specific anxiety and mood disorders for which the DSM diagnostic threshold is not reached (42). The ODIN multicentre epidemiological study (17) showed an extremely low prevalence of AD in the general population (0.3%) compared to that of depressive disorders, which was in line with expectations (6.6%). These data led the authors to surmise that a diagnostic bias exists in how AD are conceptualized in the mental disorders classification systems (both ICD and DSM) since diagnostic criteria are not specific, explicit and comprehensive, and AD diagnosis is excluded when symptoms meet the criteria for a depressive or anxiety disorder despite any chronological relationship of psychopathology onset with stressful events. The statistical analysis in the ODIN study showed that no socio-demographic or clinical variables, including the Beck Depression Inventory score, allowed distinguishing AD by depressive episodes. Moreover, the DSM-5 states that after a severe loss event (not necessarily a death), although depressive symptoms are understandable and appropriate, a possible diagnosis of a major depressive episode must still be considered. This note is a further step in the direction of not excluding the diagnosis of a major depressive episode even when the depressive symptomatology appear to be reactive to serious life events.

Mood disorders are among the most frequent psychiatric disorders: it is estimated that about 14% of the general European population presents, at least once in a lifetime, a depressive or expansive (manic/hypomanic) episode (4). Actually, all humans experience continuous mood fluctuations in response to external stimuli such as physiological phenomena which promotes the development of adaptive behaviour. When these oscillations become independent or disproportionate to external stimuli, they lose

their adaptive function and behave pathologically. In a modern view, mood episodes are classified as part of a continuum, a broad mood spectrum which includes temperamental traits, isolated and atypical symptoms, subclinical, attenuated but protracted manifestations, up to the full-blown unipolar and bipolar disorders (18, 27). Even if the sub-threshold mood spectrum manifestations were initially considered “benign” phenomena, recent epidemiological studies have shown that in the general population they were associated with an increased need of assistance for medical and mental health problems (39).

The aim of this study was to investigate personality profile and subclinical mood spectrum symptoms in a sample of workers suffering from AD or MD in work-related stressful situations who were referred to the Occupational Health Department operating in the Azienda Ospedaliero-Universitaria Pisana.

## METHODS

### Patients

The study sample consisted of 105 patients (44 M and 61 F), aged between 25 and 67 years (mean±SD=49.2±8.1), consecutively recruited between April 2013 and April 2014 at the Occupational Health Department operating in the Azienda Ospedaliero-Universitaria Pisana. We recruited a group of patients suffering from AD (n=62, 36 F (58%), mean age±SD=49.48±7.94) and a group of patients with MD (n=43, 25 F (58.1%), mean age±SD=48.9±8.40) according to the diagnostic criteria of DSM-IV-TR (5). The clinical diagnosis was confirmed by the administration of AD and MD interviews of the Structured Clinical Interview for DSM-IV axis I Patient Version (SCID-I / P) (27).

The AD group included different clinical AD subtypes provided by the DSM (with depressed mood, with anxiety, with mixed anxiety and depressed mood, with disturbance of conduct, with mixed disturbance of emotions and conduct, unspecified), while the MD group included diagnoses of a major depressive episode in the course of Depressive Disorders and Bipolar Disorders type I, II, NOS.

Exclusion criteria were the presence of psychiatric diagnoses other than those specified, the onset of current psychopathological manifestations as well as the presence of recurrent mood episodes before the onset of stressful work situations, an insufficient comprehension of Italian that prevented completion of self-report questionnaires.

The research project was approved by the Ethics Committee of the University of Pisa according to the Declaration of Helsinki (1996) and participation in the study was formalized with the collection of written informed consent.

### Clinical assessment

While staying at the Centre, patients received a general medical examination by an occupational physician and a psychiatric and psychological evaluation. They were then asked to complete questionnaires and rating scales as specified below.

A self-report form was used to collect demographic information and detailed information on work, including the type of contract, the number of years of work in the current workplace and in previous workplaces, the size and the sector of the firm.

The battery of assessments to investigate stressful events and harassment episodes in the workplace included:

- Work Harassment Scale (WHS) (9): a questionnaire that includes 24 items exploring negative and harassment episodes in the workplace. Items are coded on a 5-point Likert scale denoting the frequency of these episodes in the previous 6 months. The total score is obtained as the sum of the items and ranges from 24 to 120.

- Questionnaire on harassment (CDL) (37): this was developed in Italy to collect harassment behaviour. It includes 30 items organized into 3 areas: actions against the individual (threats, harassments), actions related to work (frequent criticism, work overload, downgrading) and actions of punishment. Items are coded on a 0 to 2 scale, where 0=never, 1=sometimes, 2=often. The questionnaire also collects information on the perpetrators of these actions.

- The levels of stress perceived by the patients were evaluated by means of the Occupational Stress Questionnaire (OSQ) (25), which allows identify-

ing and quantifying the perception by the worker of stress at work and his/her reactions to it. The 109 items investigates both central aspects, such as the content and organization of work, interpersonal relationships and the need of workers to receive the necessary support, to be satisfied with their work, and any suggestions for improving conditions. This tool does not have a cut-off that indicates a potential risk of occupational stress, but it provides a quantitative estimate of the stress felt by the worker.

Sleep disturbances, which are frequent and early symptoms of work-related stress as isolated manifestations or in full-blown psychiatric disorders (20), were studied by the administration of the Pittsburgh Sleep Quality Index (PSQI), an instrument with adequate sensitivity, accuracy and reproducibility (15). The PSQI is a 9-item questionnaire that explores over the previous month: subjective sleep quality; sleep latency (time asleep); sleep duration; habitual sleep efficiency (ratio between the hours of sleep and hours spent in bed); sleep disturbances (describing some of the most common complaints); habitual use of hypnotic drugs; the presence of interference in daily activities. The evaluation of each domain is based on a scale from 0 to 3 points, where 3 is the negative extreme and 0 the positive extreme. A score of less than or equal to 5 points is considered to be indicative of good quality sleep, a score more than 5 points poor quality sleep.

The study of personality profiles of the patients was carried out by the administration of the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (28). This consists of a clinical interview for the diagnostic evaluation of disorders and pathological personality traits according to DSM-IV-TR criteria. The disorders evaluated were: Paranoid, Schizotypal, Schizoid, Histrionic, Narcissistic, Borderline, Antisocial, Avoidant, Dependent, Obsessive-Compulsive, Passive-Aggressive and Depressive.

The Mood Spectrum-Self Report Lifetime version (MOOD-SR) (21) is a questionnaire, developed in English and Italian, focused on the presence of manic and depressive symptoms, traits and lifestyles that may characterize the 'temperamental' affective dysregulation present in both fully syndromal and sub-threshold mood disturbances. The

latter include symptoms that are either isolated or clustered in time and temperamental traits that may be present throughout the individual's lifetime. The MOODS-SR consists of 161 items coded as present or absent for one or more periods of at least 3-5 days in a lifetime. Items are organized into 3 manic-hypomanic and 3 depressive domains each exploring mood, energy and cognition, plus a domain that explores disturbances in rhythmicity (i.e. changes in mood, energy and physical well-being according to the weather, the season and the phase of menstrual cycle, etc.) and in vegetative functions (including sleep, appetite and sexual function). The sum of the scores on the three manic-hypomanic domains constitutes the score for the manic-hypomanic component (63 items) and that for the three depressive domains constitutes the score for the depressive component (62 items).

### Statistical analysis

The collected data were recorded in a database and then processed using statistical software (MedCalc version 14.8.1). The chi-square test was used for the comparison of categorical variables (gender). The comparison of quantitative variable with Gaussian distribution was carried out with the independent samples Student's t test, while the non-parametric Mann-Whitney test was used for variables with non-Gaussian distribution. Probability (p) values <0.05 were considered statistically significant.

### RESULTS

The personal characteristics of the patients and the rating scales mean scores are reported in table 1.

The two groups of patients (AD and MD) did not significantly differ in terms of age ( $p=0.48$ ) and sex ( $\chi^2=0.03$ ;  $p=0.84$ ).

Twelve patients (19.3%) in the AD group had cases of Axis I psychiatric disorders among first and second degree relatives compared to 20 patients (46.5%) in the MD group ( $p<0.01$ ).

The comparison between diagnostic groups for mean scores on scales for adversative work situations (WHS) and for work-related perceived stress (OSQ) revealed no statistically significant differences. Only the duration of exposure to adversative/stressful work situations detected through the CDL scale was significantly higher in the MD group ( $p<0.05$ ).

The severity of sleep disturbances, measured by the PSQI, was not significantly different between groups.

In the AD group ( $n=62$ ), 18 patients (29%) had pathological personality traits (also of different cluster and associated with each other) but none met the criteria for the diagnosis of a full-blown disorder (table 2). In particular, 15 patients (24%) showed obsessive-compulsive traits, 2 (3%) borderline, 2 (3%) avoidant, 1 (1.6%) narcissistic. In the MD group ( $n=43$ ), 6 patients (14%) were diagnosed with personality disorder (2 cases of Obsessive-Compulsive

**Table 1** - Socio-demographic, occupational stressful events and clinical characteristics of patients.

	AD (n=62)	MD (n=43)	p
Age (mean±DS)	49.48±7.94	48.9±8.40	0.48
Gender, F (%)	36 (58%)	25 (58.1%)	0.84
Family psychiatric history (positive), N (%)	12 (19.3%)	20 (46.5%)	<b>0.005*</b>
WHS (mean± DS)	72.03±21.28	73.5±20.59	0.73
CDL (duration, years) (media±DS)	4.73±4.9	6.1±4.43	<b>0.03*</b>
PSQI (mean± DS)	13.93±4.23	13.63±3.97	0.7
OSQ (mean± DS)	269.04±68.21	270.9±66.19	0.87
Total MOODS-SR totale (media±DS)	46.28±24.06	58.51±24.18	<b>0.019*</b>
Total depressive MOODS-SR (media±DS)	20.8±14.12	25.58±14.05	0.12
Total manic MOODS-SR (media±DS)	14.67±9.03	21.19±9.06	<b>0.001*</b>

WHS: Work Harassment Scale; CDL: questionnaire on harassment; PSQI: Pittsburgh Sleep Quality Index; OSQ: Occupational Stress Questionnaire; MOODS: Mood Spectrum-Self Report; AD: Adjustment Disorders; MD: Mood Disorders

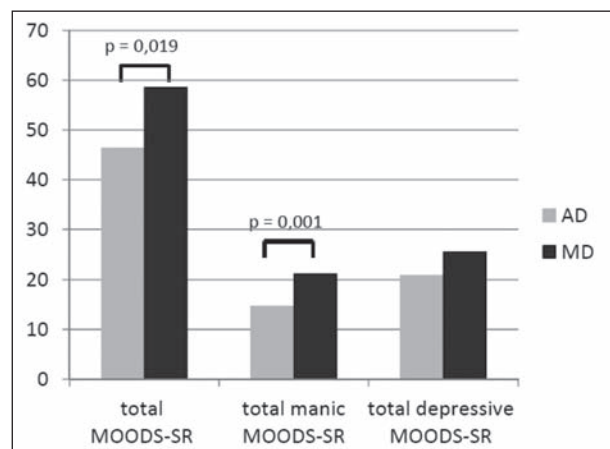
\*Statistically significant ( $p<0.05$ )

**Table 2** - Personality disorders and traits of patients

	AD (n=62)	MD (n=43)	p
Personality disorders, n (%)	0	6 (14%)	0.009*
Personality traits, n (%)	18 (29%)	36 (84%)	<0.0001*

AD: Adjustment Disorder; MD: Mood Disorders

\*Statistically significant ( $p < 0,05$ )



**Figure 1** - MOODS-SR scores in the two diagnostic groups

Personality Disorder, 1 of Avoidant, 1 of Borderline, 1 of Histrionic and 1 of Paranoid) and 36 (84%) had pathological traits. In particular, 24 (56%) had obsessive-compulsive traits, 14 (32.5%) borderline, 5 (12%) avoidant, 4 (9%) paranoid, 4 (9%) passive-aggressive, 1 (2%) histrionic.

As for the lifetime mood spectrum symptoms, the comparison between the two diagnostic groups showed a statistically significant difference relative to the total score of the MOODS-SR questionnaire ( $p < 0,05$ ) and the manic component score ( $p = 0,001$ ) with higher values in the MD group. There was no significant difference between the two groups for the MOODS-SR depressive component score (figure 1).

## DISCUSSION AND CONCLUSIONS

The first result of this study was the evidence of current comparable levels of work-related stress between patients with AD and those affected by MD. The diagnosis of AD in the DSM-IV-TR included

heterogeneous clinical syndromes characterized by emotional symptoms belonging to the anxious and/or depressive area and behavioural manifestations that for number or duration did not meet the criteria for the diagnosis of a mood or anxiety disorder. Ultimately, by considering DSM definition, our cases with AD were characterized by a milder psychopathological symptomatology than patients with MD. Therefore, on an equal score of the occupational stress scale some patients received a psychiatric diagnosis milder than others. Even from a prognostic point of view, the AD diagnosis is known to be more favourable (6).

Although the intensity of stress was similar in the two diagnostic groups, the duration of exposure to stressors was significantly greater in the MD group. This finding leads to further considerations about the possibility that some cases of "persistent" AD, secondary to prolonged stressful situations, may over time evolve into more severe psychopathological conditions such as major depression. Other authors observed such diagnostic evolution in about 40% of cancer patients diagnosed with AD during the clinical follow-up (2). Moreover, some studies suggest that AD and major depression may share clinical features, pathophysiologic and etiopathogenic patterns. The ODIN epidemiological study highlighted the critical issues in the differential diagnosis based on clinical elements between the two nosological categories (AD and depressive episodes) that may determine an underestimation of AD prevalence (17). In addition, an experimental study has shown that the perception of pain is altered, in terms of reduction of nociceptive sensitivity threshold, in the same way as in patients suffering from AD with depressed mood and in patients with major depression (10). A retrospective research has shown that psychopharmacological therapy with SSRI antidepressants in a general practice setting was equally

effective in two groups of patients, respectively AD with depressed mood and major depression (30). DSM criteria in the last decades have underlined that the concept of “reactivity” to environmental stressors does not exclude the diagnosis of major depression. Moreover, from the etiopathogenetic point of view it is widely known that there is a significant association between the onset of depression and recent stressful events (often with a synergistic interaction between the severity of stressful events and the presence of dysfunctional personality traits) (32, 33). The etiological relationship between stressors and the onset of depressive episodes becomes more complex when considering a recurrent depressive disorder. After a sufficient number of recurrences, in fact, depressive episodes begin to emerge autonomously and independently from environmental stressors due to a phenomenon known as “kindling”, which consists of a brain sensitization process with progressive reduction of the threshold for the onset of a new depressive episode (35). For this reason we decided to exclude from the study those patients with a depressive episode that started before the onset of work-related stressors or those with previous recurrent mood episodes. In fact, it would be very difficult to evaluate the etiological relationship between work-related stressors and a recurrent depressive episode which, therefore, will be unlikely to be considered an occupational disease.

The exposure to chronic stress has depressogenic effects through multiple neurobiological mechanisms (31) including neurotoxicity and subsequent cell death in many brain regions (34).

Therefore it may be hypothesized, in the case of chronic exposure to stressors, that a progression of neurotoxicity exists that would be the basis of a negative clinical evolution from AD with depressed mood to major depression. In contrast, other authors pointed out that there are clinically relevant qualitative and quantitative differences between AD and major depression. In particular, patients with AD with depressed mood have less severe symptoms, higher level of social functioning, more adaptive premorbid personality profile and better prognosis than those with major depression (12, 40). Zimmermann et al. (42) analysed a large sample for clinical differences between patients diagnosed

with depression NOS and patients with AD with depressed mood: the former presented anhedonia, increased appetite, hypersomnia and indecision more frequently, while patients with AD reported weight loss, decreased appetite and insomnia. There was no significant difference between the groups for severity of depressive symptoms or for functional impairment. Patients with depressive disorder NOS had a higher risk, even if not statistically significant, for cases of depression among first-degree relatives.

In the present study the two diagnostic groups showed some important differences as regards history and clinical features. First of all, they significantly differed regarding frequency of Axis I psychiatric disorders in first- and second- degree relatives. The frequency of positive cases was significantly higher in the MD group (46, 5% vs 19.3%) as expected on the basis of the well-known genetic predisposition for MD widely reported in the literature (7, 8).

Another important differential feature was the distribution of personality disorders and pathological personality traits. Patients with MD showed a higher frequency compared to AD patients regarding both full-blown personality disorders (14% vs 0%) and pathological traits (84% vs 29%), in particular borderline (32.5% vs 3%). These data were partly expected as the relationship between personality disorders and mood disorders is extensively described in the literature. Personality disorders represent both vulnerability factors and negative prognostic factors (3, 11, 19). Our results were also in line with a recent study that compared the prevalence of personality disorders in patients with MD and patients with AD showing a higher frequency in the former (22). In particular, the borderline personality traits, that were the most common among our patients with MD, were characterized by a pervasive and persistent emotional instability that is considered by many authors as the expression of a cyclothymic temperament and represents a core feature of the so-called soft bipolar spectrum (36).

Lastly, another element for which the two diagnostic groups were significantly different was the burden of lifetime mood spectrum symptoms. MD patients reported a significantly higher MOODS-SR total score than AD patients. In particular, the statistically significant difference concerned not

the depressive but that manic component. So, although the emotional and behavioural characteristics expressed by the items of the MOODS-SR manic component, such as high levels of energy, optimism, increased productivity, high self-esteem, may seem desirable and adaptive to stressors, they actually represent a predisposing factor to the development of psychiatric disorders of greater severity (MD). These subclinical manifestations of mania are extremely difficult to recognize because they are desirable, ego-syntonic and therefore neglected by the patients themselves. However, Judd and Akiskal (41), in a recent analysis of data from the Epidemiological Catchment Area, showed that lifetime sub-threshold manic symptoms are associated later in life with a greater need for assistance for mental illness. Moreover, the presence of lifetime manic-hypomanic sub-threshold symptoms, evaluated by means of MOOD-SR, in a population of patients with C hepatitis was associated with the development of depressive symptoms after or during interferon therapy (23). A recent study on patients with fibromyalgia showed that lifetime manic spectrum symptoms were associated with a poorer quality of life and more severe pain (22). Even in populations of patients already suffering from recurrent depression, a significant relationship was highlighted between the presence of lifetime manic spectrum symptoms and a poor prognosis as well as an increased risk of suicide (18).

The results of this study should be interpreted taking into account some important limitations. Firstly, the low number of the two diagnostic groups precluded statistical analysis on more specific diagnostic subgroups (for example, subtypes of AD). The presence of cases of Axis I psychiatric disorders among patients' relatives was investigated and defined solely on the basis of information reported by the patients. Moreover, because of the use of the MOODS-SR lifetime version and since this was a cross-sectional study, we were not able to determine if mood spectrum symptoms were prior or concomitant to the clinical evaluation.

In conclusion, management of occupational stress-related psychiatric disorders has many pitfalls for the occupational physician. In this experience we wanted to evaluate a number of factors that

may support the occupational physician in the task of preventive medical surveillance and occupational disease diagnosis.

In fact, the present study identified positive family psychiatric history, pathological personality traits and sub-threshold manic symptoms as risk factors for the development of mood disorders in workers exposed to occupational stress and therefore as a clinical marker of low resilience. Moreover, it is conceivable that a protracted exposure to stressful situations may promote a negative clinical evolution and therefore transition from AD to mood disorder. It is plausible that no differences exist in the neurobiological mechanisms of neuronal damage mediated by chronic stress in individuals who develop AD and those who develop an initial depressive episode. Further studies should investigate the neurobiological mechanisms underlying AD, maybe by exploring putative peripheral markers of neuroplasticity and resilience so far investigated in mood disorders.

In the light of these considerations, we believe that mood disorders cannot be classified in a unified manner when investigated as possible occupational diseases. Therefore, major depression can be considered an occupational disease, but this diagnosis has many confounding factors in terms of etiology. The etiologic weight of occupational stressors should definitely be considered case by case taking into account several variables, including individual predisposition (family history, personality, mood spectrum symptoms) and clinical features of the psychopathological disorder such as recurrence.

Work-related stress represents an emerging risk in occupational health, therefore in the near future it will become more and more important to focus investigations on identifying reference points for the everyday practice of the occupational physician.

NO POTENTIAL CONFLICT OF INTEREST RELEVANT TO THIS ARTICLE WAS REPORTED

## REFERENCES

1. Accordo Europeo sullo stress sul lavoro. Bruxelles, 8 ottobre 2004
2. Akechi T, Okuyama T, Sugawara Y, et al: Major depression, adjustment disorders, and post-traumatic stress



- disorder in terminally ill cancer patients: associated and predictive factors. *J Clin Oncol* 2004; 22 (suppl 10): 1957-1965
3. Akiskal HS, Hirschfeld RM, Yerevanian BI: The relationship of personality to affective disorders. *Arch Gen Psychiatry* 1983; 40 (suppl 7): 801-810
  4. Alonso J, Angermeyer MC, Bernert S, et al: Prevalence of mental disorders in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand* 2004; (suppl 420): 21-27
  5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders DSM-IV-TR. Washington, D.C.: American Psychiatric Press, 2000
  6. American Psychiatric Association: Diagnostic and statistical manual of mental disorders DSM-5. Washington, D.C.: American Psychiatric Press, 2013
  7. Andreasen NC, Rice J, Endicott J, et al: Familial rates of affective disorder. A report from the National Institute of Mental Health Collaborative Study. *Arch Gen Psychiatry* 1987; 44 (suppl 5): 461-469
  8. Berrettini WH: Genetics of psychiatric disease. *Annu Rev Med* 2000; 51: 465-479
  9. Bjorkqvist K, Osterman K, Hjelt-Back M: Aggression among University Employees. *Aggressive Behaviour* 1994; 20: 173-184
  10. Boettger MK, Bär KJ: Perception for ischemic pain shows similarities in adjustment disorder and major depression. *Eur J Pain* 2007; 11 (suppl 7): 819-822
  11. Brieger P, Ehrh U, Marneros A: Frequency of comorbid personality disorders in bipolar and unipolar affective disorders. *Compr Psychiatry* 2003; 44 (suppl 1): 28-34
  12. Bronisch T, Hecht H: Validity of adjustment disorder, comparison with major depression. *J Affect Disord* 1989; 17 (suppl 3): 229-236
  13. Buselli R: Work related stress. In *Regional Health Agency of Tuscany: Gender-Related Health in Tuscany*. Firenze (FI): Press Service srl 2015; 79-80.
  14. Buselli R, Gonnelli C, Moscatelli M, et al: Esperienza di un centro per lo studio dei disturbi da disadattamento lavorativo in tema di patologie mobbing correlate. *Med Lav* 2006; 97: 5-12.
  15. Buysse DJ, Reynolds CF 3rd, Monk TH, et al: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989; 28 (suppl 2): 193-213
  16. Casey P, Dowrick C, Wilkinson G: Adjustment disorders: fault line in the psychiatric glossary. *Br J Psychiatry* 2001; 179: 479-481
  17. Casey P, Maracy M, Kelly BD, et al: Can adjustment disorder and depressive episode be distinguished? Results from ODIN. *J Affect Disord* 2006; 92: 291-297.
  18. Cassano GB, Rucci P, Frank E, et al: The mood spectrum in unipolar and bipolar disorder: arguments for a unitary approach. *Am J Psychiatry* 2004; 161: 1264-1269
  19. Clark LA, Watson D, Mineka S: Temperament, personality, and the mood and anxiety disorders. *J Abnorm Psychol* 1994; 103 (suppl 1): 103-116
  20. Costa G: Stress e disturbi del sonno. Documento per un consenso sulla valutazione, prevenzione e correzione degli effetti nocivi dello stress sul lavoro: Congresso della Società Italiana di Medicina del Lavoro e Igiene Industriale. Parma, Ottobre 2005
  21. Dell'Osso L, Armani A, Rucci P, et al: Measuring mood spectrum: comparison of interview (SCI-MOODS) and self-report (MOODS-SR) instruments. *Compr Psychiatry* 2002; 43 (suppl 1): 69-73
  22. Dell'Osso L, Bazzichi L, Consoli G, et al: Manic spectrum symptoms are correlated to the severity of pain and the health-related quality of life in patients with fibromyalgia. *Clin Exp Rheumatol* 2009; 27 (5 suppl 56): S57-61
  23. Dell'Osso L, Pini S, Maggi L, et al: Subthreshold mania as predictor of depression during interferon treatment in HCV+ patients without current or lifetime psychiatric disorders. *J Psychosom Res* 2007; 62 (suppl 3): 349-355
  24. Doherty AM, Jabbar F, Kelly BD, Casey P: Distinguishing between adjustment disorder and depressive episode in clinical practice: the role of personality disorder. *J Affect Disord* 2014; 168: 78-85
  25. Elo AL, Leppanen A, Lindstrom K, Ropponen T: Occupational stress-questionnaire: User's instructions. Helsinki: Finland Institute of Occupational health, 1992
  26. Eurogip: What recognition of work-related mental disorders? A study on 10 European countries. Paris: EUROGIP, 2013 81/E
  27. Fiedorowicz JG, Endicott J, Leon AC, et al: Subthreshold hypomanic symptoms in progression from unipolar major depression to bipolar disorder. *Am J Psychiatry* 2011; 168: 40-48
  28. First MB, Gibbon M, Spitzer RL: User's Guide for Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II). Washington D.C.: American Psychiatric Press, 1997
  29. First MB, Spitzer RL, Gibbon M, et al: Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P). New York: Biometrics Research, New York State Psychiatric Institute, 2002
  30. Hameed U, Schwartz TL, Malhotra K, et al: Antidepressant treatment in the primary care office: outcomes for adjustment disorder versus major depression. *Ann Clin Psychiatry* 2005; 17 (suppl 2): 77-81
  31. Hill MN, Hellemans KG, Verma P, et al: Neurobiol-

- ogy of chronic mild stress: parallels to major depression. *Neurosci Biobehav Rev* 2012; *36* (suppl 9): 2085-2117
32. Kendler KS, Karkowski LM, Prescott CA: Causal relationship between stressful life events and the onset of major depression. *Am J Psychiatry* 1999; *156* (suppl 6): 837-841
33. Kendler KS, Kuhn J, Prescott CA: The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression. *Am J Psychiatry* 2004; *161* (suppl 4): 631-636
34. Lee AL, Ogle WO, Sapolsky RM: Stress and depression: possible links to neuron death in the hippocampus. *Bipolar Disord* 2002; *4* (suppl 2): 117-128
35. Monroe SM, Harkness KL: Life stress, the "kindling" hypothesis, and the recurrence of depression: considerations from a life stress perspective. *Psychol Rev* 2005; *112* (suppl 2): 417-445
36. Perugi G, Akiskal HS: The soft bipolar spectrum redefined: focus on the cyclothymic, anxious-sensitive, impulse-dyscontrol, and binge-eating connection in bipolar II and related conditions. *Psychiatr Clin North Am* 2002; *25* (suppl 4): 713-737
37. Punzi S, Cassitto MG, Castellini G, et al: Mobbing and its effects on health. The experience of the "Clinica del Lavoro Luigi Devoto" in Milan. *Med Lav* 2007; *98*: 267-283
38. Raimondi F, Milani F, Sbrana A, et al: Psychopathology and Work Harassment. *Giornale Italiano di Psicopatologia* 2009; *15*: 290-301
39. Sherbourne CD, Wells KB, Hays RD, et al: Subthreshold depression and depressive disorder: clinical characteristics of general medical and mental health specialty outpatients. *Am J Psychiatry* 1994; *151*: 1777-1784
40. Snyder S, Strain JJ, Wolf D: Differentiating major depression from adjustment disorder with depressed mood in the medical setting. *Gen Hosp Psychiatry* 1990; *12* (suppl 3): 159-165
41. Judd, Akiskal HS: The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. *J Affect Disord* 2003; *73*: 123-1231
42. Zimmerman M, Martinez JH, Dalrymple K, et al: "Subthreshold" depression: is the distinction between depressive disorder not otherwise specified and adjustment disorder valid? *J Clin Psychiatry* 2013; *74* (suppl 5): 470-476