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Opinion paper: poor response to treatment of depression in people in high occupational levels

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Abstract

The working environment may have a significant effect on response to treatment of depression and this issue has not yet been sufficiently addressed in the scientific literature. There is evidence showing that being engaged in high-level positions can be an obstacle to the success of treatment. This article discusses the few evidence in the literature and some of the possible mechanisms involved. Specific personality attributes and difficulties in adapting to depression may delay access to care and may also reduce treatment compliance. The presence of stress in jobs that require high cognitive function and lack of social support may be elements that hinder the recovery process. Residual symptoms that impact on cognitive functions may undermine adherence to treatment and adversely affect the response. The implications of these issues are potentially relevant for clinical practice in the treatment of depression and for future research.

Introduction

Work is an important part of an individual's life; it can be a source of satisfaction and fulfilment, as well as tension and worry affecting private life. Several studies have emphasized the positive effect on mental health of being employed as compared with being unemployed (Modini *et al.*, 2016). Being in work, compared with being unemployed, has been shown to be associated with a better treatment outcome in the presence of a mental illness, especially mood disorders (e.g. Drago and Serretti, 2011; van der Lem *et al.*, 2013; Jakubovski and Bloch, 2014). It has been suggested that these associations are probably mediated by a better socio-economic status (Muntaner *et al.*, 2004), since, on average, individuals who work have a higher educational level, higher income and better social inclusion compared with individuals who do not work.

Depression is common and is often a severe illness. The lifetime prevalence of major depressive disorder (MDD) is about 17% (Kessler *et al.*, 2003) and about 6.7% of the population will experience an episode of MDD in any 1 year period (Kessler *et al.*, 2005). Depression is predicted to be the leading cause of disability by 2020 (Mathers *et al.*, 2006) with substantial costs for health systems and, in working adults, indirect costs from lost working hours (absenteeism), loss of lifetime income, early retirement and, especially, loss of productivity (*presenteeism*) (Thomas and Morris, 2003; Ekman *et al.*, 2013). Consequently, screening and treatment for depression in the workplace is cost-effective and represents a worthwhile investment from the financial perspective (Evans-Lacko and Knapp, 2016).

Although a number of studies have evaluated the possible relationship between employment status (employed/unemployed) and socioeconomic status (income, educational achievement, occupational prestige), few studies have focused on occupational status as influencing the risk of developing depressive disorders, and even fewer on the outcome of treatment.

To our knowledge, only one study by Cheng *et al.* (2007) specifically evaluated the possible association of occupational level in relation to recovery rates in 67 MDD patients using a three-level occupational class, based on the *Standard Occupational Classification* (http://www.bls.gov/soc/). Although a high occupational level predicted lower rates of relapse at 1 year of follow-up [as previously reported by Tseng *et al.* (2006)], at the index episode, high occupational level was associated with a reduced chance of clinical remission.

Though these data (lower risk of relapse at follow-up – higher rates of non-remission at the index episode) may appear counterintuitive, it is possible that higher occupational level may

decrease the risk of developing a depressive illness, as shown by several studies (e.g. Fryers *et al.*, 2003), but on the other hand, a high occupational level may lower response to first-choice treatments of the episode and interfere with the expected chance of response and remission.

The hypothesis of an association between a poorer response to treatment and high occupational level is supported by our recent analysis of a larger sample of patients with MDD ($n = 654$) evaluated for response [based on clinical evaluation and Hamilton Rating Scale for depression (HAMD) scores below 17 points], remission (HAMD below 8 points) and treatment resistance (non-response to two or more adequate treatments) (Mandelli *et al.*, 2016). In patients with high occupational levels, classified according to the classification of Hollingshead (1975), we found lower rates of response and remission, and higher rates of unsuccessful treatments during the last depressive episode (treatment resistance). We found those belonging to high occupational levels (higher executives, proprietors of large, medium-sized or small independent businesses, major professionals, business managers) had a less favourable outcome than individuals in lower occupational levels (clerical and sales workers, technicians, skilled manual employees, machine operators, semi-skilled or unskilled employees) (Fig. 1).

The convergence of our data and that of Cheng *et al.* (2007) is suggestive of a link between high occupational level and poor outcome of treatment for depression, at least in the short term. Clearly, further studies in independent and larger samples are needed to explain these findings.

This paper focuses specifically on the factors that may mediate a poor response to treatment for depression in people in high occupational levels. Because of the relatively small body of evidence currently available, our considerations may be partially speculative; nevertheless, we believe that attention should be paid to certain elements that may contribute to current clinical practice.

Specific work-related stress

People in high occupational levels are exposed to specific psychosocial risk factors, which differ from those affecting other employees at lower occupational levels (Tennant, 2001). Workers in high occupational levels are expected to take on responsibilities in the management and supervision of activities of subordinate employees, to achieve customer satisfaction, to make decisions under pressure of time, and are also exposed to high levels of psychological and emotional pressure. The workload can also be very heavy in terms of hours of work. Pressure for high performance and high levels of competition among colleagues can often add to the mix. Such demanding work conditions might well be expected to represent excessive and overwhelming demands for a person with depression since the disorder is characterized by poor concentration, loss of interest and energy among other features. These conditions can represent a source of environmental stress which may easily lead to increased feelings of failure and inadequacy if the person is unable to meet the demands of work. Staying at home may also be counterproductive because a backlog of work awaits the person returning to work and this may well engender a vicious circle of further feelings of failure, hopelessness and helplessness. The return to work may therefore be more difficult for workers in high occupational levels who need to recover on a broader range of functions before returning to work.

Social support

The heavy workload and the autonomy expected in high occupational levels may also lead to social isolation in the working environment and lack of support from peers. Peers may be more competitive than supportive. Subordinates may try to take advantage while superiors may be unhelpful. No working position is completely independent from other people and those at upper intermediate levels are frequently dealing with pressures from both above and below. High occupational positions require that the worker can be independent in taking on burdensome tasks and responsibilities dealing with others and they therefore frequently come under pressure from different sources with little or no support provided. It is well known that the absence of a supportive working environment is a significant source of stress at all levels of employment (Bonde, 2008; Theorell *et al.*, 2015).

Overwork can also limit the time available to spend in activities after work (family, hobbies, friendships), resulting in isolation even outside of the workplace and/or discord in family and friendships. An extensive literature has documented an increased risk of psychological distress in workers who have difficulties balancing work and personal life (Hawksley, 2007; Couser, 2008). Individuals, especially those in high occupational levels, can suffer lack of social support, both in the workplace and outside, and may have higher levels of family discord. These factors may exert a critical interference in the recovery process in those in high occupational levels.

Personality traits

Individuals in high occupational levels are often characterized by traits of self-confidence, vigour, motivation, aptitude for leadership and success, commitment, persistence and high sense of responsibility (e.g. Judge *et al.*, 2002). They usually make efforts to prevent or deny failures and feelings of weakness; they identify with the success and the results they achieve. They need to earn appreciation from others and maintain a self-image of strength, self-sufficiency and autonomy. They may not tolerate feelings of uselessness, weakness, needing help from others and negative self-evaluation.

Depression is characterized by low mood, loss of concentration, decreased energy, and by guilt and feelings of worthlessness, lowered self-esteem and the loss of ability to function as usual (DSM5). These symptoms are possibly more destructive of ability to function in those with high occupational levels. Those with a high sense of responsibility, commitment and dedication can also develop an increased sense of guilt and shame towards colleagues and subordinates whenever they fail to meet expectations.

Self-blame

The stigma attached to mental illness is well known. Those with depression feel guilty and inclined to blame themselves. Since those in high occupational levels need to project themselves as capable and strong, it is possible that the stigma of depression in society and self-stigma are more damaging for them.

The fear of being negatively labelled, being deemed unable to perform at previous capacity due to being 'mentally ill', often magnified by the person's own stigmatizing conception of the depressive illness, may push the individual to make great but often unsuccessful efforts to hide his/her condition, both at work and outside the workplace. This may increase the

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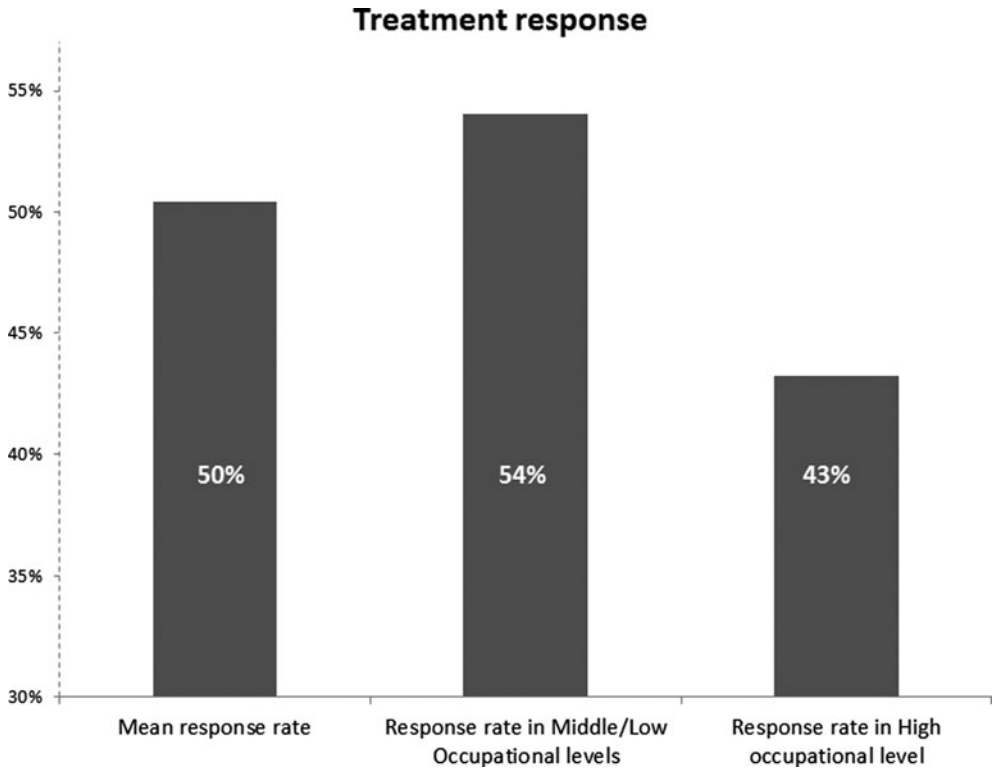

Fig. 1. Treatment response rates depending on the occupational level according to Mandelli *et al*. (2016).

individual's exposure to professional and interpersonal stressors. As well as hiding the illness from others, it may also be inwardly denied by the individual who may not recognize they have a mental problem ascribing his/her present condition to temporary external factors instead. They tend to believe the current distress should be solved with personal effort and dedication. Negative cognition and negative emotional reactions, as well as low self-esteem and withdrawal from social life are part of depression and tend to feed on each other. These might well contribute to the high rate of suicide, which has been reported in high occupational levels (Sudak *et al*., 2008; Chan *et al*., 2014; Wada *et al*., 2016). According to a systematic review of the literature, although suicidal risk is higher in low occupational levels, middle–high skilled occupations have a substantially higher risk of suicide compared with the entire working-age population (rate ratio = 0.9–1.2) (Milner *et al*., 2013). The individual may reduce participation in social life, consider themselves incapable of doing their job, to be undeserving of love from family members and friends. There is a risk of delay or even failure to request help, leading to prolonged illness duration, chronic course and poor compliance with treatment (Rusch *et al*., 2005).

Compliance with treatment

Occupational factors have been reported as barriers to treatment adherence in some medical conditions (Adisa *et al*., 2009; Coenen *et al*., 2016), but this has not hitherto been studied, to our knowledge, in psychiatric disorders. Many personal barriers exist for depressed individuals in being compliant with treatments (Frank, 1997). A number of factors contribute to poor compliance. Especially in the early stages of the illness, the individual may feel the need to cope alone, or may have poor trust in medical treatment and consequently may come late to clinical attention, sometimes after trying alternative treatment routes. They may be reluctant to take medication, to attend regularly for treatment or accept a proposal of hospitalization. They may complain of lack of time due to work obligations or the impossibility of taking time off work. Compliance may be only partial with drugs taken erratically or at lower dosages, medical appointments may be missed. Despite the need for long-term treatment, it is not uncommon for these individuals to discontinue treatment prematurely rather than wait for the full treatment benefits. Because of personality factors, work demands and life habits, individuals, especially those in high occupational levels, are often reluctant to accept treatment advice and the need for change. Work and performance are often priorities for many individuals in high occupational positions, with social relationships, family and personal care (including medical appointments) experienced as 'less important' or secondary to work commitments.

Transient side effects of drugs

Side effects can impact on treatment compliance even when they are minor (Montejo, 2009). Minor side effects may affect medication adherence but also the objective evaluation of the benefit of medication.

Jobs that are demanding from a cognitive point of view require optimal levels of psychophysical functioning (physical and mental energy, vigilance, prolonged attention, concentration) and these functions are reduced by depression. Effective treatments for depression can restore these functions (Keefe *et al*., 2014) although some can impact negatively, especially at the start of treatment, on cognitive functions, causing, for example, drowsiness (e.g. mirtazapine, amitriptyline), agitation or

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irritability [e.g. bupropion, Selective serotonine reuptake inhibitors (SSRIs) and some Serotonin–norepinephrine reuptake inhibitors (SNRIs)]. Cognition, which is already impaired as part of depression, may be further impaired by some antidepressants. Because of the anticholinergic and histaminergic effects common to many tricyclic antidepressants, reduced cognitive function may be felt early in treatment, before the therapeutic effects which comes later. Serotoninergic agents, because of their anti-anxiety properties, can impair the evaluation of critical aspects of situations and reduce motivation levels (McCabe *et al.*, 2010; Marutani *et al.*, 2011; Shannonhouse *et al.*, 2016). It has been reported that the detachment effect induced by many medications for depression such as serotoninergic inhibitors may be troublesome for some individuals (Harmer, 2008; Serretti *et al.*, 2010). The adverse cognitive effects can be particularly disturbing for individuals who need high cognitive performance at work. Despite a timely recovery from affective and somatic symptoms, the persistence of negative effects on the cognitive domain or the lack of improvement in cognitive impairments related to major depression (Papakostas and Culpepper, 2015) may interfere with compliance with treatment leading the individual to discontinue the medication. Newer medications for depression are promising (Al-Sukhni *et al.*, 2015; McIntyre *et al.*, 2015; Stahl, 2015). Anhedonia, decreased motivation and other core features of depression may persist despite an overall apparent response to treatment for depression (Yee *et al.*, 2015) and it has been suggested that some drugs for depression offer a better choice (Shelton *et al.*, 2001; Argyropoulos and Nutt, 2013). Potential side effects on body weight and sexual functioning also need to be taken into account (Serretti and Chiesa, 2009; Serretti and Mandelli, 2010).

However, many patients are often just reluctant to take medications for depression for various reasons (fear of cognitive effects, unpleasant side effects, fear of addiction, etc.). Psychotropic drugs are ascribed a moral significance and often just contemplating their use can affect how people see themselves, most commonly by suggesting personal weakness. Some patients may perceive the antidepressant medication as a barely legitimate – pharmaceutical, rather than as an established and effective treatment for a medical condition (Malpass *et al.*, 2009; Ridge *et al.*, 2015).

Residual symptoms and subjective evaluation of clinical improvement

A patient's potentially altered perception of symptomatic improvement during treatment and of residual symptoms need to be taken into account. Despite response of the major depressive symptomatology, some symptoms may persist, sometimes for a prolonged period (Fava *et al.*, 2002). For some individuals, the improvement in some symptoms such as mood, ability to engage in pleasurable activities and feelings of hope represents a significant improvement, despite the persistence of symptoms, for example, difficulties with sleep, attention and decision making (Kennedy and Foy, 2005; Fava, 2006). For other individuals, and especially those with high psychological demands at work, the same persisting symptoms (poor sleep, difficulty in sustaining attention and concentration and decision making) represent significant limitations. These individuals may continue to feel discouraged and dejected and complain of lack of benefit from treatments. Careful evaluation is needed to manage residual symptoms.

Clinical implications

Evaluation of objective and subjective stressors at work

A good clinician needs to evaluate the working life of the patient since performance at work is part of the evaluation of overall functioning. It is common for people to express spontaneously their difficulties in the workplace, the presence of pressure or tension, the fears and feelings related to their work, although in some cases, a more thorough evaluation may be needed.

Evaluation of potential or perceived stressors at work is particularly relevant in people in high occupational positions, in order to investigate the impact of the individual's working environment on the patient with depression. The clinician should identify, together with the patient, the critical problems occurring in the workplace, but also ascertain those problems produced or exacerbated by the behaviour and attitudes of the patient that result from the depression. For example, due to cognitive impairment, a patient may need to work excessive hours to complete what would be accomplished in a normal working day. Or again, due to the cognitive dysfunction, the patient may take on excessive commitments which they cannot cope with. Treatment of the depression should take into account all symptoms of depression and the need for improved support in the workplace.

Evaluation of objective and perceived availability of support

Evaluation of the availability of support at work is important. An individual may indeed be isolated from other colleagues but it can happen that concrete and emotional support potentially available from colleagues is not taken up. The perceptions, fears and emotions need to be explored to help the patient to make more use of supportive resources in the workplace. Likewise, if social networks outside of the workplace are lacking, the individual needs encouragement to explore new potential social resources. Potential sources of interference with sociability arising from excessive professional involvement (e.g. marital conflicts because of the little time to spend with the family, loss or weakening of relationships, little time to do sports, etc.) need to be evaluated.

Attitude to treatment

If the patient is involved in the decisions about the treatment, including discussion about the pros and cons of different medications for depression, compliance with the treatment and outcome have been shown to be improved. The clinician considers the individual concerns and proposes the treatment that the patient is more likely to accept and tolerate, to maximize functional restoration including professional activity. As an example, appointments can be scheduled after work or during breaks. Encouraging and enabling the patient to resume professional activity is important, and to achieve this, the clinician will consider the patient's particular needs in the choice of medication.

In the early and middle stages of the recovery, the potential persistence of residual symptoms that may hamper recovery needs to be thoroughly evaluated with the patient. The significance of these residual symptoms for the individual should not be underestimated.

Future directions

Further studies are needed to evaluate the relationship between specific aspects of higher occupational levels and outcome of

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treatment for depression. Although a large number of studies have investigated workplace risk factors for depressive disorders, greater attention needs to be paid to effective treatment and its implications for prognosis. The workplace risk factors for depression already identified (e.g. high demands, overwork, poor decision latitude, poor social support, etc.) also need to be investigated further in high occupational levels in relation to response in the short and long term.

The identification of factors that may interfere with the outcome of currently existing treatments for depressive disorders should be examined in relation to occupational level. These would undoubtedly help to improve the policies needed to promote effectiveness of current treatments. Targeting a functional and working recovery is beneficial to the individual who suffers from depression, but also has positive benefits in terms of reduced disability, absenteeism and presenteeism, increased productivity and reduction in direct and indirect costs associated with depression (Mrazek *et al*., 2014; Evans-Lacko and Knapp, 2016).

Conclusions

Work represents an important and meaningful aspect of an individual's life and it may have a particularly important role for people in high occupational levels where responsibilities and cognitive demands are great. It is important to understand the role of the professional activity as an important factor in delaying the recovery process. Currently, this is a significant gap in the scientific literature.

It appears that people in high occupational levels respond with greater difficulty to treatment for major depression (Mandelli *et al*., 2016). The reasons for this effect are not clearly established, but we can speculate that the stress factors in the workplace play a significant role.

These aspects should be carefully assessed in clinical practice. Patient education and the therapeutic alliance between clinician and patient can help improve adherence to treatment, which would lead to better outcome. Further studies are needed to fully elucidate the predictors of response in those in high-level occupations.

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