Sick and tired: psychological and physiological aspects of work-related stress

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11 General discussion

This body of research addressed the following topics in the area of work-related stress: physiological adaptation, treatment effectiveness of cognitive behavioural treatment (CBT), predictors of recovery, and the association with alexithymia. Below, the main findings are summarised per research question. Subsequently, I will discuss the main methodological issues concerning sample characteristics, design issues, and operationalisations. Then, clinical implications are provided. Finally, I will suggest directions for future research on work-related stress.

Summary of main findings

I. Is work-related stress characterised by dysregulation of the physiological stress-response system?

We found support for physiological adaptation in work-related stress resulting in physiological changes. More specifically, we observed changes in the balance between sympathetic and parasympathetic activity, HPA axis activity, and immune regulation in association with work-related stress. Concerning the balance between sympathetic and parasympathetic activity, support was found for an enhanced sympathetic tone in patients with a clinical level of work-related stress. Regarding basal activity, we observed elevated heart rate (Chapter 2), elevated systolic blood pressure (males only), reduced vagal activity, and a trend for elevated cardiac output (Chapter 3). We obtained no support for the prediction based on the reactivity hypothesis (Manuck, 1994), that is, that our patient group represents a group at risk for cardiovascular disease because of its elevated cardiovascular reactivity.

With respect to the HPA axis, support was found for its dysregulation. We found elevated morning cortisol (Chapter 2), which suggested enhanced HPA axis responsiveness. We also observed reduced cortisol *reactivity* to a psychosocial stressor (males only) and a trend for reduced basal cortisol (females only; Chapter 3). Reduced cortisol reactivity and reduced basal cortisol are indicators of reduced HPA axis responsiveness, rather than elevated HPA axis responsiveness. We do not have a clear explanation for the seemingly inconsistent results in the similar samples recruited for both studies. As the sample in the second study was larger than the sample in the first study, more weight should probably be given to the findings of the second study which supports reduced HPA axis responsiveness in association with work-related stress.

The combination of an increased sympathetic tone and reduced HPA axis responsiveness deserves further elaboration. A state of sustained cardiovascular activation suggests presence of sustained activation of the entire physiological stress system. Accordingly, increased rather than

reduced HPA axis (re)activity would be expected. Also viewed from physiological stress process models, these cardiovascular and HPA axis changes are not typical indices of the same phase of the physiological stress adaptation process. More specifically, an increased cardiac drive is associated with the initial stage of adaptation of the cardiovascular system (Palatini & Julius, 2009), while reduced HPA axis activity is commonly associated with a more progressed stage of adaptation (Cleare, 2003; Fries, Hesse, Hellhammer & Hellhammer, 2005; Miller, Chen & Zhou, 2007). As our sample demonstrated heterogeneity with respect to complaints duration, these presumed inconsistent outcomes may be caused by individual differences in the stage of physiological stress adaptation.

Concerning immune regulation, we obtained support for changed immunomodulation by the HPA axis (Chapter 4). First, in patients, dehydroepiadrosterone-sulphate (DHEAS) was associated with reduced cellular immunity, as indicated by a positive association between DHEAS and antibodies against the Epstein Barr Virus (EBV). No such association was found in healthy participants. The positive association in patients may be an indication of a shifted balance towards more anti-inflammatory activity and/or humoral immune activity. A role for DHEAS in the shift of immune activity towards more anti-inflammatory activity is in line with the findings of Mommersteeg et al. (2006a). Second, no immunostimulatory effect of cortisol was found in patients. In healthy participants, in contrast, the cortisol awakening response was positively associated with C-reactive protein (CRP), which suggests an immunostimulatory effect of cortisol. The absence of an association between the HPA axis and the inflammatory response observed in patients suggests resistance to glucocorticoids. Hence our finding supports resistance to glucocorticoids as being a consequence of prolonged exposure to stressors, as proposed by Fries et al. (2005) and Miller et al. (2002).

II. Can different phases be distinguished in the physiological stress-adaptation process?

Support was obtained for different phases in the process of physiological stress-adaptation (Chapter 8). We found that cardiovascular profiles were contingent upon the duration of complaints. Similar to cardiovascular characteristics of the initial phase in the development of hypertension (e.g., Palatini & Julius, 2009), shorter duration of complaints was associated with elevated cardiac output and a trend was found for elevated heart rate. Furthermore, longitudinally, the non-chronic patients that turned into chronic patients during the study demonstrated a reduction of cardiac output and an increase of vascular resistance, which are signs of a more progressed phase in the development of hypertension (e.g., Palatini & Julius, 2009). Our findings have enhanced the insight in the human process of physiological stress adaptation that until now has been mainly studied cross-sectionally in relatively healthy samples (e.g., Cacioppo et al., 2000; Vrijkotte, van Doornen & de Geus, 2000).

Additionally, we observed that blood pressure reduced to normal values after four months in the patients, who at the start of the study had chronic complaints already, and who did not recover in these four months. This normalisation may reflect a change towards a state of chronic fatigue.

The chronic fatigue syndrome is generally associated with normal basal functioning of basic cardiovascular measures (e.g., Peckerman et al., 2003; LaManca et al., 2001). Alternatively, blood pressure normalisation in this chronic group may indicate physiological recovery, implying that the patients with chronic work-related stress that did not recover during our four months follow-up fared well by the prolonged rest. Future studies may pit these hypotheses against each other for more definite conclusions.

III. Is cognitive behavioural treatment effective for work-related stress?

We obtained limited support for additional effectiveness of cognitive behavioural treatment (CBT) over care as usual (CAU) for a clinically elevated level of work-related stress, whether examined from work-related stress complaints or physiological outcome measures. No additional effect of CBT was found on work-resumption. With regard to complaints, support was found for superior effectiveness of individual CBT in comparison to CAU in the subgroup with a lower level of depressive complaints (Chapter 5). More specifically, this subgroup demonstrated larger reductions of emotional exhaustion, depersonalisation, and fatigue, and a larger increase of professional competence in comparison to the patients receiving CAU. Other randomised controlled trials investigating CBT for work-related stress (Bakker et al., 2007; Blonk, Brenninkmeijer, Lagerveld & Houtman, 2006; Huibers et al., 2004; van der Klink, Blonk, Schene & van Dijk, 2003) have obtained similar results regarding complaints reduction. Mixed results have been reported regarding the achievement of work-resumption with use of CBT (Bakker et al., 2007; Blonk et al., 2006; Huibers et al., 2004; van der Klink et al., 2003). Hence, we concluded that CBT for a clinical level of work-related stress needs to gain in efficacy.

Concerning physiological outcome measures, we observed superior effectiveness of group-CBT on morning cortisol (Chapter 7). More specifically, cortisol increased in the group-CBT condition, while it reduced in the individual CBT condition and in the CAU condition. A similar pattern was found for basal cortisol levels in the afternoon (Chapter 6). Although we did not observe a consistent pattern of change across all physiological variables, the similarity in the direction of cortisol changes in the two studies strengthens our conviction that the cortisol increase can indeed be ascribed to the group-CBT. The direction of change in cortisol in the group-CBT condition in accordance with the outcomes reported by others groups in a sample of patients with work-related stress (Mommersteeg, Keijsers, Heijnen, Verbraak, & van Doornen, 2006b) and in a sample of patients with chronic fatigue syndrome (Roberts, Papadopoulous, Wessely, Chalder & Cleare, 2009).

Interestingly, inconsistency in change between measurements was noted between self-reported work-related stress complaints and physiological measures. More specifically, complaints reduced considerably in the total group, while of all included physiological variables, only blood pressure changed between measurements. In addition, with regard to complaints, individual CBT yielded the largest effects, while based on physiological outcomes, group-CBT appeared the most effective. An explanation for the inconsistent patterns of change may be that complaints and physiological measures have different sources of inter-individual differences. For example, motivated misrep-

resentation related to reintegration or treatment preferences and recollection bias are factors that may have affected self-reported complaints; an influence of these factors on physiological measures is unlikely, though. Alternatively, factors may differentially influence complaints and physiological variables. For example, variation in duration of exposure to stressors may differentially affect physiological measures and self-reported complaints. For physiological variables, there is strong support for differential changes in association with a different duration of exposure to stressors (e.g., Miller et al., 2007; Fries et al., 2005; Gump & Matthews, 1999; Matthews, Gump & Owens, 2001; Melamed et al., 1999). Moreover, as noted earlier, we indeed found that variation in duration of complaints was associated with opposite physiological patterns of change (Chapter 8). These opposite physiological changes apparently cancelled out change observed in the total group. For complaints, we did not find evidence for the occurrence of opposite changes in association with variation in duration of stressor exposure in our sample (results not shown).

IV. What are predictors of recovery of work-related stress?

Reductions of work-related stress complaints were predicted by individual related, work-related, and illness related variables (Chapter 9). More specifically, male gender, less working hours, less decision authority, more co-worker support, and shorter absence duration predicted the reduction of general distress complaints (i.e., tension, fatigue, anxiety, and depressive complaints), and male gender, lower age, higher education, less avoidant coping, less decision authority, more job security, and more co-worker support predicted the reduction of burnout complaints (i.e, emotional exhaustion, depersonalisation, and professional competence). Work-resumption was only predicted by age and by a reduction of burnout complaints. No mediation of reduction of burnout complaints in the association between age and work-resumption was observed. Some of the predictors, e.g., coping and co-worker support, can serve intervention purposes. Other predictors, for example gender, age, and education, are more suitable for prognostic purposes. Our findings further confirm that a discrepancy exists between complaints reduction and work-resumption as has been observed in treatment effect studies (Bakker et al., 2007; Blonk et al., 2006; Huibers et al., 2004; van der Klink et al., 2003).

V. Is alexithymia a vulnerability factor or a consequence of work-related stress?

Based on assessment of stability and state-dependence of alexithymia, we concluded that elevation of alexithymia associated with work-related stress can best be understood as a reaction to a stressful situation rather than a vulnerability factor to develop work-related stress (Chapter 10). First, absolute stability of two alexithymia dimensions (identifying feeling, describing feelings) and relative stability of one alexithymia-dimension (identifying feelings) was lower in patients with work-related stress than in healthy participants. Second, after adjustment of alexithymia for complaints, differences between the patient- and the healthy group became small, indicating strong state dependence of alexithymia. State dependence was further supported by the finding that change in alexithymia in patients was moderately associated to symptom recovery. Our results highlight that

cross-sectional studies demonstrating associations between alexithymia and psychopathology provide insufficient evidence for alexithymia being a risk factor for psychopathology.

Methodological considerations

The main methodological aspects of our studies with regard to sample characteristics, design issues, and operationalisations are discussed below.

Sample characteristics

The patient sample studied in this thesis was a convenience sample consisting of employees predominantly working in small and medium size companies, which puts limits on the generalisation of our outcomes. For example, the CBT may have been more effective in employees working in larger companies, because in larger companies there are generally more possibilities for improving a person-job fit. In addition, the sample consisted of individuals on sickness leave. While the CBT tested in our treatment studies consisted of widely used cognitive behavioural procedures that have been proved effective in working employees (e.g., van der Klink, Blonk, Schene & van Dijk, 2001), employees on sickness-leave may require a more intensive, higher dose approach because of their more severe problems.

Second, the patient sample was heterogeneous with respect to the dominant type of complaints (i.e., depression-, anxiety-, or fatigue-related), the duration of complaints, and the extent of work-resumption. Heterogeneity suggests that the sample was naturalistic, bolstering external validity of our studies. A drawback of heterogeneity was that it presumably caused large inter-individual variation in physiological measures that may have handicapped the detection of main effects. To illustrate, generally, anxiety and fatigue complaints are associated with reduced cardiovascular activity or reactivity and reduced cortisol levels, while depressive complaints are associated with enhanced cardiovascular activity and reactivity and elevated cortisol levels (e.g., Chida & Hamer, 2008; Dahlgren et al., 2009; Matthews, Nelesen & Dimsdale, 2005; Mommersteeg, Heijnen, Verbraak & van Doornen, 2006c; Nelesen, Dar, Thomas & Dimsdale, 2008; Newton et al., 2009; Pruessner, Hellhammer, Pruessner & Lupien, 2003; Roberts, Wessely, Chalder, Papadopoulous & Cleare, 2004).

Another potential threat to the internal validity of our conclusions with respect to effectiveness of CBT was the selective drop-out. The dropout rate was larger in the CAU condition than in the CBT conditions, which was possibly due to disappointment about not receiving CBT. It is unlikely, though, that this selective dropout biased our conclusions for the following reasons. First, dropped-out patients did not differ from study completers at baseline with respect to for example severity of complaints. And second, in our differential treatment study (Chapter 5), we demonstrated that even if drop-outs would not have improved at all, superior effectiveness of CBT would still not be demonstrated.

Design issues

A general issue concerns the use of the same patient sample for different studies. This had clear practical benefits; it for example reduced the effort for sample recruitment. A disadvantage, however, was the risk of over-generalisation due to overweighing repeatedly observed patterns in the results that are caused by typical characteristics of this sample instead of typical characteristics of work-related stress.

Other design issues are specific to the treatment effect studies. First, the control group received care as usual. A restriction of this design is that we could test the relative but not the actual effectiveness of CBT. Consequently, our overall null-findings illustrated simply that CBT did not outperform care provided by the occupational physician and short psychological treatments. A strength of our design is, however, that care as usual is a credible and naturalistic control treatment. Second, the sample size enabled us to detect only medium to large between-group differences. In retrospect, though, it seems more likely that the actual differences between supposedly active interventions would be in the small to medium range.

Operationalisations

A general issue with respect to operationalisations is our definition of work-related stress as work-related adjustment disorder or burnout according to the classification of the Netherlands Society of Occupational Medicine (2000). Consequently, we have ignored potential qualitative differences between the two disorders. Our one-dimensional approach is in accordance, though, with the newest guidelines of the Netherlands Society of Occupational Medicine (2007).

When obtaining null findings in a treatment study, it behoves the researcher to rule out alternative explanations for not finding the expected results. Most importantly, did we fail to find a differential treatment effect because inadequate treatment content or implementation? With regard to content, we have tested widely used cognitive behavioural techniques that have demonstrated efficacy in anxiety- and affective disorders (Butler, Chapman, Forman & Beck, 2006) and in relatively healthy samples with work-related stress complaints (van der Klink et al., 2001). However, the strong focus on the individual of this type of techniques may be less suitable for patients on sickness leave because of work-related stress. In fact, there is now emerging evidence to suggest that the content of our cognitive behavioural intervention for stress-management places too much emphasis on changing aspects of the individual's functioning, and too little emphasis on the match between the job and the individual. First, it has been highlighted by others (e.g., Schaufeli & Buunk, 2003) that individually focused treatments put responsibility to recover and be up to the demands posed by the job again too strongly on the side of the absent employee. In addition, professional burnout is regarded as a consequence of a prolonged mismatch on the job-person relationship (Maslach, Schaufeli & Leiter, 2001). Moreover, several studies demonstrated that a state of work-related stress is to a larger extent determined by organisational aspects and perceived working conditions rather than by individual characteristics such as way of coping and personality (Maslach et al., 2001; Payne, 2001; Visser, Smets, Oort & de Haes, 2003). Whether interventions that focus on

the individual and the organisation are indeed more effective may be tested in future research.

With respect to implementation, one may question whether the therapists were sufficiently experienced. The majority of therapists indeed had less than six years clinical experience. However, other researchers have demonstrated that more experienced therapists do not necessarily obtain better treatment results (de Jong & Emmelkamp, 2000). In addition, a detailed treatment manual was provided, the therapists were thoroughly trained, and senior therapists supervised them during treatment. Hence, it is unlikely that lack of additional treatment effect was caused by inadequate therapists.

The validity of the acute psychosocial stressor is addressed because the acute cortisol reactivity in our studies was attenuated in comparison with cortisol reactivity observed by other groups using similar acute psychosocial stressors (e.g., Kirschbaum, Pirke & Hellhammer, 1993; Schmidt-Reinwaldt et al., 1999). Attenuation was most evident in females. Attenuated cortisol reactivity may have hindered traceability of between-group differences, in particular in smaller samples, and hence explain our inconsistent results with respect to changes in cortisol reactivity in work-related stress (Chapters 2 & 3). Most important topics for this discussion are the impact of the stressor, anticipatory stress, and gender relevance of the stressor. The impact of our psychosocial stressor may have been lower than the impact of for example the Trier Social Stress Test (Kirschbaum et al., 1993), because we used a camera and presence of the experimenter instead of a larger audience. Attenuated cortisol reactivity has been observed by other groups when a camera instead of a live audience was used (e.g., Roy, Kirschbaum & Steptoe, 2001; Stroud, Salovey & Epel, 2002). Against reduced impact of our psychosocial stressor pleas that no evidence for attenuated stressfulness was obtained through cardiovascular measures or subjective reports. Moreover, a few participants even refused to be exposed to the stressor a second time, because they found the session too distressing. Nonetheless, in order to rule out the risk of reduced impact, it is recommended to use a real live audience instead of a camera.

Attenuated cortisol reactivity in females may be due to lower female task relevance. Lower female task relevance implies that, according to socio-cultural norms, it may be less important for females to succeed in mental arithmetic and public speech. Consequently, less stress is induced. It has indeed been shown that gender differences in HPA axis reactivity depend on the type of stressor (e.g., Stroud et al., 2002). More specifically, Stroud et al. found that the cortisol reaction during achievement tasks (e.g., mental arithmetic and public speech) was stronger in men than in women, while during a social rejection task, the opposite pattern was found. An argument against gender differences in task relevance is the fact that we found no gender differences in subjective reactivity measured with positive and negative affect scales. Similar results have been reported by others (Stroud et al., 2002). Moreover, some researchers have even reported that women evaluated a psychosocial stressor as *more* stressful than men (e.g., Kudielka et al., 1998). Hence, based on subjective reactivity, a psychosocial stressor does not seem to be less relevant for females than for males. However, when considering cortisol reactivity, achievement tasks seem to be more valid to investigate HPA axis reactivity in males, while social rejection tasks seem to be more valid in females.

An alternative explanation for attenuated cortisol-increases in reaction to the stressor is that anticipation stress already had resulted in elevated cortisol levels. The cortisol level at the start of the laboratory stressor was considerably higher, that is 1-3 ng/ml, than the cortisol-level at midday (see Chapters 2-4), while only a small increase at the beginning of the afternoon is expected due to food intake during lunch. Although we have strived to induce physiological relaxation by allowing participants to get used to the room, anticipatory stress seems to have been induced by the laboratory environment. With regard to cortisol, the rest period of approximately 30 minutes before the first sample was taken may still have been too short to accomplish cortisol levels representative of basal HPA axis activity.

Clinical implications

Several clinical implications follow from our work. First, the finding that a substantial number of patients demonstrated pre-hypertensive diastolic and borderline hypertensive systolic blood pressure (Chapter 8) as defined by the American Heart Association (2004) suggests that blood pressure among patients with work-related stress needs to be closely monitored. Second, the presence of a particularly adverse cardiovascular profile in a subgroup of the chronic patients with work-related stress who were categorised as recovered after the treatment phase suggests that information about the phase of cardiovascular adaptation is important for treatment and reintegration purposes. Third, our findings support early identification of hypertension and subsequent monitoring after reintegration, in particular because the above mentioned subgroup of chronic patients with work-related stress upon their recovery presumable will disappear out of the medical circuit. Fourth, the loose association between self-reported work-related stress complaints and physiological measures warrants inclusion of both self-report and physiological measures in clinical assessments. Fifth, in addition to accumulating evidence from other studies (Bakker et al., 2007; Blonk et al., 2006; Huibers et al., 2004; van der Klink et al., 2003), our results of the treatment studies do not indicate routine prescription of CBT for patients on sickness leave because of work-related stress. CBT may however be beneficial for certain subgroups, e.g., those characterised by relatively low levels of depressive complaints. This suggestion awaits further cross-validation though. Sixth, the loose association between reduction of work-related stress complaints and work-resumption in the recovery process suggests that either outcome requires its own intervention strategy. Finally, since the prevalence of primary alexithymia observed among patients with work-related stress was similar to the prevalence in the general population, our study gives no rise to adapt standard CBT protocols for work-related stress.

Future research

Main challenges regarding research about work-related stress are a) to elucidate the nature and development of physiological adaptation associated with work-related stress, b) to unravel the rela-

tion between physiological characteristics and self-reported work-related stress complaints, c) to improve treatment efficacy of work-related stress, d) to enhance insight in the process of recovery of work-related stress, and e) to sharpen the conceptualisation of work-related stress.

Nature and development of physiological adaptation

To progress on the elucidation of the nature and development of physiological changes associated with work-related stress we suggest the following future directions. First, in order to explain inconsistent findings that have been reported about physiological changes in work-related stress, it is suggested to search for explanatory variables for individual differences in physiological changes. Our studies described in Chapters 3 and 8 highlight the relevance of gender and complaints duration, respectively, in association with physiological changes. Considering the literature, the following variables are also promising explanatory variables for individual differences in physiological changes: a) the dominant type of complaints (Chida & Hamer, 2008; Dahlgren et al., 2009; Matthews et al., 2005; Mommersteeg et al., 2006c; Nelesen et al., 2008; Newton et al., 2009; Pruessner et al., 2003; Roberts et al., 2004), b) the duration of stressor exposure (Cacioppo et al., 2000; Henry, Meehan & Stephens, 1967; Herman, Adams & Prewitt, 1995; McCarthy, Horwatt & Konarska, 1988; Palatini & Julius, 2009; Vrijkotte et al., 2000), and c) situational characteristics (e.g., presence/absence of a stressor; Kudielka, Bellingrath & Hellhammer, 2006; Ostrander et al., 2006).

Second, in order to obtain a more refined view of physiological changes in work-related stress, it is suggested to study the interplay between physiological stress sub-systems, that is, the sympathetic system, the parasympathetic system, the HPA axis, and the immune system. These physiological stress sub-systems have long been treated as separate and mainly independently regulated systems. However, evidence has been accumulating that these physiological stress sub-systems are highly integrated and have mutual effects (e.g., Sapolsky et al., 2000; de Kloet, Vreugdenhil, Oitzl & Joels, 1998). Our results that regulatory changes may be present in absence of changes in the individual stress sub-systems (Chapter 7) provide initial support for the relevance of studying the interplay between physiological stress mechanisms for detection of physiological changes in work-related stress.

Third, insight in changed physiological functions may be enhanced through conducting challenge tests. The use of challenge tests is scarce in the field of work-related stress. Our findings regarding reduced cortisol reactivity (Chapter 3) highlight the importance of the use of challenge tests, since changes may otherwise remain undetected. In addition, in particular chemical challenge tests can provide more detailed information about functional changes in different levels of the HPA axis. For example, by conducting the dexamethasone suppression test, support for enhanced sensitivity to central glucocorticoid feedback in the HPA axis in patients with work-related stress has been found (Sonnenschein et al., 2007).

Fourth, genetic research can add to the detection of vulnerability factors for work-related stress. With respect to cardiovascular responding, support for a genetic component associated with cardiovascular reactivity to stressors has been found (e.g., Mei et al., 2009). It remains to be demon-

strated though, that enhanced reactivity is a vulnerability factor for work-related stress complaints, and/or the adverse cardiovascular conditions associated with it. Regarding the HPA axis, by demonstrating associations between glucocorticoid receptor polymorphisms and cortisol reactivity to a psychosocial stressor, Wüst et al. (2004) provided initial support for individual differences in vulnerability for developing changes in HPA axis activity. Again, it remains to be shown that this genetic profile is a vulnerability factor for work-related stress complaints and/or the changes of HPA axis activity found in association with work-related stress.

Finally, in order to refine the physiological process models, including the General Adaptation Syndrome (Selye, 1975) or the theory of allostatic load (McEwen & Wingfield, 2003), future research should focus at developmental pathways of physiological adaptation to stressors. An example of a more refined model is the model described by Fries et al. (2005), which specifically describes the development of hypocortisolism associated with chronic stress. Validation of existing models and more detailed descriptions of pathways and mechanisms may be reached by conducting longitudinal research in stressed samples, whereby information about for example the type (e.g., social, physical), severity, duration, and pattern (single, continuous, or repeated) of the stressor is assembled and physiological variables and self-reported complaints are repeatedly measured.

Incongruence physiological characteristics and subjective complaints

For unravelling the relation between physiological characteristics and self-reported work-related stress complaints we suggest to assess sources of incongruence between these measures. In addition to the previously discussed confounders such as presence/absence of a stressor, duration of stressor exposure, recollection bias, and motivational misrepresentation that probably differentially affect self-report measures and physiological measures, a main source of incongruence is likely to be found in data collection methods. For example, a source of incongruence may be the time lag between measurement of physiological variables and self-reported work-related stress complaints. It is common practise to relate physiological variables to self-reported complaints that have been collected using retrospective questionnaires. Moreover, physiological variables are generally assembled over short periods of minutes to hours, while questionnaires generally cover periods of several weeks. Presumably, physiological variables more strongly reflect a momentary state, while inquiry of complaints by questionnaire results in a more global measure. A recent study has illustrated that stronger associations between cortisol and self-reported work-related stress complaints can indeed be obtained when data are collected simultaneously on a day-to-day basis (Sonnenschein et al., 2007). Consequently, when the aim of a study is to search for between-group differences in self-reported complaints and physiological variables rather than assess intra-individual associations between physiological measures and self-reported complaints, it may be worthwhile to explore whether intra-individual fluctuations in physiological measures can be reduced by increasing the number of physiological measurements and extending the number of sampling days.

Another possible source of incongruence is distorted measurement of physiological dysregulation. More specifically, peripheral measurement of physiological measures may, for example

through compensatory mechanisms, not adequately reflect physiological dysfunctions that are located centrally. Further research on central disturbances, including changed neurotransmitter balances, and related peripheral changes may clarify this issue.

Treatment efficacy of work-related stress

To improve treatment efficacy, we suggest that future research will be targeted at: a) investigating the effectiveness of a dual treatment approach, b) examining pharmacotherapy, c) clarifying the specific effects of CBT elements, and d) exploring predictors of treatment effectiveness.

A dual treatment approach that is targeted at the individual and the work-situation is promoted by the view that work-related stress develops as a consequence of a prolonged mismatch of the job-person relationship (e.g., Maslach et al., 2001). Our results reported in Chapter 9 indeed lend support to the notion that complaint reduction and work-resumption are influenced by individual-related and job-related variables (Chapter 9). Focusing on the organisation in addition to the individual is more common in preventive interventions than in clinical interventions. Initial support for positive effects of organisational interventions in patients on sickness-leave because of work-related stress has been reported (Nieuwenhuijsen, Verbeek, Siemerink & Tummers-Nijsen, 2003). Considering the psychological expertise of the psychologist and the occupational expertise of the occupational physician and his/her contacts with the employer, a dual treatment approach may be operationalised as a multidisciplinary treatment by the psychologist and occupational physician.

Effectiveness of pharmacotherapy for work-related stress complaints with for example corticosterone or DHEA has not been explored yet. Positive effects of replacement or supplementation may be expected for the following three reasons. First, we have demonstrated changes in cortisol levels (Chapters 2 & 3) and alteration of immune regulation by cortisol and DHEAS (Chapter 4). Second, support for the role of cortisol in the association between stress on the one hand, and concentration, memory, and emotional problems on the other, has been obtained from animal (Conrad, Lupien & McEwen, 1999; Ohl, Michaelis, Vollman-Honsdorf, Kirschbaum & Fuchs, 2000; Song, Che, Min-Wei, Murakami & Matsumoto, 2006) and human research (Erickson, Drevets & Schulkin, 2003; Skosnik, Chatterton, Schwisher & Park, 2000). In addition, the brain structures involved in concentration, memory, and emotion, e.g., the amygdala, the hippocampus, and the prefrontal cortex, appear to be sensitive to cortisol (de Kloet et al., 1998). Third, initial positive findings of treatment with a low dose of hydrocortisone in normalising the cortisol level and on complaints have been reported for chronic fatigue syndrome (Cleare, 2003). The role of DHEA in concentration, memory, and emotional complaints is currently less clear yet (Buvat, 2003). However, DHEA supplementation in healthy elderly women yielded positive effects on memory functions (Buvat, 2003). In addition, some preliminary support has been reported for positive effects of treatment with DHEA on complaints in patients with chronic fatigue syndrome with reduced levels of DHEA (Himmel & Seligman, 1999) and in patients with depressive symptoms (Buvat, 2003).

In order to clarify the effects of CBT elements, we suggest repeated measurement of potential

precursors of complaint reduction and work-resumption that relate more directly to the CBT components in a treatment effect study. Candidates for precursor variables are self-esteem, mastery, lifestyle, cognitions, and interpersonal capacities. Support for a precursor – complaint association has been reported; reductions of irrational cognitions appeared to be associated with reductions of anxiety, depressive, and stress complaints in a sample with common mental disorders (Nieuwenhuijsen, Verbeek, de Boer, Blonk & van Dijk, 2007). Another strategy to enhance insight in treatment effectiveness is to dismantle the CBT program, and study the effects of the separate components. With this approach, the beneficial effect of social support in group CBT (suggested in Chapter 7) could also be investigated.

Assessments of predictors of treatment success may aid to improve treatment efficacy. Superior effectiveness of individual CBT was observed in patients with a lower level of depressive complaints (Chapter 5). While this finding requires cross-validation, it provides tentative evidence that empirically informed matching of patient characteristics with treatment modalities may yield superior overall treatment gains. We therefore suggest exploration of the level of depressive complaints as a predictor for treatment success.

The recovery process

To arrive at a better understanding of the process of recovery, we suggest longitudinal assessment of potential individual, illness-related, and work-related predictors and mediators during the period of sickness absence. Regarding potential mediating individual characteristics, we suggest measures of coping and cognitions be included. While we obtained zero-outcomes for cognitions, repeated measurements of the theoretically relevant cognitions may yield different results because of a more optimal timing of measurement. Further support for this notion was reported by the research group of Nieuwenhuijsen et al. (2007). Concerning illness-related variables, we suggest exploration of the predictive value of physiological changes for recovery of complaints and work-resumption. In addition, investigating the predictive value of severity of anxiety and depressive complaints is promoted by a study in that reported that a diagnosis of anxiety or depression predicted extended sickness leave (Nieuwenhuijsen, Verbeek, de Boer & van Dijk, 2006). Regarding work-related predictors, we suggest to found variable selection on the Demand Induced Strain Compensation (DISC) model (de Jonge & Dormann, 2003). This model integrates the Job-Demand Control Support (JDCS) model and the Effort Reward Imbalance (ERI) model. Our study promotes selection of work-related variables based on the Job-Demand Control Support (JDCS) model (Chapter 9) and clinical impressions supported the relevance of effort-reward imbalance for a lack of well-being.

Conceptualisation of work-related stress

To improve construct validity of work-related stress and formulation of associated clinical diagnoses, further conceptual research is recommended. Sharper conceptualisation may for example result in implementation of a diagnosis of work-related adjustment disorder or burnout in diagnostic

classification systems, which will facilitate future research on work-related stress. To progress on this issue, we propose to investigate conceptual relations between work-related adjustment disorder and burnout on the one hand and major depression and anxiety disorders on the other. The main conceptual question is whether work-related adjustment disorder and burnout reflect qualitatively different disorders, or sub-clinical levels of anxiety or mood disorders. Other researchers have proposed shared neurobiological mechanisms in the development and treatment of depression and burnout (Ericksson & Wallin, 2004). Furthermore, the finding that only the severity, but not the type, of irrational beliefs differed between adjustment disorder and anxiety or depression (Nieuwenhuijsen et al., 2006) serves as initial evidence that adjustment disorder is not qualitatively different from anxiety or major depression. Further research is necessary, though.

Second, we suggest that future research be targeted at investigating work-related stress as an overarching construct containing work-related stress complaints, work-related adjustment disorder, and burnout, as proposed by the Netherlands Society of Occupational Medicine (2000). In order to test dimensional or categorical conceptualisation of work-related adjustment disorder and burnout, we propose to investigate whether the main distinctions between the clinical diagnoses for work-related adjustment disorder and burnout, that is, a) presence/absence of a stressful event, and b) duration of the developmental path, are associated with different behavioural, cognitive, emotional, and/or physiological characteristics. Moreover, we propose to assess whether these distinctive characteristics have differential prognostic value for treatment effectiveness and recovery.

Conclusions

Progression has been made in the elucidation of physiological and psychological characteristics of work-related stress and of effectiveness of CBT for work-related stress. The main findings of this disseration are as follows. First, work-related stress is indeed characterised by physiological changes that indicate dysregulation of the physiological stress response system. In addition, different phases appear to exist in long-term cardiovascular stress adaptation. Second, support was found for superior effectiveness of individual CBT on work-related stress complaints in patients with less severe depressive complaints. Furthermore, a stronger treatment effect of group-CBT on cortisol was observed. Third, recovery of complaints was predicted by various individual-related predictors, work-related predictors, and an illness related predictor, while work-resumption was only predicted by age and reduction of burnout complaints. In addition, complaints reduction and work-resumption appeared to be loosely related processes. And fourth, alexithymia appeared to be a consequence rather than a risk-factor for work-related stress.

An important challenge within the field of work-related stress is to improve the efficacy of treatment for work-related stress, by for example exploring the effectiveness of treatments that are targeted at the individual and the workplace. Other challenges are to elucidate the development of physiological adaptation associated with work-related stress and to enhance insight in the process of recovery of work-related stress through for example longitudinal studies.

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