State-dependent factors and attention in Whiplash Associated Disorder

Mariëtte Blokhorst

ADDRESS OF CORRESPONDENCE:

Mariëtte Blokhorst
Roessingh Research and Development
PO Box 310
7500 AH Enschede
The Netherlands
+31 (53) 4875777
m.blokhorst@rrd.nl

ISBN 90-365-2111-4

Layout, figures and cover: TerHeyne Communicatie & Design, Enschede
Printed by Robine B.V., Twello

DE PROMOTIECOMMISSIE IS ALS VOLGT SAMENGESTELD:

Voorzitter en secretaris:	
Prof. dr. W.H.M. Zijm	Universiteit Twente
Promotor:	
Prof.dr. G. Zilvold	Universiteit Twente
Assisstent promotor:	
Dr. R. Lousberg	Roessingh Research and Development Universiteit Maastricht
Referent:	
Dr. F. Winter	Medische Psychologie, te Eerbeek
Leden:	
Prof. dr. E. Seydel	Universiteit Twente
Prof. dr. H. Hermens	Universiteit Twente
Prof. dr. B. Schmand	Universiteit van Amsterdam
Prof. dr. A. Vingerhoets	Universiteit van Tilburg
Dr. P. Eling	Radboud Universiteit Nijmegen

Paranymfen:

Drs. O. Lof
Drs. J. Wittrock

State-dependent factors and attention in Whiplash Associated Disorder

PROEFSCHRIFT

ter verkrijging van
de graad van doctor aan de Universiteit Twente,
op gezag van de rector magnificus,
prof.dr. F.A. van Vught,
volgens besluit van het College voor Promoties
in het openbaar te verdedigen
op vrijdag 21 januari 2005 om 16.30 uur

door

Mariëtte (M.G.B.G.) Blokhorst
Geboren op 28 maart 1962
te Goor

DIT PROEFSCHRIFT IS GOEDGEKEURD DOOR:

Prof. Dr. G. Zilvold (promotor)
Dr. R. Lousberg (copromotor)

This study was generously supported by grants from the St. Hubertus Foundation and Nardy Roeloffzen foundation. The publication of this thesis was supported by Revalidatiecentrum het Roessingh, Enschede

Voor Paul

Contents

Chapter 1

Introduction and outline of the thesis

INTRODUCTION

The chronic whiplash syndrome, also called Whiplash Associated Disorder (WAD), has been known for decades.[1] Because the majority of WAD patients are in the employable age, the syndrome constitutes, apart from the personal suffering, a frequent contributor to the ever increasing financial strain on insurers as well as the healthcare system.[1,2]

There is ample evidence that WAD patients have attention problems, which interfere with their daily functioning.[1-12] However, the causes of these cognitive problems are not clear.[2,13] Evidence of traumatic brain injury is not convincing and it is suggested that state-dependent factors, such as headache, neck pain, fatigue or distress, might play a significant role.[1-8]

The main aim of this thesis is to investigate this relationship between state-dependent factors and attention in WAD patients. Furthermore, the focus is on noise-distractibility and noise-intolerance, which are symptoms related to attention, often mentioned by WAD patients and which are neglected subjects in whiplash research so far.[3,5,14]
In this chapter, a brief overview is given of the definition, classification and epidemiology of WAD. Next, a review of results on cognitive functioning in WAD will be presented. In the last paragraph, the remaining chapters of this thesis are introduced.

Definition, classification and epidemiology of WAD

The term WAD is defined by the Quebec Task Force in 1995 as follows:

> *'Whiplash is an acceleration-deceleration of energy transfer to the neck. It may result from rear-end or side-impact motorvehicle collisions, but can also occur during diving or other mishaps. The impact may result in bony or soft-tissue injuries (whiplash injury), which in turn may lead to a variety of clinical manifestations (Whiplash Associated Disorder)'.*[13]

The clinical manifestations of WAD are rather diverse with respect to the kind and severity of the symptoms.[3,15] After neck pain (part of the definition of the disorder), headache (76%) and shoulder pain (62%) are also very common symptoms. Dizziness (29%), visual (43%) and auditory symptoms (tinnitus, sensitivity to noise) (38%), sleeping problems and fatigue (76%) also regularly occur.[4,15] Furthermore, WAD patients frequently show emotional distress (anxiety, depression, irritability) (67%) and report problems with cognitive functioning (inability to concentrate, forgetfulness) (38%).[4,15] There is however a large difference between percentages of complaints in several studies, due to a selection bias of patients included in the study.[4,5,13,15]

In 1995, the Quebec Task Force developed a classification system that reflects these differences in symptoms and signs.[13] This grading system is shown in Table 1.[13,15]
Most WAD patients have grade I or II symptoms, called 'soft tissue injuries'.[2,15] This thesis will focus on these first two grades (that is, patients without cervical spine fractures, dislocations, or clear-cut, objective neurological lesions).
There are substantial variances in the epidemiology of whiplash in different countries, partly due to different study objectives and methodologies, and likely also because of real differences in recovery rates in countries as a result of different insurance/compensation systems.[2,15] Annual incidence rates of whiplash injuries vary between 16 per 100.000 in New Zealand to 70 per 100.000 in Quebec (Canada), while the Netherlands scores 40 per 100.000.[15,16]

Table 1: The Quebec Task Force on Whiplash Associated Disorder (WAD) classification scheme.[4]

Grade:	Injury and symptoms:	Signs:
1	Neck stiffness only	No tenderness and normal range of motion. Normal reflexes and muscle strength in the limbs.
2	Probable muscle and/or ligament sprain	Any combination of neck pain with or without back pain, jaw pain, jaw locking, jaw clicking, limb, numbness, dizziness. Paraspinal tenderness and restricted spine range of motion.Normal reflexes and muscle strength in the limbs.
3	Probable disc protusion with nerve root impingement.	Neck pain, often arm pain or numbness. Abnormal reflexes and/or muscle weakness, often with sensory changes in a dermatomal pattern suggesting nerve root impingement (typically due to disc protusion).
4	Cervical fracture and/or dislocation	Neck pain, possibly neurological symptoms in limbs, urinary incontinence due to spinal cord involvement. Possible hyperreflexia, positive Babinski's sign, motor weakness and sensory changes suggesting spinal cord injury.Radiograph reveals fracture and/or dislocation.

Cognitive functioning in WAD

Neuropsychological profile and the course of cognitive dysfunction

The daily problems concerning cognitive functioning WAD patients complain of, are objectivated in several neuropsychological studies.[5,6,9,10,17] In a meta-analysis, Kessels et al. (2000) analysed the results of published studies on cognitive functioning after whiplash injury and concluded that WAD patients show an overall impaired performance on tests measuring working memory, attention (divided and focused attention), immediate and delayed recall, visuomotor tracking and cognitive flexibility.[6]
With respect to the course of the attention problems, a prognostic study of Radanov et al.[3] showed that patients who were symptomatic two years after the injury, showed significantly poorer results on attention tasks in the acute stage of the WAD compared to asymptomatic patients. Following an average improvement, regarding all aspects of attentional functioning in both groups during the first months, the subsequent performance of symptomatic patients was poorer on almost all tests of attention.

Possible causes of cognitive dysfunction

It is still unknown what exactly causes the cognitive problems in WAD patients. In the eighties and early nineties of last century, a common opinion of researchers was that the cognitive deficits were due to *organic brain lesions*, as a result of the head swerve. The cognitive symptoms WAD patients complained of were quite similar to those of patients with a mild traumatic brain injury.[5] However, inconsistent with this 'organic-lesion' explanation is the absence of typical 'brain-injury signs' such as unconsciousness and amnesia in WAD patients.[5,12] Furthermore, EEG- and MRI-research showed normal results and did not correlate with neuropsychological test results.[4,5,7,8,12] Therefore, in contrast with this 'organic brain-lesion' explanation, some researchers argue(d) that the WAD syndrome is a *functional disorder*, which refers to conditions which involve disturbance of function without physical abnormality. This explanation implies that the signs and symptoms of WAD are caused by psychological factors and processes, such as neuroticism, pre-injury existent stress vulnerability, symptom-expectation, symptom amplification and/or malingering.[5,18,19] With respect to malingering it is proposed and objectivated that WAD patients may *simulate* cognitive problems or are under-performing during neuropsychological research, due to conscious or unconscious reasons (e.g. financial interests, attention seek-

ing).[5,6,20] Whereas research has demonstrated that pre-injury life-events nor personality-characteristics have a significant predictive value with respect to chronicity of symptoms in WAD patients,[3,5] recent research showed that cultural and psychological factors seem to play a significant role in the course of the whiplash syndrome.[2,21,22,23,24] There is enough evidence that WAD patients exhibit a great amount of *emotional distress*.[1,21,22,25,26,27] This distress is believed to be a direct response to the whiplash injury[22,26] and is also seen as an indirect response as a result of the perceived disabilities in daily life.[1,21,25,27]
The link between emotion and cognition is expressed in the so called 'processing efficiency theory': it is known that a constant high level of emotional distress is related to attention deficits, because the pre-occupation with psychological problems occupies a part of the (limited) information processing capacities and therefore has a negative effect on cognition and mental performances in general.[28,29,30] In other words, the information process is less efficient in case of a high level of distress. Therefore, one might assume that the cognitive problems WAD patients complain of, might (in part) be related to the high level of distress or tension.[5,31,32,33] In the present thesis this assumption was investigated.

Recent research demonstrated that, besides psychological factors, neurophysiological factors are (also) crucial in the development of chronic whiplash-related complaints leading to dysfunctional pain processes in the central nervous system.[34,35,36] In line with this neurophysiological view, it is also possible that the chronic high level of distress in WAD patients might cause an imbalance in the stress-hormone system, leading in turn to cognitive deficits[37,38,39] or other whiplash related complaints such as 'noise-intolerance'. Research is still required to clarify whether a dysfunction of the stress-hormone system does exist in WAD. In this thesis, it was investigated whether cortisol levels are significantly elevated in WAD patients compared to healthy people.

Likely, the *pain* WAD patients experience, is another important factor of negative influence on cognitive functioning.[5,6,12,40] The relationship between pain and cognition is described in the so called 'Cognitive-Affective model of the interruptive function of pain'.[40] Pain is in fact a warning of danger to an organism: it interrupts, distracts and demands attention. The cognitive-affective model describes that pain interrupts ongoing activities, dependent on several pain-related characteristics (e.g. the intensity, novelty, predictability and threat) and the characteristics of the environmental demands (e.g. task difficulty, emotional arousal).[40] Radanov et al. found some evidence for the relationship between headache and cognitive functioning in WAD patients.[8] However, more studies are needed and in this thesis the relationship between pain and cognition in WAD patients was further investigated.

Related to 'pain' is *fatigue*: WAD patients are quickly tired after physical or mental endurance tasks or even during relaxation, for example because of sleeping problems.[3,5] Likely, fatigue induces cognitive deficits in WAD patients[5,11] as was demonstrated in patients with a chronic fatigue syndrome.[41] In view of the 'state-regulation model' of Hockey (1986), one might argue that WAD patients have to invest 'compensatory mental effort' during cognitive task-performance. By this is meant a surplus of effort needed when individuals find themselves in a suboptimal state, in order to control task performance on a stable level. An impaired performance quality emerges when the individual's energetical resources are low.[42,43] Although the influence of fatigue on daily functioning and especially on cognition has been recognized, the influence of fatigue on attention performance was never systematically investigated in WAD patients.[5,11]

Pain medication of influence on the central nervous system can diminish attentional performance. Radanov et al.[11] demonstrated that the impaired performance of WAD patients on attention tasks, is (partly) caused by the adverse effect of analgesics used regularly by many of the symptomatic patients. Another study reported that 80% of the whiplash patients used medication which could have a negative effect on cognitive performance.[44] Apparently, in studies concerning cognition, this factor is a confounding factor and therefore needs special attention, as was done in this thesis.

Recently, several researchers have suggested that the whiplash phenomenon can be at best understood from a 'bio-psycho-social' viewpoint.[2,45-48] In this bio-psycho-social model, it is assumed that several of the above mentioned (psychological, social-cultural and neurophysiological) factors simultaneously influence the development and maintainence of WAD-associated complaints. The bio-psycho-social model recognises physical and psychological sources of (cognitive) symptoms, but fundamentally recognises that the chronic whiplash syndrome is not only the result of a "chronic injury".[2,45-48]

OUTLINE OF THIS THESIS

The main aim of this thesis is to investigate the relationship between state-dependent factors (headache, neck pain, fatigue, distress) and attention in WAD patients. Furthermore, the focus is on 'noise-distractibility' and 'noise-intolerance', which are symptoms related to attention and often mentioned by WAD patients.[3,5,14]

The first two studies of this thesis are related to distress, the functioning of the stress-hormone system and the relationship with chronic everyday problems (daily hassles) in WAD patients. The aims of the first study were to investigate the amount and nature of daily hassles and to determine the relationship between daily hassles and distress in WAD patients (chapter two).
In the second study, an experiment was carried out to explore cortisol levels and cortisol response as a result of a mental stress task in WAD patients, compared to healthy subjects and subjects in a relax-control condition. In addition, it was investigated whether the amount and appraisal of the severity of daily hassles predicted cortisol response (chapter three).
The third study concentrated on focused attention and the relationship with state-dependent factors such as pain, fatigue and distress (chapter four).
In order to objectivate the complaint of 'noise-intolerance' in daily life, an experiment was carried out to investigate systematically to which extent WAD patients are more intolerant of different noise-intensities compared to healthy matched controls. In addition, the relationship between state-dependent factors and noise-intolerance level was investigated (chapter five).
The aim of the last experiment was to test whether WAD patients have significantly more attentional problems in a noisy surrounding compared to healthy matched control subjects. In this study, the results of the studies described in chapter four en five are combined into a new experiment: focused attention was systematically investigated with different levels of noise-distractors. Again, the relationship with state-dependent factors was explored.
In the last chapter, a general overview is given of the main findings and conclusions that have arisen from the preceding chapters. The results of the various studies are discussed and imbedded into current models.

REFERENCES

1. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical review: Whiplash Injury. *Pain*, 283-307.

2. Ferrari, R. (2002). Prevention of chronic pain after whiplash. *Emerg. Med. Journal*, 19, 526-530.

3. Radanov, B.P., Sturzenegger, M. & Di Stefano, G. (1997). Long-term outcome in whiplash injury. In: *The aftermath of road accidents: psychological, social and legal consequences of an everyday trauma* (ed. Mitchell, M.). London: Routlegde, 70-88.

4. Borchgrevink, G., Smevik, O., Haave, I., Haraldseth, O., Nordby, A., Lereim, I. (1997). MRI of cerebrum and cervical columna within two days after whiplash neck sprain injury. Injury, 28(5-6),331-335.

5. Van Zomeren, A.H., & Saan, R. (1997). Whiplash. In B.G. Deelman, P.A.T.M. Eling, E.H.F. de Haan, A. Jennekens-Schinkel, A.H. van Zomeren (Ed.), *Klinische neuropsychologie* (pp. 290-298). Amsterdam: Boom.

6. Kessels, R.P.C., Aleman, A., Verhagen, W.I.M. & Luijtelaar, E.L.J.M. (2000). Cognitive functioning after whiplash injury: a meta-analysis. *Journal of the International Neuropsychological Society*, 6, 271-278.

7. Radanov, B.P., Hirlinger, I., Di Stefano, G. & Valach, L. (1992). Attentional processing in cervical spine syndromes. *Acta Neurol Scand*, 85, 358-362.

8. Radanov, B.P. , Dvorak, J. & Valach, L. (1992). Cognitive deficits in patients after soft tissue injury of the cervical spine. *Spine*, 17, 127-131.

9. Taylor, A.E., Cox, C.A., & Mailis, A. (1996). Persistent neuropsychological deficits following whiplash: evidence for chronic mild head traumatic brain injury*? Arch Phys Med Rehab, 77,* 529-535.

10. Kischka, U., Ettlin, T.M., Heim, S., & Schmid, G. (1991). Cerebral symptoms following whiplash injury. *European Neurology, 31,* 136-140.

11. Radanov, B.P., di Stefano, A., Schnidrig, M., Sturzenegger, & Augustiny, K.F. (1993). Cognitive functioning after common whiplash. *Archives of Neurology*, 50, 87-90.

12. Radanov, B.P., Bicik, I., Dvorak, J., Antinnes, J., von Schulthess, G.K., & Buck, A. (1999). Relation between neuropsychological and neuroimaging findings in patients with late whiplash syndrome. *Journal of Neurology Neurosurgery and Psychiatry, 66*, 485-489.

13. Spitzer, W.O., Skovron, M.L., Salmi, L.R. et al. (1995). Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders. *Spine*, 20, 7-73S.

14. Tjell, C., Tenenbaum, A. & Rosenhall, U. (1999). Auditory function in whiplash-associated disorders. *Scand Audiol,* 28, 203-209.

15. Skovron, M.L. (1998). Epidemiology of Whiplash. In: *Current concepts in Prevention, Diagnosis and Treatment of the Cervical Whiplash Syndrome* (Gunzburg, R. & Szpalski, M., eds). Philadelphia: Lippincott-Raven publ., 61-67.

16. Versteegen, G. (2001). Sprain of the neck & Whiplash Associated Disorder. A study from epidemiological and psychological perspective (Thesis). Groningen: RUG.

17. Klein, M. (1997). *Cognitive Aging, Attention and mild traumatic Brain Injury* (Thesis). Maastricht: Neuropsych. Publishers.

18. Radanov, B.P., Di Stefano, G., Schnidrig, A., Sturzenegger, M. (1994). Common whiplash: psychosomatic or somatopsychic? *J. Neurol. Neurosurg. Psychiat.*, 57, 486-490.

19. Berry, H. (2000). Chronic Whiplash syndrome as a Functional Disorder. Arch. Neurol., 57, 592-594.

20. Schmand, B., Lindeboom, J. Schagen, S. Heijt, R. Koene, T., Hamburger, H.L. (1998). Cognitive complaints in patients after whiplash injury: the impact of malingering. *J Neurol Neurosurg Psychiatry*, 64, 339-343.

21. Sterling, M., Kenardy, J., Jull, G. & Vincenzino, B. (2003). The development of psychological changes following whiplash injury. *Pain*, 106, 481-489.

22. Smed, A. (1997). Cognitive function and distress after common whiplash injury. *Acta Neurologica Scandinavica*, 95, 73-80.

23. Schrader, H. Obelieniene, D., Bovim, G. et al. (1996). Natural evolution of late whiplash syndrome outside the medicolegal context. *Lancet*, 347, 2107-1211.

24. Castro, W.H., Meyer, S.J., Becke, M.E., Nentwig, C.G., Hein, M.F., Ercan, B.I., Thomann, S., Wessels, U., Du Chesne, A.E. (2001). No stress-no whiplash? Prevalence of "whiplash" symptoms following exposure to a placebo rear-end collision. *Int J Legal Med.*, 114(6), 316-322.

25. Wallis, B.J., Lord, S.M., Barnsley, L., & Bogduk, N. (1996). Pain and Psychologic Symptoms of Australian Patients with Whiplash. *Spine*, 21, 804-810.

26. Drottning, M., Staff, P.H., Levin, L. & Malt, U.F.R. (1995). Acute emotional response to common whiplash injury predicts subsequent pain complaints. *Nord. J. Psychiatry*, 49, 293-299.

27. Radanov, B.P., Begre, S., Sturzenegger, M. & Augustiny, K.F. (1996). Course of psychological variables in whiplash injury – a 2-year follow-up with age, gender and education pair-matched patients. *Pain*, 64, 429-434.

28. Ouwerkerk van, R.J., Meijman, T.F. & Mulder, G. (1994). *Arbeidspsychologische taakanalyse*. Utrecht: Lemma b.v.

29. Eysenck, M.W. & Calvo, M.G. (1992). Anxiety and performance: the processing efficiency theory. *Cognition and Emotion*, 6, 409-434.

30. Brand, N. Hanson, E. & Godaert, G. (2000). Chronic stress affects blood pressure and speed of short-term memory. *Perceptual and Motor skills*, 91, 291-298.

31. Brand, N., & Jolles., J. (1987). Information processing in depression and anxiety. *Psychological Medicine*, 17, 145-153.

32. Kolb, B. & Wishaw, I.Q. (1994). Emotional Processes. In: *Fundamentals of human neuropsychology* (3rd ed.). New York: Freeman and Company, 607-642.

33. Eling, P. (2003). Denkkaders in de psychiatrie. Een inleiding vanuit historisch perspectief. In: *Cognitieve Neuropsychiatrie* (Eling, P., de Haan, E., Hijman, R. & Schmand, B., Eds). Amsterdam: Boom, 17-45.

34. Sterling , M., Jull, G., Vizenzino, B., Kenardy, J. (2003). Sensory hypersensitivity occurs soon after whiplash injury and is associated with poor recovery. *Pain,* 104(3), 509-517.

35. Lidbeck, J. (2002). Central hyperexcitability in chronic musculoskeletal pain: a conceptual breakthrough with multiple clinical implications. *Pain Res Managem.*, 7, 81-92.

36. Banic, B., Petersen-Felix, S., Andersen, O.K., Radanov, B.P., Villiger, P.M., Arendt-Nielsen, L., Curatolo, M. (2004). Evidence for spinal cord hypersensitivity in chronic pain after whiplash injury and in fibromyalgia. *Pain*, 107(1-2), 7-15.

37. van Steegeren, A. (2003). Stress en geheugen: de rol van noradrenaline en de amygdala bij emotionele informatieverwerking. *Neuropraxis*, 141-151.

38. Newcomer, J.W., Selke, G., Melson, A.K., Hershey, T., Craft, S., Richards, K., Alderson, A.L. (1999). Decreased memory performance in healthy humans induced by stress-level cortisol treatment. *Arch Gen Psychiatry.*, 56(6), 527-533.

39. Vedhara, K., Hyde, J., Gilchrist, I.D., Tytherleigh, M., Plummer, S. (2000). Acute stress, memory, attention and cortisol. *Psychoneuroendocrinology*, 25(6), 535-549.

40. Eccleston, C., Crombez, G. (1999). Pain demands attention: a cognitive-Affective model of the interruptive function of pain. Psychol. Bulletin, 356-366.

41. Vercoulen, J.H.M.M., Swanink, C.M.A., Fennis, J.F.M., Galama, J.M.D., Van der Meer, J.W.M., & Bleijenberg, G. (1994). Dimensional assessment of chronic fatigue syndrome. *Journal of Psychosomatic Research, 38 (5),* 383-392.

42. Wiethof, M. (1997). *Task analysis is heart work* (Thesis). Delft: University Press.

43. Hockey, G.R.J. (1986). Changes in operator efficiency as a function of environmental stress, fatigue and environmental rhythms. In: Boff, K.R., Kaufmann, L. and Thomas, J.P. (eds.). *Handbook of Perception and Human Performance*, vol 2. New York: Wiley.

44. Di Stefano, G. & Radanov, B.P. (1995). Course of attention and memory after common whiplash: a two-years prospective study with age, education and gender pair-matched patients. *Acta Neurologica Scandinavica*, 91, 346-352.

45. Reinders, H. (2002). The post-whiplash syndrome: don't treat, but unravel. *Ned Tijdschr Geneeskunde*, 146(34), 1565-1568.

46. Scholten-Peeters, G.G., Bekkering, G.E., Verhagen, A.P., van Der Windt, D.A., Lanser, K., Hendriks, E.J., Oostendorp, R.A. (2002). Clinical practice guideline for the physiotherapy of patients with whiplash-associated disorders. *Spine*, 27(4), 412-422.

47. Bosma, F. & Kessels, R.P.C. (2002). Cognitive impairments, psychological dysfunction and coping styles in patients with chronic Whiplash Syndrome. *Neuropsychiatry, Neuropsychology and Behavioral Neurology*, 15(1), 56-65.

48. Ferrari, R. & Schrader, H. (2001). The late whiplash syndrome: a biopsychosocial approach. *J Neurol Neurosurg Psychiatry*, 70(6), 722-726.

Chapter 2

Daily hassles and stress-vulnerability in patients with Whiplash Associated Disorder

Mariëtte Blokhorst[1,] M.S., Richel Lousberg[1,4], Ph.D., Ad Vingerhoets[3], M.D., Ph.D., Frits Winter[5], Ph.D., Gerrit Zilvold, M.D. [1,2], Ph.D.

[1] Roessingh Research and Development, Enschede
[2] University of Twente, Enschede
[3] Department of Clinical Health Psychology, Tilburg
[4] Dept. of Psychiatry and Neuropsychology, University of Limburg, Maastricht

Published in: International Journal of Rehabilitation Research 2002; 25, 173-179.

INTRODUCTION

There is ample evidence that patients with a Whiplash Associated Disorder (WAD) experience a great deal of emotional distress following the onset of physical symptoms.[1-11]
Most authors agree that the distress WAD sufferers report is a consequence of their physical injury (acute stressor) itself and its profound effects on daily life (chronic everyday stressors). Mayou (1997) argues that even a minor injury may have significant social consequences (e.g., financial problems, problems at work or limitation of travel).[4] Moreover, Drottning *et al.* (1995) concluded that the initial emotional responses to the whiplash injury are the strongest predictors of maintenance of pain symptoms four weeks later.[2] Consequently the initial reaction to the whiplash injury appears to be crucial.

The extent, to which the course of the WAD is influenced by pre-morbid and co-morbid stressors that are *not* related to the injury, remains a matter of discussion. In a series of prospective studies, Radanov *et al.* (1991, 1993, 1994, 1996) found no relationship between the distress or physical injury related complaints and life-events present prior to or immediately after the accident. These results led the authors to conclude that distress is caused by problems that occur as a consequence of the whiplash injury itself.[6,7,8,14]
There is also some evidence that psychosocial factors, unrelated to the WAD, play a significant role in the course of the whiplash syndrome.[11,12] For example, Mayou (1993) reported that social and emotional problems that preceded the accident, predicted emotional disorders in 18% of the WAD patients.[12] Similarly, Smed (1997) found that WAD patients who reported negative life-events that occurred *after* the accident, perceived more distress one and seven months after the injury than patients who reported no stressors in addition to the accident.[11]
The discrepant results in these studies may be accounted for by several factors including the use of different assessment methodologies (for example interview compared with questionnaire), differences in post-injury interval at the time of assessment and the nature of the life-events that were evaluated (acute compared with chronic stressors). Perhaps most importantly, however, the discrepancies may be explained by the fact that most studies considered only the *number* of negative life-events reported. Investigators have rarely evaluated the WAD patients' *appraisals* of the stressful life events, although numerous studies have emphasized the critical role of people's appraisals or evaluations of the meaning and importance of particular stressors in the development of emotional distress.[13]

The aim of the present study was to obtain more insight into the degree of exposure to and the appraisal of whiplash-related and whiplash-independent stressors in the everyday life of WAD patients *after* the injury. We systematically examined the frequency of self-reported daily stressors of WAD patients, while making a distinction between person-dependent stressors (representing events and conditions probably caused by the individuals themselves, which are dependent on the functioning and mental status of a person) and person-independent stressors (representing situations beyond human control). Because WAD patients experience all kinds of problems and stressors in their daily lives, we hypothesized that both their self-reported frequencies and seriousness ratings of the problems related to personal functioning would be higher, compared to normal healthy individuals. In addition, we expected that the seriousness ratings, but not the frequency scores of person-independent negative hassles would also be high, reflecting a stronger impact of these stressors on these vulnerable people. Because it is unlikely that WAD patients with chronic complaints would be more frequently exposed to distressing life-events that occur independently of their functioning, we anticipated no differences in person-independent problems compared to healthy control participants. The anticipated higher seriousness ratings for person-independent daily stressors is assumed to reflect the vulnerability of chronic WAD patients to emotional stimuli.[14]
Finally, we examined the level of distress in both groups as well as the extent to which the level of emotional distress of WAD patients is predicted by the kind and amount of stressors and/or seriousness ratings. Because previous studies showed a negative relationship between educational level and level of distress in a healthy population[15], we examined this relationship in the WAD group expecting that patients with a low educational level exhibit more psychological complaints than patients with a high educational level.

METHODS

Participants

Forty-seven WAD patients (62% of whom were women), who were referred to a rehabilitation centre for treatment because of chronic whiplash-related complaints participated in the study. The mean age of the patients was 34 years (SD= 6.9) and approximately half of them (51%) had a high educational level, while the other half had a low educational level. The injury causing the WAD occurred more than six months ago (mean interval=47 months; SD=24). All patients suffered a WAD following an automobile-accident (45 patients had a rear-end collision and only two patients had a side collision).

None of the respondents was to blame for the accident. In order to obtain a homogeneous group of patients, people who reported that they had lost consciousness after the whiplash injury, those who had recent narcoses or head injury and those with a psychiatric history were excluded.
Following the Quebec Task Force's clinical-anatomic axis that corresponds to the severity of the whiplash injury[16], only patients with chronic complaints classified in levels 1 and 2 (the lowest of the four levels with neck complaints of pain, stiffness, or tenderness accompanied by muscular-skeletal signs and without fractures or significant neurological signs) were included. The control group consisted of 47 healthy participants, matched for sex (62% women), age (mean=33.7; SD=7.3) and educational level (51% had a high educational level).

Measures

Daily Problem Checklist

The Daily Problem Checklist (DPC) is a 114-item self-report questionnaire that assesses both the frequency and perceived seriousness of chronic everyday problems during the preceding two months.[17] This questionnaire includes items from several domains including: (1) family life, (2) living conditions, (3) working conditions, (4) physical appearance and general performance, (5) transactions, (6) social developments and (7) confrontations (as witness or as victim). Respondents were asked to check the items describing events and/ situations that they had experienced in the past two months. Three scores can be calculated from this questionnaire: (1) total number of items checked (frequency-score); (2) the mean intensity score or seriousness rating (intensity-scre); and (3) the product of these two scores (total score). This score reflects the amount of self-perceived stress load.
In the original instrumental development study of the DPC, a panel of judges determined that 28 of the items were person-dependent (for example 'you could not realise your ambitions', or 'you had problems with friends') and 22 were person-independent (for example 'things you wanted to buy were suddenly more expensive' or 'someone of the family was the victim of a crime'). The remainder of the items may or may not be caused by the behaviour or mental status of the individual.
The DPC has a good test-retest reliability for the three scores: frequency: 0.87; intensity: 0.85; total score: 0.85. A previous study has shown that the relationship between the DPC-factors and distress is moderately positive in a general population.[17] Furthermore, results have indicated that self-reported everyday problems are of direct influence on subjective health com-

plaints.[17] There is also evidence that the DPC scores are related to immune activity, cardio-vascular functioning and stress-hormone release, indicating the validity of the test. The DPC has previously been used with patients with rheumatic arthritis (RA) and patients with systemic lupus erythematosus (SLE) and results revealed that the DPC scores are positively related to pain, anxiety and depression.[17]

The Symptom Check List

In order to investigate the level of distress in our population, the Dutch version of the Symptom Check List (SCL-90) was administered.[18] The SCL-90 is a self-reporting, multidimensional symptom checklist composed of 90 items, each describing a physical or psychological symptom.[18,19] The instructions require patients to respond on a five-point scale (ranging from 'not at all' to 'extremely') to indicate how much an item has bothered them over the past week. In addition, eight subscales have been derived: anxiety (anx), phobic anxiety (pho), depression (dep), somatic complaints (som), insufficiency (insuf), interpersonal sensitivity (sen); hostility (hos), sleeping problems (sle). The global severity index (GSI) is a measure of general distress that is obtained from the subscale scores and other items of the questionnaire not included in these scores.
The SCL-90 has proven to be a useful device for describing the distress of chronic pain patients in general, including the psychological and physical symptoms after a whiplash injury.[9, 20] Wallis *et al.* (1996) found a homogeneous pattern of responses that described a profile of whiplash patients characterised by high somatic complaints and elevated scores on the variables 'obsessive-compulsive behaviour' and 'depression'.[9] The profile of pain patients does not describe any diagnostic personality disorder or neurotic disorder and there is evidence that the psychological distress exhibited by WAD patients is secondary to chronic pain.

Statistical procedure

Statistical Package for Social Sciences (SPSS) was applied for all data analyses.[21] Frequency distribution, mean and standard deviation were calculated for the DPC and the SCL-90 variables. Next, non-parametric tests (Mann-Whitney *U* tests) were performed to test the differences between the WAD-group and the healthy control group. Regression-analysis was performed in order to investigate the relationship between the DPC and the SCL-90. All reported *P*-values are two tailed.

RESULTS

Frequency analyses showed that the DPC scales as well as the SCL-90 scales were not normally distributed (they all showed skewed distributions). Because attempts to transform these variables into normality failed, non-parametric tests were performed.[22]
Mann-Whitney *U* tests were performed to compare the DPC scores of WAD patients and healthy control participants. The results indicated that the person-dependent frequency, serious ratings and total scores of the WAD group were all significantly higher than those of the control-group (see Table 1).

There was, however, no significant group difference in the person-independent frequency score, whereas the seriousness rating was statistically significant ($P<.001$).
To summarize, WAD patients seemed to experience more person-dependent, but not person-independent stressors, but they perceived both kinds of stressors as more serious than control participants did.
The scores on the SCL-90 sub-scales and the GSI-scale were significantly higher in the WAD-group than in the control-group, indicating more distress in the patient group (see Table 2).

In order to investigate to what extent the DPC scores predict the level of distress in WAD patients, regression analysis was performed within the WAD group. After a logarithmic transformation of the GSI score, normality was achieved for this variable in the WAD group. DPC variables were entered in

Table 1: Means and standard deviations of the daily problem checklist scales for the WAD group and the control group.

	WAD group mean(SD)	Control group mean(SD)	P-value*
Person-Dependent Frequency	8.5 (4.7)	5.2 (3.4)	<.001
Person-Dependent Intensity	1.6 (0.6)	0.9 (0.7)	<.001
Person-Dependent Total	14.9 (10.7)	5.6 (5.4)	<.001
Person-Independent Frequency	5.4 (3.5)	4.3 (2.7)	NS
Person-Independent Intensity	1.4 (0.7)	1.1 (0.6)	<.001
Person-Independent Total	8.3 (7.4)	5.1 (4.4)	<.005
Total DPC	51.2 (36.2)	22.4 (17.0)	<.001

WAD, Whiplash Associated Disorder; DPC, Daily Problem Check List. *Two-tailed significance

Table 2: Means and standard deviations of the SCL-90 scales for the WAD group and the control group.

	WAD group mean(SD)		Control group mean(SD)		P-value*
Anxiety	17	(5.5)	11	(1.6)	<.001
Phobic Anxiety	10.2	(3.8)	7.2	(0.4)	<.001
Depression	31.1	(11.8)	18.9	(3.8)	<.001
Somatic Complaints	28.3	(8.0)	14.7	(3.1)	<.001
Insufficiency	25.9	(8.4)	11.2	(2.8)	<.001
Sensitivity	28.9	(10.7)	21.1	(4.3)	<.001
Hostility	10.7	(5.1)	7.0	(2.0)	<.001
Sleeping problems	7.5	(3.3)	3.9	(1.5)	<.001
Global Severity Index	172.6	(50.0)	105.0	(17.2)	<.001

WAD, Whiplash Associated Disorder. *Two-tailed significance

Table 3: Regression analyses in the WAD-group: prediction of global severity index out of the daily problem checklist (n=47).

Variable	B	SE B	ß	P-value
Step 1*				
Person-dependent frequency	-.0146	.003	.59	.000
Step 2*				
Person-dependent frequency	-.0138	.003	.55	.000
Educational level	-.0871	.026	-.37	.001
Step 3*				
Person-dependent frequency	-.0113	.003	.45	.000
Educational level	-.0861	.023	-.37	.000
Person-independent seriousness rating	-.0632	.017	.37	.001

WAD, Whiplash Associated Disorder; DPC, Daily Problem Checklist. *R^2=.35 for step 1 (p<.001); $R^{2\ change}$= .14 for step 2 (p<.001); $R^{2\ change}$=.12 for step 3 (p<.001)

a linear regression analysis as independent variables, combined with sex, age, educational level and pain interval; the log transformed GSI scale was the dependent variable. A stepwise procedure was performed. Results revealed a model in which the GSI scores were predicted by the person-dependent frequency variable, together with the person-independent serious rating and educational level. This model explained 61% of the variance of GSI scale (see Table 3).

DISCUSSION

The first aim of the present study was to obtain more insight into how WAD patients experience daily stressors. We assessed frequency and seriousness of two types of self-reported everyday stressors of WAD patients who are in the chronic phase.
As expected, the results of this study revealed a clear difference between the exposures to person-dependent compared with person-independent stressors, indicating that chronic WAD patients appear more often to be confronted with stressors that may be related to their personal functioning or mental status. In contrast, stressors not related to their personal functioning were not elevated compared to a healthy control group. These results are consistent with those reported by Radanov *et al.* (1996), who argued that many of the problems and stressors encountered by WAD patients are a consequence of the whiplash injury.[8]
The results further revealed significant differences in patients' appraisals of severity of their daily problems, indicating that stressors, in general, have a greater impact on WAD patients than on healthy people. This finding further supports the notion that WAD patients who are in the chronic phase become easily aroused by all kinds of stressors.
Corroborating previous results, the results of this study demonstrated that the level of distress is significantly higher in WAD patients than in healthy people.[1-11] The results of the regression analysis suggested that the distress in WAD patients is strongly related to the number of daily hassles related to personal functioning and to appraisal of stressors independent of personal functioning.
Furthermore, the results indicate that WAD-patients with a low-educational level report more general distress than patients with a high-educational level, which may imply that the low-educational group is probably more vulnerable.
To what extent pre-existing dispositions are of influence on the reported distress and appraisals of daily problems remains to be established. In other words, it is possible that the injury is only an eliciting factor, which triggers pre-existing stress sensitivity. Future studies focusing on pre-morbid characteristics of the patients may yield results answering this question.
One limitation of this study is that a selection bias might have occurred, because the participants in the present study were all patients who have been referred to a rehabilitation centre for a treatment, which prevents generalizing the present findings to the WAD population at large. Despite this limitation, the results of this and previous studies suggest that it is important in

the early stage following a WAD, to assess both the frequency of problems (daily stressors) as well as patients' appraisals. Treatment must focus on the reduction of the daily stressors associated with personal functioning (active, problem oriented coping strategies), combined with emotional coping strategies, aiming at changing the perceived seriousness of daily problems. Adequate, early interventions may prevent excessive emotional distress in many of these patients.

In conclusion, WAD patients report high degrees of daily stressors, which are related to their personal functioning. These problems are likely to be a consequence of the whiplash injury. What appears to be important is not only the amount of self-perceived daily problems, but also how WAD patients appraise their daily problems and life-events. Our results revealed that both the amount of person dependent problems, as well as WAD patient' excessively negative interpretations of stressors contribute to psychological distress, which may lead to the exacerbation and maintenance of their physical symptoms. To what extent the stress-responses of WAD patients, after the whiplash injury, are caused by pre-existing disposition factors, is a question for future research. Patients with a low educational level seem to be particularly vulnerable and tend to react with more distress compared to patients with a high educational background.
It is reasonable to assume that coping and psychological stress responses play an important role in the maintenance or worsening of whiplash associated complaints. In order to gain more insight into the observed vulnerability, future studies should focus on the effects of educational level, personality factors, coping-abilities and stressors on the course of whiplash related symptoms.

REFERENCES

1. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical Review: Whiplash Injury. *Pain,* 283-307.

2. Drottning, M., Staff, P.H., Levin, L. & Malt, U.F.R. (1995). Acute emotional response to common whiplash injury predicts subsequent pain complaints. *Nord. J. Psychiatry*, 49, 293-299.

3. Mayou, R., Radanov, B.P. (1996). Whiplash Neck Injury. *Journal of Psychosomatic Research*, 5, 461-474.

4. Mayou, R. (1997). *The psychiatry of road traffic accidents.* In: Mitchell, M., ed. The Aftermath of Road Accidents, London/New York: Routledge. 33-48.

5. Merksey, H. (1993). *Psychological consequences of whiplash*. In: Teasell R.W., & Shapiro AP, eds. *Spine State of the Art Reviews. Cervical Flexion-Extension/Whiplash Injuries*. Philadelphia: Hanley and Belfus, 471-480.

6. Radanov, B.P., Di Stefano, G., Schnidrig, A. & Sturzenegger, M. (1993). Psychosocial stress, cognitive performance and disability after common whiplash. *Journal of Psychosomatic Research*, 37, 1-10.

7. Radanov B.P., Di Stefano, G., Schnidrig, A., Sturzenegger, M. (1994). Common whiplash: psychosomatic or somatopsychic*? J of Neurology, Neurosurgery, and Psychiatry,* 57, 486-490.

8. Radanov, B.P., Begre, S., Sturzenegger, M. & Augustiny, K.F. (1996). Course of psychological variables in whiplash injury – a 2-year follow-up with age, gender and education pair-matched patients. *Pain,* 64, 429-434.

9. Wallis, B.J., Lord, S.M., Barnsley, L., & Bogduk, N. (1996). Pain and Psychologic Symptoms of Australian Patients with Whiplash. *Spine*, 21, 804-810.

10. Wallis, B.J., Lord, S. & Bogduk, N. (1997). Resolution of psychological distress of whiplash patients following treatment by radiofrequency neurotomy: a randomised, double blind, placebo-controlled trial. *Pain,* 73, 15-22.

11. Smed, A. (1997). Cognitive function and distress after common whiplash injury. *Acta Neurol. Scand.*, 95, 73-80.

12. Mayou, R., Bryan, B., Duthie, R. (1993). Psychiatric consequences of road traffic accidents. *British Medical Journal*, 307, 647-651.

13. Cohen, S, Kessler, R.C., Underwood Gordon, L. (1995). *Strategies for measuring stress in studies of psychiatric and physical disorders.* In: Cohen S, Kessler RC, Underwood Gordon L, editors. Measuring Stress; a Guide for Health and Social Scientists. Oxford: Oxford University Press, 3-26.

14. Radanov B.P., Di Stefano, G., Schnidrig, A., & Ballinari, P. (1991). Role of psychosocial stress in recovery from common whiplash. *The Lancet* , 338, 712-715.

15. Sivera van der Sluijs, I.J., van de Mheen, H., Stronks, K. & Mackenbach, J.P. (1996). Blootstelling aan en omgang met psychosociale stressoren: sociaal-economische verschillen. *Tijdschrift voor Sociale Geneeskunde,* 2, 71-77.

16. Spitzer, W.O., Skovron, M.L., Salmi, L.R., *et al.* (1995). Scientific monograph of the Quebec task force on whiplash-associated disorders: redefining "whiplash" and its management. *Spine,* 20, 7-73.

17. Vingerhoets, A.J.J.M., & Van Tilburg, M.A.L. (1994). *Alledaagse Problemen Lijst (APL).* Lisse: Swets en Zeitlinger.

18. Arrindel, W.A. & Ettema, J.H.M. SCL-90 (1986). *Handleiding bij een psychopathologie-indicator.* Lisse (The Netherlands): Swets & Zeitlinger.

19. Derogatis, L.R. (1983). SCL-90R. *Annual II. Clinical Psychometric research*. Towson: Clinical Psychometric Research.

20. Bernstein, I.H., Matthew, E.J. & Hinkley, B.S. (1994). On the utility of the SCL-90-R with Low-Back Pain Patients. *Spine*, 19, 42-48.

21. Norusis, M.J. (1992). *SPSS-user Guide*; version 5.0; Chicago.

22. Hair, J.S., Anderson, R.E., Tatham, R.L., Black, W.C. (1998). *Multivariate data analysis.* London: Prentice Hall.

Chapter 3

Cortisol responses to experimental stress in patients with Whiplash Associated Disorder

Mariëtte Blokhorst[1], Pinel Schrijver[1], Stefan Meeldijk[1], Rob Hermans[2], Richel Lousberg[1,3], Gerrit Zilvold[1].

[1] Roessingh, Research and Development, Enschede
[2] Dept. Pharmacol.Toxicol., Cardiovasc. Res. Inst. Maastricht, University of Limburg, Maastricht
[3] Dept. of Psychiatry and Neuropsychology, University of Limburg, Maastricht

Accepted as a chapter in 'Psychology of Stress' (in press): NovaSciences (New York)

INTRODUCTION

There is consistent evidence that patients with a Whiplash Associated Disorder (WAD) experience a great deal of emotional distress following the onset of physical symptoms.[1-9] A WAD is a hyper-extension / flexion trauma of the neck, resulting after an injury (often an automobile accident) and is accompanied by pain in the neck, headache, fatigue, dizziness, attention problems and emotional distress.[10] Most authors agree that the distress WAD sufferers report is a consequence of the physical injury itself and its profound effects on daily life.[4,7,8] Recent results revealed that both the amount of problems related to personal functioning, as well as WAD patient's excessively negative interpretations of stressors contribute to the level of distress.[8]

It seems reasonable to assume that the emotional distress WAD patients exhibit, leads to activation of the Hypothalamic-Pituitary-adrenocortical (HPA) axis and release of the stresshormones ACTH and cortisol. Whereas research in chronic pain syndromes like Fibromyalgia and Rheumatoid Arthritis has provided evidence of HPA-axis disturbances[11], HPA-axis research in WAD patients has not yet been conducted. A valid method to examine the functioning of the HPA-axis is to investigate the changes in cortisol levels in response to an experimental psychological challenge or a stress-task.[12] The purpose of the present study was to examine changes in salivary cortisol levels, after performing a mental stress-task, in both WAD patients and healthy control participants, and to compare these changes to a relax-control condition. The concentration of salivary free cortisol has proved to be a reliable method for assessing cortisol responses in man.[12,13] It was hypothesized that WAD patients will show an increase in complaints (pain, fatigue, tension) and cortisol levels after performing a mental stress-task, compared to healthy control participants and subjects in a relax-control condition.

Another important issue investigated in this study is whether the amount of daily hassles predicts cortisol response induced by a mental stress-task, in WAD patients and healthy control subjects. 'Daily hassles' means the chronic everyday problems (or chronic life stress) patients may perceive in several domains of their life (for example the problems in family life, living conditions, working conditions of physical appearance and general performance).[8] Various studies suggest a possible link between chronic life stress and the stress hormone system. For instance, Brosschot et al. (1994) showed that high numbers of daily hassles are associated with a more pronounced decrease in immune cell traffic, induced by an acute stressor in healthy hu-

man subjects.[14] This suggests that a high degree of life stress 'sensitizes' the individual to subsequent stress. Daily hassles may lead to sustained physiological activation, which in turn changes the magnitude or duration of physiological responses. Pike et al. (1997) demonstrated that cortisol levels of persons undergoing chronic life stress, remained increased above base line during recovery, after they had undergone a psychological challenge, indicating sustained activation. In contrast, persons with a low level of stress returned to base line cortisol levels during recovery.[15] Smyth et al. (1998) reported that the numbers of daily hassles were significantly related to cortisol levels in normal healthy subjects.[16]
Based on these previous results, it was hypothesised that the amount of daily hassles predicts significantly cortisol response induced by a mental stress-task.
Because HPA-axis activation is also associated with an inability to cope with stressful events and helplessness,[12,16,17] it was further hypothesised that (besides the self-reported frequencies of daily hassles) the seriousness or intensity ratings of these problems significantly predicts cortisol response.

METHODS

Participants

Twenty-eight WAD patients (16 women), referred to a rehabilitation centre for treatment because of chronic whiplash related complaints, participated in this research project. The patients in this study had a mean age of 32 years (± 7 years). The injury occurred more than six months before testing, which means that all patients were in the chronic phase (mean interval= 38 months; ± 24 months). All patients encountered the whiplash injury in a car-accident (rear-end collision); none was to blame for the accident. All patients were still in litigation. Patients, who reported that they had lost consciousness after the whiplash injury, had recent narcoses or pre-morbid head injury, were excluded to eliminate the possibility of significant head trauma. Psychiatric comorbity and premorbid migraine were also exclusion criteria. Fifty-seven percent of the patients had a low/middle educational level and the other 43 percent of patients had a middle/high educational level. Thirty-nine percent of the patients were able to work, whereas 57% had a worker's compensation. Following the Quebec Task Force's clinical-anatomic axis that corresponds to severity of the whiplash injury, this study concerns only patients with chronic complaints after a W.A.D. Grade I and II. This means neck complaints of pain, stiffness, or tenderness eventually accompanied by muscular-skeletal sign(s).[10]

Twenty-eight healthy control subjects (16 women), far most working in the rehabilitation centre, were selected and matched for educational level and age. These variables are related to performance on the mental stress task[18] used in this experiment and should therefore be controlled for (see procedure). The distribution of the variable 'sex' is shown in Table 3: in both experimental groups are more women included compared to both control groups. None of the participants reported to be under treatment with medication. At the moment of testing, none of the subjects had used medication of influence on the central nervous system. All subjects gave their written informed consent. A medical ethical committee approved the study.

Measures

Salivary cortisol

Saliva samples were collected. At the beginning of the session, each subject was given a 20-ml polyethylene vial with a mark on the side at the 5-ml level. Subjects collected saliva in their mouths and deposited it into the vials up the 5-ml marks on the side. Samples were stored at −60° C until cortisol determination. For the determination of cortisol in salivary samples an HPLC method was used based on previously described methods.[19-22] Briefly, 30 pmol of 4-androsten-11, 17- diol-3-one-17- carboxylic acid (Steraloids, New Port, USA) was added to the saliva samples to serve as internal standard. Following acidification of the saliva with HCl, steroids were extracted and derivatized with sulfuric acid essentially as described.[19-21] Subsequently, the obtained fluorescent products were extracted with a 4/1 v/v mixture of diethyl ether (Merck Darmstadt, Germany) and methylene chloride (Biosolve, valkenswaard the Netherlands) in order to remove the sulphuric acid. Fluorescent products were analysed on HPLC within 18 hours. The HPLC consisted of a Nucleosil C18 column (150x3.2 mm, Supelco-Sigma, St Louis, USA) as stationary phase and a 1/640/360 v/v/v mixture of trifluoroacetic acid (Sigma st. Louis, USA), methanol (Biosolve, Valkenswaard, the Netherlands) and water as mobile phase. Cortisol and internal standard were detected by their fluorescence at excitation and emission wavelengths of 367 and 532 nm respectively. Cortisol concentrations were derived by calculating peak area ratios and comparing them with calibration curves. For every subject all samples were analyzed within one assay. The HPLC method had a detection limit of about 0.3 pmol and an intra-assay variation of 13 %.

Daily Hassles

The Daily Problems Checklist (DPC) is a 114-item self-report questionnaire that assesses both the frequency and perceived severity or impact of daily hassles during the preceding two months.[23] This questionnaire is partly based on the Daily Hassles Scale of Lazarus and co-workers.[14,24,25] The scale has a test-retest reliability of R=0.87. Both questionnaires are claimed to be valid (including validity in predicting psychological and physical complaints)[23,26,27] and are among the tests most widely used for stress research in Dutch-speaking countries.

Respondents were asked to check the items, describing events and/ situations that they experienced in the past two months (frequency of daily hassles). Next, they are asked to rate the level of severity of the stressor, indicating the impact of the stressor on subjects' daily life (intensity of daily hassles). The questionnaire discriminates between person-dependent and person-*in*dependent stressors. Person-dependent stressors represent events and conditions that are likely caused by the individuals themselves and that depend on the functioning and mental status of a person. An example is 'you could not realise your ambitions', or 'you had problems with friends. The person-*in*dependent stressors represent situations beyond human control (for example 'things you wanted to buy were suddenly more expensive' or 'someone of the family was the victim of a crime').

SCL-90

In order to investigate the level of distress in our population, the Dutch version of the SCL-90 was applied.[28] The SCL-90 is a self-report symptom checklist composed of 90 items, each describing a physical or psychological symptom.[28, 29] The instructions require patients to respond on a 5-point scale (ranging from 'not at all' to 'extremely') to indicate how much an item has bothered them over the past week. The global severity index (GSI) is a measure of general distress that is obtained from the eight subscale scores and other items of the questionnaire not included in these scores. The SCL-90 has proven to be a useful device for describing the distress of chronic pain patients in general, including the psychological and physical symptoms after a whiplash injury.[30, 31] Psychometric properties (such as test-retest reliability, internal consistency and validity coefficients) are satisfactory.[28, 29]

State-dependent measures: Headache, Neck pain, Fatigue, Tension

Subjective 'state' dependent feelings were measured by means of Visual Analogue Scale (VAS). Patients were asked to rate the level of headache, neck pain, fatigue and tension several times during the experiment (see procedure). A 10-cm line was provided with written anchors at the two extremes: e.g. 'no pain' and 'unbearable pain'.

Laboratory task

The 'Synwork' task, a divided attention task, was used as a mental stress task.[18, 32] This task consists of four subtasks: a memory task, an arithmetic task, a visual monitoring task and an auditive monitoring task. The subject has to alternate his attention on those four tasks. Every seven minutes, the task becomes more complex by increasing the speed of stimulus presentation and/or raising the number of target items (in the working memory task and the auditive monitoring task). The arithmetical task is self-paced: a new stimulus is presented just after a response is given. The test consists of six sessions of seven minutes. Subjects get 10 points for every right reaction and they lose 10 points when they neglect certain stimuli (stimuli of the visual monitoring task). They are instructed to collect as much points as possible. Their score is visible in the middle of the screen. Before the test starts, subjects perform a practice-session (lasting 10 minutes), in which initially every subtask is executed separately before all subtasks are presented together. Subjects may choose which task they want to perform and in which order they execute the tasks, so in fact they may develop their own strategy.
Synwork is known as a dynamic and complex task, which simulates the many-sidedness of worksituations.[18] The task is also used in mental capacity assessment.[32]
In order to investigate the self-perceived effort to perform this task, subjects were asked to rate the level of effort by means of a Visual Analogue Scale (VAS-scale), ranging from zero (no effort) through 10 (extreme effort) after they had executed the task.

Experimental stress procedure

All subjects were instructed not to use any coffee/tea, not to smoke and not to take medication of influence on the central nervous system. They had a light breakfast at least two hours before the experiment started. All subjects arrived one hour before baseline measurement. After arriving, subjects

filled in a state-check list. In all groups, half of the subjects started at 8.30 AM with pre-measurement and at 9.30 AM with base line measurement (T-0), while the other half started with pre-measurement at 10.30 AM and at 11.30 AM with base line measurement (T-0). The first saliva sample was collected as soon as subjects came in (Pre-1). Thirty minutes later, another saliva sample was collected and subjects rated their state-related feelings (Fatigue, Neck pain, Headache, Tension) (Pre-2).
Next, all subjects underwent a noise-tolerance test for twenty minutes: subjects were offered five different noise-intensities (ranging from 57dB - 95dB) by means of an audiometer. The results of this test will be published elsewhere.[33]
The base line sample (T-0) was collected just before the intervention took place (mental stress condition or relax condition). Subjects also rated their complaints (fatigue, neck pain, headache and tension). After this, half of the WAD-patients and half of the healthy subjects performed the mental stress task (WAD-experimental group and Healthy-experimental group) which lasted for about 60 minutes. Subjects were instructed as follows:

> *"You have to perform an attention task on this computer. This task measures your ability to execute several tasks at the same time. The task consists out of four parts. Task 1 is a letter-recognition task: you have to recognize a letter out of several other letters. Task 2 is an arithmetical task: you have to add two numbers. In task 3, you have to prevent that a vertical dash is more than one second at both ends of a horizontal line. In task 4 you have to push your left-mouse button on a rectangle on your screen, when you hear a high sound."*

Next, subjects were able to practice all four tasks separate and later on together (practice session lasted about ten minutes).
After the practice-session, the test began and subjects got the following instruction:

> *"As you have seen, you get ten points for every right reaction. Your score is visible in the middle of the screen. However, when you forget to react to the visual-monitoring task (the "dash-task"), your score will decrease. The better you are able to react to all the different tasks, the higher your score will be. The test consists of six sessions of seven minutes. Try to increase your score with every new session!"*

The two control groups (WAD-control and Healthy-control) had to rest and were allowed to relax. After completion of Synwork, saliva samples were collected in the four groups (T+60 min) and VAS-scales were rated concerning state-related feelings and subjective feeling of effort relating to the stress-task in the two experimental groups. Next, all subjects got again the same noise-tolerance test. After this test, saliva samples were collected (T+90 min) and after thirty minutes rest again (T+120 min).

Statistical Procedure

Statistical analyses were performed with the Statistical Package for Social Sciences.[36] The mental stress-task performance and subjective feelings of mental effort were calculated for the two experimental groups and expressed in means and standard deviations.
In order to investigate differences on state-related variables (in time) between the four groups, non-parametric tests were performed.
Differences between the frequency and intensity of daily hassles (DPC-variables) were investigated by means of MANOVA between the WAD-patients and healthy subjects. A *t*-test was performed regarding the data of the Synwork task.

Normality tests revealed that the cortisol data were not distributed normally. As was indicated by Hair (1998), the cortisol data were log-transformed.[34] This transformation resulted in normally distributed data. ANOVA for repeated measures was performed in order to measure cortisol changes from Pre-1 to Base line (T-0). Next, ANOVA for repeated measures were applied on the four different moments (T-0. T+60, T+90, T+120), in order to investigate the differences in cortisol response between the four groups. Start time and sex were entered as covariates in the analyses, because these factors influence acute cortisol stress responsivity that would otherwise complicated the analyses.[12, 35]

Cortisol responsivity was calculated as changes in cortisol from baseline to the three post stress-task measures (T+60, T+90, T+120) and expressed as percentages relative to baseline levels.[37] In order to investigate the relationship between daily hassles/ severity appraisals on the one hand and the cortisol responsivity after a mental stress-task (independent variables) on the other hand, separate regression analyses were performed within the two experimental groups, with respect to the three different post-task cortisol responsivity measures.

RESULTS

Frequency of daily hassles and self-perceived stress-load

The data of the DPC-variables were normally distributed. Mean and standard deviations are listed in Table 1. MANOVA revealed significant differences between WAD patients and healthy subjects on the person-dependent frequency and intensity variables (one-tailed) (see Table 1). The person-*in*-dependent variables showed no significant differences between the WAD-patients and healthy subjects.

Mental stress performance

An independent t-test was conducted to explore whether performance on the mental stress task (Synwork) was different between the WAD-experimental group and the Healthy-experimental group. The results revealed no significant differences, indicating that both groups performed equally well on this test (P=0.3).
Subjective feelings of mental effort were recorded just after the mental stress task. A Mann-Whitney U test revealed no significant difference between the two experimental groups on the mental-effort VAS-scale (P= 0.40); WAD-group: M=62 mm ± 23; Healthy-group: M=54 mm ± 22.

State-characteristics of the WAD and control group

The question ‘How tensed are you at this moment?’ was used in order to check whether the abstention of cigarettes, coffee and tea had possibly caused an abnormal high level of tension. The responses ranged from ‘not at all’ through ‘extremely tensed’ (five-point scale). The results revealed that none of the subjects was ‘fairly tensed’ or ‘extremely tensed’. Twenty-

Table 1: Means and standard deviations of Daily Problem Checklist in WAD patients and Healthy subjects.

DPC	WAD group mean (SD)	Control group mean (SD)	P*
Person-dependent FREQ	7.0 (4.0)	5.1 (3.4)	0.03
Person-dependent INT	1.5 (0.5)	0.9 (0.6)	0.001
Person-independent FREQ	4.1 (2.7)	4.1 (2.5)	0.45
Person-independent INT	1.4 (0.7)	1.1 (0.6)	0.09

*P-values are one-tailed and refer to MANOVA-analysis

one percent of the WAD patients and 7% of the healthy subjects said to be a little tensed and the other 79% of the WAD patients and 93% of the healthy subjects was not tensed (at all). This indicated that the influence of the abstention of cigarettes and coffee/tea on the subjective feeling of tension was not relevant.
Mann-Whitney U tests showed that the ‘state’-levels just before the mental stress-task (base line) (headache, neck pain, fatigue, tension) were not significantly different between the two WAD-groups (all *P*-values 0.1). However, WAD patients had significantly more complaints on all moments compared to healthy-subjects (all *P*-values 0.001). Performance of the mental stress task did not induce more complaints in both healthy groups (all *P*-values 0.14). In addition, the subjects of both control groups did not perceive more complaints (see Table 2).

In contrast, the level of state-variables in the experimental WAD-group increased significantly, just after the mental stress task was performed (see Table 2). Wilcoxon Signed Ranks Tests revealed that at T+90, neck pain and tension remained on the same level, while headache en fatigue increased further in the experimental WAD group (all *P*-values 0.02). At T+120 all levels remained the same compared to T+90, except for the variable fatigue, which significantly decreased, after a relax period of thirty minutes.
The level of headache and fatigue in the WAD control-condition did not change during the experiment (all *P*-values 0.09). The level of neck pain increased at T+90 (*P*= 0.01). The level of tension decreased after a relax-period (*P*=0.05) and remained on the same level after this.
The data of the global severity index (GSI) were not normally distributed (transformations of the data did not succeed in a normal distribution).

Table 2: State-measures in mm of the four groups, before and after a mental stress task (experimental groups) or rest (control-groups) (n=56).

	Headache mean (SD)			Neck Pain mean (SD)			Fatigue mean (SD)			Tension mean (SD)		
	Before	After	P*	Before	After	P	Before	After	P	Before	After	P
WAD exp.	20 (23)	31 (28)	.005	34 (19)	50 (25)	.002	29 (24)	43 (25)	.003	10 (11)	17 (21)	.01
Healthy exp.	1 (3)	1 (2)	.32	1 (3)	3 (4)	.14	4 (6)	5 (6)	.48	2 (5)	2 (5)	.59
WAD cont.	32 (22)	36 (21)	.24	40 (24)	37 (21)	.92	36 (22)	39 (29)	.47	22 (23)	16 (20)	.08
Healthy cont.	2 (4)	2 (3)	1.0	1 (5)	1 (3)	.32	5 (8)	5 (8)	.57	2 (5)	2 (4)	.68

*All P-values (two-tailed) refer to Wilcoxan Signed Ranks Tests

A Kruskall-Wallis Test showed that the difference on the GSI-index between the WAD-groups and the healthy-groups is significant (*P*= 0.001): the GSI-index of WAD patients is much higher than the index of healthy subjects, indicating more distress in the patient groups (WAD-group: *M*= 156 ± 45; Healthy-group: *M*= 114 ± 33).

Cortisol response in experimental- and control groups

Cortisol data were incomplete for four WAD patients and two healthy controls due to technical difficulties in assay or not having enough saliva. Repeated measures of variance of the three pre-treatment cortisol samples showed no significant main effect for Time (pre-1, pre 2, T-0), Group (WAD / healthy), Condition (experimental / control), nor significant interaction effects. Start time and sex were covariates: Start time was significant (P<0.002) and sex was not.
The raw average salivary cortisol values recorded during the laboratory session for both WAD and healthy groups from base line to the end of the experiment are shown in Table 3.

Repeated measures of variance was conducted with the four cortisol samples as dependent variables ('Time': T-0, T+60, T +90, T+120) and Group (=Patient/ Healthy), Condition (= Mental stress-task/ Rest) as independent variables. Start time (Early/ Late in the morning) and sex (male/female) were entered as covariates in the analysis. Results showed a main effect for Group (F (1, 49)= 9.2, P=0.004); as can be seen from Table 3, the average

Table 3: First colum: distribution of the variable 'sex'. Colum 2-5: mean levels and standard deviations of raw cortisol concentrations in saliva (nmol/l) recorded in WAD and Healthy groups before (base line) and at three moments after a mental stress task (experimental groups) or before and after a break (control- groups) (n=56).

	Sex (women)	T-0 (base line*)		T+60		T+90		T+120	
WAD-exp.	11	2.8	(1.7)	5.4	(7.4)	6.0	(8.7)	3.1	(2.2)
WAD-control	5	4.5	(5.9)	3.5	(4.9)	4.3	(7.5)	5.3	(8.3)
Healthy-exp.	12	1.8	(1.5)	1.1	(1.0)	1.2	(1.0)	0.9	(0.7)
Healthy-control	4	4.3	(3.1)	2.4	(1.4)	1.7	(1.3)	1.8	(2.0)

*In every group half of the cortisol concentrations were measured at 9.30 AM and half at 11.30 AM.

cortisol level of WAD patients is higher than the average cortisol level of healthy subjects. Furthermore, a significant main effect of Time was present (F (3, 47)= 5.5, P<0.003). An interaction effect of Time by Group was also significant (F (3, 47)=3.1, P<0.03). Inspection of Table 3 demonstrated that the cortisol levels of WAD patients remained stable or increased in time, whereas the cortisol levels of healthy subjects decreased.

Results showed that the factor 'sex' was significant in this analysis, indicating a different stress response for men and women (F (1,49)=4.1, P=0.05). Inspection of the means showed higher mean cortisol levels for men compared to women, during all measurements.

Relationship between daily hassles and cortisol responsivity.

In order to investigate the relationship between daily hassles / severity appraisal and cortisol change as result of a mental stress task, separate regression analyses were performed within the two experimental groups with respect to the cortisol change at T+60, T+90 and T+120.

The basic model consisted of the new calculated dependent variable T+60-change, T+90-change or T+120-change and the basic predictor variables 'Group and Start time'. This basic model did not predict cortisol change significantly at moments T+60, T+90 and T+120.
Furthermore, the variables 'duration of complaints', 'age' and the 'GSI-index' were not significant predictors.

With respect to the daily stressors, both the frequency and intensity measures of the *in*dependent stressors were not related to T+60, T+90 of T+120 cortisol change. In contrast, both the frequency and the intensity measures related to personal functioning were significant predictors for T+60 cortisol change (see Table 4).

Only the person-dependent intensity variable is still a significant predictor of T+90-change in the experimental groups (P=0.03). Because the person-dependent variables are significantly related to Group (Patient/Healthy), this last variable disappeared in the best predicting model for T+90-change (see Table 4). The best predicting model of T+120-change was the level of tension just before the mental stress-task (T-0), combined with the variables Group, Start time and sex (R^2=0.55; P=0.003).

Table 4: Prediction of percentage cortisol change at several Post-task moments as result of a mental stress task: regression analyses in WAD and Healthy Intervention groups (n=25).

	B	SE B	ß	P
Model 1(dependent: cortisolchange at T+60)*				
Constant	-.74	.32		.03
Starttime	-.02	.24	-.01	.93
Person-dependent intensity	.83	.22	.73	.001
Person-dependent frequency	-.09	.04	-.52	.01
Model 2(dependent: cortisolchange at T+90)*				
Constant	-.93	.39		.03
Starttime	.14	.30	.09	.63
Person-dependent intensity	.60	.26	.47	.03
Model 3(dependent: cortisolchange at T+120)*				
Constant	-1.60	.45		.002
Starttime	.84	.33	.41	.02
Patient/Healthy	.83	.34	.41	.02
Male/Female	.84	.43	.31	.06
Tension at baseline (T-0)	-.07	.02	-.57	.004

*R^2=0.44 for Model 1 (P=0.009); R^2= 0.21 for Model 2 (P<0.09); R^2=0.55 for Model 3 (P<0.003)

DISCUSSION

In line with the results of previous studies, the WAD patients in this study reported more general distress and daily hassles (related to personal functioning) and perceived them as more serious than healthy subjects.[8, 31]
The results showed no differences in performance on the mental stress-task between WAD patients and healthy subjects. Furthermore, both groups perceived the stress-task as equally strenuous. This implicates that the WAD patients in this study were not underperforming or aggravating (because in case of underperformance or aggravation, the performance and complaints of WAD patients should have been worse compared to healthy subjects).[38] Hence, the results can be interpreted as valid.
Confirming the expectations, the mental stress-task did not induce complaints of fatigue, pain or tension in healthy subjects. However, WAD patients did report significantly more headache, neck pain and were more fatigued and tensed after performing the mental stress-task. In contrast, the complaints of WAD patients in the relax-condition stayed roughly the same (headache, neck pain, fatigue) or decreased (tension).

Results demonstrated that WAD patients had significant higher cortisol levels compared to healthy subjects during the experiment. Furthermore, cortisol levels of WAD patients showed a different time-course during the experiment: cortisol levels in WAD patients remained the same or increased, whereas the cortisol concentrations in healthy subjects decreased. Despite the fact that the interaction term between Group x Time x Condition was not significant, it can be seen from Table 3 that there is a trend towards an increase in cortisol concentrations in WAD patients, after performing a mental stress task. It is conceivable that extension of this experiment with more subjects will reveal a significant change in cortisol concentration in the experimental WAD group compared to control groups.

In conclusion, WAD patients may perform as well as healthy subjects on a mental stress task, but in order to achieve this 'normal' result, it probably requires extra effort for them, whereas their processing resources are limited.[33, 39] This enhanced effort results into more pain, fatigue, tension and a higher cortisol secretion.

The results of this study are in accordance with the results of previous studies, which demonstrated elevated cortisol concentrations in other chronic pain syndromes like fibromyalgia and rheumatoid arthritis.[11, 40]
Analysis revealed a significant relationship of the factor 'sex' with cortisol levels, indicating higher cortisol levels for men. This result is in line with previous results.[35]

Because previous studies have demonstrated a high level of distress in WAD patients, which is related to the chronic daily stressors patients perceive (related to personal functioning), it was hypothesised that the amount of daily hassles predicts significantly cortisol response induced by a mental stress-task in WAD patients and healthy persons.[4, 7, 8] It was further hypothesised that (besides the self-reported frequencies of daily hassles) the seriousness ratings of these problems by the subjects significantly predicts cortisol response. Results demonstrated that cortisol responsivity in the experimental groups is indeed predicted by both the amount of daily hassles and appraisal of severity of the daily problems. Especially this last factor has proven to be a significant predictor of cortisol responsivity 30- and 60 minutes after termination of the stressor. These results are in agreement with other results concerning the positive relationship between frequency and intensity ratings of daily hassles and cortisol secretion as result of an acute psychological stressor.[14, 15,16]

The present findings have to be interpreted with care, because of the relatively small group of subjects. Definite conclusions cannot be drawn. Nevertheless, the present results offer new, interesting perspectives in the WAD phenomenon.
To substantiate our findings and in order to reveal the mechanisms behind the observed differences between healthy subjects and WAD patients, further research is necessary. Investigating cortisol levels and cortisol response at various time points post-injury, may give an indication about the time course of the changed HPA-axis sensitivity and may offer insight into the natural development of this syndrome, including different contributing factors, as is explained by the 'bio-psycho-social model'.[41] Of particular interest is the investigation of the cortisol stress-reaction in the acute phase of the WAD syndrome. Previous results have revealed that the initial emotional response to the injury and the existence of stressors independently of the injury are significant prognostic factors.[5, 8, 9, 42] Therefore, a cortisol stress-reaction in the acute phase will be expected in those subjects who exhibit this strong emotional distress in the acute phase. This kind of evidence would further objectivate a vulnerability to stress in some WAD patients.

In conclusion: although the number of subjects in the present study is relatively small and therefore no definite conclusions can be drawn, the results indicated significant higher cortisol concentrations in WAD patients compared to healthy persons. Furthermore, the results demonstrated that the cortisol change as result of an acute mental stressor is related to the amount of daily hassles (related to personal functioning) and especially the appraisal of severity of daily problems. Likely, WAD patients have become more sensitive to subsequent stressors after the whiplash injury, because of chronic daily hassles and dysfunctional coping strategies. For this reason 'stress management' should be an important topic in rehabilitation programs for chronic WAD patients.
It is concluded that study of HPA-axis in WAD patients offer new, interesting perspectives in the WAD phenomenon.

REFERENCES

1. Radanov, B.P., Di Stefano, G., Schnidrig, A. & Ballinari, P. (1991). Role of psychosocial stress in recovery from common whiplash. *The Lancet,* 338, 712-715.

2. Merksey, H. (1993). Psychological consequences of whiplash. In: *Spine state of the art reviews; Cervical flexion-extension/Whiplash injuries* (Teasell, R.W. & Shapiro, A.P., eds.). Philadelphia: Hanley & Belfus, 471-480.

3. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical review: Whiplash Injury. *Pain*, 283-307.

4. Radanov, B.P., Di Stefano, G., Schnidrig, A., Sturzenegger, M. (1994). Common whiplash: psychosomatic or somatopsychic*? J. Neurol. Neurosurg. Psychiat.,* 57, 486-490.

5. Drottning, M., Staff, P.H., Levin, L. & Malt, U.F.R. (1995). Acute emotional response to common whiplash injury predicts subsequent pain complaints. *Nord. J. Psychiatry*, 49, 293-299.

6. Radanov, B.P., Begre, S., Sturzenegger, M. & Augustiny, K.F. (1996). Course of psychological variables in whiplash injury – a 2-year follow-up with age, gender and education pair-matched patients. *Pain*, 64, 429-434.

7. Mayou, R. (1997). The psychiatry of road traffic accidents. In: *The Aftermath of Road Accidents* (Mitchell, M., ed.). London/New York: Routledge, 33-48.

8. Blokhorst, M.G.B.G., Lousberg, R., Vingerhoets, A.J.J.M., Winter, F.A.M., Zilvold, G. (2002). Daily hassles and stress-vulnerability in patients with a Whiplash Associated Disorder. *International Journal of Rehabilitation Research,* 25, 173-179.

9. Sterling, M., Kenardy, J., Jull, G. & Vicenzino, B. (2003). The development of psychological changes following whiplash injury. *Pain*, 106(3), 481-489.

10. Spitzer, W.O., Skovron, M.L., Salmi, L.R., et al. (1995). Scientific monograph of the quebec task force on whiplash-associated disorders: redefining "whiplash" and its management. *Spine*, 20 (7), 7-73.

11. Catley, D, Kaell, A.T., Kirschbaum, C. & Stone, A.A. (2000). A naturalistic evaluation of cortisol secretion in persons with fibromyalgia and rheumatoid arthritis. *Arthritis Care Research*, 13 (1), 51-61.

12. Cohen, S., Kessler, R.C., Underwood, G..L. (1995). Strategies for measuring stress in studies of psychiatric and physical disorders. In: *Measuring Stress; a Guide for Health and Social Scientists* (Cohen S, Kessler RC, Underwood, G.L, eds.). Oxford: Oxford University Press, 3-26.

13. Hawk, L.W. & Baum, A. (2001). Endocrine assessment in behavioral medicine. In: *Assessment in Behavioral Medicine* (Vingerhoets, A., Ed.). East-Sussex: Brunner-Routledge, 413-440.

14. Brosschot, J.F., Benschop, R.J., Godaert, G.L.R., Olff, M., De Smet, M., Heijnen, C.J. & Ballieux, R.E. (1994). Influence of Life Stress on Immunological Reactivity to Mild Psychological Stress, *Psychosomatic Medicine*, 56 (3), 216-224.

15. Pike, J.L., Smith, T.L., Hauger, R.L., Nicassio, P.M., Patterson, T.L., McClintick, J, Costlow, C. & Irwin, M.R. (1997). Chronic life stress alters sympathetic, neuroendocrine, and immune responsivity to an acute Psychological Stressor in Humans. *Psychosomatic Medicine*, 59, 447-457.

16. Smyth, J., Ockenfels, M.C., Porter, L., Kirschbaum, C., Hellhammer, D.H., Stone, A.A. (1998). Stressors and mood measured on a momentary basis are associated with salivary cortisol secretion. *Psychoneuroendocrinology*, 23 (4), 353-370.

17. Peters, M.L., Godaert, G.L.R., Ballieux, R.E., van Vliet, M., Willemsen, J.J., Sweep, F.C.G.J. & Heijnen, C.J. (1998). Cardiovascular and endocrine responses to experimental stress: effects on mental effort and controllability. *Psychoneuroendocrinology*, 23 (1), 1-17.

18. Elsmore, T.F. (1994). Synwork 1: A PC-based tool for assessment of performance in a simulated work environment. Behavior Research Methods, *Instruments & Computers*, 26 (4), 421-426.

19. Gotelli, G.G., Wall, J.H., Kabra, P.M., and Marton, L.J. (1981). Fluorometric liquid-chromatographic determination of serum cortisol. *Clin. Chem.*, 27, 441-443.

20. Nozaki, O., Ohata, T., Ohba, Y. 1991. Determination of serum cortisol by reversed-phase liquid chromatography using precolumn sulphuric acid-ethanol fluorescence derivatization and column switching. *J. Chrom.,* 570, 1-11.

21. Mason, S.R., Ward, L.C., Reilly, P.E.B. (1992). Fluorimetric detection of serum corticosterone using high-performance liquid chromatography. *J. Chrom.*, 581, 267-271.

22. Hermans, J.J.R., Van Essen, H., Struijker-Boudier, H.A.J., Johnson, R.M., Theeuwes, F. & Smits, J.F.M. (2002). Pharmacokinetic advantage of intrapericardially applied substances in the rat. *Journal of Pharmacol. Exp. Ther.,* 301, 672-678.

23. Vingerhoets, A.J.J.M. & Van Tilburg, M.A.L. (1994). *Alledaagse Problemen Lijst (APL).* Lisse: Swets en Zeitlinger.

24. Kanner, A., Coyne, J.C., Schaefer, C. et al. (1981). Comparison of two modes of stress measurements: Daily hassles and uplifts versus major life events. *J. Beh. Med.*, 4, 1-39.

25. DeLongis, A., Coyne, J.C., Dakof, G. et al. (1982). Relationship of daily hassles, uplifts, and major life events to health status. *Health Psychol.,* 1, 119-136.

26. Van de Willige, G., Schreurs, P., Tellegen, B. & Zwart, F. (1985). Het meten van 'life-events': de vragenlijst recent meegemaakte gebeurtenissen (VRMG). *Nederlands Tijdschrift voor de Psychologie*, 40, 1-19.

27. Vingerhoets, A.J.J.M., Jeninga, A., & Menges, L.J. (1989). Het meten van chronische en alledaagse stressoren: eerste onderzoekservaringen met de Alledaagse Problemen Lijst (APL) II. *Gedrag en Gezondheid*, 17, 10-17.

28. Derogatis, L.R. (1983). *SCL-90R. Annual II. Clinical Psychometric research*. Towson: Clinical Psychometric Research.

29. Arrindel, W.A. & Ettema, J.H.M. (1986). *SCL-90: Handleiding bij een psychopathologie-indicator.* Swets & Zeitlinger, Lisse (The Netherlands).

30. Bernstein, I.H., Matthew, E.J. & Hinkley, B.S. (1994). On the utility of the SCL-90-R with Low-Back Pain Patients. *Spine,* 19*,* 42-48.

31. Wallis, B.J., Lord, S.M., Barnsley, L., & Bogduk, N. (1996). Pain and Psychologic Symptoms of Australian Patients with Whiplash. *Spine,* 21*,* 804-810.

32. Cremer, R. (1998). *Mentaal Belastbaarheids Onderzoek*, internal report TNO, Amsterdam.

33. Blokhorst, M.G.B.G., Meeldijk, S. van Luijtelaar, G., van Toor, T., Lousberg, R. & Ganzevles, P. (in press). Noise intolerance and state-dependent factors in patients with Whiplash Associated Disorder. Accepted for publication in: *Journal of Whiplash and Related Disorders*, 2005, vol. 4 (1)

34. Hair, J.S., Anderson, R.E., Tatham, R.L., Black, W.C. (1998). Multivariate data analysis. London: Prentice Hall.

35. Kirschbaum, C., Wust, S. & Hellhammer, D. (1992). Consistent sex difference in cortisol responses to psychological stress. *Psychosomatic Medecine*, 54 (6), 648-657.

36. Norusis, M.J. (1999). *SPSS-user Guide: version 9.0.*, Chicago.

37. Negrão, A.B., Deuster, P.A., Gold, P.W., Singh, A., Chrousos, G.P. (2000). Individual reactivity and physiology of the stress response. *Biomed. & Pharmacother.,* 54, 122-128.

38. Schmand, B., de Sterke, S. & Lindeboom, J. (1999). *Amsterdamse Korte Termijn Geheugen Test*. Lisse: Swets & Zeitlinger Publishers.

39. Klein, M. (1997). Attentional performance in Young and Old patients with Cervical Acceleration Deceleration Injury. In: *Cognitive Aging, Attention, and Mild Traumatic Brain Injury (Thesis).* Maastricht: Neuropsych Publishers. 155-170.

40. Crofford, L.J., Pillemer, S.R., Kalogeras, K.T., Cash, J.M., Michelson, D. Kling, M.A., Sternberg, E.M., Gold, P.W. Chrousos, G.P., Wilder, R.L. (1994). Hypothalamic-pituitary-adrenal axis pertubations in patients with fibromyalgia. *Arthritis Rheum*, 37, 1583-1592.

41. Ferrari, R. & Schrader, H. (2001). The late whiplash syndrome: a biopsychosocial approach. *Journal of Neurosurg Psychiatry*, 70, 722-726.

42. Smed, A. (1997). Cognitive function and distress after common whiplash injury. *Acta Neurologica Scandinavica*, 95, 73-80.

Chapter 4

Noise-intolerance and state-dependent factors in patients with Whiplash Associated Disorder

Mariëtte Blokhorst[1], Stefan Meeldijk[1], Gilles van Luijtelaar[3], Thijs van Toor[4], Richel Lousberg[1, 2], Paul Ganzevles[5]

[1] Roessingh Research and Development, Enschede
[2] Dept. of Psychiatry and Neuropsychology, University of Limburg, Maastricht
[3] NICI, Radboud University, Nijmegen
[4] Audiologisch Centrum Twente, Hengelo
[5] Mediant, Enschede

Accepted for publication in: Journal of Whiplash & Related Disorders; vol. 4 (1), 2005

INTRODUCTION

It is well known that patients with a Whiplash Associated Disorder (WAD) complain of pain, fatigue, dizziness, attention problems, heightened irritability, sensitivity for light and noise-intolerance.[1-5] Lowered tolerance to sound stimuli is a subjective symptom that is frequently present in WAD patients, but has received little scientific attention compared to other symptoms. It is reported that percentages ranging from twenty-seven to sixty-three of all WAD patients complain about increased intolerance to sounds after a whiplash injury.[6-7] This undue sensitivity to noise or loud sounds is a common complaint given different names (hyperacusis, hypersensitivity, phonophobia, audio-sensitivity or loudness intolerance). In this chapter only the term 'tolerance' will be used and is defined as the subjective ability to endure higher intensities of sound stimuli.[8] Characteristic of noise-intolerance is the intolerance to everyday sounds in the presence of normal hearing. Sounds that are bothersome may include higher pitch sharp noises such as silverware or dishes, sudden sounds such as dogs barking, screaming children, or even lower steady noises such as computer fans, motor noises and party noise or television emissions.[9] Results of recent studies revealed normal hearing patterns in WAD patients as was measured by means of pure tone audiometric tests.[7,10]

Noise in general (especially loud, intermittent, unpredictable and uncontrollable noise) is often an environmental stressor in healthy persons, which effects performance negatively.[11] Noise-intolerance is characterized by substantial individual variation, which is determined by factors such as gender, age, personality dimensions and health state.[12]

There are several clinical conditions reported to co-occur with noise-intolerance, after excluding middle ear and cochlear conditions, for example: migraine, depression, benzodiazepine dependence, post-traumatic stress disorder, chronic post-viral fatigue syndrome (CFS)[13] and mild head injury (MHI).[14] Sound induced discomfort-thresholds in patients with migraine and tension-type headache appear to be significant lower than controls.[15,16] Recently, the level of uncomfortable loudness (UCL) was assessed in WAD patients.[10] Results revealed that WAD patients have a lower threshold than healthy controls.

While most studies investigated the maximal threshold of tolerance, Bohnen et al. (1991) assessed also sub maximal levels of lowered tolerance in patients with MHI, by applying a graded tolerance scale for each stimulus.[8,14] Results revealed that MHI patients were significantly less tolerant to stimuli of intensities from 71dB, three to six days after the trauma, compared to controls. It was concluded that 'as these intensities are common in daily life, MHI patients may easily get disturbed by many daily life situations'.[8] Because of the reported association between noise-intolerance on the one hand and pain, fatigue and anxiety on the other hand,[10,13] it seems relevant to investigate the relationship between noise-intolerance in WAD patients and these kind of state-dependent factors, as these symptoms go along together in WAD patients.[4,17]

The aims of the present study are to test the following three hypotheses: first it is hypothesized that WAD patients do not differ from healthy matched controls with respect to loudness perception of a 1000 Hz pure tone of different intensities, given the normal results on pure tone audiometric tests in WAD patients.[7,10]
Secondly, it is expected that WAD patients will be less tolerant to moderate and strong sound intensities compared to healthy matched controls. Moreover, since the level of pain, fatigue and tension in WAD patients is thought to be related to the amount of work performed,[19] a mental stress task will be used with the expectation that mental stress will induce more headache, neck pain, fatigue and tension in the experimental WAD group, compared to a WAD control and a healthy experimental and healthy control group.
Thirdly, it is hypothesised that the WAD group will show an increase in noise-intolerance for moderate and strong noises after performing the mental stress task, compared to the experimental healthy group and the WAD control group. In other words, it is expected that an increase in headache, neck pain, fatigue or distress is associated with an increase in noise-intolerance in WAD patients, considering the previous reported relationship between state-dependent complaints and noise-intolerance.[10,13,15,16]

METHODS

Participants

Twenty-eight WAD patients (14 males and 14 females), referred to a rehabilitation centre for treatment because of chronic whiplash related complaints, participated in this research project. The patients in this study had a mean age of 32 years (± 7 years). The injury occurred more than six months before testing, which means that all patients were in the chronic phase (mean interval = 38 months; ± 24 months). All patients encountered the whiplash injury in an automobile-accident (rear-end collision); none was to blame for the accident. All patients were still in litigation. Patients, who reported that they had lost consciousness after the whiplash injury, had recent narcoses or pre-morbid head injury, were excluded, to eliminate the possibility of significant head trauma. Psychiatric comorbity and premorbid migraine were also exclusion criteria. Patients were only included if they had a normal peripheral hearing (threshold at 500, 1000, 2000 and 4000 Hz; 15dB HL or better) as was investigated by means of a standard audiological test procedure (pure tone and speech audiometry). One patient was excluded because of tinnitus and one healthy subject was excluded because of an abnormal audiogram. Fifty-seven percent of the patients had a low/middle educational level and the other 43 percent of patients had a middle/high educational level. Thirty-nine percent of the patients were able to work, whereas 57 percent had a worker's compensation. Following the Quebec Task Force's clinical-anatomic axis that corresponds to severity of the whiplash injury,[4] this study concerns only patients with chronic complaints after a WAD grade I and grade II. The definition for grade I is: no tender points and normal range of neck motion; the only symptom is 'neck stiffness'. Grade II is defined as: tender points and restricted range of motion. The symptoms are 'probable muscle and/or ligament sprain'.[4] In the experimental WAD group, two patients are diagnosed as WAD grade I and only one patient in the WAD-control group is diagnosed for having a WAD grade I.

Twenty-eight healthy control subjects, far most working in the rehabilitation centre, were selected and matched for educational level and age. These variables are related to performance on the mental stress task used in this experiment and should therefore be controlled for (see procedure).[18]

At the moment of testing, none of the subjects used medication that is known to influence the central nervous system. All subjects were informed of the possibility that the tests could increase or provoke complaints and gave signed permission before starting. A medical ethical committee approved the study.

Materials

Noise-stimuli

Five different noise intensities of 1000 Hz were offered to patients and control subjects, by means of an audiometer (type: Madson OB77-12769-M1) with headphone. Intensities were: 57dB, 71dB, 81dB, 89dB and 95dB. These stimuli were chosen because the human ear is well able to perceive these tones and they represent a large range of intensities.[8] Every stimulus was offered six times in a semi-randomized order. A stimulus-session consisted of thirty stimuli. A certain stimulus was never followed by the same stimulus. The sound stimuli lasted for four seconds at every level, with an eight-second interstimulus interval. During the experiment, these stimulus-sessions were presented four times (see procedure). Every stimulus-session was identical within and between persons, for both the two loudness perception sessions and the two noise-intolerance sessions.

Experimental task

The 'Synwork' task, a divided attention computer task, was used as a mental stress task.[18,19,20] This task consists of four subtasks: a memory task, an arithmetic task, a visual monitoring task and an auditory monitoring task. The subject has to alternate his attention on those four tasks. Every seven minutes, the task becomes more complex by increasing the speed of stimulus presentation and/or raising the number of target items (in the working memory task and the auditive monitoring task). The arithmetical task is a self-paced task: a new stimulus is presented just after a response is given. The test consists of six sessions of seven minutes. Subjects get 10 points for every right reaction and they lose 10 points when they neglect certain stimuli (the stimuli of the visual monitoring task) or give a wrong answer (in case of the memory task and the arithmetical task). They are instructed to collect as much points as possible. Their score is visible in the middle of the screen. Before the test starts, subjects perform a practice-session (lasting 10 minutes), in which initially every subtask is executed separately before all subtasks are presented together. Subjects may choose which task they want to perform and in which order they execute the tasks, so in fact they may develop their own strategy. Synwork is known as a dynamic and complex task, which simulates the many-sidedness of work situations.[18] The task is also used in mental capacity assessment.[19]

Loudness and Noise-intolerance VAS-scales

Loudness and noise-intolerance perception was measured by means of a Visual Analogue Scale (VAS). During the experiment, the subjects were asked to rate the level of loudness and (dis)comfort of every stimulus, on a 10 cm line. In order to get an impression of the range of the noise-intensities, every subject underwent a practice-session for a few minutes.

State- dependent variables: Headache, Neck pain, Fatigue, Tension

Subjective, state-dependent complaints were measured by means of a Visual Analogue Scale (VAS). During the experiment, patients were asked six times to rate the level of headache, neck pain, fatigue and tension (see also procedure). A 10 cm line was provided with written anchors at the two extremes: e.g. 'no pain' and 'unbearable pain'.

Subjective perception of noise-intolerance in daily life.

In order to get more insight into the subjective perception of noise intolerance in daily life, a few questions were asked to WAD patients: the first question was 'are you more intolerant to noise since the whiplash injury?' In addition, the second question was 'How much is everyday noise more annoying for you since the whiplash injury?'.

Subjective perception of effort regarding the mental stress task.

The perceived effort of the Synwork task in the experimental groups was measured by means of a VAS-scale. A 10 cm line was provided with written anchors at the two extremes: no effort needed – very much effort needed.

SCL-90

In order to check the relationship between global distress on the one hand and noise-intolerance level on the other hand, the Dutch version of the SCL-90 was administered.[21] The SCL-90 is a self-report, multidimensional symptom checklist composed of 90 items, each describing a physical or psychological symptom.[21,22] The instructions require patients to respond on a 5-point scale (ranging from 'not at all' to 'extremely') to indicate how much an item has bothered them over the past week. The global severity index (GSI) is a measure of general distress, which is obtained from the eight sub-scale scores and other items of the questionnaire not included in these scores.

Procedure

WAD patients were randomly assigned to the experimental-group or the relax-control group. All subjects were instructed not to use any coffee/tea, not to smoke and not to take medication of influence on the central nervous system. Due to practical reasons, half of the subjects of each of the four groups group started at 8.30 AM in the morning, while the other half started at 10.30 AM (start times were counter-balanced across the four groups). The first state-dependent measurement was collected just before the noise-intolerance test (T-0) (see Figure 1). Subjects rated their state-dependent feelings (headache, neck pain, fatigue and tension) and a cortisol sample was collected. The results of the cortisol values are described elsewhere.[20]

Figure 1: experimental procedure in time

Next, subjects underwent the loudness and noise-intolerance test. The order of these tests was counter-balanced across the groups. The instruction for the loudness-test was:

> *"After this instruction you hear some sounds. You have to indicate how you perceive this sound. You have to draw a vertical bar on this line. For example, if you perceive the sound as very loud, you draw a bar near the anchor 'extreme loud'. On the other hand, if you perceive the sound as very soft, you draw a bar near the other anchor 'extreme soft'.*

The instruction of the noise-intolerance test was:

> *"After this instruction you hear some sounds. You have to indicate how comfortable or uncomfortable this sound is to you. You have to draw a vertical bar on this line. For example, if you perceive the sound as very bearable, you draw a bar near the anchor 'very bearable'. On the other hand, if you perceive the sound as very uncomfortable, you draw a bar near the anchor 'very unbearable sound'.*

Again, a state-dependent measurement was carried out (T+30). After this, half of the WAD-patients and half of the healthy subjects performed the mental stress task (WAD-experimental group and Healthy-experimental group) that lasted for about 60 minutes. Subjects were instructed as follows:

> *"You have to perform an attention task on this computer. This task measures your ability to execute several tasks at the same time. The task consists out of four parts. Task 1 is a letter-recognition task: you have to recognize a letter out of several other letters. Task 2 is an arithmetical task: you have to add two numbers. In task three, you have to prevent that a vertical dash is more than one second at both ends of a horizontal line. In task 4 you have to push your left-mouse button on a rectangle on your screen, when you hear a high sound."*

Next, subjects were able to practice all four tasks separate and later on together (practice session lasted about ten minutes). After the practice-session, the test began and subjects got the following instruction:

> *"As you have seen, you get ten points for every right reaction. Your score is visible in the middle of the screen. However, when you forget to react to the visual-monitoring task (the "dash-task"), your score will decrease. The better you are able to react to all the different tasks, the higher your score will be. The test consists of six sessions of seven minutes. Try to increase your score with every new session!"*

The two control groups (WAD-control and Healthy-control) had to rest and were allowed to relax. After this session, VAS-scales were rated concerning state-dependent feelings (in the experimental and control groups) and subjective feeling of effort relating to the stress task in the two experimental groups (T+90). Next, all subjects again underwent the loudness and noise-intolerance test. After this test, the state related measures were collected (T+120) and again after thirty minutes rest (T+150 min).

Data analyses

Statistical analyses were performed with the Statistical Package for Social Sciences.[23] Data of the loudness-tests were analysed by means of non-parametric tests because these data were not distributed normally. Noise-intol-

erance data were analysed by means of MANOVA for repeated measures. In order to investigate differences on state-dependent variables (in time) between the four groups, non-parametric tests were used.
The relationships between the state-dependent variables and noise-intolerance were analysed by means of multiple regression analyses. Other relevant variables on personal status and duration of complaints were also included in the model. A correlation-matrix was calculated in order to investigate the relationship between the changes in complaints and the changes in noise-intolerance. The level of significance was set at $P=0.05$.

Results

Subjective noise-intolerance perception in daily life.

Ninety two percent of the WAD patients answered with 'yes' regarding the question 'are you more intolerant to noise since the whiplash injury?' The second question was 'How much is everyday noise more annoying for you since the whiplash injury?': the results showed a mean of 6.0 (sd: 3.1) on a VAS-scale from 0-10 cm in both WAD-groups.

Mental stress performance

An independent *t*-test revealed no significant differences between the two experimental groups regarding the perceived effort of the mental stress task (Synwork) ($P=0.36$). Furthermore, an independent *t*-test was conducted to explore whether performance on the Synwork task was different between the WAD-experimental group and the healthy-experimental group. The results revealed no significant differences, indicating that both groups performed equally well on this test ($P=0.30$).

Post-hoc analyses showed no significant differences between the WAD-experimental group and the healthy-experimental group regarding the six different subtasks of Synwork (*P*-values ranging from 0.4 - 0.9).

SCL- 90

The data of the global severity index (GSI) of the SCL-90 were not distributed normally (transformations of the data did not succeed in a normal distribution). A Kruskal-Wallis Test showed that the difference on the GSI-index between the WAD and the healthy-groups is significant ($P<0.001$): the GSI-index of WAD patients is much higher than the index of healthy subjects, indicating more distress in the patient groups (WAD-group: mean= 156; sd=45; healthy-group: mean= 114; sd=33).

'State' characteristics of the WAD and control group

The mean values of headache, neck pain, fatigue and tension are listed in Table 1. For coherence of this chapter, only the data of pre- and post condition are presented. Neither the two healthy groups, nor the two WAD groups differed significantly between each other on moment T-0 (base line) with respect to the four state related factors, as was investigated by a non-parametric tests (the Kruskal-Wallis test).
Non-parametric tests revealed that the level of headache, neck pain, fatigue and tension increases significantly during the experiment in the WAD-experimental group and not in the three other groups (see also Table 1). Healthy subjects hardly complain about headache, neck pain, fatigue or tension. No significant differences were found between men and women regarding the level of state-dependent complaints.

Loudness perception

Mean scores and standard deviations of the loudness VAS-scales are presented in Table 2.
Normality tests revealed that the data of the loudness scales are not distributed normally. Non-parametric tests (Kruskal-Wallis test) revealed that there are no differences in subjective loudness perception at base line between WAD patients and healthy controls (*P*-values ranging from 0.06-0.49). Post-condition measurement revealed significant differences in subjective loudness perception between WAD patients and healthy subjects, only at the two highest intensities (89dB: $P<0.01$; 95dB: $P<0.001$). WAD patients rated these intensities as louder compared to healthy controls (see also Table 2). Mann-Whitney U tests only revealed a significant change on 95dB between

Table 1: Median values of headache, neck pain, fatigue and tension VAS-scales in WAD patients and Healthy control participants before and after the experimental condition.

	Headache			Neck Pain			Fatigue			Tension		
	Before	After	P*	Before	After	P	Before	After	P	Before	After	P
WAD exp.	15.6	33.5	.005	31.3	46.5	.002	25.0	40.0	.003	7.0	11.0	.01
Healthy exp.	0.36	0.36	.32	0.36	2.0	.14	1.3	2.5	.48	0.6	0.6	.59
WAD cont.	33.0	35.0	.24	40.5	35.0	.92	34.5	42.5	.47	11.0	7.0	.08
Healthy cont.	0.25	1.0	1.0	0.30	0.30	.32	1.8	1.0	.57	0.6	0.5	.68

* All P-values (two-tailed) refer to Wilcoxan Signed Ranks Tests

Table 2: Median values of subjective loudness perception (by means of VAS-scales) in WAD patients and Healthy subjects for five different noise intensities, before and after a mental stress task/relax period.

	WAD-experimental (N=14)	WAD-control (N=14)	Healthy-Experimental (N=14)	Healthy-Control (N=14)
	Median	Median	Median	Median
57 db-pre	9.0	5.7	7.0	5.8
57 db-post	8.6	8.1	7.5	7.5
71 db-pre	25.5	19.4	17.0	18.0
71 db-post	29.1	20.3	20.6	21.6
81 db-pre	44.7	44.5	35.5	41.0
81 db-post	48.2	47.2	41.5	40.5
89 db-pre	76.4	77.2	72.7	65.7
89 db-post	82.5	83.5	71.6	62.8
95 db-pre	96.5	92.7	88.9	85.7
95 db-post	97.8	96.7	81.1	80.4

pre- and post measurement with respect to WAD patients and healthy controls (P=0.02). WAD patients rated on average at post measurement a stimulus of 95dB as significantly louder compared to the base line measurement, in contrast to healthy subjects. No significant changes were found between both WAD groups or between both healthy groups regarding the loudness perception of a stimulus of 95dB. Furthermore, no significant differences were found in the four groups regarding the difference scores of pre- and post measurement on the four other intensities.

In order to investigate whether the significant differences in loudness perception of 89dB- and 95dB stimuli between WAD patients and healthy subjects were related to the level of headache, neck pain, fatigue or tension at post-measurement, post-hoc a correlation-matrix was calculated between these state-dependent variables and the loudness-perception data of the five intensities. Results revealed significant correlations between 89dB and the level of headache (R=0.36; P=0.006), neck pain (R=0.44; P=0.001) and fatigue (R=0.32; P=0.01) at post-measurement. Also, an intensity of 95dB was significantly related to the level of headache (R=0.36; P=0.007), neck pain (R=0.46; P=0.000), and fatigue (R=0.006; P=0.36). Tension was not related to any of the five intensities. None of the state-dependent variables was related to the other three intensities.

Noise-intolerance level

Mean scores and standard deviations of the noise-intolerance VAS-scales are presented in Table 3.

Despite an outlier at 71dB, data were distributed normally. This outlier did not influence the results. A MANOVA was conducted on the base line data with the Intensities (5) as 'within subject' factor and Group (WAD group versus healthy group) as 'between group' factor. The results showed a significant main effect for Intensities (F (4,51)=382; P<0.001), a main effect for Group (F(1,54)=18.8; P<0.001) and an interaction effect for Group by Intensities (F(4,51)=4.2; P<0.005). Inspection of the data showed that the difference between WAD patients and healthy subjects increased with increasing noise-intensity.

Multivariate analyses showed significant differences between the four groups on all intensities (P-values ranging from 0.01 – 0.000) (see also Table 3). Contrast analyses indicated no significant differences between the two WAD groups as well as the two healthy groups, on the pre- and post measurement.

MANOVA for repeated measures was conducted with Intensities (5) and Time (2) (pre- and post condition) as 'within subject' factors and Condition (2) (Relax- and Experimental group) and Group (WAD group versus healthy group) as 'between subject' factors. The results showed a significant main effect for Intensities (F (4,49)=361; P<0.001) (in every group the noise-intolerance increased by increasing intensity), a main effect for Time (F(1,52)=19.7; P<0.001) (noise-intolerance increased at post-measurement for every group), a main effect for Group (F(1,52)=21; P<0.001) (WAD patients are more intolerant for noises; see also Table 3). Furthermore, an interaction effect for Intensities by Group (F (4,49)=3.8; P<0.009) was found. Inspection of the data showed again that the difference between WAD patients and healthy subjects increased, with increasing noise-intensity. Results revealed no significant 'Condition effect', nor any interaction effects with the variable 'Condition'.

Table 3: Means, standard deviations and median values of noise intolerance (by means of VAS-scales) in WAD patients and Healthy subjects for five different noise intensities before and after a mental stress task/ relax period.

	WAD-experimental (N=14)			WAD-control (N=14)			Healthy-Experimental (N=14)			Healthy-Control (N=14)		
	M	(SD)	Med	M	(SD)	Med	M	(SD)	Med	M	(SD)	Med
57 db-pre	18.0	(11.0)	16.0	14.4	(6.6)	13.5	9.9	(10.0)	8.0	10.6	(5.6)	11.1
57 db-post	19.1	(12.1)	17.5	16.9	(7.7)	15.0	12.5	(12.0)	8.4	10.2	(5.1)	8.9
71 db-pre	31.6	(14.0)	28.3	26.0	(8.3)	27.5	20.9	(14.8)	14.6	21.0	(8.9)	22.5
71 db-post	33.3	(14.4)	36.9	31.3	(7.8)	32.3	24.1	(13.8)	19.1	21.9	(9.3)	20.7
81 db-pre	50.4	(8.9)	49.4	46.8	(12.4)	50.6	33.0	(17.5)	32.0	36.4	(13.9)	38.1
81 db-post	55.5	(18.6)	58.9	52.2	(10.7)	54.0	37.2	(15.5)	34.9	39.2	(9.9)	38.7
89 db-pre	76.3	(17.7)	79.9	73.5	(12.5)	75.8	56.4	(19.9)	56.6	55.5	(10.2)	54.5
89 db-post	78.2	(17.9)	82.7	79.1	(11.0)	79.0	59.1	(16.9)	62.7	58.7	(12.7)	53.3
95 db-pre	88.4	(15.5)	91.6	89.6	(8.7)	91.3	70.1	(17.2)	74.3	72.1	(8.8)	72.7
95 db-post	90.7	(14.3)	96.4	90.8	(7.7)	93.8	72.7	(17.1)	76.3	74.7	(11.1)	76.5

Relationship between noise-intolerance and state-dependent factors

In order to investigate the relationship between the level of noise-intolerance and state dependent factors (headache, neck pain, fatigue, tension and global distress), separate regression-analyses were performed within the two WAD groups with respect to the pre- and post condition results (with the different intensities as dependent variables). The basic model consisted of the dependent variable 57dB, 71dB, 81dB, 89dB or 95dB and the predictor variables 'sex' (male or female), 'Educational level' and 'Duration of complaints'. Results showed that the only significant predicting factor was 'sex', on three intensities (57dB, 71dB and 81dB: R^2 varies from 14% to 16%; *P*-values ranged from 0.03-0.05). Post-hoc analyses revealed that female WAD patients were more intolerant for certain intensities compared to male WAD patients. MANOVA revealed significant differences between males and females on 71dB ($P<0.03$), 81dB ($P<0.04$) at base line measurement and on 71dB ($P<0.03$), 81dB ($P<0.03$) and 89dB ($P<0.05$) at post-measurement. Inclusion of the state-dependent variables (headache, neck pain, fatigue, tension and global distress) to this basic model revealed no significant improvements.

In order to investigate whether an increase in complaint (headache, neck pain, fatigue, tension) is related to an increase in noise-intolerance in WAD patients, a correlation matrix was calculated. The results revealed a significant correlation between an increase in intolerance for an intensity of 57dB and an increase in fatigue in WAD patients ($R=0.40$; $P<0.02$). The increasing level of intolerance for intensities of 81dB and 89dB in WAD patients is related to an increase of headache in these patients (81dB: $R=0.40$; $P<0.03$; 89dB: $R=0.30$; $P<0.04$).

DISCUSSION

Most of the chronic WAD patients in this study (92%) experienced noise as more annoying since the whiplash injury. Results revealed that the loudness perception in WAD patients is not different from healthy subjects on base line measurement. In contrast, on post-measurement there is a significant difference on the two strongest noise intensities (e.g. 89dB and 95dB) between WAD patients and healthy subjects. Neither the two WAD groups, nor the two control groups differ from each other on the measured intensities. Post-hoc analyses revealed a significant relationship between these two strong intensities and state-dependent variables. Likely, the loudness perception of extreme noise-intensities is influenced by the physical well being of persons. No effect on loudness perception is seen because of the mental stress task. In fact, except from very strong intensities, loudness perception is stable. Given the above mentioned results, we may conclude that there is no audio sensitivity in WAD patients, because 'audio sensitivity' means that not only sounds of strong intensities, but also sounds of moderate-strong intensities are perceived as louder than 'normal'.[24] Furthermore, because of the lack of differences at base line measurement between WAD patients and healthy control subjects and the fairly stable loudness perception in time, it is concluded that there are no signs for subliminal cochlear lesions in these WAD patients. These results are in accordance with previous results that also indicated no evidence for hearing loss associated with whiplash injury or dysfunctions of the brainstem startle circuitry [(5,7,10)].

In contrast to the results of loudness perception, the noise-intolerance level is significantly different for all investigated noise-intensities ranging from 57dB to 95dB. WAD patients are more intolerant for these noise-intensities, compared to healthy subjects. As was expected, both WAD patients and healthy subjects became increasingly more intolerant for stronger noise-intensities. The data showed that the difference in intolerance level, between WAD patients and healthy subjects, increases with increasing noise-intensity. These results are comparable with previous results in patients with a mild head injury.[8]

The experimental condition, by means of a mental stress task, did induce significantly more complaints in WAD patients (as was expected). However, the experimental WAD group showed no significant increase in noise-intolerance level compared to the other groups, after performing the mental stress task. In fact, the data showed that the subjects of all groups (WAD and healthy groups) became more intolerant for noises as the hours went by.

Despite a lack of condition-effect on noise-intolerance, results did however reveal significant correlations between an increase in WAD patients' complaints and an increase in noise-intolerance level in the total WAD group. More specifically, an increase in fatigue is related to an increase in intolerance level for an intensity of 57dB, and an increase in headache is related to an increase in intolerance level for noise-intensities of 81dB and 89dB (at pre-and post-measurement). This association between an increase in headache and an increase in intolerance of moderate-strong noise-intensities of 81dB and 89dB is not surprising, because one might assume that headache does not interfere with low noise-intensities. Furthermore, it is conceivable that high noise-intensities (such as 95dB) are not comfortable for any subject, despite the level of headache. This association between headache and noise-intolerance is in concordance with previous results of lowered noise-discomfort levels in migraine patients and patients with tension-type headaches,[15,16] as well as the recently found significant correlation between UCL-levels (Uncomfortable Loudness) and headache in WAD patients.[10]

A relationship between anxiety/ tension or global distress on the one hand and noise-intolerance on the other hand was not found. These findings suggest that the reported responses to noise were independent of the global emotional status of the patients. Perhaps, noise-intolerance is related to emotional distress only for those situations in which WAD patients have to concentrate on catching what persons say in a noisy surrounding, which is a strenuous task for WAD patients.[3,4,7,28] Future research must give more insight into the relationship between noise intolerance and focused attention in WAD patients.

Although the results indicated a relationship between headache and noise-intolerance, other (demographic) factors seem to be more important, given the moderate percentage explained variance of the factor headache. Post-hoc analysis revealed that female WAD patients are more intolerant to moderate strong noises than male-patients. It is known from previous studies that women with and without medical disorder generally tend to report more symptoms and more severe symptoms.[25] This could be related to a process called ‘symptom amplification’ and is also thought to be related to whiplash complaints in general.[26] Amplification refers to a perceptual style and means that persons who have a heightened attentional focus on bodily sensations (hypervigilance), have a tendency to select out and concentrate on certain relatively weak and infrequent sensations, and have a disposition to react to somatic sensations with affect and cognitions that intensify them and make them more alarming and disturbing.[26,27] Another explanation is that women express emotions and easier and faster than men.
Another (neurophysiological) explanation is that women might have a higher level of neck proprioceptive activity than males, after a similar impact. Previous results revealed that disturbances of the proprioceptive input from the neck to the central nervous system and/or of the central processing of such input, influence the postural control in many patients with WAD.[29-32] Possibly, the noise-intolerance is also related to this heightened proprioceptive activity and dysfunctional pain processes.

The results of the Synwork task showed no differences between WAD patients and healthy subjects. It seems contradictory that WAD patients performed as well as healthy subjects on this divided attention task, because previous studies showed worse performances on divided attention tasks in WAD patients compared to healthy subjects (for example on the often used PASAT task).[5,6,29] To understand these results it is important to look at the kind of task which is used. We might say that the Synwork task is more or less a self-paced task: one of the four tasks is clearly a self-paced task (the arithmetical task) and furthermore, subjects may choose to which task they attend and may determine the order of carrying out the different tasks. Interestingly, a previous study of Klein (1997) has demonstrated that WAD patients perform a self-paced version of the PASAT as good as healthy control subjects.[33] In conclusion, the results of this study are in accordance with these previous results: apparently WAD patients are able to perform normal on self-paced divided attention tasks in contrast to time-pressure tasks as the standard version of the PASAT. However, they can do so only by investing 'compensatory mental effort', which is a surplus of effort needed when individuals find themselves in a suboptimal state.[34] As Hockey (1986) stated before: "The maintenance of performance under increased fatigue may attract increased 'costs' ".[35]

It is concluded that WAD patients are more intolerant to noise in general compared to healthy subjects and that this intolerance increases significantly with increasing noise-intensity. These results confirm the subjective complaint of WAD patients with respect to the intolerance to everyday sounds, in the presence of normal hearing. Given the fact that moderate-strong noise intensities are common in daily life, it is concluded that this noise-intolerance is an important disability for many WAD patients. Results revealed a relationship between headache and gender on the one hand and noise-intolerance on the other hand. However, other (related) factors may be important in the development of noise intolerance. More research is needed in order to get insight into the role of these (neuro) psychological/physiological mechanisms in the development of chronic whiplash associated symptoms.

REFERENCES

1. Barnsley, L., Lord, S. & Bogduk, N. (1994). Clinical review: Whiplash Injury. *Pain,* 283-307.

2. Dvorak., J. (1998). Soft-Tissue Injuries of the Cervical Spine: Classification and diagnosis. In: Gunzburg, R. & Szpalski, M. (eds). *Whiplash Injuries. Current concepts in prevention, diagnosis, and treatment of the Cervical Whiplash Syndrome.* Philadelphia: Lippincott- Raven publishers, 53-60.

3. Blokhorst, M.G.B.G., Swinkels, M., Lof, O., Lousberg, R. & Zilvold, G. (2002a). The Influence of State related Factors on Focused Attention Following Whiplash Associated Disorder. *Journal of Clinical and Experimental Neuropsychology,* 24, 471-478.

4. Spitzer WO, Skovron ML, Salmi LR, et al. (1995). Scientific monograph of the Quebec task force on whiplash-associated disorders: redefining "whiplash" and its management. *Spine,* 20,7-73.

5. Kessels, R.P.C., Keyser, A., Verhagen, W.I.M. & van Luijtelaar, E.L.J.M. (1998). The whiplash syndrome: a psycho-physiological and neuropsychological study towards attention. *Acta Neurologica Scandinavica,* 97, 188-193.

6. Radanov, B.P., Sturzenegger, A. & Di Stefano, G. (1997). Long-term outcome in whiplash injury. In: Mitchell M. (ed). *The Aftermath of Road Accidents. Psychological, social and legal consequences of everyday trauma.* London: Routledge, 70-88.

7. Tjell, C., Tenenbaum, A. & Rosenhall, U. (1999). Auditory function in whiplash-associated disorders. *Scand Audiol,* 28, 203-209.

8. Bohnen, N., Wijnstra, A., Kroeze, J. & Jolles, J. (1991a). A Psychophysical Method for Assessing Visual and Acoustic Hyperesthesia in patients with Mild Head Injury. In: N. Bohnen (ed), *Mild head injury and postconsussive sequelae: a study of brain and behavior relationships.* Maastricht: Datawyse Maastricht, 19-23.

9. American Hyperacusis Association. (2003). What is Hyperacusis? Internet

10. van Toor, T., Neijenhuis, K., Snik, A. & Blokhorst, M.G.B.G. (2003). Evaluation of auditory processing disorders after whiplash. In: *Auditory Processing Disorders. Development and evaluation of a test battery.* Nijmegen: Dissertation Radboud University, 109-129.

11. Brand, N., Schneider, N. & Arntz, P. (1995). Information processing efficiency and noise. Interactions with personal rigidity. *Personal Individual Differences,* 18 , 571-579.

12. Topf, M. (1989). Sensitivity to noise, personality hardiness and noise-induced stress in critical care nurses. *Environment and Behavior,* 21, 717-733.

13. Marriage, J. & Barnes, N.M. (1995). Is central hyperacusis a symptom of 5-hydroxytryptaminse (5-HT) dysfunction? *The Journal of Laryngology and Otology,* 109, 915-921.

14. Bohnen, N., Twijnstra, A., Wijnen, G. & Jolles, J. (1991b). Tolerance for light and sound of patients with persistent postconsussional symptoms six months after mild brain injury. In: N. Bohnen, (ed)., *Mild head injury and postconsussive sequelae: a study of brain and behavior relationships.* Maastricht: Datawyse Maastricht, 50-55.

15. Vanagaite Vingen, J., Pareja, J.A., Støren, O., White, L.R. & Stovner, L.J. (1998a). Phonophobia in migraine. *Cephalalgia,* 18, 243-249.

16. Vanagaite Vingen, J. & Stovner, L.J. (1998b). Photophobia and phonophobia in tension-type and cervicogenic headache. *Cephalalgia,* 18, 313-318.

17. Blokhorst, M.G.B.G., Lousberg, R., Vingerhoets, A.J.J.M., Winter, F.A.M. & Zilvold, G. (2002b). Daily hassles and stress-vulnerability in patients with a Whiplash Associated Disorder. *International Journal of Rehabilitation Research,* 25, 173-179.

18. Elsmore, T.F. (1994). Synwork 1: A PC-based tool for assessment of performance in a simulated work environment. *Behavior Research Methods, Instruments & Computers;* 26, 421-426.

19. Cremer R. (1998). *Mentaal Belastbaarheids Onderzoek*, Amsterdam: internal report TNO.

20. Blokhorst, M.G.B.G., Schrijver, P., Meeldijk, S., Hermans, R., Lousberg, R. & Zilvold, G. (in press). Cortisol responses to experimental stress in patients with Whiplash Associated Disorder. Accepted for publication in: *Psychology of Stress*. New York: Nova Sciences.

21. Arrindel, W.A. & Ettema, J.H.M. (1986). *Handleiding bij een psychopathologie-indicator.* Lisse: Swets & Zeitlinger.

22. Derogatis, L.R. (1983). *SCL-90R. Annual II. Clinical Psychometric research.* Towson: Clinical Psychometric Research.

23. Norusis, M.J. (1999). *SPSS-user Guide*: version 9.0. Chicago.

24. Gordon, K.G. (1986). Abnormal middle ear muscle reflexes and audiosensitivity. *British journal of Audiology,* 20, 95-99.

25. Pennebaker, J.W. (1988). *The Psychology of Physical Symptoms*. New York: Springer-Verlag.

26. Ferrari, R. (2002). Prevention of chronic pain after whiplash. *Emerg Med Journal,* 19, 526-530.

27. Barsky, A.J., Goodson, J.D., Lane, R.S. & Cleary, P.D. (1988). The amplification of somatic symptoms. *Psychosomatic Medicine,* 50, 510-519.

28. van Zomeren, A.H. & Saan, R. (1997). Whiplash. In: Deelman BG, Eling PATM, de Haan EHF, Jennekens-Schinkel A & van Zomeren AH (Eds.), *Klinische neuropsychologie*. Amsterdam: Boom, 290-298.

29. Gimse, R., Björgen, I.A., Tjell, C., Tyssedal, J.S. & Bö, K. (1997). Reduced cognitive functions in a group of whiplash patients with demonstrated disturbances in the posture control system. *Journal of Clinical and Experimental Neuropsychology*, 19, 838-849.

30. Michaelson, P., Michaelson, M., Jaric, S., Latash, M.L., Sjolander, P., Djupsjobacka, M. (2003). Vertical posture and head stability in patients with chronic neck pain. *J Rehabil Med.*, 35(5), 229-235.

31. Lidbeck, J. (2002). Central hyperex citability in chronic musculoskeletal pain: a conceptual breakthrough with multiple clinical implications. *Pain Res Managem.*, 7, 81-92.

32. Sterling , M., Jull, G., Vizenzino, B., Kenardy, J. (2003). Sensory hypersensitivity occurs soon after whiplash injury and is associated with poor recovery. *Pain,* 104(3), 509-517.

33. Klein, M. (1997). *Cognitive Aging, Attention and mild traumatic Brain Injury* (Thesis). Maastricht: Neuropsych. Publishers.

34. Wiethof, M. (1997). *Task analysis is heart work* (Thesis). Delft: University Press.

35. Hockey, G.R.J. (1986). Changes in operator efficiency as a function of environmental stress, fatigue and environmental rhythms. In: Boff, K.R., Kaufmann, L. and Thomas, J.P. (eds.). *Handbook of Perception and Human Performance*, vol 2. New York: Wiley.

Chapter 5

The influence of state-dependent factors on focused attention following Whiplash Associated Disorder

Mariëtte Blokhorst[1], Minke Swinkels[1],
Onno Lof[1], Richel Lousberg[1, 2], Gerrit Zilvold[1, 3.]

[1] Roessingh Research and Development, Enschede
[2] Dept. of Psychiatry and Neuropsychology, University of Limburg, Maastricht
[3] University of Twente, Enschede

Published in: Journal of Clinical and Experimental Neuropsychology 2002; 24, 471-478

INTRODUCTION

Attention deficits resulting from a Whiplash Associated Disorder (WAD) have been the subject of investigation in the last decade. The results indicate that the nature of the attentional problems is related to divided and sustained attention.[1-3] In general, WAD patients are slower responding on all kinds of time-pressure tasks compared to healthy persons, while the performance on self-paced tasks is not different.[3]
There seems to be no deficit of focused attention (the capacity to select relevant information for processing and to ignore irrelevant material).[2-6] However, many WAD patients complain that they are easily distracted in daily life and have difficulty ignoring irrelevant stimuli (e.g. concentrate on a conversation at a cocktail party).[2,7]

Focused attention is typically indexed by the Stroop Colour Word Test.[8] The Stroop test is a perceptual interference task and is comprised out of three parts: the reading of colour names printed in black ink (subtask 1), the naming of coloured rectangles (subtask 2), and the naming of colours when printed as letters in ink of a conflicting colour (subtask 3). In this last subtask, the automatic reading response must be suppressed in order to meet the demands of the test. The difference in time, required for finishing subtask 2 and 3, has often been taken as a measure of interference susceptibility.[9]
The discrepancy between 'interference' complaint and test results has also been recognised in patients with closed-head injury.[6,10,11] Patients with closed-head injury are slower responding on all Stroop tasks compared to healthy subjects, but interference-scores lay in the normal range, which means that there are no signs for focused attention problems.
Bohnen et al. (1991a) have hypothesized that the Stroop test may not be sufficiently demanding to elicit subtle cognitive difficulties and suggested that this test does not reflect the complexity of daily life.[10] Therefore, they added a modified colour-word interference condition (subtask 4) in which a box was drawn around one fifth of the items comprising the colour-word subtask. On the boxed items, subjects were asked to read the word rather than name the colour of the print. The different instructions imply that individuals have to shift their attention continuously during the execution of the task. As a result, this task is more complex than the classical Stroop task. Shifting attention can be described as the process of alternately monitoring two or more sources of input.[3] This modified subtask has proved to be a sensitive method to discriminate head injured patients from healthy controls.[10,12] Results showed that WAD patients are significantly slower responding on this

modified interference task compared to healthy persons, but there are no signs for specific attention problems.[3] The first aim of the present study is to replicate the study of Klein (1997) and to investigate whether the modified Stroop task is a more sensitive method than the classical Stroop version for assessing an attention deficit of WAD-patients.[3] The question is whether WAD patients are disproportionately slow on subtask 4 (related to subtask 2) as compared to control subjects. A significant difference would indicate subtle attention difficulties in WAD patients. This would correspond to WAD patients' complaint of interference susceptibility and attentional shifting problems in daily life.

The most important issue, addressed in this study, is the possible relationship between emotions (e.g. general tension, anxiety), pain (headache, neck pain) and fatigue on the one hand and cognition on the other hand. It is known that pain, fatigue and emotional factors as tension or anxiety have a negative influence on cognitive processes.[11,13-20] This implies that the level of pain, fatigue or anxiety is possibly of influence on the task performance in test and daily life situations. Previous results have shown that, (apart from age, practice or personality factors), sub-optimal health (e.g. pain) may influence performance on the Stroop test.[3,16,21] In an extensive review Radanov et al. (1996) argue that these 'state factors' are probably important factors causing cognitive impairments in WAD patients: 'An impairment in the long term may result from pain, medication, or psychological problems resulting from difficulties in adjusting to trauma-related symptoms' (p. 393).[14] Radanov et al. (1999) found significant negative correlations between emotional factors (state-anxiety, depression), and pain-intensity at the moment of testing on the one hand and performance on a divided attention task and a working memory task on the other hand.[18]
In order to gain more insight into the relationship between state-factors (e.g. pain, fatigue, tension and anxiety) and cognitive functioning in WAD patients, we examined to what extent the performance on the modified Stroop task is influenced by pain (neck pain or headache), fatigue, anxiety or general tension.

Based on previous results, it is hypothesised that the Stroop subtasks 1 through 4 have an increasing level of complexity, which means that response latencies increase for the different subtasks, both in WAD patients and in healthy individuals.[3,10,22] It is expected that WAD patients respond significantly slower on the Stroop tasks and that they are disproportionately slow on the modified subtask, compared to healthy subjects.[3] It is further hypothesized that the state variables are significant predictors for the performance on the Stroop subtasks and the interference scores. With respect to the state factor 'pain' it seems relevant to make a distinction between the intensity of pain and pain-localisation. As Radanov et al. (1992) have stated, especially headache, due to cervical pathology, seems to be related to the impaired attentional functioning of WAD patients.[23] We assume therefore that, especially the intensity of headache is related to the response latencies of the Stroop task in WAD patients.

METHODS

Participants

Forty-eight WAD patients, referred to a rehabilitation centre for treatment because of chronic whiplash related complaints, participated in a research project of which this study was the first part. In the second part of the project, an experiment was performed concerning the relationship between noise-intensity and attention, with the same subjects. Because of the coherence of this manuscript, it was decided to publicise the results of this second part later on. The patients in this study (30 females and 18 males) had a mean age of 33.83 years (*SD*=6.86). The injury occurred more than six months before testing, which means that all patients were in the chronic phase (*mean interval*= 47.17 months; *SD*=24.04). All patients encountered the whiplash injury in an automobile-accident (forty-six patients had a rear-end collision and two patients had a side-collision); none was to blame for the accident. All patients were still in litigation. Patients suffering from migraine before the whiplash injury were excluded, because research has shown that this is a complicating factor which has a prognostic value in the course of the whiplash syndrome.[24] Patients who reported that they had lost consciousness after the whiplash injury, had recent narcoses or pre-morbid head injury were also excluded, to eliminate the possibility of significant head trauma. Psychiatric comorbity was another exclusion criterion.

Half of the subjects had a low educational level (12 years of education) and the other half had a high educational level (14 years of education). Forty-eight percent of the patients were able to work, while fifty-two percent had a worker's compensation. Following the Quebec Task Force's clinical-anatomic axis that corresponds to severity of the whiplash injury, this study concerns only patients with chronic complaints after a WAD, grade I and II. This means neck complaints of pain, stiffness, or tenderness eventually accompanied by muscular-skeletal sign(s).[25]

Forty-eight healthy control subjects were selected, matched for sex, educational level and age. Research has shown that these variables are influencing the performance of the Stroop task.[9,22] Most of the control subjects worked in the Rehabilitation Clinic or in the Research Department. Twenty-one percent of the control subjects were students or housekeepers. None of the participants reported to be under treatment with medication. At the moment of testing, none of the subjects had used medication of influence on the central nervous system. All subjects gave their written informed consent. A medical ethical committee approved the study.

Materials

Stroop task

The Stroop Colour Word Interference Test[8], as available in the Netherlands[9], was used in the present study. Time, taken to read 100 words, was recorded for the word, colour, and colour-word subtask (subtask 1 - 3). The modified colour-word subtask (subtask 4) as described by Bohnen et al. (1991) was also administered.[10]

State-dependent variables: Headache, Neck pain, Fatigue, Tension

Subjective state-dependent feelings were measured by means of Visual Analogue Scale (VAS). Patients were asked to rate the level of headache, neck pain, fatigue and tension just before and after the Stroop task was performed. A 10-cm line was provided with written anchors at the two extremes: e.g. 'no pain' and 'unbearable pain'.

STAI

State- and Trait anxiety was measured using the Dutch version of the State-Trait Anxiety Scale (STAI).[26, 27] This is a self-report measurement in order to assess two anxiety concepts: State-Anxiety (STAI-dy 1) and Trait-Anxiety (STAI-dy 2). The STAI-dy1, reflecting how the respondent feels at the moment of investigation, was used as a state-related variable. The STAI-dy 2 was used as a trait-variable, indicating a general tendency to react with fear.

Amsterdam Short-term Memory Test (ASMT)

The ASMT, a recently developed memory test to investigate suboptimal performance, was used as a validity check for the Stroop test scores.[28] This test is easy to perform and does not tax memory largely. Research has shown that patients with memory disorders due to closed head injury as well as patients with amnesic syndromes of various origins perform well on the test.[28] The test consists of thirty items and two practice items. In each item the subject is presented with five printed words from the same semantic category (for example, Holland, France, Belgium, England, Germany), which the subject has to read aloud and must try to remember. Then the subject is distracted with a simple written addition or subtraction task, which is to be solved mentally. Finally, five words from the same semantic category as before are presented. The subject has to indicate the three words that had been presented in the first series (for example: Russia, France, Germany, Greece, Belgium). The maximum score is ninety (thirty items x three words correct).

SCL-90

In order to check the relationship between global distress on the one hand and state related variables and Stroop performances on the other hand, the Dutch version of the SCL-90 was administered.[29] The SCL-90 is a self-report, multidimensional symptom checklist composed of 90 items, each describing a physical or psychological symptom.[29,30] The instructions require patients to respond on a 5-point scale (ranging from 'not at all' to 'extremely') to indicate how much an item has bothered them over the past week. The Global Severity Index (GSI) is a measure of general distress that is obtained from the eight sub-scale scores and other items of the questionnaire not included in these scores.

Procedure

First, participants filled in the four state-related VAS-scales and the STAI. Next, the modified Stroop task was conducted. Thereafter, subjects filled in the SCL-90 and the ASMT was executed. Finally, subjects were debriefed.

Data analyses

Statistical analyses were performed with the Statistical Package for Social Sciences.[31] MANOVA for repeated measures were applied in order to compare the scores on the four different Stroop tasks for the WAD group and the Control group. Two interference scores were calculated for both groups: first, the classical interference score: response time of subtask 3 minus the response time of subtask 2. The second interference score was based on the modified Strooptask: subtask 4 minus subtask 2.

A frequency distribution of the ASMT was performed and means of both groups were calculated, to check for validity of the Stroop scores.
Non-parametric tests were used to test the differences in both groups on the VAS-scales, the State-anxiety scales and GSI-scale. Next, a Spearman correlation matrix was calculated, to investigate the correlation between the several scales in the WAD group.

Because the distribution of the state scores in the control group was skewed, it was decided to test the relationship between the state variables (independent variables) and the Stroop conditions (dependent variables) in the WAD group, by means of multiple regression analyses. Other relevant variables on personal status and global distress were included in the model, to control for *confounding or mediating* factors.
Next, the relationships between the two interference measures (dependent variables) and the state-variables combined with educational level, sex, age and group, were investigated by means of linear regression analyses. The level of significance was generally set at $P=0.05$.

RESULTS

Results on the modified Stroop task

Mean scores and standard deviations of the four Stroop subtasks are presented in Table 1. In addition, the two mean interference scores of both groups are listed.
Normality tests (a combined skewness and kurtosis test)[32] revealed that the data of the Stroop tasks were not distributed normally. Along the lines described by Hair et al. (1998), data of the Stroop subtasks and the interference scores were transformed.[33] The inverse transformations resulted in normally distributed data.
In order to investigate whether the response latencies increase from subtask 1 through 4, MANOVA was conducted with the Stroop subtasks (4) as within factor and Group (WAD group vs. Control group) as between factor. The results showed a significant main effect for the Stroop subtasks ($F_{(3,91)}=629.8$; $P<0.001$) and a main effect for Group ($F=14.14$; $P<0.001$). Univariate analyses showed significant differences between the two groups on every subtask (see Table 1). There also was a significant interaction effect ($F_{(3,91)}=7.11$, $P<0.001$).
The same analysis was performed on the two different interference-scores. Results revealed no significant differences between the WAD group and the Control group for the 'classical' interference score (Interference 1: $P=0.09$;

Table 1: Mean time and standard deviations (in seconds) of four Stroop subtasks and two interference scores in the WAD- and the Control group.

	WAD Group (N=48)		Healthy Group (N=48)		
	M	(SD)	M	(SD)	F
Subtask 1	50.6	(14.4)	40.4	(6.4)	21.427***
Subtask 2	64.8	(18.1)	54.1	(10.4)	10.232**
Subtask 3	106.6	(52.3)	84.9	(20.3)	7.462**
Subtask 4	126.9	(64.9)	99.4	(23.5)	8.074**
Interference 1	41.8	(38.6)	30.8	(14.6)	1.686
Interference 2	62.1	(51.2)	45.3	(18.4)	3.148*

- P-values refer to univariate analyses of the inverse-scores of the four subtasks
* P< 0.05 one sided
** P< 0.01 one sided
*** P<0.001 one sided

one-sided). However, the interference score of the modified subtask was significant (Interference 2: P=0.04; one-sided).
To control for invalid Stroop scores, the ASMT was used. Frequency distributions of the ASMT were calculated and results revealed a skewed distribution in both groups.
Inspection of the data revealed three outliers (more than two standard deviations below the mean). The difference between both groups disappeared when these outliers were excluded (mean in WAD group: 86.06, *SD*: 3.5; mean in control group: 87.2, *SD*: 2.2). Again, a MANOVA was conducted with the Stroop subtasks (4) as within factor and Group (WAD group vs. Control group) as between factor. Despite the fact that the differences between the groups became smaller on all subtasks, the differences remained significant.

Relationship between Stroop performance and state variables

Mean scores and standard deviations of the state variables, the trait-anxiety variable and the GSI are presented in Table 2.
Mann-Whitney U tests revealed that the two groups significantly differed on all the state-variables and the GSI (Table 2). Independent t-test revealed a significant difference on the STAI-dy 2 between both groups (t= 6.8; P<0.001). The correlation matrix showed that headache, neck pain and fatigue are

Table 2: Means (and SD) on the VAS-scales, the STAI-dy 1 & 2 and GSI-scale in the WAD- and the Control group.

	WAD Group (N=48)		Control Group (N=48)		
VAS Scales	M	(SD)	M	(SD)	P
Headache	26.35	(20.4)	2.53	(4.7)	< 0.001
Neck pain	35.95	(20.6)	2.65	(5.0)	< 0.001
Fatigue	36.25	(23.8)	7.77	(11.7)	< 0.001
Tension	18.94	(19.6)	5.92	(14.7)	< 0.001
STAI-dy1	37.77	(9.2)	30.04	(6.1)	< 0.001
STAI-dy2	43.70	(10.4)	30.90	(7.5)	< 0.001
GSI	172.00	(49.7)	105.00	(17.0)	< 0.001

moderately strong correlated (see Table 3). The variables related to tension, anxiety (STAI-dy1 & 2) and the GSI-scale are significantly related to each other, but not related to pain and fatigue.

In order to investigate the relationship between the state variables and the Stroop subtasks, multiple linear regression analyses were performed (each subtask as a dependent variable). The three outliers on the ASTM were removed from further analyses, because these might indicate non-valid Stroop scores. Because of co-linearity between the state variables, these variables were introduced as predictor variables in separate analyses. In first instance, this state variable was analysed alone and then together with GSI, STAI-dy2 (trait-anxiety) and some subject characteristics (sex, age, educational level, working status and duration of complaints).

Table 3: Spearman Rho correlation coefficients between state variables, trait-anxiety and GSI-scale in the WAD-group.

	Neck pain	Fatigue	Tension	STAI-dy1	STAI-dy2	GSI
Headache	R=0.66; P=.001	R=0.40, P=.006	R=0.35; P=.02	R=0.10; n.s.	R=0.13; n.s.	R= 0.09; n.s.
Neck pain		R=0.50, P=.001	R=0.36; P=.01	R=0.20; n.s.	R=0.27; n.s.	R= 0.05; n.s.
Fatigue			R=0.50; P=.001	R=0.01; n.s.	R=0.25; n.s.	R=-0.08; n.s.
Tension				R=0.53; P<.001	R=0.43; P=.002	R= 0.29; P=.05
STAI-dy1					R=0.64; P=.001	R= 0.44; P=.002
STAI-dy2						R= 0.73; P=.001

Table 4: Regression analyses in the WAD-group: prediction of the inverse scores of Subtask 1 and 4 out of Headache and other subject characteristics (n=45).

	Subtask 1				Subtask 4			
	B	SE B	ß	P	B	SE B	ß	p
Model 1*								
Constant	-.0246	.001			.0169	.001		<.001
Headache	-.0001	.001	-.508	.001	<-.0001	<.001	-.397	.008
Model 2*								
Constant	.0199	.001		<.001	.0098	.001		<.001
Headache	-.0001	.001	-.487	.030	<-.0001	<.001	-.389	.001
Educational level	.0025	<.001	.262	.003	.0020	.001	.414	<.001
Duration of Complaints	<.0001	<.001	.359	<.001	<.0001	<.001	.358	.001
Working status	-	-	-	-	-.0013	.001	-.262	.016

• Subtask 1: R2=.26 for model 1; R2= .44 for model 2;
• Subtask 4: R2=.16 for model 1; R2= .56 for model 2;
WAD=Whiplash Associated Disorder

Results revealed that a model, which consists of a constant together with the variables headache, educational level, and duration of complaints, predicts the results on the four Stroop subtasks most optimal (see also Table 4). Total explained variance for subtask 1 is 44%; for subtask 2: 49%; for subtask 3: 45%; and for subtask 4: 56%. Headache alone predicts 26% of the variance on subtask 1, 16% of the variance on subtask 2, 12% of the variance on Subtask 3 and 16% of the variance on subtask 4.
The other state variables, the GSI and trait-anxiety showed not to be significant predictors.
The model fit (R^2) varied from 0.001-0.09 for the different dependent variables (subtask 1-4).

In order to investigate the relationship between the state variables and the interference scores, similar regression analyses were performed (each interference score as a dependent variable). Interference score 1 was only predicted by educational level (R^2=0.24; p=0.001). The second interference score was significantly related to headache, in combination with educational level and working status (R^2=0.43; p=0.001).

DISCUSSION

The results showed that response latencies increase significantly for both WAD patients and healthy control subjects on the four different subtasks of the modified Stroop task. Furthermore, the results revealed that WAD patients are significantly slower compared to healthy individuals on every subtask of the Stroop. This general slowness of information processing is in accordance with previous studies.[2-5]
The results showed that the differences between WAD patients and healthy control subjects increase from subtask 1 through 4. In other words, WAD patients are increasingly slower in responding when tasks become more complex and demand more attention compared to healthy participants. With respect to focused attention, no differences could be demonstrated between the two groups on the classical-interference score. However, the modified Stroop task (subtask 4) did give extra information, compared to the classical Stroop task, because of the significant interference-score. This implies that WAD patients have subtle attentional difficulties, which become manifest only in complex tasks.
The second part of this study confirmed the expectation that headache is related to task performance. As was expected, a significant relationship between intensity of headache and Stroop performance was found. Fourteen to twenty-six percent of the variance of the subtasks can be explained by headache. The negative correlation between headache-intensity and the inverse Stroop scores implies that subjects with severe headache tend to have greater response latencies than subjects with low levels of headache. Besides pain-intensity, also pain-location (headache vs. neck pain) seems to be important. The general disruptive effect of pain on attention has been noted in some previous studies[13-16] and has recently been described in a cognitive-affective model of the interruptive function of pain.[34]

This study demonstrated that there is no relationship between the more ‘somatic’ state factors (headache, neck pain, fatigue) and emotional factors (e.g. tension, state-anxiety, trait-anxiety or general feelings of distress).

The results of this study confirmed the complaint of WAD patients concerning interference susceptibility in daily life. It is possible that the interference susceptibility of WAD patients is also related to external factors such as noise and light, rather than the complex visual-cognitive distraction, which is investigated by the modified Stroop task. Given the fact that headache is negatively related to cognitive functioning, combined with the notion that headache patients are sensitive to noise[35], one might assume that external stressors such as intense noise or light stimuli, are moderating factors which influence the effect of pain on information processing. Especially patients with a high somatic awareness seem to be vulnerable for the disruptive effects of internal and external stimuli on attention.[36]

The aforementioned results imply that, for clinical practice, neuropsychological test results of WAD patients have to be interpreted with caution: scores on attention tasks of WAD patients are just a momentary result and are, as this study indicated, dependent on the amount of headache present at the moment of investigation and may be also dependent on external circumstantial factors.

To get more insight into the effects of state factors on cognitive functioning in WAD patients, future studies have to investigate the relationship between these internal state factors (such as pain intensity, pain location, fatigue, tension) and attention performance, in combination with environmental state factors (such as noise-intensity, task-complexity) and coping styles (e.g. somatic awareness, catastrophic thinking, avoidance behaviour, aggravation).

REFERENCES

1. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical Review: Whiplash Injury. *Pain, 58,* 283-307.

2. Van der Vlugt, H., & Erven-Sommers, J. van. (1992). Neuropsychologie en het whiplash-trauma. In A.J.E.M. Fischer, H., Kingma, J. & Pathijn, (Eds.), *Het whiplash-probleem.* (pp 159-177). Utrecht, The Netherlands: Bruna.

3. Klein, M. (1997). Cognitive Aging, Attention, and Mild Traumatic Brain Injury. *Thesis*; Maastricht: Neuropsych Publishers.

4. Kischka, U., Ettlin, T.M., Heim, S., & Schmid, G. (1991). Cerebral symptoms following whiplash injury. *European Neurology, 31,* 136-140.

5. Etlin, T.M., Kischka, U., Reichmann, S., Radii, E.W., Heim, S., à Wengen, D., & Benson, D.F. (1992). Cerebral symptoms after whiplash injury of the neck: a prospective clinical and neuropsychological study of whiplash injury. *Journal of Neurology, Neurosurgery and Psychiatry, 55,* 943-948.

6. Van Zomeren, A.H., & Saan, R. (1997). Whiplash. In B.G. Deelman, P.A.T.M. Eling, E.H.F. de Haan, A. Jennekens-Schinkel, A.H. van Zomeren (Ed.), *Klinische neuropsychologie* (pp. 290-298). Amsterdam: Boom.

7. Van Zomeren, A.H., & Brouwer, W.H. (1994). *Clinical Neuropsychology of Attention*. New York: Oxford University Press.

8. Stroop, J.R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18,* 643-662.

9. Hammes, J.W.G. (1978). De Stroop Kleur-woord Test; Handleiding. Lisse: Swets & Zeitlinger.

10. Bohnen, N., Jolles, J. & Twijnstra, A. (1991a). Modification of the Stroop Color Word Test improves differentiation between patients with mild head injury and matched controls. In N. Bohnen, (Ed.), *Mild head injury and postconcussive sequelae: A study of brain and behavior relationships* (pp 24-28). Maastricht: Datawyse Maastricht.

11. Batchelor, J., Harvey, A.G., & Bryant, R.A. (1995). Stroop colour word test as a measure of attentional deficit following mild head injury. *The Clinical Neuropsychologist, 9 (2),* 180-186.

12. Bohnen, N., Jolles, J. & Twijnstra, A. (1991b). Neuropsychological deficits in patients with persistent symptoms six months after mild head injury. In N. Bohnen, (Ed.), *Mild head injury and postconcussive sequelae: A study of brain and behavior relationships* (pp 56-62). Maastricht: Datawyse Maastricht.

13. Taylor, A.E., Cox, C.A., & Mailis, A. (1996). Persistent neuropsychological deficits following whiplash: evidence for chronic mild head traumatic brain injury*? Arch Phys Med Rehab, 77,* 529-535.

14. Radanov, B.P., & Sturzenegger, M. (1996). Predicting recovery from common whiplash. *European Neurology, 36,* 48-51.

15. Eccleston, C. (1994). Chronic pain and attention – A cognitive approach. *British Journal of Clinical Psychology, 33*, 535-547.

16. Grisart, J.M. & Plaghki, L.H. (1999). Impaired selective attention in chronic pain patients. *European Journal of Pain, 3*, 325-333.

17. Olsnes, B.T. (1989). Neurobehavioral findings in whiplash patients with long-lasting symptoms. *Acta Neurologica Scandinavica, 80,* 584-588.

18. Radanov, B.P., Bicik, I., Dvorak, J., Antinnes, J., von Schulthess, G.K., & Buck, A. (1999). Relation between neuropsychological and neuroimaging findings in patients with late whiplash syndrome. *Journal of Neurology Neurosurgery and Psychiatry, 66*, 485-489.

19. Brand, N., & Jolles, J. (1987). Information processing in depression and anxiety. *Psychological Medicine, 17,* 145-153.

20. Vercoulen, J.H.M.M., Swanink, C.M.A., Fennis, J.F.M., Galama, J.M.D., Van der Meer, J.W.M., & Bleijenberg, G. (1994). Dimensional assessment of chronic fatigue syndrome. *Journal of Psychosomatic Research, 38 (5),* 383-392.

21. Dulaney, C.L. & Rogers, W.A. (1994). Mechanisms underlying reduction in Stroop interference with practice for young and old adults. *Journal of Experimental Psychology: Learning, Memory and Cognition, 20* (2), 470-484.

22. Mac Leod, C.M. (1991). Half a Century of Research on the Stroop Effect: An Integrative Review. *Psychological Bulletin, 109*, 163-203.

23. Radanov, B.P., Hirlinger, I., Di Stefano, G., & Valach, L. (1992). Attentional processing in cervical spine syndromes. *Acta Neurologica Scandinavica, 85,* 358-362.

24. Radanov, B.P., Dvorak, J. (1996). Impaired cognitive functioning after whiplash injury of the cervical spine. *Spine, 21,* 392-397.

25. Spitzer, W.O., Skovron, M.L., Salmi, L.R., et all. (1995). Scientific monograph of the quebec task force on whiplash-associated disorders: redefining "whiplash" and its management. *Spine,20 (7),*7-73.

26. Ploeg van der,H.M. , Defares, P.B., Spielberger, C.D. (1981). Handleiding bij de Zelf-Beoordelings Vragenlijst. Lisse: Swets & Zeitlinger.

27. Spielberger, C.D., Gorsuch, R.L., Lushene, R.E. (1993) *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.

28. Schmand, B., de Sterke, S. & Lindeboom, J. (1999). *Amsterdamse Korte Termijn Geheugen Test*. Lisse: Swets & Zeitlinger Publishers.

29. Arrindel, W.A. & Ettema, J.H.M. (1986). *Handleiding bij een psychopathologie-indicator.* Lisse: Swets & Zeitlinger.

30. Derogatis, L.R.. (1983). *SCL-90R. Annual II. Clinical Psychometric research.* Towson: Clinical Psychometric Research.

31. Norusis, M.J. (1999). *SPSS-user Guide*: version 9.0. Chicago.

32. D'Agostino, R.B., Balanger, A. & D'agostino jr., R.B. (1990). A suggestion for using powerful and informative tests of normality. *The American Statistician, 44*, 316-321.

33. Hair, J.S., Anderson, R.E., Tatham, R.L., Black, W.C. (1998). Multivariate data analysis. London: Prentice Hall.

34. Eccleston, C. & Crombez, G. (1999). Pain demands Attention: A Cognitive-Affective Model of the Interruptive Function of Pain. *Psychological Bulletin, 3,* 356-366.

35. International Headache Society (I.H.S.). (1988). Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia, 8*.

36. Eccleston, C., Crombez, G., Aldrich, S. & Stannard, C. (1997). Attention and somatic awareness in chronic pain. *Pain, 72*, 209-215.

Chapter 6

Influence of background noise and state-dependent factors on attention in Whiplash Associated Disorder

Mariëtte Blokhorst[1], Onno Lof[1], Richel Lousberg[1, 2], Gilles van Luijtelaar[3], Paul Eling[3], Willem Kersing[4] & Gerrit Zilvold[1,5].

[1] Roessingh Research and Development, Enschede
[2] Department of Psychiatry and Neuropsychology, University of Limburg, Maastricht
[3] NICI, Biological Psychology, Radboud University, Nijmegen
[4] Medisch Spectrum Twente, Enschede
[5] University of Twente, Enschede

Submitted for publication

INTRODUCTION

Several symptoms are related to a Whiplash Associated Disorder (WAD) such as pain, fatigue, dizziness, attention problems, increased irritability, sensitivity for light and noise-intolerance.[1-3] A WAD is a hyper-extension / flexion trauma of the neck, caused by an injury (often a car accident).[4] Recent studies have shown that, despite normal audiograms, patients with a chronic WAD are more intolerant to noise compared to healthy persons, as was indicated by lowered 'uncomfortable loudness' or UCL-levels and higher noise-intolerance levels of various intensities.[5-7] These results confirm the subjective complaint of WAD patients that moderate everyday sounds are more annoying for them since the whiplash injury (e.g. screaming children, silverware or dishes, even lower steady noises such as computer fans, party noise).[8]
This noise-intolerance is also related to the frequently expressed complaint of WAD patients having difficulty of focusing attention to a conversation, while neglecting other sources of environmental noise.[3,7,9,10]
There is indeed evidence that WAD patients have a subtle focused attention deficit, as was demonstrated by means of the modified Stroop task, which is a more complex version of the classical Stroop task.[3]

Given the strong evidence that WAD patients are intolerant to noise, the aim of the present study is to investigate whether external noise (e.g. cocktail-party noise) acts as a distracter when patients have to concentrate on other, complex auditory stimuli.
It was hypothesised that the intensity level of background noise is negatively related to the performance on a simultaneously presented complex auditive attention task, both in WAD patients and healthy persons. This negative 'noise' effect was not expected in case of an easy auditive attention task. It is known that noise in general (especially loud, intermittent, unpredictable and uncontrollable noise) is an environmental stressor in healthy persons, which increases the task difficulty and therefore effects complex mental performance negatively, by interfering negatively with working memory processes and reducing the accuracy.[11,12] Recent studies have shown an increased noise-intolerance in WAD patients,[5] as well as a focused attention deficit.[3] It was expected that WAD patients perform significantly worse on a complex auditive attention task with noise, compared to healthy persons, especially in conditions with high background noise.
Recent studies have investigated the influence of sub-optimal health or state-dependent factors, for example 'pain' and 'fatigue', on cognitive functioning.[3,13-16] In WAD patients, headache is negatively related to perform-

ances on the Stroop task as well as to noise-intolerance.[3,5] Therefore, it was hypothesised that the level of 'headache', 'neck pain' and 'fatigue' are significant predictors in explaining the variance of the performance on a complex auditive attention task, especially in conditions with high background noise.

Another important state-dependent factor is emotional distress or tension. WAD patients exhibit a great deal of emotional distress following the onset of physical symptoms.[17-20] There is ample evidence that emotional distress, for example depression or anxiety, is negatively related to cognitive functioning.[21-23] It was hypothesised that emotional distress is negatively related to the performance on a complex auditive attention task in WAD patients, especially in situations with a high level of background noise. External noise was supposed to have a disrupting effect on information processing in those persons who are emotional unstable at that moment, because the noise serves as another stressor.[11]

In order to manipulate the level of state-dependent factors, an experimental condition was designed in which subjects were exposed to strong cocktail-party noises for a while, with the expectation that this would induce an increase in state-dependent complaints and subsequently also an worsening of performance on a complex auditive attention task in the presence of background noise.

METHODS

Participants

Forty-eight WAD patients, referred to a rehabilitation centre for treatment because of chronic whiplash related complaints, participated in a research project of which the present study was the second part. The results of the first part of this project were published before.[3] The patients in this study (30 females and 18 males) had a mean age of 33.8 years (SD=6.8). All patients were in the chronic phase (mean interval =47.17 months; SD=24.04), after they had encountered a whiplash injury in a car accident. Exclusion criteria were: premorbid migraine, premorbid head injury, premorbid psychiatric treatment, patients with recent general anaesthesia or who reported that they lost consciousness after the whiplash injury. Because educational level is of influence on the tasks used in this experiment, this variable was kept under control by matching: half of the subjects had a low educational level (12 years of education) and the other half had a high educational level

(15 years of education). Nearly half of the subjects were able to work (48%), while the other half had a worker's compensation (52%). Following the Quebec Task Force's clinical-anatomic axis, that corresponds to severity of the whiplash injury, this study concerns only patients with chronic complaints after a WAD Grade I and II. This means neck complaints of pain, stiffness, or tenderness eventually accompanied by muscular-skeletal sign(s).[4]
Forty-eight healthy control subjects were selected, matched for gender, educational level and age (mean age: 33.6 years; *SD*=6.9), because these variables are influencing the performance on cognitive tasks used in this experiment and so must be kept under control.[24,25] Patients were only included if they had a normal peripheral hearing (threshold at 500, 1000, 2000 and 4000 Hz; 15dB HL or better) as was investigated by means of a standard audiological test procedure (pure tone and speech audiometry). At the moment of testing, none of the subjects had used medication of influence on the central nervous system. All subjects gave their written informed consent. A medical ethical committee approved the study.

Materials

Subjective perception of noise-intolerance and concentration in daily life

All WAD patients were asked three questions regarding their subjective perception of noise-intolerance and problems with focused attention in noisy surroundings. Patients were asked to answer the level of change on a Visual Analogue Scale (VAS): a 10-cm line was provided with written anchors at the two extremes: e.g. 'no change' and 'a lot of change'.

Question 1 was:
'Do you think your concentration has altered since the whiplash injury?'
Question 2 was:
'Do you perceive noise in general as more annoying since the whiplash injury?'
Question 3 was:
'Do you think you are more distracted by noises since the whiplash injury?'

Amsterdam Short-Term Memory Test (ASMT)

The ASMT was used to investigate sub-optimal performance in subjects.[3] It serves as a validity check for the performances on experimental tasks.[26] This test is easy to perform and does not tax memory largely. Instructions and procedure have been published before.[3]

Audio-material

All audio information was submitted to the subjects by means of a CD-player (trademark: Philips). The target- and distracting stimuli were simultaneously presented over loudspeakers in a sound-attenuated room in which the subject was seated. Two loudspeakers were equally spaced before the subject around the frontal hemisphere ± 30° to the left and to the right, at a distance of 1.5m from the subject and at a height of approximately 1.2m (approximately the height of the head of the subject when seated).
Two other, smaller, loudspeakers were spaced behind the subject, ± 30° to the left and to the right, at a distance of 1.5m, in order to get a Dolby Surround effect, which simulates real life noise rather well. The loudspeaker outputs were matched in dB-A output by means of a sound level meter (LC-electronics: CB-2050).

Auditive arithmetical task

An easy arithmetical task was developed in order to investigate the influence of external noise on tasks, which require a minimum of concentration, because of the subjects' highly trained arithmetical skills. During this task, subjects had to add up digits between 1 and 6 (e.g. 2+3; 1+6). Twelve parallel versions were developed. Twenty-two responses were asked for each subtest. The interval between consecutive digits remains constant and was 3 seconds. The arithmetical tests were digitally recorded in a studio in order to prevent uncontrollable noise recording. Three conditions were developed: in the first condition, four versions with target stimuli of 60dB and no background noise were presented to subjects (condition 1). An intensity of 60dB was chosen in order to be sure that subjects are able to perceive the target stimuli well. It is known that the healthy human ear is well able to perceive speech of 60dB: the performances on the so-called 'Word-recognition test' revealed an average of 100% correct responses, with target stimuli of 60dB when offered in a silent room.[27] The second condition consisted of four versions with target stimuli of 60dB and a background noise of 55dB. This background noise consisted of standardised cocktail-party noise, used by audiologists as an auxiliary tool in the research of speech-discrimination or speech- intelligibility (so called 'real-life environment sound examples; trademark: Widex Compact Disc). A stimulus-noise ratio of 5dB was chosen, because the human ear is able to discriminate between those two intensities, as is tested by the standard speech-in-noise-test.[6] The third condition consisted out of target stimuli of 75dB and background noise of 70dB. To be sure, subjects were competent to add up, they got some practice items before they were included in the experiment.

Complex auditive attention task: Pasat

The Paced Auditory Serial Addition Task (Pasat) is a widely used neuropsychological test for the assessment of impairments in divided and sustained attention and is used in whiplash research on cognitive functioning.[25,28-32] While listening to a recorded series of single digits, patients have continuously to add up digits, always two at a time: the second to the first, the third to the second and so on, verbally reporting the results to the clinician. The interval between consecutive digits remains constant. The standard test consists of five trials containing 60 digits each. The interval between consecutive digits is shortened for each subsequent trial.[30] Because the standard version is very long with different stimulus-intervals, it was not suitable for this experiment. Therefore, it was decided to develop a series of relatively short parallel-versions, based on the Pasat principle. The purpose was to make a test that WAD patients can execute rather well in a quiet condition (without external noise). A pilot study revealed that most subjects (WAD patients and healthy persons) perform relatively well on a short 'Pasat' task, with a stimulus-interval of 3 seconds. Even normal scores on Pasat tests with a stimulus-interval of 2.0 seconds in WAD patients were reported.[32,33] However, deviating results have also been published with the PASAT test in WAD patients.[30,31,34] The Pasat is very sensitive in detecting subtle attention deficits[25] and requires strong concentration.[7]

Twelve parallel versions were developed consisting out of 28 digits between 1 and 6. The tests were also digitally recorded in a studio. In four of the twelve versions, the target stimuli (e.g. digits) were offered with an intensity of 60dB (condition 1: no noise). In another four versions, the target stimuli (e.g. digits) were offered with an intensity of 60dB and a background noise of 55dB (condition 2: moderate noise). Background noise consists out of the same cocktail party noise as mentioned above. In order to investigate the influence of stronger noise on attention performance, the last four versions are offered with an intensity of 75dB and a background noise of 70dB (condition 3: strong noise).
Because performances on the Pasat test are related to educational level,[35,36] subjects were selected and matched on educational level, as was mentioned earlier (see 'participants').

State- dependent variables: Headache, Neck pain, Fatigue, Tension

Subjective state-dependent feelings were measured by means of Visual Analogue Scale (VAS) (see also ‘Procedure’). Patients were asked to rate the level of headache, neck pain, fatigue and tension six times during the experiment (see figure 1: Procedure). A 10-cm line was provided with written anchors at the two extremes: e.g. ‘no pain’ and ‘unbearable pain’.

Symptom Check List-90

In order to check the relationship between global distress and performances on the Pasat task (in the various conditions) the Dutch version of the SCL-90 was administered.[37] The SCL-90 is a self-report, multidimensional symptom checklist composed of 90 items, each describing a physical or psychological symptom.[37,38] The instructions require patients to respond on a 5-point scale (ranging from ‘not at all’ to ‘extremely’) to indicate how much an item has bothered them over the past week. The Global Severity Index (GSI) is a measure of general distress that is obtained from the eight sub-scale scores and other items of the questionnaire not included in these scores. The subscales are anxiety, agoraphobia, depression, somatic complaints, insufficiency, sensitivity, hostility, sleeping problems.[37]

Spielberger Trait Anxiety Inventory

State- and Trait anxiety was measured using the Dutch version of the State-Trait Anxiety Scale (STAI).[39,40] This is a self-report measurement in order to assess two anxiety concepts: State-Anxiety (STAI-dy 1) and Trait-Anxiety (STAI-dy 2). The STAI-dy1, reflecting how the respondent feels at the moment of investigation, was used as a state-dependent variable and was measured six times during the experiment, just as the other state-dependent variables. The STAI-dy 2 was used as a trait-variable, indicating a general tendency to react with fear.

Procedure

Participants were invited for an interview on admission to the project. Person-related data were registered, subjects filled in some questionnaires (Spielberger Trait Anxiety Inventory, NEO-PI-R) and they were informed about the procedure of the project. Next, they went to an audiologist to exclude significant hearing loss.

Within one month after the audiological investigation, participants came to the laboratory for the first experiment of this project. As mentioned before, the results of the first part of the study have already been published.[3] On the next day, with a maximum test-interval of two weeks, subjects came to the laboratory for the second part of the study. First, participants filled in the state-dependent VAS-scales (State 1). Next, subjects performed the Pasat and the easy arithmetical task (the order of presentation was counter-balanced within the four groups (low- vs. high educational level group and whiplash vs. healthy control-subjects). Both tasks were presented in three different conditions (condition 1: no background noise; condition 2: background noise of 55dB; condition 3: background noise of 70dB). These three conditions were also counter-balanced within the different groups mentioned above.

Next, subjects filled in the state-dependent VAS-scales for the second time (State 2). The procedure was repeated in order to extend the reliability of the data and after this, subjects filled in the state-dependent VAS-scales for the third time (State 3). Half of the subjects underwent an experimental manipulation consisting out of listening to cocktail-party noise for 15 minutes (at a level of 70dB), whereas the other half of the subjects had a period of relaxation. After this, subjects rated on a VAS-scale the level of annoyance of the experimental condition and all subjects rated the state-dependent variables (State 4). At post-condition, the procedure of the pre-condition was repeated with parallel versions of the Pasat and the arithmetical task. At the end, subjects filled in the SCL-90.

Data analyses

Statistical analyses were performed with the Statistical Package for Social Sciences.[41] Because of non-normality of some of the data and because transformations were unsuccessful in obtaining normal distributed scores, non-parametric tests were used to test the difference between WAD patients and healthy subjects regarding the data on the subjective perception of noise-intolerance, ASMT, SCL-90, the state-dependent VAS-scales and the easy arithmetical task.

MANOVA for repeated measures was applied in order to analyse the data of the Pasat. The relationships between the state-dependent variables and Pasat in three different conditions were analysed by means of multiple regression analyses. Other relevant variables on personal status and duration of complaints were also included in the model. All reported P-values are two-tailed.

RESULTS

Subjective perception of noise-intolerance and concentration

The responses on the subjective perception of noise-intolerance and concentration are listed in Table 1.
The results revealed that WAD patients experience strong changes in their concentration since the whiplash injury. They perceive noise in general as more annoying and they are easily distracted by noise in their environment. A Mann-Whitney test revealed no significant differences between patients with a low- and with a high educational level on all the three questions. Furthermore, age, gender and duration of complaints are not related to the level of annoyance.

ASMT

Frequency distributions of the ASMT were calculated and results revealed a skewed distribution in both groups. Consequently, non-parametric tests were used. WAD patients perform significantly worse compared to healthy subjects (P=0.04). Two outliers were found on the easy arithmetical- or the complex task; these two were removed from further analyses. The difference between both groups was no longer significant, when these two outliers were excluded (mean in WAD-group: 86.06, *SD*: 3.5; mean in healthy group: 87.2, *SD*: 2.2; P=0.08).

SCL-90

The data of the SCL-90 were not normally distributed. Consequently, non-parametric tests were used. The results of Mann-Whitney tests revealed significant differences between WAD patients and healthy persons regarding all the sub-scales and the GSI (global severity index) (P<0.001). After

Table 1: Responses on VAS-scales (range: 0-100 mm) of WAD patients regarding three questions on concentration, noise-intolerance and distractibility, since the whiplash injury (n=47).

	Mean	SD
Altered concentration	69.7	19.7
Noise-intolerance	68.1	24.9
Noise-distractibility	67.5	23.0

applying Bonferroni corrections, no differences were found between the healthy groups with a low- and high educational level. In contrast, in the WAD group, Mann-Whitney tests showed that patients with a low-educational level exhibit significantly more complaints on the sub-scales Depression (P=0.01), Insufficiency (P=0.004), Hostility (P=0.006) and on the GSI (P=0.008), compared to the high educational WAD group, thus indicating more emotional distress.

STAI

As can be seen from the data in Table 2, WAD patients with a low educational level report more anxiety on the trait and on the two state-dependent anxiety scales. ANOVA tests (with Bonferroni corrections) showed significant differences between this low-educational WAD group and the other three groups on the trait-anxiety scale (all *P-values* < 0.001). The high educational WAD group differ significantly from the high educational Healthy group (P<0.002), but not from the low educational Healthy group.

Table 2: Means and standard deviations of WAD patients and healthy persons, divided in low- and high educational level, on the eight sub-scales of the SCL-90, the Global Severity Index and the Spielberg Trait and State Anxiety Inventory (STAI) (n=96).

	WAD-low	WAD-high	Healthy-low	Healthy-high
Anxiety	18.0 (6.5)	14.2 (3.5)	11.1 (1.8)	10.7 (1.3)
Agoraphobia	10.6 (4.3)	8.4 (2.1)	7.2 (0.5)	7.0 (0.2)
Depression	32.4 (12.8)	24.7 (8.0)	19.2 (4.2)	18.1 (2.9)
Somatic compl.	28.0 (8.9)	24.8 (6.8)	14.9 (3.5)	14.2 (2.5)
Insufficiency	27.9 (8.1)	20.9 (7.4)	11.9 (3.2)	10.5 (1.8)
Sensitivity	29.8 (13.2)	25.1 (6.9)	22.4 (5.1)	19.4 (2.2)
Hostility	11.2 (5.1)	8.3 (2.6)	7.2 (1.9)	6.6 (2.1)
Sleep problems	8.1 (3.5)	6.3 (3.5)	3.8 (1.5)	3.8 (1.2)
GSI	179.9 (55.9)	143.8 (35.5)	108.3 (20.4)	99.7 (11.8)
STAI-trait	49.1 (8.8)	37.7 (8.6)	32.6 (8.6)	29.0 (5.7)
STAI-state 3*	44.9 (9.4)	34.2 (7.2)	29.2 (7.0)	26.9 (5.1)
STAI-state 4**	45.8 (9.0)	38.3 (10.2)	29.0 (5.8)	26.8 (5.8)

* STAI-state 3 reflects mean scores on the state-anxiety scale just before the stress/relax period.
** STAI-state 4 reflects mean scores on the state-anxiety scale just after the stress/relax period.

With respect to the state-anxiety scales, ANOVA analyses revealed significant differences between the low educational WAD group and the other three groups on all moments (1 to 6); (*P*-values ranging from 0.02-0.001). At moment 1 (at baseline), the high educational WAD group did not differ from the high educational Healthy group. However, at all other moments the differences between these two groups were significant and as can be seen from the results presented in Table 2, the high educational WAD group is more anxious compared to the high educational Healthy group.

Results on the auditive arithmetical task

As mentioned before, frequency distributions showed two outliers on the easy arithmetical task as well as on the ASTM in the WAD group, which were removed from further analyses. Normality tests revealed that the data of this easy task were still not distributed normally. Transformations did not succeed to achieve normality. Therefore, non-parametric tests were used. Mann-Whitney tests revealed no significant difference between patients and the healthy group regarding condition 1 (no background noise) (see Table 3).

In contrast, the differences in the other two conditions between WAD patients and healthy control subjects were significant (condition 2: $P=0.01$; condition 3: $P=0.003$). Post-hoc analyses revealed that the difference between the low-educational WAD group and the low-educational Healthy group was significant for these two conditions (condition 2: $P=0.01$; condition 3: $P=0.005$), whereas the difference in both high-educational groups was not.

Table 3: Means and standard deviations of total errors on parallel Arithmetical-tasks for three conditions (1: no background noise; 2: 55dB background noise; 3: 70dB background noise) for WAD (experimental and control) patients and healthy (experimental and control) subjects, at pre- and post-condition.

	WAD (n=46)				Healthy (n=48)			
	Exp. group		Control group		Exp. Group		Control group	
	Pre-	Post	Pre-	Post	Pre-	Post	Pre-	Post
Condition 1: no noise	0.2 (0.5)	0.2 (0.9)	0.2 (0.4)	0.9 (0.4)	0.3 (1.0)	0.2 (0.6)	0.1 (0.4)	0.2 (0.6)
Condition 2: 55 dB	0.3 (0.7)	0.9 (2.1)	0.3 (0.8)	1.5 (2.0)	0.1 (0.4)	0.3 (0.5)	0.3 (1.6)	0.2 (0.5)
Condition 3: 70 dB	0.9 (2.1)	0.9 (2.7)	1.8 (4.1)	1.6 (3.1)	0.4 (1.0)	0.1 (0.3)	0.5 (1.8)	0.1 (0.3)

Results on the complex auditive attention task: Pasat

Normality tests showed that the data of the Pasat tasks were not distributed normally. Along the lines described by Hair (1998), the raw scores were log-transformed.[42] These transformations resulted in normally distributed data. The raw scores (total faults) on the Pasat in the three different noise-conditions (e.g. condition 1: 'no background noise', condition 2: 'background noise of 55dB', condition 3: 'background noise of 70dB') for the WAD and the healthy groups (pre- and post condition) are listed in Table 4.

In order to investigate whether the amount of faults is significantly increasing from condition 1 through 3 in time for the different groups, a MANOVA was conducted with 'Background noise-level' (3) (0dB, 55dB, 70dB) and 'Time' (2) (pre- and post condition) as within factors and 'Group' (2) (WAD group versus Healthy group), 'Condition' (2) (experimental vs. control) and 'Educational level' (2) (low/high) as between factors. The results showed a significant main effect for 'Background noise-level' (F (2, 94) =28.5; P=0.001): as can be seen from Table 4 the groups made more faults when background noise increases. There is also a main effect for 'Time' (F (1,95) =61.9; P<0.001) (taken all subjects together, they perform better at post-condition, indicating a practice effect) and a main effect for Group (F (1,95)=23.7; P<0.001) (WAD patients made more faults than healthy subjects). There is also a main effect for Educational level (F (1,95)= 23.0; P<0.001). Results demonstrated that the mean fault score on the Pasat of both low educational groups in the three conditions is higher compared to both high educational groups (low-educational groups: mean=57.3; sd=49.1; high-educational groups: mean=26.3; sd=34.4).

Table 4: Means and standard deviations of total errors on parallel PASAT-tasks for three conditions (1: no background noise; 2: 55dB background noise; 3: 70dB background noise) for WAD (experimental and control) patients and healthy (experimental and control) subjects, at pre- and post-condition.

	WAD (n=46)				Healthy (n=48)			
	Exp. group		Control group		Exp. group		Control group	
	Pre-	Post	Pre-	Post	Pre-	Post	Pre-	Post
Condition 1: no noise	8.3 (8.0)	8.3 (7.8)	8.0 (7.4)	7.2 (7.2)	4.4 (4.9)	2.2 (3.9)	6.7 (8.5)	4.2 (6.6)
Condition 2: 55 dB	10.1 (8.2)	11.2 (8.9)	8.1 (6.7)	9.6 (8.9)	4.6 (5.3)	2.4 (4.1)	6.5 (8.7)	4.5 (7.5)
Condition 3: 70 dB	12.4 (9.4)	10.4 (9.6)	9.9 (8.6)	10.3 (9.6)	4.7 (5.1)	2.5 (4.1)	6.7 (8.7)	4.7 (7.3)

The significant interaction effect between Noise-level by Group (*F* (2,94) =3.3; *P*<0.04) and inspection of the data showed that with increasing noise-level, WAD patients made more errors on the Pasat tasks compared to healthy subjects (see Table 4). There is a significant interaction effect between Time by Group (*F* (1,95)=21.6; *P*<0.001): as can be seen from Table 4, healthy subjects showed a strong reduction in faults in all three conditions (practice-effect), whereas the WAD groups have only a slight reduction in faults and even an increase in faults.

Relationship between Pasat and state-dependent variables

The mean scores and standard deviations of the state-dependent variables are presented for the pre- and post-condition in Table 5.
Mann-Whitney tests revealed that the WAD-groups differ significantly from the healthy groups on all the state-dependent factors both pre- and post condition (all *P*-values < 0.001), indicating more complaints in the WAD group (see Table 5).

Wilcoxon Signed Ranks Tests were conducted in each of the four groups (WAD-experimental / WAD-control / Healthy-experimental / Healthy-control group) to investigate whether state-dependent factors changed because of the experimental/control condition. Results demonstrated that state-dependent factors did not change significantly in both experimental groups. In contrast, the WAD-control group perceived a significant decrease in head-

Table 5: Means (and SD) on the 'State-dependent' factors in the WAD- and the Healthy groups, pre-and post-condition (VAS-scales; range: 0-100) (n=96).

	WAD Groups				Healthy Groups			
	Exp. Gr. (n=24)		Contr.Gr. (n=24)		Exp. Gr. (n=24)		Contr.Gr. (n=24)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Headache	52.8 (22.4)	54.4 (24.1)	50.8 (22.9)	45.1 (23.8)	4.7 (6.8)	4.8 (8.7)	6.0 (8.3)	3.9 (4.9)
Neck pain	49.8 (27.1)	52.6 (28.5)	50.5 (26.1)	47.6 (25.2)	2.7 (4.3)	1.9 (2.8)	4.7 (5.8)	4.2 (4.7)
Fatigue	52.2 (21.6)	55.7 (23.5)	52.9 (23.1)	48.8 (23.0)	10.2 (14.3)	10.2 (13.9)	12.5 (13.7)	8.2 (12.2)
Tension	35.8 (25.1)	40.4 (28.2)	37.9 (24.9)	34.9 (24.3)	5.2 (7.0)	4.6 (7.7)	7.5 (10.6)	4.8 (6.3)

ache, neck pain and fatigue, whereas the Healthy-control group reported significantly less headache and fatigue.
In order to investigate the relationship between the state-dependent variables and the performances of the Pasat-test in the three different conditions, multiple linear regression analyses were performed within the total WAD group (each total (log-transformed) fault-score on the three conditions were successively taken as a dependent variable).
Because of strong correlations between the four state-dependent variables, four separate models were calculated for each condition. Condition 3 (strong background noise) is predicted most optimal by a model which consists of the variables educational level together with the mean fatigue VAS-score (adjusted R^2=0.41; P<0.001) (see Table 6). Furthermore, a model with the variables educational level and the mean headache-VAS score is also significant (adjusted R^2=0.35; P<0.001) and for neck pain the model is significant after removal of two outliers (adjusted R^2=0.35; P<0.001). The variable 'tension' is not a significant predictor for condition 3.
Condition 2 (moderate background noise) is also predicted at best by the variables educational level and fatigue (see Table 6). Headache, neck pain and tension are not related to condition 2.

Table 6: Regression analyses in the WAD-group: Prediction of performances on the PASAT task in condition 2 (with moderate background noise) and condition 3 (with strong background noise) (n=46).

	Condition 2 *				Condition 3**			
	B	SE B	ß	P	B	SE B	ß	p
<u>Model 1</u>								
Constant	5.0	.90		<.001	4.4	.95		<.001
Educational level	-1.4	.39	-.46	.001	-1.3	.41	-.41	.002
Fatigue	0.02	.01	.28	.03	0.03	.01	.40	.002
<u>Model 2</u>								
Constant	5.2	.93		<.001	5.2	.90		<.001
Educational level	-1.4	.40	-.46	.001	-1.3	.40	-.42	.003
Headache	0.02	.01	.25	.06 ns	0.03	.01	.34	.011
<u>Model 3</u>								
Constant	5.6	.84		<.001	5.3	.85		<.001
Educational level	-1.5	.40	-.48	.001	-1.4	.42	-.44	.001
Neck pain	0.01	.009	.20	.13 ns	0.02	.009	.33	.012

* Condition 2: adjusted R2=0.33 and p<.001 for model 1; adjusted R2= 0.31 and p<.001 for model 2; adjusted R2=0.29 an d p<.001 for model 3.
** Condition 3: adjusted R2=0.38 and p<.001 for model 1; adjusted R2= 0.26 and p<.001 for model 2; adjusted R2=0.35 and p<.001 for model 3.

Results revealed that condition 1 is also predicted at best by the variables educational level and fatigue, after removal of three outliers (n=43; $R^2=0.33$; $p<0.001$). None of the other state-dependent variables showed to be significant predictors of this condition (no background noise).
A model consisting out of educational level and GSI (global severity index) is not significant for any of the three conditions, because, as mentioned above, GSI in the WAD group is strongly related to educational level (the low educational WAD group exhibit significant more distress compared to the high educational WAD group). A correlation matrix showed significant correlations between GSI and condition 1 ($R=0.33$; $P<0.03$), condition 2 ($R=0.42$; $P<0.005$) and condition 3 ($R=0.34$; $P<0.03$). Furthermore, trait-anxiety is significant correlated with GSI ($R=0.63$; $P<0.001$) and with condition 3 ($R=0.30$; $P<0.05$).

DISCUSSION

In accordance with the first hypothesis, a main effect of background noise was found and data showed that both WAD patients and healthy control subjects made increasingly more errors on a complex auditive attention task (Pasat task) in conditions with rising background noise. However, WAD patients performed significantly worse in all conditions, even in the silent condition. As the Pasat task measures 'divided attention',[28,29] we may conclude that WAD patients have problems in shifting their attention quickly between several sources of information. This is in concordance with some of the literature.[30,34] Furthermore, the results indicated that WAD patients have problems with 'focusing attention' as well, especially in situations with strong noises: as the background noise increases, WAD patients made increasingly more errors on the Pasat task, compared to healthy control subjects. Results demonstrated that the low-educational groups performed significantly worse compared to the high educational groups. The low educational WAD-group performed significantly worse on our easy arithmetical task compared to the low educational healthy group, however, only in the two conditions with background noise. It is concluded that the low educational WAD-group is easily distracted by background noise, even when performing an ordinary, elementary mental task.
Obviously, state-dependent complaints are significantly stronger in WAD patients compared to healthy subjects. At variance with the hypothesis, complaints did not change significantly as result of the noise-condition in the experimental WAD group, despite a trend towards an increase of com-

plaints. Probably, a fifteen-minute 'noise' condition is too short to increase state-dependent complaints. Both control groups showed significantly less state-dependent complaints as result of the fifteen minutes relax-condition. These results indicated that individuals in general take advantage of a break in a silent surrounding.

The outcomes of the regression-analyses showed that several state-dependent factors together with educational level are significant predictors of the performance in condition 3 within the WAD group (e.g. fatigue, headache and neck pain), however, only fatigue was still a significant predictor in condition 1 and 2. This confirms our hypothesis.
The WAD group exhibit more distress compared to healthy subjects; this is in concordance with previous results.[17,19] Furthermore, the sub-group of WAD patients with a low-educational level perceives more distress compared to WAD patients with a high-educational level, as was measured by means of the SCL-90 and the Spielberger Trait and State anxiety Inventory.[17] Emotional distress was significantly related to the performance on the Pasat in all three conditions; this confirms our hypothesis. However, contrary to the expectation, for the general distress index (as was measured by the SCL-90) this relationship was not stronger in condition 3 compared to condition 1 or 2. However, the 'trait' scale of the STAI was significantly correlated only with condition 3 (strong background noise).
It is concluded that emotional distress has a negative relationship with divided attentional performance, independent of background noise. These results are in accordance with the results of Radanov et al. (1999) who found a significant correlation between state-anxiety and the performance on a divided attention task.[31] They concluded that 'a close relation between emotional and cognitive problems may be the basis for a vicious circle...' (p. 488). Likely, persons with a general tendency to react with fear are more distracted by a high level of background noise.

It is concluded that the performance of WAD patients on cognitive tasks is significantly reduced in the presence of background noise, compared to healthy subjects. In other words, WAD patients are easily distracted by noise in their surrounding, indicating a focused attention deficit. Furthermore, this distraction increases with the rising of background noise. Especially, WAD patients with a low educational level are easily distracted, even when executing an easy mental task. Furthermore, this group exhibit more emotional distress compared to WAD patients with a high educational level, confirming the vulnerability of this group.[17]

Results indicated a significant negative relationship between state-dependent factors (fatigue, headache, neck pain, global emotional distress) and attention performance.

The present results confirm the frequently expressed complaint of WAD patients regarding the difficulty of focusing attention to a conversation, while neglecting other sources of noise surrounding them. In this respect WAD patients could benefit from the use of special hearing plugs with a moderate acoustic filter, which reduces the surrounding noise-value, without reduction of the speech-intelligibility of persons nearby, when concentrating in a noisy surrounding. Given the relationship between state-dependent factors and attention performance, a multidisciplinary rehabilitation program, aimed at reducing both the physical and emotional symptoms, will also improve cognitive functioning.

REFERENCES

1. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical review: Whiplash Injury. *Pain,* 283-307.

2. Dvorak, J. (1998). Soft-Tissue Injuries of the Cervical Spine: Classification and diagnosis. In: *Current concepts in Prevention, Diagnosis and Treatment of the Cervical Whiplash Syndrome* (Gunzburg, R. & Szpalski, M., Eds). Philadelphia: Lippincott-Raven publ., 53-60.

3. Blokhorst, M.G.B.G., Swinkels, M., Lof, O., Lousberg, R., Zilvold, G. (2002a). The Influence of State related Factors on Focused Attention Following Whiplash Associated Disorder. *Journal of Clinical and Experimental Neuropsychology,* 24, 471-478.

4. Spitzer, W.O., Skovron, M.L., Salmi, L.R., Cassidy, J.D., Duranceau, J., Suissa, S., & Zeiss, E. (1995). Scientific monograph of the Quebec task force on whiplash-associated disorders: redefining "whiplash" and its management. *Spine*, 20 (7), 7-73.

5. Blokhorst, M.G.B.G., Meeldijk, S., van Luijtelaar, G., van Toor, T., Lousberg, R. (in press). Noise intolerance and state-dependent factors in patients with Whiplash Associated Disorder. Accepted for publication in: *Journal of Whiplash and Related Disorders*, 2005, vol. 4 (1).

6. Van Toor, T., Neijenhuis, K., Snik, A. & Blokhorst, M.G.B.G. (2003). Evaluation of Auditory processing disorders after whiplash. In: *Auditory Processing Disorders. Development and evaluation of a test battery.* (K. Neijenhuis, Thesis). Nijmegen: Radboud University, 109-129.

7. Tjell, C., Tenenbaum, A. & Rosenhall, U. (1999). Auditory function in whiplash-associated Disorders. *Scand Audiol*, 28, 203-209.

8. American Hyperacusis Association (2003). *What is Hyperacusis?* Internet.

9. Van Zomeren, A.H., & Saan, R. (1997). Whiplash. In B.G. Deelman, P.A.T.M. Eling, E.H.F. de Haan, A. Jennekens-Schinkel, A.H. van Zomeren (Ed.), *Klinische neuropsychologie,* 290-298. Amsterdam: Boom.

10. Heering de, A. (1998). The Whiplash Syndrome: neurolinguistic and attention disorders. In: *Whiplash Injuries. Current Concepts in prevention, diagnosis and treatment of the Cervical Whiplash Syndrome.* Gunzburg, R. & Szpalski, M. (Eds). Philadelphia: Lippincott-Raven Publishers, 143-159.

11. Brand, N., Schneider, N. & Arntz, P. (1995). Information processing efficiency and noise. Interactions with personal rigidity. *Personal & Individual Differences,* 18 (5), 571-579.

12. Ouwerkerk, R.J., Meijman, T.F. & Mulder, G. (1994). Mentale belasting. In: *Arbeidspsychologische taakanalyse*. Utrecht: Lemma b.v., 19-47.

13. Vercoulen, J.H.M.M., Swanink, C.M.A., Fennis, J.F.M., Galama, J.M.D., Van der Meer, J.W.M., & Bleijenberg, G. (1994). Dimensional assessment of chronic fatigue syndrome. *Journal of Psychosomatic Research, 38 (5),* 383-392.

14. Eccleston, C. & Crombez, G. (1999). Pain demands Attention: A Cognitive-Affective Model of the Interruptive Function of Pain. *Psychological Bulletin, 3,* 356-366.

15. Grisart, J.M. & Plaghki, L.H. (1999). Impaired selective attention in chronic pain patients. *European Journal of Pain, 3*, 325-333.

16. Sjøgren, P., Olsen, A.K., Thomsen, A.B., Dalberg, J. (2000). Neuropsychological performance in cancer patients: the role of oral opioids, pain and performance status. *Pain*, 86, 237-245.

17. Blokhorst, M.G.B.G., Lousberg, R., Vingerhoets, A.J.J.M., Winter, F.A.M., Zilvold, G. (2002b). Daily hassles and stress vulnerability in patients with a Whiplash Associated Disorder. *International Journal of Rehabilitation Research,* 25, 173-179.

18. Mayou, R. (1997). The psychiatry of road traffic accidents. In: *The Aftermath of Road Accidents.* M. Mitchell (Ed). London/New York: Routledge, 33-48.

19. Wallis, B.J., Lord, S., Barnsley, L. and Bogduk, N. (1996). Pain and psychologic symptoms of Australian patients with whiplash. *Spine*, 21, 804-810.

20. Smed, A. (1997). Cognitive function and distress after common whiplash injury. *Acta Neurologica Scandinavica*, 95, 73-80.

21. Brand, N., & Jolles., J. (1987). Information processing in depression and anxiety. *Psychological Medicine*, 17, 145-153.

22. Kolb, B. & Wishaw, I.Q. (1990). Emotional Processes. In: *Fundamentals of human neuropsychology* (3rd Ed.). New York: Freeman and Company, 607-642.

23. Eling, P. (2003). Denkkaders in de psychiatrie. In: *Cognitieve neuropsychiatrie* (Eling, P., de Haan, E., Hijman, R. & Schmand, B., Eds.). Amsterdam: Boom, 17-45.

24. Hammes, J.W.G. (1978). *De Stroop Kleur-woord Test*; Handleiding. Lisse: Swets & Zeitlinger.

25. Kessels, R.P.C. (2002). Measuring attention with the Paced Auditory Serial Addition Task (PASAT). *Gedrag & Gezondheid*, 30(1), 37-43.

26. Schmand, B., de Sterke, S. & Lindeboom, J. (1999). *Amsterdamse Korte Termijn Geheugen Test*. Lisse: Swets & Zeitlinger Publishers.

27. Rodenburg, M. & Hanssens, K. (1998). *Audiometrie, methoden en klinische toepassingen* (4th edition). Bussum: Couthino, 45-50.

28. Gronwall, D.M.A. (1977). Paced Auditory Serial-Addition Task: a measure of recovery from concussion. *Perceptual and Motor Skills*, 44, 367-373.

29. Lezak, M.D. (1995). *Neuropsychological Assessment* (3rd Ed.). New York: Oxford University Press.

30. Radanov, B.P., Hirlinger, I., Di Stefano, G. & Valach, L. (1992). Attentional processing in cervical spine syndromes. *Acta Neurol Scand*, 85, 358-362.

31 Radanov, B.P., Bicik, I., Dvorak, J., Antinnes, J., von Schulthess, G.K., & Buck, A. (1999). Relation between neuropsychological and neuroimaging findings in patients with late whiplash syndrome. *Journal of Neurology Neurosurgery and Psychiatry, 66*, 485-489.

32. Bosma, F.K. & Kessels, R.P.C. (2002). Cognitive impairments, psychological dysfunction and coping styles in patients with chronic whiplash syndrome. *Neuropsychiatry, neuropsychology and behavioural Neurology*, 15 (1), 56-65.

33. Gimse, R., Björgen, I.A., Tjell, C., Tyssedal, J.S. & Bö, K. (1997). Reduced cognitive functions in a group of whiplash patients with demonstrated disturbances in the posture control system. *Journal of Clinical and Experimental Neuropsychology*, 19, 838-849.

34. Kessels, R.P.C., Keyser, A., Verhagen, W.I.M., van Luijtelaar, E.L.J.M. (1998). The whiplash syndrome: a psychophysiological and neuropsychological study towards attention. *Acta Neurologica Scandinavica*, 97, 188-193.

35. Diehr, M.C., Heaton, R.K., Miller, W & Grant, I. (1998). The Paced Auditory Serial Addition Task (PASAT): Norms for age, education and ethnicity. *Assessment*, 5, 375-387.

36. Egan, V. (1988). PASAT: Observed correlations with IQ. *Personality and Individual Differences*, 9, 179-180.

37. Arrindel, W.A., & Ettema, J.H.M. (1986). *Handleiding bij een psychopathologie-indicator.* Lisse: Swets & Zeitlinger.

38. Derogatis, L.R.. (1983). *SCL-90R. Annual II. Clinical Psychometric research.* Towson: Clinical Psychometric Research.

39. Ploeg van der, H.M., Defares, P.B., Spielberger, C.D. (1981). *Handleiding bij de Zelf-Beoordelings Vragenlijst*. Lisse: Swets & Zeitlinger.

40. Spielberger, C.D., Gorsuch, R.L., Lushene, R.E. (1983) *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.

41. Norusis, M.J. (1999). *SPSS-user Guide*: version 9.0. Chicago.

42. Hair, J.S., Anderson, R.E., Tatham, R.L., Black, W.C. (1998). *Multivariate data analysis*. London: Prentice Hall.

Chapter 7

General discussion and conclusions

GENERAL DISCUSSION

In this last chapter, the results of the studies described in chapters two through six are discussed and imbedded in current theories. First, the results concerning daily hassles and distress in WAD patients are discussed. Next, the subject of noise-intolerance, attention and the relationship with state-dependent factors in WAD patients are passed under separate review. Finally, implications are given for whiplash research, clinical neuropsychological assessment, and treatment of WAD patients.

Daily hassles, distress and stress-vulnerability in WAD patients

In line with previous results, it was concluded that WAD patients exhibit a high level of emotional distress.[1-9] Whereas the initial emotional response in the acute phase is related to the whiplash injury itself [5,9], in the chronic phase the distress perceived by WAD patients is mainly a reaction caused by the complaints and limitations they confront in daily life. Evidence which supports this secondary emotional reaction was the observed relationship between the reported distress and the frequency of person-dependent daily hassles (this thesis) and the reduction of distress when pain and other symptoms decrease.[4]
The results described in this thesis revealed that the appraisals of different kinds of daily stressors (e.g. person-dependent and person-independent stressors) differ significantly between WAD patients and healthy subjects, indicating that WAD patients view their daily stressors as more severe than healthy control subjects. It seems that all kinds of stressors (e.g. person-dependent and person-independent stressors) have a greater impact on WAD patients compared to healthy control subjects. This heightened sensitivity to stressors was further objectivated by the cortisol study described in this thesis (chapter three): it was concluded that chronic WAD patients have higher cortisol levels compared to healthy subjects and study of the HPA-axis in WAD patients can offer a new perspective in the WAD phenomenon. Because both the amount and appraisal of the severity of daily problems were significant predictors of cortisol responsivity as a result of an acute mental stressor, it is plausible that a subgroup of WAD patients (e.g. patients with high levels of frequency and intensity rating scores regarding daily stressors) is more vulnerable to subsequent stressors after the whiplash injury.

It is still not clear whether WAD patients become gradually more sensitive to subsequent stressors during the course of the whiplash syndrome and/or that they have a premorbid vulnerability to stressors in general. In other words, to what extent pre-morbid characteristics of individuals affect the reported distress and appraisals of daily problems after a whiplash injury, remains to be established. Previous research revealed that global personality dimensions (e.g. neuroticism, extraversion, altruism) as well as previous life-events are not significant predictors of the course of the whiplash syndrome.[6,10] The results of predictive studies on personality traits in chronic pain patients in general have been inconsistent. Although some studies have found a relationship between certain personality dimensions (e.g. hypochondriasis, hysteria and depression) and long term functioning, other studies have found no evidence of such relationships.[11] In conclusion, further research on personality factors in relation to WAD is necessary. Perhaps the questionnaires used so far to assess personality characteristics in WAD patients are too global and perhaps one should look for more specific personality dimensions, ones that can be measured for example by means of the NEO-PI.[12]

The results described in this thesis demonstrated that another important personal or socio-demographic characteristic related to stress-vulnerability was 'educational level' (chapter two and six). Although post-hoc analyses demonstrated that the low educational WAD group perceived the same amount of daily hassles and perceive them as equally serious compared to WAD patients with a high educational level, the results of two separate studies described in this thesis showed higher levels of distress for WAD patients with a low educational level. Possibly, stressors have more impact on these patients due to the use of different coping strategies. From previous studies it is known that the use of active coping strategies (i.e. staying busy, ignoring pain, distraction) are associated with less pain, whereas passive coping strategies (i.e. restricting activities due to pain, engaging in wishful thinking, depending on others to relieve pain) are associated with more severe pain.[13] In addition, from 'stress' research it is known that people with a low educational level in general have a tendency to use more passive coping strategies, whereas persons with a high educational level use more active coping strategies.[14] Recently, the relationship between educational level and use of coping strategies and cognitions in patients with chronic spinal pain was investigated with respect to level of disability.[15] Results revealed that after controlling for relevant covariates (e.g. age, sex, pain duration, litigation status), persons with a low educational level possessed a greater belief that pain is a 'signal of harm', unrelated to emotional experience and that pain is disabling and uncontrollable. They also endorsed more passive and maladaptive coping strategies, including a tendency to catastrophize about their pain.[15]

It was concluded that persons with lower educational levels are more likely to develop maladaptive pain beliefs and coping strategies. Likely, these patients not only use maladaptive coping strategies, but also have fewer coping resources.[15] Despite the importance of coping strategies /coping resources for future functioning of patients[15,6,17] and the relationship between educational level and coping strategies/ coping resources, little attention has yet been given to this educational factor in pain research.

Another largely ignored factor in pain research in general and specifically in whiplash research, is related to the differences in how men and women report a variety of symptoms associated with common health problems and specifically with respect to pain and distress. Miaskowski (1999) concluded that in most studies, researchers have treated the two genders as equals.[18] However, research showed the striking fact that there is a female predominance of sprain in the neck after a car accident.[6,19] Furthermore, research has indicated that women are more sensitive to painful stimuli than men (women have lower pain thresholds and they exhibit less tolerance to pain stimuli than men).[18,20] Moreover, it is known from previous studies that women, both with and without medical disorder, generally tend to report more symptoms and more severe symptoms.[21] Besides the differential influences of the socialisation process and culture on pain-perception and expression in males and females, another interesting possible explanation is the influence of gonadal hormones on nociceptive processing. Fllingim and Ness (2000) argued in an extensive review that there is an impressive evidence for sex-related hormonal influences on nociceptive responses.[22] They noted that extreme hormonal conditions, such as those accompanying pregnancy, can produce robust effects on nociceptive processing. Further integration of hormonal factors into basic science and clinical research endeavors attempting to enhance the understanding and management of pain.
However, the results described in this thesis concerning gender and distress are consistent: post-hoc analyses (Mann-Whitney U-tests) on the data of the studies described in chapter four and five revealed no significant differences between males and females within the WAD group regarding the frequency and intensity ratings of daily hassles, nor regarding the level of distress. However, the study on noise intolerance revealed that female WAD patients are more intolerant to noise compared to male patients (this thesis; see also below).

In conclusion, future studies should not only focus on specific personality factors (or sub-facets of the global personality dimensions), but should also take into account factors such as educational level and sex.

Noise-intolerance in WAD patients

All patients included in the study had a normal profile on a pure tone audiometric test, carried out in order to exclude possible hearing loss. In chapter four it was described that the loudness perception of WAD patients is not different from healthy matched control subjects (except for the very strong intensities) and is stable in time. Therefore, it was concluded that there is no proof of inner ear lesions in these patients. These results are in accordance with previous results which also indicated no evidence for hearing loss associated with whiplash injury or dysfunctions of the brainstem startle circuitry.[23,24,25]
However, results demonstrated an increased intolerance for noise intensities (even for low intensities) in WAD patients compared to healthy matched control subjects (> 57dB). The data showed that the difference in intolerance level between WAD patients and healthy subjects increases with increasing noise-intensity. Furthermore, strong fatigue was related to noise intolerance for low intensities (57dB), whereas strong headache was associated with noise intolerance for moderately strong noise-intensities (81dB and 89dB). Likely, a suboptimal state in persons increases noise intolerance. Given the variability of pain and fatigue in time, these results explain why WAD patients perceive also a considerable amount of variance in the degree of noise intolerance over the course of a day. Post-hoc analysis revealed that female WAD patients are more intolerant to moderately strong noises than male patients.
The results showed that the reported responses to noise were independent of the level of distress. It was suggested that noise intolerance is related to emotional distress only for those situations in which WAD patients also have to concentrate on understanding people in a noisy environment, which is a strenuous task.[24] The results of the study described in chapter six showed that this is indeed the case (see also below).
Despite the absence of an association between noise intolerance and distress, this does not imply that noise intolerance is independent of psychological processes. For example, theoretically, it is possible that some WAD patients amplify their complaints, but at the same time have unique coping strategies, resulting in low distress. As Ferrari (2004) argued in a recent discussion, we should not confuse the very important concept of 'symptom amplification' or 'hypervigilance' with 'psychological distress'.[26] Symptom amplification refers to a perceptual style and means that persons who have a heightened attentional focus on bodily sensations (hypervigilance) have a tendency to select out and concentrate on certain relatively weak and in-

frequent sensations, and are disposed to react to somatic sensations with affect and cognitions that intensify them and make them more alarming and disturbing.[24,25] Hypervigilance is defined as constant scanning of the body for somatic and, particularly, pain sensations. Increased attention to pain and other somatosensory signals is defined as specific hypervigilance, whereas increased attention directed towards irrelevant (neutral) stimuli (for example 'noise') is referred to as general hypervigilance. It is known that individuals who are hypervigilant for bodily sensations, have a lower pain-threshold.[27] Hypervigilance, in combination with negative appraisals of the perceived symptoms, may predispose individuals for all kinds of chronic complaints after a whiplash injury.[26] With respect to noise intolerance, besides the influence of a suboptimal state on noise intolerance (e.g. fatigue and headache), it is conceivable that the process of symptom amplification, and more specifically hypervigilance, plays a significant role. Future research must answer this intriguing question.
On the other hand, it is possible that noise intolerance is independent of psychological processes. Perhaps, as was suggested in chapter four, disturbances of the proprioceptive input from the neck to the central nervous system and/or of the central processing of such input, not only influence the postural control in many patients with WAD,[28,29] but perhaps also enhance noise-intolerance.

Attentional difficulties in WAD patients

Focused attention difficulties

'Stroop' distraction

In chapter five, it was concluded that WAD patients exhibit subtle focused attention problems, as was measured by means of the modified Stroop task. Results revealed no significant differences between the WAD group and the healthy control group with respect to the 'classical' interference score. However, the interference score of the modified Stroop task was significantly different between both groups. Hence, it was concluded that the results demonstrated signs of interference susceptibility and reduced capacity to shift attention. Furthermore, this result illustrates that the modified interference score is a relevant supplement to the classical interference score in neuropsychological assessment in WAD patients. Important to note is that the modified Stroop task is a more complex task and requires more controlled attention than the classical Stroop task, because of the additional cognitive strategy change which is needed in order to execute the task successfully.

'Noise' distraction

In the study described in chapter six, multivariate analysis showed a main effect of background noise, which demonstrated that both WAD patients and healthy control subjects made increasingly more errors on a complex auditive attentional task (Pasat task) in conditions with rising background noise. However, WAD patients performed increasingly worse with increasing background noise compared to healthy participants. Furthermore, it was concluded that especially WAD patients with a low educational level are easily distracted, even when executing an easy mental task. In addition, this group exhibit more emotional distress compared to WAD patients with a high educational level, confirming the vulnerability of the former group (see also chapter two). These results indicate that coping resources are probably less available in WAD patients with a low educational level.

Comparison of the different interference measures

We may conclude that both visual and auditive stimuli may serve as distractors, when offered with other competing stimuli. The question is which interference measure (the Stroop interference measures or the 'Pasat in noise' interference measures) is the most sensitive test in detecting focused attention problems? We have already concluded that the modified Stroop interference measure is a more subtle measure as compared to the classical Stroop interference measure (see above).

In order to investigate which condition of the Pasat in noise is the most subtle measure, it was necessary to execute a few post-hoc analyses. Two interference scores were calculated: the difference score of condition three (high background noise) minus one (no background noise) (3-1), and the difference score of condition two (low background noise) minus one (2-1). These difference scores give an indication of the influence or distractibility of noise on performance. Mann-Whitney *U*-tests revealed that both scores were significantly different between the WAD-group and healthy control participants ($P<0.001$). However, results showed that the difference score between both groups is stronger for the 3-1-interference score than for the 2-1-interference score (see Table 1). Therefore, it is concluded that the 3-1 interference score is a more subtle interference measure.

Table 1: Median values of the Pasat-in noise interference scores.

	2-1 interference	3-1 interference
WAD group	3.5	5.0
Healthy control group	0.0	0.2

In order to investigate the relationship between the two interference scores of the Stroop task on the one hand and the two interference scores of the 'Pasat in noise' on the other hand, post-hoc a correlation matrix was calculated. As can be seen from Table 2, the associations are more or less the same. The strongest associations are the ones between the modified Stroop interference score and the interference scores of the Pasat.

A relevant question is whether the 'Pasat in noise' has a surplus value compared to the modified Stroop task. Despite the fact that there is a moderately strong shared variance (R^2=0.37) between the two 'most subtle' interference scores (e.g. Stroop 4-2 and Pasat 3-1), they both have a considerable amount of unique variance. In order to gain more insight into this question, we have looked for associations between these two interference scores and the subjective perception of WAD patients regarding noise-distractibility in daily life. Results showed that the correlation between the modified Stroop interference score and the perceived noise-distractibility in daily life by WAD patients is significant (R=0.44; P=0.002), whereas the correlation between the noise-interference scores and subjective noise-distractibility is not significant.

In conclusion, these results demonstrated that the modified Stroop interference score is an objective and subtle measure of focused attention and easy to assess.
Despite the fact that the 'Pasat in noise' test seems not to be the most effective way to measure *focused* attention, the principle of systematically adding noise (cocktail party noise, office noise) as a kind of background distraction

Table 2: Spearman's rho correlations between two Stroop Interference scores and the Pasat interference scores. (n=96)

	Stroop Interference 1 (3-2)		Stroop Interference 2 (4-2)	
Pasat Interference 1 (2-1)	R=0.10	n.s.	R=0.30	P=0.006
Pasat Interference 2 (3-1)	R=0.25	P=0.02	R=0.34	P=0.001

during neuropsychological assessment likely will enhance the ecological validity of the procedure and could be used in future assessment procedures to investigate *sustained* attention.

Divided attention problems

WAD patients performed significantly worse on a series of parallel versions of the Pasat, even in a silent condition. As the Pasat task measures 'divided attention'[30,31] and because it is a high time-pressure task, we may conclude that WAD patients have problems in quickly shifting their attention between several sources of information. This is in concordance with some of the literature.[32,33,34]

However, the results of the Synwork task (chapter four), which is also a divided attention task, showed no differences between WAD patients and healthy subjects. In fact, during the Synwork task, subjects may use their own strategy to perform the task and in a way it is a self-paced task. Therefore, it was concluded that WAD patients apparently are able to perform normally on self-paced divided-attention tasks in contrast to time-pressure tasks such as the standard version of the Pasat. This result is in line with a previous result of Klein (1997).[35]

Influence of state-dependent factors on cognitive functioning

Influence of pain and fatigue on attention in WAD patients

The demonstrated slowing of response on complex attention tasks may have different causes, as was described in the introduction. The slowing of response may be due to a general slowing in information processing because of organic brain injury. However, as there is no convincing evidence for brain lesions in the WAD syndrome, other causes apparently play a part.[36,37,38,39]

Besides brain injury, task performances may be negatively influenced by 'malingering'. Therefore, in this thesis, results were controlled for 'malingering' or underperformance by means of a specific and valid test.[40] In order to exclude possible influences on cognitive functioning due to pain medication, the use of medication of influence on the central nervous system, was an exclusion criterion.

State-dependent factors (headache, neck pain, fatigue, tension and distress) are suggested to be relevant factors, influencing cognitive functioning negatively.[36,37,39,41] Of course, pain, fatigue and suffering in general are private, internal events that cannot be directly observed by clinicians or assessed

via bioassays.[42] In order to assess pain experience, we have to rely on self-reports.[42] The kind of self-report used in this thesis is the Visual Analogue Scale (VAS)-scale. There is much evidence supporting the validity of the VAS-scales for pain intensity and fatigue,[42] so the use of a VAS-scale is a valid way to assess state-dependent factors. It is beyond the scope of this discussion to reveal the results on validity research, however, one of the important advantages of the use of VAS-scales is that it is sensitive to change in pain- or fatigue intensity because of the high range of response categories (e.g. a 10-cm VAS can be considered as having 101 response levels).[42]
In both the Stroop (chapter five) and the Pasat study (chapter six), we found evidence for the influence of these state-dependent factors on attentional performance. The results concerning the influence of state-dependent variables indicated that, besides educational level and duration of complaints, the intensity of headache predicts most optimally the performance on the four Stroop-subtasks. Only the modified Stroop interference score was significantly related to headache, in combination with educational level and working status ($R^2=0.43$; $P=0.001$).
The results of the Pasat task in the condition with strong background noise are predicted most optimally by a model which consists of the variables education level together with fatigue ($R^2=0.41$), although headache and neck pain are also significant predictors. A model consisting of fatigue only predicts the results of the Pasat task with low background noise. The results revealed that fatigue is associated with poor attentional performance in situations with different noise levels and even in situations with no noise at all. Likely, fatigue interferes very quickly with the performance on high time-pressure tasks.

In conclusion: the intensity of pain and fatigue is significantly associated with noise intolerance, as well as with performance on attention tasks. Besides pain intensity, also pain location (headache versus neck pain) seems to be important, because headache is more often and more strongly associated with noise intolerance and attention than neck pain. These results are in line with recent evidence on attention in other chronic pain patients.[43,44] Recently, results demonstrated a significant relationship between state-dependent factors and cognitive functioning in patients with Fibromyalgia.[43]

Influence of tension and distress on cognitive functioning in WAD patients

In chapter six it was described that the global severity index (GSI), a measure for global distress, is a significant predictor of the Pasat without and with

two levels of background noise in WAD patients, but only when the factor educational level was excluded (because educational level is strongly related to distress). With respect to the Stroop results (chapter five), the GSI showed not to be a significant predictor on the Stroop results when educational level is also included in the model. However, post-hoc analyses revealed that the GSI alone is significantly associated with the scores of subtask 1 (R=0.37) and subtask 4 (R=0.30), again indicating a significant collinearity between educational level and distress.
There is another important link between emotion and cognition, which is a neurophysiological link: it is possible that the chronic high level of distress in WAD patients causes an imbalance in the stress-hormone system, leading in turn to cognitive deficits or other whiplash-related complaints such as 'noise intolerance'.[45,46,47] The results discussed in this thesis indeed revealed signs of a heightened cortisol response due to mental stress and a relationship between chronic daily hassles, appraisal and cortisol responses (chapter two). However, future research must investigate whether heightened cortisol levels are also associated with reduced cognitive functioning in WAD patients.

Concluding remarks concerning cognitive functioning in WAD

The above mentioned results illustrate that the performance on attention tasks should be interpreted in the context of state-dependent complaints.
With respect to chapter five and six of this thesis, the results indicate that WAD patients exhibit a slowing of task performance on complex, high time-pressure tasks, which require controlled attention. This slowing increases when tasks become more complex and require more controlled attention. Since, in chapter five the results of the modified Stroop task showed that response latencies on the four different subtasks were significantly higher for WAD patients compared to healthy control subjects. Furthermore, the difference in response latencies between both groups increases from subtasks 1 through 4, which indicate that responses became slower as tasks became more complex. In chapter six, the results were described of a parallel version of the Pasat-test. The Pasat is sensitive in detecting subtle attention problems[33] and requires strong controlled attention.[24] Analyses demonstrated worse performances on the Pasat in the classical condition (without noise) in WAD patients compared to healthy control subjects.
In conclusion, so far results demonstrated that the performance of WAD patients on high time-pressure tasks, which require strong controlled attention, is significantly worse compared to healthy persons. Clearly, WAD patients

cannot keep pace with the offered stimuli. In contrast, self-paced tasks are well executed, at the expense of an increase in state-dependent complaints.

The question is which cognitive model explains these results most optimal? After this, the above mentioned results are applied within two frequently used information processing models: the information processing model of Shiffrin and Schneider[48,49] and the State-regulation model of Hockey.[50,51,52]

Information processing model of Shiffrin and Schneider

Shiffrin and Schneider demonstrated the two kinds of attention problems described above: focused attention deficit and divided attention deficit.[48,49] These attention problems cause a slowing of task performance and an increase in the frequencies of errors during task performance. One of the basic assumptions of this model is the difference between automatic and controlled information processing. Automatic information processing does not require attention, in contrast to controlled information processing. Controlled information processing is thought to be a sequential process which is limited in time. When external stimuli such as noise, as well as internal stimuli such as pain, distract and therefore demand attention, part of the limited information capacity is continuously occupied, resulting in slow or bad task performances on tasks which require controlled attention.
How much attention a pain stimulus gets, is dependent of several factors, as was described in the so called 'Cognitive-Affective model of the interruptive function of pain.[41] This model describes that pain interrupts ongoing activities, dependent on several pain-related characteristics (e.g. the intensity, novelty, predictability and threat) and the characteristics of the environmental demands (e.g. task difficulty, noise).

The State-regulation model of Hockey

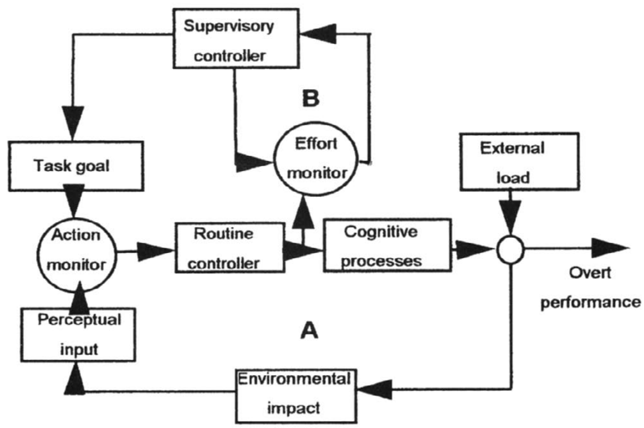
A basic notion in the 'State-regulation' model of Hockey (1986) is that the present or momentary task state often deviates from the required task state (task goal). The model assumes that every individual has a routine control system for maintaining behavioural stability, in which the so called action monitor plays a central role. This monitor has the function of monitoring the present state of the task, and to compare the actual state with the required task state, and after detecting a discrepancy activating adjustments in order to overcome that situation by investment of 'mental effort'. Mental effort is an energetical construct for active control.[50,51,52]

However, there are instances in which this routine type regulation is overruled by a more active control loop, which is assumed to be activated in case the discrepancy between required task state and the momentary state is too high, and the action monitor signals a high need for effort investment. This active control loop has several options for control.[50,51,52]

- *Direct control:* further increase of effort investment ('trying harder'), which will result in affective and psycho-physiological effects.
- *Indirect control:* downwards adjustment of the performance goals (or adjustment of motivational priorities), for example by choosing a less effortful strategy. This results in a less effective performance (e.g. slower task performances, or neglect of certain aspects of the task).
- *Failure to control:* when individuals are continuously striving for direct control, but are unable to resolve the discrepancy, and are unwilling or unable to relinquish the task goals. This state may give rise to sustained stress and can be regarded as a failure to control the situation, resulting into more state-dependent complaints (pain, fatigue and distress) as well as ineffective performances.

Probably, this active control loop is often needed and used by WAD patients. Mulder (1994) argues that when individuals find themselves in a suboptimal state (pain, fatigue, distress), a surplus of effort is needed in order to control task performance on a stable level.[50] However, as Hockey has asserted: "the

Figure 1: State-Regulation model of Hockey[50]



The diagram illustrates optional modes of control that may be used to resolve the discrepancy between work demands and current cognitive resources. Loop A: the routine control system. Loop B: superior control system to be activated as the discrepancy is too high.

maintenance of performance under increased fatigue may attract increased 'costs'", expressed on the subjective level as more pain, fatigue and distress and on the neurophysiological level expressed as an increase in stress-hormones, EMG-activity and other physiological indices.[50] In view of this State-regulation model one might argue that WAD patients have to invest 'compensatory mental effort' during cognitive task-performance in order to perform well, as Klein (1997) has already suggested.[35] With respect to the results of the Synwork task (chapter three and four), it was concluded that WAD patients perform equally well as healthy individuals, but the execution of this task resulted on the subjective level in significantly more complaints and on the neurophsyiological level in an increase of the stresshormone cortisol, which can be interpreted as indications of 'compensatory mental effort'.
The results on the modified Stroop task, demonstrating significant slower task performances in WAD patients compared to healthy subjects, can be seen as examples of indirect control: a downwards adjustment of the performance goals.
Adding noise, as a kind of background distraction, when executing the Pasat-test, resulted in significant worse performances of WAD patients compared to healthy individuals (this thesis). Noise may increase the task load, because it serves as a distractor. As a result, more mental effort is needed when individuals have to perform a complex cognitive task (requiring controlled attention), in a noisy surrounding. In view of this model, the results demonstrated that healthy individuals are able to keep their performances stable in those situations, by using the routine control system. In contrast, WAD patients have to use their active control system: it seems that the WAD patients came in a 'failure to control' situation, because results demonstrated an increase of pain, fatigue and tension (an indication of extra mental effort investment) as well as an ineffective task performance (they made significantly more errors). From clinical experience it is known that many WAD patients are absent for sick-leave because of a strong increase of state dependent complaints, after they have worked well for a few weeks or months. In view of the State-regulation model this is an indication that, presumably, in the end the direct control strategy fails and that these patients are unwilling or not able to relinquish task goals (don't use the indirect control strategy), thus bringing them in a 'failure to control' situation.

Comparison of the two models

One important limitation of the model of Shiffrin and Schneider when applied to state-dependent complaints in relation to cognitive functioning, is

that this model is 'static' in the sense that it takes no account of the intra-individual variances in cognitive functioning due to continuously changing intensities of pain and fatigue[48], as is the case with WAD patients.
Another limitation is that, although the model of Shiffrin and Scheider can adopt a concept like 'pain' as a kind of internal distractor which occupy part of the limited information capacity, it does not account for the influence of motivation on task performance and the choice individuals have to use certain cognitive strategies dependent on their own task-goals.
With the 'State-regulation' model of Hockey[50,51,52] those phenomena are more easy to account for. Another advantage of the State-regulation model is that it can explain (in part) the chronic stress WAD patients may perceive in many daily situations in which mental effort plays in important role, because of the perceived cognitive difficulties and the often resulting ineffective job performances.
It is concluded that the State-regulation model can be used in future research concerning the relationship between state dependent factors and cognitive functioning in WAD patients.[50,51,52]

Recommendations for whiplash research

The results in this thesis concerning cortisol levels in WAD patients demonstrated that investigation of the HPA-axis offers a new perspective in the WAD phenomenon. These are in line with the bio-psycho-social model of WAD.[9,26,29,34,51] It is important to repeat this cortisol study with other kinds of (cognitive and emotional) stressors, in order to learn more about the possible imbalance of the stress-hormone system in WAD patients. The mental stressor used in this study was more or less a self-paced task, however, it is likely that high time-pressure tasks are more stressful and will cause more stress-responses.
It is interesting to know whether an imbalance of the stress-hormone system is already present after the initial emotional response of the whiplash injury, or whether it develops gradually in the course of the whiplash syndrome as a response to the continously perceived whiplash-related complaints and the person-dependent daily hassles.
As was noted before, not only stress-hormones may play a significant role in pain-perception, another interesting link is the influence of gonadal hormones on nociceptive processing.[22]
It is conceivable that a psychological process such as symptom amplification mediates the relationship between external stressors (whether this is the acute stressor of the whiplash injury or the perceived chronic daily has-

sles afterwards) and neurophysiological responses (e.g. dysfunctional stress-hormone system and/or dysfunctional pain-mechanisms). Therefore, more research is needed concerning the role of hypervigilance, appraisals, coping strategies and coping resources in the development of chronic whiplash-associated complaints. Research must focus on the precise relationship between 'hypervigilance' (which is a psychological process) and the existing neurophysiological process of 'hypersensitivity' in WAD patients.
Moreover, it would be interesting to know whether some WAD patients are '*hypo*vigilant', which means that they have an extreme tendency to neglect bodily symptoms in order to finish all activities they started, which is a kind of extreme suppressive coping behaviour.[52] It is thought that this kind of coping strategy will lead to an overuse of muscles and joints with a repetitive combination of muscular hyperactivity and pain. These repetitive pain experiences will also elicit neurophysiological processes of sensitization.[52]
Furthermore, future research should pay more attention to largely neglected factors such as educational level and sex.

With respect to *neuropsychological* research in WAD patients, further investigation of the relationship between the functioning of the HPA-axis and cognitive functioning in WAD patients appears an interesting subject. Several studies have demonstrated that increased cortisol levels, due to experimentally induced stress in healthy persons, are significantly associated with worse performances on memory tasks, related to neutral information.[53-58] Elevated cortisol levels are also associated with a better recall of (positive or negative) emotional stimuli.[59,60] It is advisable to perform this kind of investigation also in WAD patients.
The results revealed that WAD patients have a focused attention problem. More specifically, WAD patients are easily distracted by noise and are intolerant to everyday sounds of moderate strong intensities, in the presence of normal hearing. Likely, WAD patients will benefit from the use of special hearing plugs with a moderate-strong acoustic filter. These plugs reduce the surrounding noise-value, without reduction of the speech-intelligibility of persons nearby. Future research must clarify whether these special ear plugs do indeed enhance attention of WAD patients in noisy environments and which (dis)advantages may exist.
Research aimed at developing a more dynamic neuropsychological assessment method is necessary, because the current methods used by most neuropsychologists, are incomplete and unsuitable to give answers to questions regarding mental-cognitive functioning of these patients in daily life situations. Questions that have to be answered particularly within the context of legislation-

and insurance-procedures. A dynamic assessment approach is more suited to objectivate the subtle and changing cognitive capacities of WAD patients in daily life. Therefore, neuropsychologists may profit from new tools and procedures that are more sophisticated (see also below) and aimed at the investigation of the variability of cognitive functioning in WAD patients.

In conclusion, further integration of (neuro)psychological-, (neuro)physiological and (neuro)endocrinological research is necessary in order to gain more insight into the development of chronic whiplash-related complaints.

Implications for clinical neuropsychological assessment

Based on the results in this thesis, it is concluded that the health state of WAD patients is significantly related to attentional functioning. Given the fact that the intensity of state-dependent complaints varies during the course of the day(s) in WAD patients and the significant association between these complaints and attentional functioning, attentional functioning may also vary considerably in WAD patients' daily life, possibly leading to inconsistent work performances. Given this variability in functioning and the necessity of valid judgements concerning cognitive capacities of WAD patients and chronic pain patients in general, a more dynamic approach is required, as was argued above.

This implies:

- *Careful analysis of (biological) life-events and personality profile.*[61] Life-events (present before or after the whiplash injury) or personality characteristics (for example fear of failure, depression) may influence the test-performances in a negative way.
- *Inventory of pain medication or other medication and intoxications influencing the central nervous system.*[39,61]
- *Repeated measurements* should be included in the assessment to enable investigation of the variability of cognitive capacities.[62]
- *Subjective evaluation of state-dependent complaints* should be used (for example by means of VAS-scales) to enable more profound interpretations of the performances of neuropsychological tests.
- *Assessment under suboptimal conditions.* Standard neuropsychological assessment-procedures are aimed at reducing distractions and protection from fatigue in order to obtain the best performance of the pa-

tients.[31] This standard assessment procedure often reveals normal test results in WAD patients. In order to be able to objectivate the subtle cognitive deficits of these patients and to investigate the sustained attention in relation to state-dependent complaints, the test setting has to change in such a way that it reflects daily life situations better. This implies that tasks should be more complex and that the test situation should vary systematically in order to investigate the influence of external stimuli on attentional functioning.

- Assessment procedures must include a standard *'malinger' test* in order to control for suboptimal performance, because research has shown that WAD patients may *simulate* cognitive problems or under-perform during neuropsychological investigation for conscious or unconscious reasons.[39,63-65]

Some years ago, a group of researchers has begun to develop a new assessment method called 'Mental-endurance' assessment.[62] This method includes a systematical assessment of subjective complaints and attention in a more long-lasting test condition, with a pre- and post measurement paradigm, in order to measure the variability in attentional performance. For the years to come, the challenge is to enhance the ecological validity of this method, by implementing tasks that are more complex and varying the conditions of the test setting.

Implications for treatment

Recently some guidelines were developed by the medical advisary board of the whiplash foundation and the board for physiotherapists, concerning treatment of WAD patients in the acute- and subacute stage.[66,67] One of the guidelines concerns the advice for general practitioners to prescribe pain medication in order to relieve the pain of their patients significantly. Previous research revealed that in the acute stage after a whiplash injury, high pain intensity is a strong predictor for delayed functional recovery for WAD patients,[68] so pain relief is indeed important. Given the significance of initial pain intensity for long-term functioning, a systematic evaluation of the level of pain-relief perceived by the patient should be incorporated in the guideline, because this is a crucial step in achieving adequate pain control.[69] This implies that in the acute phase after the whiplash injury, the practitioner should see the patient on a regular basis and assess systematically the levelof pain-relief, for example by means of a VAS-scale.

Another significant prognostic factor for long-term functioning is the level of distress in the acute stage of the whiplash injury.[5,9,68,70] Given the importance of this primary emotional response for long-term functioning, as well as the possibility of an increasing vulnerability to stressors over the course of the months after the whiplash injury (this thesis), early reference to a psychologist or multi-disciplinary centre is necessary for individuals at risk.[26] This implies that general practitioners, as well as physiotherapists, have to judge the (changes in) level of distress in their patients.
Given the multi-dimensional character of the WAD syndrome, the most effective approach to chronic WAD patients is a multi-disciplinary treatment. An important implication of the bio-psycho-social model for rehabilitation treatment is the underlying vision that WAD-related symptoms (grade I and II) are caused by various interacting factors, resulting in dysfunctional pain processes and other neurophysiological imbalances.[26,29] This implies that when neurophysiological mechanisms are in balance again, the symptoms may gradually disappear, provided that the dysfunctional mechanisms did not cause structural changes in the central nervous system, which may happen when present for a long time.[29] In accordance with this view, the message to WAD patients must be that they can learn to elicit their own recovery process, by attending to a variety of bio-psycho-social factors. Given the relationship between state-dependent factors and attentional performance, a multi-disciplinary rehabilitation program, aimed at reducing both the physical and emotional symptoms, may also improve cognitive functioning. Treatment of chronic WAD patients should focus on pain- as well as on stress-management in the broadest sense. This implies for example: reduction of negative emotions related to the injury itself (e.g. post-traumatic stress symptoms, phobic reactions), reduction of daily stressors by using compensatory strategies and changing unhealthy life-style, awareness of the influence of personality factors on general functioning, restructuring of catastrophic (pain) cognitions, use of several different (pain)coping strategies, relaxation training, problem-solving training, social-skills training and increase of social support.[71,72] Given the stress-vulnerability of WAD patients with a low educational background, special attention must be given to developing effective treatments for this group, aimed at changing dysfunctional coping strategies into healthy strategies and using available personal coping-resources.

REFERENCES

1. Radanov, B.P., Di Stefano, G., Schnidrig, A. & Ballinari, P. (1991). Role of psychosocial stress in recovery from common whiplash. *The Lancet,* 338, 712-715.

2. Merksey, H. (1993). Psychological consequences of whiplash. In: *Spine state of the art reviews; Cervical flexion-extension/ Whiplash injuries* (Teasell, R.W. & Shapiro, A.P., eds.). Philadelphia: Hanley & Belfus, 471-480.

3. Barnsley, L., Lord, S., & Bogduk, N. (1994). Clinical review: Whiplash Injury. *Pain*, 283-307.

4. Radanov, B.P., Di Stefano, G., Schnidrig, A., Sturzenegger, M. (1994). Common whiplash: psychosomatic or somatopsychic*? J. Neurol. Neurosurg. Psychiat.,* 57, 486-490.

5. Drottning, M., Staff, P.H., Levin, L. & Malt, U.F.R. (1995). Acute emotional response to common whiplash injury predicts subsequent pain complaints. *Nord. J. Psychiatry*, 49, 293-299.

6. Radanov, B.P., Begre, S., Sturzenegger, M. & Augustiny, K.F. (1996). Course of psychological variables in whiplash injury – a 2-year follow-up with age, gender and education pair-matched patients. *Pain*, 64, 429-434.

7. Mayou, R. (1997). The psychiatry of road traffic accidents. In: *The Aftermath of Road Accidents* (Mitchell, M., ed.). London/New York: Routledge, 33-48.

8. Blokhorst, M.G.B.G., Lousberg, R., Vingerhoets, A.J.J.M., Winter, F.A.M., Zilvold, G. (2002). Daily hassles and stress-vulnerability in patients with a Whiplash Associated Disorder. *International Journal of Rehabilitation Research,* 25, 173-179.

9. Sterling, M., Kenardy, J., Jull, G. & Vicenzino, B. (2003). The development of psychological changes following whiplash injury. *Pain*, 106(3), 481-489.

10. Borchgrevink, G.E., Stiles, T., Borchgrevink, P.C. & Lereim, I. (1997). Personality profile among symptomatic and recovered patients with neck sprain injury, measured by MCMI-I acutely and 6 months after car-accidents. *Journal of Psychosomatic Research*, 42(4), 357-367.

11. Weisburg, J.N. & Keefe, F.J. (1999). Personality, individual differences and psychopathology in chronic pain. In: *Psychosocial Factors in Pain* (Eds. Gatchel, R.J. & Turk, D.C.). New York: the Guilford Press, 56-73.

12. Trull, T.J. and Useda, J.D. (1995). Comparison of the MMPI-2 personality Psychopathology Five (PSY-5), the NEO-PI and the NEO-PI-R. *Psychological Assessment*, 7(4), 508-516.

13. Gatchel, R.J. & Epker, J. (1999). Psychosocial predictors of chronic pain and response to treatment. In: *Psychosocial Factors in Pain* (Eds. Gatchel, R.J. & Turk, D.C.). New York: the Guilford Press, 412-434.

14. Sivera van der Sluijs, I.J., van de Mheen, H., Stronks, K. & Mackenbach, J.P. (1996). Blootstelling aan en omgang met psychosociale stressoren: sociaal-economische verschillen. *Tijdschrift voor Sociale Geneeskunde,* 2, 71-77.

15. Lazarus,R.S., Folkman,S. (1984). *Stress, appraisal and coping.* New York: Springer Publishing Co.

16. Roth, R.S. and Geisser, M.E. (2002). Educational achievement and chronic pain disability: mediating role of pain-related cognitions. *Clin J Pain*. 18(5), 286-96.

17. Endler, N.S. and Johnson, J.M. (2001). Assessment of coping with health problems. In: *Assessment in behavioral medicine*. (Ed. Vingerhoets, A.). New York: Brunner-Routledge, 135-160.

18. Miaskowski, C. (1999). The role of sex and gender in pain perception and responses to treatment. In: *Psychosocial Factors in Pain* (Eds. Gatchel, R.J. & Turk, D.C.). New York: the Guilford Press, 401-411.

19. Versteegen, G.J. Kingma, J. ten Duis H.J. (2000). Neck sprain after motor vehicle accidents in drivers and passengers. *Eur. Spine J*, 9, 547-552.

20. Keefe, F.J., Lefebvre, J.C., Egert, J.R., Affleck, G., Sullivan, M.J. & Caldwell, D.S.(2000). The relationship of gender to pain, pain behavior, and disability in osteoarthitis patients: the role of catastrophizing. *Pain,* 87, 325-334.

21. Pennebaker, J.W. (1988). *The Psychology of Physical Symptoms*. New York: Springer-Verlag.

22. Fillingim, R.B. & Ness, T.J. (2000). Sex-related hormonal influences on pain and anlgesic responses. *Neuroscience and biobehavioral reviews*, 24, 485-501.

23. Kessels, R.P.C., Keyser, A., Verhagen, W.I.M. & van Luijtelaar, E.L.J.M. (1998). The whiplash syndrome: a psycho-physiological and neuropsychological study towards attention. *Acta Neurologica Scandinavica*, 97, 188-193.

24. Tjell, C., Tenenbaum, A. & Rosenhall, U. (1999). Auditory function in whiplash-associated disorders. *Scand Audiol*, 28, 203-209.

25. Van Toor, T., Neijenhuis, K., Snik, A. & Blokhorst, M.G.B.G. (2003). Evaluation of auditory processing disorders after whiplash. In: *Auditory Processing Disorders. Development and evaluation of a test battery.* Nijmegen: Dissertation Radboud University, 109-129.

26. Ferrari, R. (2004). The clinical relevance of symptom amplification. *Pain*, 107, 276-279.

27. Peters, M.L., Vlaeyen, J.W.S., Kunnen, A.M.W. (2001). Is pain-related fear a predictor of somatosensory hypervigilance in chronic low back pain patients? *Behaviour Research and Therapy*, 40, 85-103.

28. Gimse, R., Björgen, I.A., Tjell, C., Tyssedal, J.S. & Bö, K. (1997). Reduced cognitive functions in a group of whiplash patients with demonstrated disturbances in the posture control system. *Journal of Clinical and Experimental Neuropsychology*, 19, 838-849.

29. Lidbeck, J. (2002). Central hyperexcitability in chronic musculoskeletal pain: a conceptual breakthrough with multiple clinical implications. *Pain Res Managem.*, 7, 81-92.

30. Gronwall, D.M.A. (1977). Paced Auditory Serial-Addition Task: a measure of recovery from concussion. *Perceptual and Motor Skills*, 44, 367-373.

31. Lezak, M.D. (1995). *Neuropsychological Assessment* (3rd Ed.). New York: Oxford University Press.

32. Radanov, B.P., Hirlinger, I., Di Stefano, G. & Valach, L. (1992). Attentional processing in cervical spine syndromes. *Acta Neurol Scand*, 85, 358-362.

33. Kessels, R.P.C. (2002). Measuring attention with the Paced Auditory Serial Addition Task (PASAT). *Gedrag & Gezondheid*, 30(1), 37-43.

34. Bosma, F.K. & Kessels, R.P.C. (2002). Cognitive impairments, psychological dysfunction and coping styles in patients with chronic whiplash syndrome. *Neuropsychiatry, neuropsychology and behavioural Neurology*, 15 (1), 56-65.

35. Klein, M. (1997). *Cognitive Aging, Attention and mild traumatic Brain Injury* (Thesis). Maastricht: Neuropsych. Publishers.

36. Radanov, B.P., Bicik, I., Dvorak, J., Antinnes, J., von Schulthess, G.K., & Buck, A. (1999). Relation between neuropsychological and neuroimaging findings in patients with late whiplash syndrome. *Journal of Neurology Neurosurgery and Psychiatry,* 66, 485-489.

37. Van Zomeren, A.H., & Saan, R. (1997). Whiplash. In B.G. Deelman, P.A.T.M. Eling, E.H.F. de Haan, A. Jennekens-Schinkel, A.H. van Zomeren (Ed.), *Klinische neuropsychologie,* 290-298. Amsterdam: Boom.

38. Borchgrevink, G., Smevik, O., Haave, I., Haraldseth, O., Nordby, A., Lereim, I. (1997). MRI of cerebrum and cervical columna within two days after whiplash neck sprain injury. Injury, 28(5-6),331-335.

39. Kessels, R.P.C., Aleman, A., Verhagen, W.I.M. & Luijtelaar, E.L.J.M. (2000). Cognitive functioning after whiplash injury: a meta-analysis. *Journal of the International Neuropsychological Society*, 6, 271-278.

40. Schmand, B., de Sterke, S. & Lindeboom, J. (1999). *Amsterdamse Korte Termijn Geheugen Test*. Lisse: Swets & Zeitlinger Publishers.

41. Eccleston, C., Crombez, G. (1999). Pain demands attention: a cognitive-Affective model of the interruptive function of pain. Psychol. Bulletin, 356-366.

42. Jensen, M. & Karoly, P. (2001). Self-report Scales and procedures for assessing pain in adults. In: *Handbook of Pain Assessment* (Turk, D. & Melzack, R., Eds.). New York: Guilford Press, 15-34.

43. Suhr, J.A. (2003). Neuropsychological impairment in fibromyalgia: relation to depression, fatigue and pain. *J Psychosom Res.*, 55(4),321-329.

44. Grisart, J.M. & Plaghki, L.H. (1999). Impaired selective attention in chronic pain patients. *European Journal of Pain,* 3, 325-333.

45. Eysenck, M.W. & Calvo, M.G. (1992). Anxiety and performance: the processing efficiency theory. *Cognition and Emotion,* 12, 697-713.

46. Brand, N., & Jolles., J. (1987). Information processing in depression and anxiety. *Psychological Medicine*, 17, 145-153.

47. Kolb, B. & Wishaw, I.Q. (1994). Emotional Processes. In: *Fundamentals of human neuropsychology* (3rd ed.). New York: Freeman and Company, 607-642.

48. Eling, P. & van Zomeren, E. (1997). Aandacht. In: *Klinische neuropsychologie*. (Deelman, B.G. et al., Eds.). Amsterdam: Boom. 125-144.

49. Brouwer, W. (1995). De psychologie van de aandacht. In: *Aandachts-stoornissen*. (Eling, P. & Brouwer, W., Eds.). Lisse: Swets & Zeitlinger, 29-47.

50. Wiethof, M. *Task analysis is heart work* (Thesis). 1997. Delft: University Press.

51. Hockey, G.R.J. Changes in operator efficiency as a function of environmental stress, fatigue and environmental rhythms. (1986). In: Boff, K.R., Kaufmann, L. and Thomas, J.P. (eds.). *Handbook of Perception and Human Performance*, vol 2. New York: Wiley.

52. Ouwerkerk, R.J., Meijman, T.F. & Mulder, G. (1994). *Arbeidspsychologische taakanalyse.* Het onderzoek van cognitieve en emotionele aspecten van arbeidstaken. Utrecht: Uitgeverij Lemma.

53. Ferrari, R. & Schrader, H. (2001). The late whiplash syndrome: a biopsychosocial approach. *J Neurol Neurosurg Psychiatry*, 70(6), 722-726.

54. Hasenbring M, Hallner D, Klasen B.(2001). Psychological mechanisms in the transition from acute to chronic pain: over- or underrated? *Schmerz*, 15(6), 442-447.

55. Van Steegeren, A. (2003). Stress en geheugen: de rol van noradrenaline en de amygdala bij emotionele informatieverwerking. *Neuropraxis*, 141-151.

56. Newcomer, J.W., Selke, G., Melson, A.K., Hershey, T., Craft, S., Richards, K., Alderson, A.L. (1999). Decreased memory performance in healthy humans induced by stress-level cortisol treatment. *Arch Gen Psychiatry.*, 56(6), 527-533.

57. Vedhara, K., Hyde, J., Gilchrist, I.D., Tytherleigh, M., Plummer, S. (2000). Acute stress, memory, attention and cortisol. *Psychoneuroendocrinology*, 25(6), 535-549.

58. Lupien, S.J., Gaudreau, S., Tchiteya, B.M., Maheu, F., Sharma, S., Nair, N.P.V., Hauger, R.L., McEwen, B.S. & Meaney, M.J. (1997). Stress-induced declarative memory impairment in healthy elderly subjects: relationship to cortisol reactivity. *Journal of Clinical Endocrinology and Metabolism*, 82(7), 2070-2075.

59. Buchanan, T.W. & Lovallo, W.R. (2001). Enhanced memory for emotional material following stress-level cortisol treatment in humans. *Psychoneuroendocrinology*, 26, 307-317.

60. Geraerts, E., Jelicic, M., Merckelbach, H. & Guerrieri, R. (2004). Het effect van acute stress op neutraal en emotioneel geheugen. *Neuropraxis*, 2, 54-59.

61. Bruins, J. (2004). Knelpunten en valkuilen bij neuro-psychologisch expertise onderzoek. *Neuropraxis*, 2, 48-53.

62. Cremer, R. (1998). *Mentaal Belastbaarheids Onderzoek*, internal report TNO, Amsterdam.

63. Schmand, B., Lindeboom, J. Schagen, S. Heijt, R. Koene, T., Hamburger, H.L. (1998). Cognitive complaints in patients after whiplash injury: the impact of malingering. *J Neurol Neurosurg Psychiatry*, 64, 339-343.

64. Smith, G.P. & Burger, G.K. (1997). Detection of malingering: validation of the Structured Inventory of Malingered Symptomatology (SIMS). Journal of the Academy of Psychiatry and the Law, 25, 180-183.

65. Merckelbach, H., Koeyvoets, N., Cima, M. & Nijman, H. (2001). De Nederlandse versie van de SIMS. Psychodiagnostisch gereedschap. *De Psycholoog*, 586-591.

66. Whiplash Stichting Nederland (2000). Richtlijnen voor huisartsen in de acute fase na een whiplash injury.

67. Bekkering, G.E., Hendriks, H.J.M., Lanser, K., Oostendorp, R.A.B., Peeters, G.G.M., Verhagen, A.P., van der Windt, D.A.W.M. (2001). KNGF-richtlijn Whiplash. Nederlands Tijdschrift voor Fysiotherapie. 3 (suppl.), 1-24.

68. Scholten-Peeters, G.G., Verhagen, A.P., Neeleman-van der Steen, C.W., Hurkmans, J.C., Wams, R.W. & Oostendorp, R.A. Randomized clinical trials of conservative treatment for patients with whiplash-associated disorders: considerations for the design and dynamic treatment protocol. *J. Manipulative Physiol. Ther.*, 26(7), 412-420.

69. Cepeda, M.S., Africano, J.M., Polo, R., Alcala, R. & Carr, D.B. (2003). What decline in pain intensity is meaningful to patients with acute pain? *Pain*, 105, 151-157.

70. Smed, A. (1997). Cognitive function and distress after common whiplash injury. *Acta Neurologica Scandinavica*, 95, 73-80.

71. Timmerman, I.G.H., Emmelkamp, P.M.G. & Sanderman, R. (1998). The effects of stress-management training program in individuals at risk in the community at large. *Behaviour Research and Therapy*, 36, 863-875.

72. Turk, D. (2003). Chronic pain and Whiplash Associated Disorder: Rehabilitation and secondary prevention. *Pain. Res. Manage.*, 8(1), 40-43.

Summary

SUMMARY

Chapter 1

Previous research has demonstrated that patients with a Whiplash Associated Disorder (WAD) have attention deficits, which interfere with their daily functioning. However, the causes of these cognitive problems are not clear. Evidence of traumatic brain injury is not convincing and it is suggested that state-dependent factors, such as headache, neck pain, fatigue or distress, might play a significant role. The main aim of this thesis was to investigate this relationship between state-dependent factors and attention in WAD patients. Furthermore, the focus was on 'noise-intolerance' and 'noise-distractibility', which are symptoms often mentioned by WAD patients and neglected topics in whiplash research so far. In the first chapter, a brief overview was given of the definition and classification of WAD. Next, a review of results on cognitive functioning in WAD was presented. In the last paragraph, the remaining chapters of the thesis were introduced.

Chapter 2

The objectives of the study described in chapter two were to examine the self-reported, daily problems of patients with a Whiplash Associated Disorder (WAD) and healthy controls, with the hypothesis that WAD patients would report more person-dependent hassles and perceived them as more serious than healthy controls, due to the prior experience of a whiplash injury. In addition, it was expected that the person-independent serious rating would be elevated, reflecting the increased vulnerability of WAD patients to common stressors. Finally, a strong relationship was expected between frequency and/or seriousness of daily problems on the one hand and level of distress on the other hand. Forty-seven WAD patients seeking treatment and forty-seven matched healthy controls, completed the Daily Problems Checklist (DPC). The level of distress was measured by the Symptom Check List (SCL-90).

As was expected, most DPC-scores in the WAD group were higher than the scores of healthy subjects. Regression-analysis further revealed that 61% of the variance in general distress in the WAD group could be explained by DPC-scores and educational background.

In conclusion, chronic WAD patients report a high stress-load, which is related specifically to personal functioning after the whiplash injury. In addition, WAD patients (especially those with a low educational level) appear to be more vulnerable and react with more distress than healthy persons, to all kinds of stressors. It was concluded that stress-responses likely play an important role in the maintenance or deterioration of whiplash-associated complaints.

Chapter 3

In chapter three the results of an experiment were described which was carried out to explore cortisol levels and cortisol response as result from a mental stress task, in patients with a Whiplash Associated Disorder (WAD) compared to healthy subjects and subjects in a relax-control condition. In addition, it was investigated whether the amount and appraisal of severity of daily hassles predicted cortisol response. It was expected that WAD patients had higher cortisol levels in time and that they showed a stronger increase in cortisol levels after performing a mental stress-task, compared to healthy subjects and subjects in a relax-control condition. Both the frequencies and appraisal of daily problems were assumed to be significant predictors of cortisol responsivity.

As was hypothesized, results revealed that WAD patients had significant higher cortisol levels in time. Although the differences were not significant, there seems to be a trend towards an increase in cortisol concentrations after performing a mental stress task in the experimental WAD group, compared to the healthy control group and relax control groups. Cortisol responsivity in the experimental groups is predicted by the amount of daily hassles and especially by the appraisals of severity of daily problems. The frequency and intensity ratings of daily hassles are significant higher in WAD patients compared to healthy persons.

It was concluded that chronic WAD patients have higher cortisol levels compared to healthy subjects. Because both the amount and appraisal of severity of daily problems are significant predictors of cortisol responsivity due to an acute mental stressor, it is plausible that a subgroup of WAD patients is more vulnerable to subsequent stressors after the whiplash injury. For this reason, 'stressmanagement' should be an important topic in rehabilitation program mes for chronic WAD patients. It was concluded that study of HPA-axis in WAD patients offer new, interesting perspectives in the WAD phenomenon.

Chapter 4

In chapter four, the results were described of an complementary experiment on the study presented in chapter three. An experiment was carried out in

which the level of noise-intolerance in patients with a Whiplash Associated Disorder (WAD) was compared to healthy matched control subjects. In addition, the relationship between state-dependent factors (as headache, neck pain, fatigue and tension) and noise-intolerance level was investigated. Twenty-eight WAD patients and controls were exposed to state-measurements and noise-intensities ranging from 57dB-95dB before and after a mental stress task.
WAD patients were significantlly more intolerant to all noise-intensities than healthy subjects. This intolerance increased with increasing noise-intensity. Noise-intolerance was not increased after the execution of a mental stress task. These results confirm the subjective complaint of WAD patients being more intolerant to everyday sounds, in the presence of normal hearing. In accordance with the hypothesis, a positive association was found between the increase in headache and the increase in noise-intolerance for moderate intensities. Besides headache, gender was related to noise-intolerance.
It was concluded that more research is needed in order to get more insight into the relationship between noise-intolerance and possible other (neuro)psychological/ physiological factors.

Chapter 5

The modified Stroop task was presented to forty-eight patients with a Whiplash Associated Disorder (WAD) and forty-eight healthy matched control participants to investigate possible attentional impairments in relation to state related factors (headache, neck pain, fatigue, tension and state-anxiety). It was expected that performance on the Stroop task is negatively associated by these state related variables.
In accordance with the expectations, the results showed that response latencies increase for subtasks 1 through 4, for both groups. In addition, WAD patients performed significantly worse on all subtasks. There was a significant interaction between the two groups and the four subtasks. The results demonstrated signs for interference susceptibility or reduced capacity to shift attention on the modified Stroop task. The results concerning the influence of state variables indicated that the intensity of headache was significantly related (demonstrating a worsening) to Stroop task performance in the WAD-group.
It was concluded that WAD patients exhibit a general slowing of information processing, especially on tasks, which require controlled attention. There are signs for subtle deficits in focused attention, related to the intensity of headache. Clinical implications were discussed.

Chapter 6

An experiment was carried out to explore the influence of the level of background noise on attention in forty-eight patients with a Whiplash Associated Disorder (WAD) compared to forty-eight healthy matched control subjects. In addition, the relationship between state-dependent factors such as headache, fatigue, tension, global distress, and task performance in three conditions with different levels of background noise was investigated.
As was expected, all subjects made increasingly more errors on an attention task, with increasing background noise. However, WAD patients performed increasingly worse with increasing background noise, as compared to healthy subjects. Furthermore, whereas healthy subjects showed a practice-effect in time, WAD patients did not. Besides educational level, three state-dependent variables (fatigue, headache, neck pain) were significant predictors of the performance on an attention task with strong background noise, whereas in the other two conditions (low background noise and no background noise) only fatigue was a significant predictor. Furthermore, emotional distress was negatively related to attentional performance in all three conditions.
It was concluded that WAD patients have a focused attention deficit, when surrounded by noise. Given the relationship between state-dependent factors and attentional performance, a multidisciplinary rehabilitation program, aimed at reducing both the physical and emotional symptoms, may also improve cognitive functioning.

Chapter 7

In the last chapter, the results of the different experiments were reviewed, discussed and imbedded in current theories. Next, recommendations for future research were described and clinical implications were given for neuropsychological assessment as well as rehabilitation.

Samenvatting

SAMENVATTING

Hoofdstuk 1

Uit onderzoek is gebleken dat patiënten met een Whiplash Associated Disorder (WAD) een gestoorde aandachtsfunctie hebben. Ook is vastgesteld dat deze cognitieve beperking een negatieve invloed heeft op hun dagelijks functioneren. Aangezien er weinig evidentie is voor een traumatisch hersenletsel, is door enkele onderzoekers gesuggereerd dat toestands-gerelateerde factoren, zoals hoofdpijn, nekpijn, vermoeidheid of emotionele spanningen, waarschijnlijk significant gerelateerd zijn aan het cognitief functioneren bij WAD-patiënten. Het belangrijkste doel van dit promotie onderzoek is dan ook meer zicht te krijgen op deze samenhang tussen toestandsfactoren en de aandachtsfunctie binnen deze patiënten groep.
In het bijzonder werd onderzocht in hoeverre er bij WAD-patiënten sprake is van een intolerantie voor geluiden. Daaraan gekoppeld werd onderzocht of deze patiënten in verhoogde mate afleidbaar zijn door geluid. WAD-patiënten benoemen deze klachten namelijk regelmatig, terwijl tot op heden geen onderzoek is verricht naar de objectiveerbaarheid van deze klachten, dan wel óf en in hoeverre er een samenhang is met toestandsgerelateerde factoren.
In het eerste hoofdstuk wordt een kort historisch overzicht gegeven. Begonnen wordt met de definitie, classificatie en epidemiologische gegevens van het WAD-syndroom. Daarna komen de onderzoeksresultaten aan de orde met betrekking tot het cognitief functioneren van WAD-patiënten. In de laatste paragraaf zal vervolgens worden vooruitgelopen op de hoofdlijnen van het onderzoek.

Hoofdstuk 2

In het tweede hoofdstuk worden de resultaten gepresenteerd van een (deel)-onderzoek naar de frequentie en intensiteit van alledaagse problemen bij enerzijds een groep WAD-patiënten en anderzijds een gezonde controle groep.
De hypothese was dat WAD-patiënten, in vergelijking met een gezonde controle groep, significant meer problemen waarnemen die gerelateerd zijn aan het persoonlijk functioneren en ook, dat deze problemen als meer bedreigend ervaren worden als gevolg van het doorgemaakte whiplash ongeval. Verder werd verwacht dat WAD-patiënten ook niet-persoons gerelateerde stressoren (i.e. stressoren waar men geen invloed op heeft) als significant meer bedreigend ervaren, hetgeen kortom een algehele kwetsbaarheid zou

weerspiegelen voor allerlei soorten stressoren. Ten slotte werd verwacht dat er eveneens een significant verband zou bestaan tussen de frequentie en/of intensiteit van de alledaagse problemen enerzijds en de mate van emotionele spanningen anderzijds.
Vierennegentig proefpersonen, waar van zevenenveertig WAD-patiënten en zevenenveertig gezonde controle personen, gematcht op leeftijd, geslacht en opleidingsniveau, vulden de Alledaagse Problemen Lijst (APL) in. Het niveau van emotionele spanningen, psychoneuroticisme, werd gemeten met behulp van de Symptom Check List (SCL-90).
In overeenstemming met de hypothese, laten de resultaten zien dat vrijwel alle scores op de Alledaagse Problemen Lijst in de WAD-groep, significant hoger zijn dan de scores van de gezonde referentiegroep. De resultaten van een regressie-analyse tonen aan dat 61% van de variantie in psychoneuroticisme verklaard kon worden uit de APL-variabelen tezamen met opleidingsniveau.
Geconcludeerd werd dat WAD-patiënten, in vergelijking met de gezonde groep, een hogere subjectieve belasting ervaren, gerelateerd aan het persoonlijk functioneren. Bovendien lijken WAD-patiënten (metname diegenen met een laag opleidingsniveau) kwetsbaarder te zijn voor allerlei soorten van stressoren. Waarschijnlijk spelen stressreacties een belangrijke rol bij het in stand houden, of bij de toename van whiplash gerelateerde symptomen.

Hoofdstuk 3

In het derde hoofdstuk vindt u de resultaten van een experiment waarbij het cortisolgehalte en de cortisolrespons werd gemeten voor- en na de uitvoering van een mentale stresstaak, in een groep WAD-patiënten en in een groep gezonde proefpersonen. Vervolgens werden deze cortisolgehaltes vergeleken met die van een groep WAD-patiënten en een groep gezonde proefpersonen in een relax-controle conditie. Ook werd onderzocht of de frequentie en beoordeling van alledaagse stressoren een voorspellende waarde heeft met betrekking tot de cortisolrespons. Verwacht werd dat WAD-patiënten, in vergelijking met de overige twee groepen, een significant hoger cortisolgehalte hebben en dat zij een significante toename in cortisol vertonen na een mentale stresstaak te hebben uitgevoerd.
Conform de hypothese tonen de resultaten aan dat WAD-patiënten op verschillende tijdstippen gedurende het experiment een significant hoger cortisolgehalte hebben. Vergeleken met de overige groepen, is er bij de experimentele WAD-groep een toename in cortisol waarneembaar, ofschoon niet significant. Zoals verwacht, kan de cortisolrespons worden voorspeld door

de hoeveelheid alledaagse stressoren, in het bijzonder door de mate waarin deze stressoren door patiënten als bedreigend worden beoordeeld.

Samenvattend kan worden gesteld dat chronische WAD-patiënten een hoger cortisolgehalte hebben in vergelijking met gezonde mensen. Aangezien zowel de frequentie, als de beoordeling van alledaagse problemen, significante predictoren van de cortisolrespons (als gevolg van de uitvoering van een mentale stresstaak) zijn, moet worden geconcludeerd dat een subgroep van WAD-patiënten naar aanleiding van het whiplashongeval waarschijnlijk kwetsbaarder is geworden voor opeenvolgende stressoren. Om die reden dient 'stressmanagement' een belangrijk thema te zijn in revalidatiebehandelprogramma's voor chronische WAD-patiënten. Nog een belangrijke conclusie is dat het onderzoek naar de HPA-as in WAD-patiënten een nieuwe, interessante invalshoek is, die het ont- en bestaan van chronische whiplash gerelateerde klachten wellicht (mede) kan verklaren.

Hoofdstuk 4

Als vervolg op het onderzoek in hoofdstuk drie, vindt men in hoofdstuk vier de resultaten beschreven van een aanvullend experiment, waarin werd onderzocht of WAD-patiënten, vergeleken bij gematchte, gezonde proefpersonen, intoleranter zijn voor geluiden. Verder werd het al of niet bestaan van een verband onderzocht tussen toestandsfactoren (zoals hoofdpijn, nekpijn, vermoeidheid, spanning, etc.) en de mate van geluidsintolerantie. Zesenvijftig personen (28 WAD-patiënten en 28 gezonde proefpersonen) werden blootgesteld aan geluidsintensiteiten (variërend van 57dB tot 95dB) en de daaraan gekoppelde toestandsmaten, vóór- en nadat een mentale stresstaak werd uitgevoerd.

De conclusie hier is dat WAD-patiënten, in vergelijking met gezonde proefpersonen, significant intoleranter zijn voor alle aangeboden geluidsintensiteiten. Deze intolerantie nam verhoudingsgewijs toe, naarmate de geluidsintensiteit toenam. De geluidsintolerantie nam echter niet significant toe na het uitvoeren van een mentale stresstaak.

Deze resultaten bevestigen de klacht van veel WAD-patiënten dat zij alledaagse geluiden na het ongeval als hinderlijker ervaren, terwijl het gehoor niet is aangetast. In overeenstemming met de hypothese ging een toename van hoofdpijn gepaard met een toename van geluidsintolerantie met betrekking tot matig-sterke geluidsintensiteiten. Behalve hoofdpijn, kon ook de variabele 'geslacht' significant gerelateerd worden aan geluidsintolerantie (vrouwen zijn intoleranter voor diverse geluidsintensiteiten).

Ten einde meer inzicht te verkrijgen in de relatie tussen geluidsintolerantie enerzijds en (neuro-)psychologische/neurofysiologische factoren anderzijds, is aanvullend onderzoek gewenst.

Hoofdstuk 5

Ten einde eventuele aandachtstekorten te onderzoeken in relatie tot specifieke toestandsvariabelen (hoofdpijn, nekpijn, vermoeidheid, spanning en toestandsangst) werd een gemodificeerde versie van de Stroop taak aangeboden aan 96 personen (48 WAD-patiënten en 48 gematchte, gezonde proefpersonen). Verwacht werd dat de prestatie op de Strooptaak negatief samenhangt met deze toestandsvariabelen. De resultaten met betrekking tot de invloed van toestandsvariabelen demonstreren dat de intensiteit van de hoofdpijn significant gerelateerd is aan de prestatie op de Strooptaak (hoe meer hoofdpijn, des te trager de Strooptaak werd uitgevoerd).
Geconcludeerd moet worden dat WAD-patiënten een tragere informatieverwerking vertonen, in het bijzonder op taken die veel bewuste aandacht vergen. Er zijn aanwijzingen voor subtiele tekorten in de gerichte aandacht die verband houden met de intensiteit van hoofdpijn. Ter afsluiting worden de klinische implicaties besproken.

Hoofdstuk 6

In hoofdstuk 6 worden de resultaten van een experiment beschreven waarbij de sterkte van achtergrondlawaai, in relatie tot de prestatie op een aandachtstaak, werd onderzocht bij 96 proefpersonen (48 WAD-patiënten in vergelijking met 48 gematchte, gezonde proefpersonen). Het verband tussen toestandsvariabelen (zoals hoofdpijn, nekpijn, vermoeidheid, spanning) en taakuitvoering in drie condities met verschillend niveau van achtergrondruis, werd systematisch onderzocht.
Zoals werd verwacht maakten alle proefpersonen meer fouten op een aandachtstaak naarmate het achtergrond lawaai toenam. Echter, naarmate het achtergrond lawaai toenam, presteerden WAD-patiënten disproportioneel slechter dan de gezonde controlegroep. Terwijl gezonde proefpersonen gedurende verschillende trials een leer-effect te zien gaven, was dat bij WAD-patiënten niet het geval. Naast opleidingsniveau, blijken, in de conditie met een sterk achtergrond lawaai, drie toestandsvariabelen significante predictoren te zijn voor de prestatie op een aandachtstaak. In de andere twee condities (laag niveau of geen achtergrond lawaai) was alleen de variabele 'vermoeidheid' een significante voorspeller. De factor 'emotionele spanning' was

negatief gerelateerd aan de prestatie op de aandachtstaak in alle drie condities waarbij de factor 'opleidingsniveau' buiten beschouwing werd gelaten. De conclusie is dat WAD-patiënten in verhoogde mate afgeleid worden door achtergrondlawaai. Gezien de samenhang tussen toestandsvariabelen en de prestatie op aandachtstaken, is te verwachten dat de aandachtsfunctie zal verbeteren indien fysieke- en emotionele klachten verminderen.

Hoofdstuk 7

In het laatste hoofdstuk worden de resultaten uit de verschillende experimenten tenslotte samengevoegd, bediscussieerd en geïmplementeerd in hedendaagse theorieën. Vervolgens worden enkele aanbevelingen gegeven voor toekomstig whiplash research. Als laatste worden enkele relevante klinische implicaties beschreven voor zowel het toekomstig neuropsychologisch assessment, als de behandeling van WAD patiënten.

Dankwoord

DANKWOORD

Het leek er even op dat het einde van dit proefschrift telkens verschoof naarmate het onderzoek vorderde, gelijk een horizon tijdens een wandeling, maar eindelijk is het zo ver dat ik het dankwoord kan typen. Tijdens het onderzoek en de verslaglegging hiervan heb ik van veel mensen ondersteuning en begeleiding gekregen. Een aantal van hen wil ik hier graag met name noemen.

Allereerst mijn copromotor Richel Lousberg. Richel, ontzettend bedankt voor al je kritiek, adviezen, morele steun, vertrouwen en geduld in de afgelopen jaren. Ik heb het erg prettig gevonden om met je samen te werken! Jouw enthousiasme voor het onderzoek was heel stimulerend.
Ook ben ik veel dank verschuldigd aan mijn promotor Prof. dr. Gerrit Zilvold voor de ruimte en het vertrouwen dat mij gegeven werd om dit onderzoek op te zetten en uit te voeren. Gerrit creëerde de noodzakelijke randvoorwaarden; zonder zijn inzet was dit onderzoek niet mogelijk geweest. Uiteraard is de betrokkenheid en de genereuze financiële ondersteuning van mw. Nardy Roeloffzen ook van cruciaal belang geweest om dit onderzoek te kunnen realiseren.

Mijn dank gaat ook uit naar de vier stagiaires van de Radboud Universiteit Nijmegen die mij in de afgelopen jaren voortreffelijk hebben geholpen met het uitvoeren van het onderzoek: Onno Lof, Stefan Meeldijk, Minke Swinkels en Pinel Schrijver. Een speciaal woordje van dank voor Onno: jij behoorde tot de mensen van het eerste uur en hebt zelfs je studieduur aanmerkelijk verlengd om het onderzoek te kunnen afronden. We hebben vaak het nuttige met het aangename verenigd en destijds heel wat rookpauzes ingelast om te brainstormen over de opzet van het onderzoek. Ik kijk met veel plezier terug op deze periode, hoewel ik blij ben dat ik inmiddels gestopt ben met roken.

Thijs van Toor, Paul Ganzevles, Rob Hermans en Willem Kersing eveneens bedankt voor jullie professionele inbreng. En ook aan Gilles van Luijtelaar en Paul Eling die op de achtergrond, vanuit hun functie als stagebegeleider aan de faculteit Psychologie van de Radboud Universiteit, regelmatig hebben meegedacht. Paul, jij zat in 1988 in mijn afstudeercommissie psychologie en het doet mij deugd dat je ook zitting wilde nemen in de promotiecommissie. De overige promotiecommissieleden, professor Erwin Seydel, professor Hermie Hermens, professor Ben Schmand, professor Ad Vingerhoets en dr. Frits Winter ben ik zeer erkentelijk voor hun bijdrage. Hermie, ik kan mij voorstellen dat je uit hoofde van je functie blij bent dat het onderzoek nu af is. Ad, mede dankzij jou heb ik geleerd dat je ook in de wetenschap moet doorzetten. Frits, je directe bijdrage aan dit onderzoek is niet zo groot geweest, maar je indirecte bijdrage des te meer! Ik heb ontzettend veel van je geleerd en ik dank je voor de fijne tijd dat we hebben samengewerkt in het Roessingh.

Dan mijn andere (ex)collega's binnen het RCR, RRD en RDG. Dank voor jullie samenwerking, belangstelling en inbreng. In het bijzonder Marc Nederhand, Nicole Vrijens, Anneke Wulferink, Jan Blanksma, Silvia Kienhuis, Jan Willems, Lucas Slot, Maja van Liere, Ailien de Boer, Bernadette Wassink, Machteld Faber, Michael Eissink, Annika Bekmann, José Wittrock en Karlein Schreurs. Karlein, in de eindfase van het schrijven van dit proefschrift heb ik erg veel gehad aan jouw kritiek en adviezen. Bedankt dat je tijd wilde vrijmaken terwijl je zo druk bent. José, volgens mij kunnen wij binnenkort ons 12,5 jarig samenwerkingsjubileum vieren; wat gaat de tijd toch snel (als je aan een proefschrift werkt!)

Caro Bedorf en Sacha Jagt bedank ik voor alle artikelen die ze telkens weer voor mij hebben aangevraagd. Diane Muller ben ik erkentelijk voor de secretariële ondersteuning.

Ook dank aan alle vrienden en familieleden voor de voortdurende interesse in de voortgang van mijn onderzoek: gelukkig kan ik tegen jullie allemaal zeggen dat het af is. Van Bea heb ik de nodige hulp gehad wat betreft het Engelse correctiewerk. Bedankt dat je daarbij ook hebt willen luisteren naar mijn alledaagse stressoren met betrekking tot de voortgang van mijn proefschrift. Nu dit boekje af is, zul je zien dat ik meer 'power' krijg om te 'walken'. Ook Margret, door wie de kinderen wanneer nodig opgevangen konden worden, wil ik hier met name noemen.

Helaas leven mijn ouders niet meer, maar ik ben hen erg dankbaar voor hun stimulans en de ruimte die ze mij hebben gegeven om mijn eigen interesses te kunnen volgen. Dankzij de vele fijne herinneringen zullen zij voor mijn gevoel altijd in mijn nabijheid zijn.

Lieve Gido en Mauro, eindelijk is dit werkje af. Ik hoop dat ik nu nóg meer tijd krijg om spelletjes met jullie te doen.
Lieve Paul, bedankt voor alle tijd en energie die je hebt gestoken in de layout van dit boekje en vooral ook dank voor al het andere. Zonder jou zou dit proefschrift zeker niet zijn verschenen!

Curriculum Vitae

CURRICULUM VITAE

Mariëtte Blokhorst werd geboren op 28 maart 1962 in het Overijsselse Goor. In 1980 behaalde zij haar VWO-diploma aan het Twickel College te Hengelo, waarna ze eerst een jaar sociologie studeerde aan de Universiteit van Nij–megen, om het jaar daarna over te stappen naar de studie psychologie. Na het kandidaatsexamen werd de afstudeerrichting neuro- en revalidatiepsychologie gevolgd. Het doctoraalexamen behaalde zij in 1988. In 1999 kreeg zij een registratie als gezondheidszorg psycholoog in het BIG register.

In het kader van haar studie liep zij stage in het AMC te Amsterdam en daarna in revalidatiecentrum Het Roessingh.
Na deze stage kreeg zij een functie als psycholoog binnen de afdeling Psychologie van Het Roessingh en een aantal jaren later bij de pijnkliniek van Het Roessingh. Daarnaast werkte zij tevens als psycholoog bij de Roessingh Diensten Groep, met als belangrijkste taak het verrichten van expertise-onderzoeken o.a. in het kader van letselschade- en WAO-procedures. Zij is ook al enige jaren als onderzoeker verbonden aan Roessingh Research & Development. Verder is zij gastdocente aan de postdoctorale GGZ-opleiding in Oost-Nederland.