

REVIEW

Reactivity and recovery from different types of work measured by catecholamines and cortisol: a systematic literature overview

Judith K Sluiter, Monique H W Frings-Dresen, Theo F Meijman, Allard J van der Beek

Abstract

Objectives—To review occupational health, laboratory, and sports literature on neuroendocrine reactivity and recovery from mental, combined mental and physical, or physical tasks.

Methods—A systematic literature search was performed in eight databases. Studies with catecholamines or cortisol as effect variables measured in blood, urine, or saliva were included.

Results—After application of inclusion and exclusion criteria, 77 studies from the initial 559 identified were taken into account. In occupational settings it was found that relatively few studies were conclusive about recovery, which formed a contrast with sports research. For reactivity and recovery up to 1 hour after performing the task, half of the studies considered physical tasks and more than two thirds showed incomplete recovery compared with baseline excretion of catecholamines and cortisol. Recovery extending to 3 days after the task was performed was often incomplete for cortisol after combined mentally and physically demanding tasks, and less often after solely mental or physical tasks. This type of recovery was more often incomplete for adrenaline (epinephrine) than for noradrenaline (norepinephrine), which was the case after mental as well as combined mental and physical tasks.

Conclusions—The results from laboratory and sports research may be transferable to some occupations, but more research is needed on the course of recovery relative to health effects in occupational settings.

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Keywords: neuroendocrine reactivity; neuroendocrine recovery; occupational task

Occupationally induced fatigue is thought to play a major part in causing psychological overload when, repeatedly, too little opportunity for recovery is given. This suggests that the short term effects of insufficient recovery from a working period will lead to long term effects on health. The prevalence of burnout,

overtraining, chronic fatigue syndrome, musculoskeletal disorders, and chronic cardiovascular disorders have been rising. As Frankenhaeuser¹ proposed in her biopsychosocial stress model, stress is determined by the balance between the person's evaluation of the demands from the environment and his or her perceived mental resources to meet these demands. Physiologically, the human body has to maintain a balance between catabolic and anabolic mechanisms to function optimally. This balance has to be required continuously, and more time to recover is needed when a state of dysbalance remains relatively too long. Reactivity and recovery after physical or mental exertion takes place in many subsystems of the human body. The cardiovascular-respiratory system, for example, reacts naturally with increases in heart rate, blood pressure, and respiration rate when stressful situations occur or when body movements are asked for during sporting and working situations. Total recovery of this system is achieved when the heart rate, blood pressure, and respiration rate return to baseline levels.

A review of psychoneuroendocrine research on stress and coping² discussed the classic studies from Canon to Selye, and from Ursin to Levi and Frankenhaeuser. From these studies, it can be concluded that, when people unwind neuroendocrinologically too slowly after exertions, and thereby, show tonic sustained activation (spillover) of neuroendocrine reactivity, recovery to baseline levels is incomplete. In the long term, when accumulated, this might lead to chronic fatigue that in turn might lead to health problems. The starting point of this (partly assumed) vicious circle is the way in which people recover from tasks. To clarify this picture, it seems obvious to focus on what is known about neuroendocrine reactivity and recovery. By contrast with occupational research, this mechanism is well studied in sports research. This empirical knowledge can be transferred to occupational settings.

The two neuroendocrine systems in this context are the sympathetic-adreno-medullary system (SAM) and the hypothalamus-pituitary-adrenal system (HPA). For decades measurements of these two systems have formed the basis for psychoneuroendocrine

Coronel Institute for Occupational and Environmental Health, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

J K Sluiter
M H W Frings-Dresen
A J van der Beek

University of Groningen, Experimental and Work Psychology, Groningen, The Netherlands

T F Meijman

Correspondence to:
Dr Judith Sluiter, Coronel Institute for Occupational and Environmental Health, Academic Medical Center, University of Amsterdam, PO Box 22700, 1100 DE Amsterdam, The Netherlands
email j.sluit@amc.uva.nl

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stress research starting with Cannon (SAM) and Selye (HPA).^{2,3} Differences between people in HPA activity have been found in cortisol excretion at baseline and reactivity during work. Especially the morning baseline concentrations were found to increase with chronic or traumatic stress, and were shown to be associated with genetic and personality traits.⁴ The SAM activity is measured by concentrations of peripheral catecholamines and indicates general arousal reflecting the acute mental (adrenaline) and physical (noradrenaline) workload to which the subject is exposed. Thus, the reactivity of the neuroendocrine system is different when mental or physical exertion is asked for, and the excretion rates of adrenaline, noradrenaline, and cortisol could be seen as indicators of the effect of different task and environmental demands on healthy people. A further distinction exists between acute and chronic effects, and these effects may depend upon short term and long term demands.

Reactivity and recovery are time and activity dependent, and both psychological and physiological body systems react at different speeds and at different times. Most studies use different time lags to assess their recovery variables. Because working life is most often organised in fixed time schedules, and to facilitate the comparison of outcomes in the different studies a categorisation of recovery time is proposed:

- reactivity
- mesorecovery
- metarecovery
- macrorecovery.

In this study, the different categories have been defined.

Reactivity is the time during which a task or activity is performed. Because of the micro-pauses that people take during performance of a task, reactivity is partly entangled with what might be called microrecovery. The first minutes after performance of a task might be seen as microrecovery. Mesorecovery includes the recovery period between 10 minutes and about 1 hour after performance of a task. Metarecovery is the time to recover from performance of a task that occurs between 2 days or periods of work. This period starts about 1 hour after work—for example, the evening, or overnight—and may expand to 2 days (weekend period). Finally, macrorecovery is defined as that period which begins 2 days after performance of a task.

This literature overview is focused on the reactivity and recovery of part of the neuroendocrine system (cortisol and the peripheral catecholamines). Measurements of these hormones in the different studies take place in urine, blood, and saliva. Urinary measurements of free adrenaline and noradrenaline provide a reliable measure of the circulating concentrations of these hormones in blood.⁵ Also, salivary cortisol was also found to be highly associated with the free cortisol fraction in blood.⁶ Thus, the outcomes of the different studies are comparable. To investigate relations between work or task demands, psychological variables, and reactivity in catecholamines and

cortisol, empirical research has been carried out in both laboratory and field studies.

Field studies cover a whole range of occupations with different natures of work, as well as different sports. The main focus of work related studies is on work stress and work related fatigue relative to health complaints—such as, burnout or chronic fatigue. In neuroendocrine sports research, two major research lines are distinguishable: assessments among endurance (aerobic) athletes, and assessments among sportsmen who mainly perform resistance training (anaerobic workouts). The main topic in both kinds of research is “overtraining”. Overtraining is defined as an increase in training volume or intensity of exercise with inadequate recovery periods between workouts, resulting in long term performance decrements (several weeks or months).^{7,8} A shorter or less severe variation of overtraining is referred to as overreaching.^{7,9} Recovery from overtraining is said to take weeks to months, whereas recovery from overreaching would take just a few days. The jargon used in occupational and sports research seems to be compatible, and both make a distinction in severity of symptoms, in which the acute fatigue and overreaching occur in advance of both chronic fatigue and overtraining.

In laboratory settings, mostly short term controlled tasks are used to assess neuroendocrine reactivity. Well known, work related mentally demanding tasks in the laboratory are arithmetic tasks, the Stroop test, public speaking tests, emotionally loaded films, word search tasks, and simulated work tasks. In laboratory sports research, submaximal or maximal tests on cycle ergometer, treadmill, and row ergometer are used as stressors. Compared with work related research, sports research often combines laboratory measurements with real life training or competition measurements. An exception is the study of Lundberg *et al*¹⁰ who compared the same group of workers in laboratory and naturally mentally demanding settings, and showed that the correlation within subjects between measurements in the laboratory and those in real life situations were high. Furthermore, they reported consistency within a person in urinary catecholamine and cortisol excretion over different experimental conditions and time intervals ranging from 24 hours to 12 weeks.

The nature of tasks under study can be divided into mainly mental tasks, mainly physical tasks, and a combination of mental and physical tasks. In occupational laboratory research the focus is often on mental performance of a task, while laboratory sports research mainly focuses on physical tasks. In occupational field studies, some occupations may be classified as a combination of mental and physical tasks, and the same goes for sports research in which subjects are studied during games or races.

The purpose of this literature overview is threefold. Firstly, to get insight into the extent to which neuroendocrine reactivity and recovery is investigated, in terms of the definitions of the four recovery periods, relative to work as

Table 1 Summary of research on reactivity or microrecovery

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑ = increase ↓ = decrease ≡ = no change)	Controlled variables
Bergerson 1991 ¹⁴	10 M	II Tennis players	(1) Treadmill maximal test until voluntary exhaustion (2) On court tennis match (95 min)	a	C	B	Immediately after 5 Min after 5 Min after	1) ↓ 2) ↓ A/NA/C: ↑	No food 2 h before Time of day (0730)
Berk 1990 ¹⁵	9 M	I Marathon runners	Marathon run in laboratory	a	A NA C	B	Immediately after	↑	Food and drink intake
Nieman 1989 ¹⁶	1 F	I Marathon runners	Monitoring winter training season: 15x200 m freestyle tests after (1) 6 Weeks (2) 12 Weeks (3) 24 Weeks	a	C	B	Immediately after	↑	Food and drink intake
Carstensen 1994 ¹⁸	1) 12 2) 8 3) 22	I / III Students	(1) 10 Min bicycle ergometer test at constant workload of 150 W (2) Cold pressure study (5 min hand immersion in ice water) (3) 65 Min medical students end of year examination	a	A NA	B: (a) Plasma (b) Platelets	1,2,3: Immediately after test	A: ↑ 1a ≡ 1b, 2ab, 3 NA: ↑ 1a, 2ab : ≡ 1b, 3	4 Consecutive shifts
Costa 1997 ¹⁹	10 F	II Nurses	A morning shift was compared to an afternoon and two night shift	a	A	U	A/NA: 1st half of shift compared with 2nd half of shift sample C: start, middle, and end After jump	NA: ↑ 1st half night shift C: ≡ ↑ Jump 1,2,3 ↓ Peak value from jump 2 to 3	Caffeine, alcohol, nicotine, fat intake
Deinzer 1997 ²⁰	10 M 6 F	II Parachute jumpers	3 Consecutive parachute jumps	d	NA C C	U B S	Immediately after test	A: ↑ NA: ↑ Handball ↑ Swimmers Sedentary women ≡	Food intake
Deschenes 1998 ²¹	10 M	I Students	4 Exhaustive aerobic power bicycle ergometer tests were performed at 0800, 1200, 1600, and 2000	a	A NA	B	Immediately after test	A/NA: ≡	
Filaire 1996 ²²	31 F	I Handball players Swimmers	In 24 h (a training day), 6 samples of saliva cortisol. Three groups were compared	a	NA C	S	After training		
Gao 1990 ²³	23 M 6 F	III Students	Two groups of 150 min VDT data entry: (1) Simple (2) Complicated	a	A NA	U	Immediately after		
Gerra 1996 ²⁴	20 F	III Students	(1) Emotional or violent film (2) A neutral (Walt Disney) film	a	A NA C	B	During and immediately after test	A: ≡ NA: ≡ C: ≡	Time of day (morning), menstrual phase, food intake
Gilberg 1986 ²⁵	9 M	I Different activities: Lying, sitting, standing, walking, bicycling, running	Activities lasting for 1 h (except running: 45 min), with testing before and after of 1 h sitting	a	A NA	U	Immediately after	A/NA: ↓ lying run A: ≡ sit, stand, walk, cycle	Time of day
Gratas-Delamarche 1994 ²⁶	6 M 6 F	I Sprinters	Wingate test (30 s bicycle pedalling at highest possible rate against previous determined load)	a	A NA	B	Immediately after	NA: ↑ cycl/run NA: ≡ sit, stand, Walk	
Häkkinen 1993 ²⁷	10 M	I Power lifters, body builders, weight lifters	Heavy resistance training leg extensors: (A) Maximal (20x1RMx100%) (B) Submaximal (10x10x70%)	d	C	B	Immediately after	ANA: ↑	Time of day
Heikamp 1996 ²⁸	10 F	I Marathon runners	Two run tests: (A) Maximal test treadmill (B) Non-competitive marathon run	a b	C	B	A: 3 min after B: 1.2 h during run, 3 min after	A: ≡ B: 1 h during ≡ 2 h During 3 Min after ↑	Food intake, time of day
Hoogeveen 1996 ²⁹	10 M	I Professional cyclists	Maximal ergometer test before and after 3 months of extensive training.	a	C	B	Immediately after	↑	Humidity, temperature, time of day
Jin 1992 ³⁰	48 F 48 M	III Laboratory stress test	(1) Mental 1 h stress test, and (2) Emotional 1 h stress test	a	A NA C	U U S	Immediately after	A: 1: ↑, 2: ≡ NA: 1,2 ↑ C: 1,2 ↑	Caffeine and alcohol intake, time of day
Kakimoto 1988 ³¹ Nakamura 1989 ³²	17 M	III Transport aircraft cockpit personnel	One day of flying compared to 1 day of ground work; 3 groups: pilots, copilots, and flight engineers	d (ground work)	C	S	1) After take off 2) During flight 3) After landing	1) ↑ Pilots 2) ↑ Pilots/co-pilots 3) ↑ Co-pilots	Time of day

Table 1 Continued

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Kirschbaum 1995 ³³	20 M	III Students	Subjects were exposed to the trier social stress test five times. High responders(H) were compared to low responders(L)	a	C	S	Immediately after test	↑ Day 1 to 5 (H) ↑ Day 1 (L)	Time of day, alcohol and nicotine intake, diseases
Kobayashi 1997 ³⁴	12 F	II Nurses	Comparison of reactivity during : nightshift after day shift, night shift after half-day shift, and day shift after day shift	a	C	B	Immediately after shift	Morning-level ↓ after nightshift than after day shift	Nicotine intake, time of day, phase of menstrual cycle
Kraemer 1998 ³⁵	13 M 8 F	I Untrained subjects	8 Weeks short term heavy resistance training (lower limb, 3 muscle groups, 3/week) T1=week 1, T2=week 6, T3=week 8	a	C	B	Immediately and 5 min after test	M ↑ T1, T2, T3 F ↑ T2, T3	Medication intake, endocrine disorders, time of day
Lac 1997 ³⁶	5 M 4 F	I Sports students	Laboratory: 30 min submaximal bicycle ergometer test.	d	C	S	During and few minutes after test	↑	Time of day (10 am)
Lehmann 1991 ³⁷	8 M	I Middle and long distance runners	Increase in volume of training during 4 weeks: 3 Maximal tests (comparison between day 0, 14, 28).	a	A NA	B	After test	A: ≡ between days NA: ↑ on day 28	Diseases, time of day
Liederbach 1992 ³⁸ , 1994 ³⁹	6 F 6 M	I Ballet dancers	Dancers were followed during a 5 weeks performance season: Before and after performance	a	A NA	U	After performance	A: ↑ NA: ↑ F ↑ M	Time of day
Mathur 1986 ⁴⁰	12 M	I Long distance runners	Within/between subjects design: Long distance runners were compared with control non-athletes during bicycle ergometer maximal test	a	C	B	Immediately after test	C: ↑ both groups	Time of day (0730 after 30 min rest)
McKay 1997 ⁴¹	15 M	II Golfers	An 18 hole golf match (M) was compared with a practice round (P) as day off	d	C	S	During (2 samples) and immediately after	C: ↑ (M > P) ↑ During > after	Time of day
Miki 1997 ⁴²	16 M 2 F	III Students	Prolonged mental tasks were performed on day A and only one mental task in the morning and additional rest on test day B	a	A NA C	U S	Before and after tasks	A: ↑ day A > B NA: ↑ day A > B C: ≡	Time of day
Nieman 1989 ⁴³	20 M	I Marathon runners	Marathon runners were compared with control non-athletes during a graded maximal treadmill test	a	A NA C	B	5 Min after test	A ↑ both groups NA ↑ both groups C ↑ both groups	Time of the day
O'Connor 1987 ⁴⁴	8 M	I Non-athletes	30 min cycling at 75% of their VO _{2max}	a	C	B	Immediately after test	≡	Time of day (1800-1920)
O'Connor 1991 ⁴⁵ , 46	22 M 18 F	I Swimmers	A paced swim test of 182.9 m was performed four times (before and after a W/E/W flight crossing four time zones	a	C	S	Immediately after test	≡	Time of day
Oberbeck 1998 ⁴⁷	8 M	II Parachute jumpers	A first time tandem parachute jump was assessed	a (4 h Before test)	A NA C	B	Immediately after jump	A, NA: ↑ C: ≡	All baseline measurements made at 0800
Obminsky 1997 ⁴⁸	48 M	III Students military aviation college	A routine acceleration test on a centrifuge (radius length—11 m, linear acceleration gradient of 0.2 G/s) for 30-40 s	a	C	S	3 Min after test	C: ↑ (blood) ≡ (Saliva)	Time of day (1100-1200)
Odagiri 1996 ⁴⁹	21 M	I Triathlon athletes	Measurements before and after a triathlon match	d	C	B	Immediately after triathlon	↑	Time of day, 2 days before test and after test
Ragatt 1997 ⁵⁰	10 M	III Bus drivers	1 Workday (W) 12 h shift was compared with a (2nd) day off (B).	d	A NA C	U	Before, during (1100, 1500) and after (1900) work	All samples: A: W ↑ B NA: W ↑ B C: W ≡ B	Alcohol intake, caffeine and tobacco usage
Richter 1996 ⁵¹	43 M	II Parachute jumpers	Measurements before, during, and after a parachute jump	a	A NA C	B	During and immediately after jump	A ↑ NA ↑ C ↑	Time of day (between 1000 and 1200)
Rudolph 1998 ⁵²	26 M	I University crosscountry runners (1) and control students (2)	30 Min treadmill run at 60% VO _{2max}	a	C	S	During and at end of test	↑ 1,2	Blood sampled continuously! Time of day (1500-1700), food intake
Schnabel 1984 ⁵³	10 M	I Students	An exhaustive short term supramaximal treadmill exercise was performed	a	A NA C	B	A, NA, C: Immediately after test C: 6 min after test	A, NA: ↑ C: ≡	Time of day (0800-1030)

Table 1 Continued

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Schreinicke 1990 ⁵⁴	77 M	III Experimental subjects	A VDU time stress test of 30 min	a	C	S	5 Min after test	↑	Time of day (0900)
Schwartz 1990 ⁵⁵	12 M	I Non-specifically trained subjects	Laboratory: an exhausting incremental graded step test and a 1 min anaerobic cycle ergometer exercise	a	A NA C	B	Immediately and 5 min after test	A: ↑ both tests NA: ↑ both tests C: ↑ step test	Time of day (morning)
Shiota 1996 ⁵⁶	10 M	III Cockpit crewmembers	During 8 days of which 5 days off and a two flights from Tokyo to Los Angeles (and vice versa) were measured. Two groups: one outdoor exercise group and one control group	d	A NA 17-OHCS	U	During and immediately after flights	A, NA ↑	Time of day
Sinyor 1988 ⁵⁷	6 M	II Sedentary men	The effect of 10 weeks of aerobic training on sympathoadrenal responses to a psychosocial stress was measured	a	A NA	B	Immediately after test, and 5 min after test	A, NA : ≡	Morning
Sluiter 1998 ⁵⁸	10 M	III Long distance coach drivers	A long distance trip of three (1,2,3) working days or nights and one consecutive day off was compared with a (2nd day off) baseline day. Overall means (M) and separate samples were compared to baseline	d	A NA C	U	During work (7 samples per 24 h: 7, 11, 14, 17, 20, 23, 4am)	A: ↑ MI (1: 14,20,23; 2: 7,20,23; 3: 7,11) A: ↓ (2: 14,17) NA: ↑ (1:7,20; 2:4,7,14; 3:4,7) C: : ↑ M2,3 ≡ samples A: ↑ R,C,T A: ↓ R,T	Alcohol, caffeine, nicotine intake
Strobel 1993 ⁵⁹	28 M	I Long distance runners (R) Triathletes (T) Controls (C)	An incremental treadmill test to exhaustion was assessed. Besides plasma free catecholamines, sulphated catecholamines were measured.	a	A NA	B	Immediately after test	↑ R,C,T A: ↑ R,T	Food, alcohol, and caffeine intake, time of day
Strüder 1998 ⁶⁰	19 M	I Distance runners (8) Sedentary controls	A 30 min cycle ergometer test (65% VO _{2max}) was performed	a	C	B	Immediately after test	↑ Both groups	Time of day (1115), and food intake
Stupnicki 1995 ⁶¹	74 M	I Rowers (R) Wrestlers (W)	A graded exercise was performed by junior and senior athletes:	a	C	B	2 Min after test	↑ Senior male rowers + wrestlers ≡ Females + junior male athletes	Time of day (morning), and food intake before test
Tanaka 1992 ⁶²	9 M 9 F	III Students	(1) At a rowing ergometer (R) (2) At a cycle ergometer (W) Three groups were compared (1) VDT word search task with large print, (2) VDT word search task with small print, (3) Reference hard copy word search task One work day and evening were assessed	a	A NA	U	Immediately after test	A: ≡ NA: ↓ (3)	Time of day (0900), duration of tests 2 h followed by a rest period of 2 h Coffee, alcohol, and medication intake
Van der Beek 1995 ⁶³	32 M	II Lorry drivers	Three 30 min running evaluations were performed before, immediately after, and 3 weeks after the training volume was increased with 38% during the middle 3 weeks	d	A NA C	U	Sampled at 10, 14, 17, 30 h 5 Min after test	A ↑ NA ↑ C: ↑ before training increase	Time of day (afternoon)
Verde 1992 ⁶⁴	10 M	I Distance runners	Two measurements were performed during 100 min work: (1) After a period of low traffic, and (2) After a period of high traffic	a	C	B	Immediately after work	a) ↑ (2) ≡ (1) b) ↑ (2) ≡ (1)	Time of day (morning)
Zeier 1994, ⁶⁵ 1996 ⁶⁶	170 M	III Air traffic controllers: (a) Area control centre (b) Airport control tower	(1) After a period of low traffic, and (2) After a period of high traffic	a	C	S	Immediately after work	a) ↑ (2) ≡ (1) b) ↑ (2) ≡ (1)	Time of day (morning)

F/M=Female or male; jobnature: I=physical and mental, II=physical, III=mental; a=before test, b=morning, c=day or night mean, d=day off; hormone: A=adrenaline, NA=noradrenaline, C=cortisol; bodily fluid: B=blood, U=urine, S=saliva; ↑=increase, ↓=decrease, ≡=no change.

Table 2 Summary of findings from 51 studies that assessed reactivity or microrecovery (relative frequency (number of subjects))

Reactivity or microrecovery (n=101)	Studies that assessed microrecovery				Total
	Mental task	Mental/physical tasks	Physical tasks		
			Aerobic	Anaerobic	
Adrenaline (n=29):					
Increase	6/13 (156)	3 / 4 (83)	7/10 (102)	2/2 (24)	18/29 (365)
No change	7/13 (225)	1 / 4 (10)	3/10 (39)	0/2 (—)	11/29 (274)
Decrease	0/13 (—)	0 / 4 (—)	0/10 (—)	0/2 (—)	0/29 (—)
Noradrenaline (n=29):					
Increase	7/13 (252)	4 / 4 (93)	10/10 (141)	2/2 (24)	23/29 (510)
No change	5/13 (111)	0 / 4 (—)	0 / 10 (—)	0/2 (—)	5/29 (111)
Decrease	1/13 (18)	0 / 4 (—)	0 / 10 (—)	0/2 (—)	1/29 (18)
Cortisol (n=43):					
Increase	8/12 (534)	3/7 (74)	15/20 (311)	3 / 4 (31)	29/43 (950)
No change	4/12 (218)	2/7 (18)	5/20 (50)	1 / 4 (40)	12/43 (326)
Decrease	0/12 (—)	2/7 (22)	0/20 (—)	0 / 4 (—)	2/43 (22)

Some studies performed several measurements at the same time. The 101 assessments are categorised by nature of the task and effect found for the different hormones.

well as sports. Secondly, to get insight into which bodily fluids have been measured in these studies, and thirdly to find out what is known about the reactivity in stress hormones during the different periods of recovery and consecutive periods of recovery relative to the different natures of tasks at hand.

Methods

The present literature search on reactivity and recovery includes occupational as well as sports research, as the differentiation between physical, mental and physical, and mental work demands is used. Classification on job title only has been used often in differentiating the nature of work according to physical, mental and physical, or mental work demands.^{11 12} Fewer studies—for example, Ainsworth *et al.*¹³—have differentiated the nature of work on the basis of energetic demands in terms of metabolic equivalent (MET), creating the opportunity to include professional sports as occupational jobs.

Search for literature was started in Medline, Psycom, Nioshtic, Psc Med, Current contents life sciences, Current contents med sciences, Psyclit, and Sportdisc. Initially, two broad searches on keywords were performed—namely: (1) catecholamines; adrenaline, noradrenaline, epinephrine, norepinephrine, cortisol, corticosterone, and (2) health complaints; fatigue, recovery, workstress, workload.

These two searches were combined 1+2 to get a first inclusion criterion, resulting in 559 identified publications. Studies were included which measured SAM and HPA reactivity as well as recovery relative to performed jobs or tasks. Subsequently, the following criteria were used:

Inclusion criterion: publication between 1983 and August 1998.

Exclusion criteria: animal experimentation; toxicological experiments or specific patient groups; language other than English; reviews (no original article); general knowledge experiments in which no physical or work task was performed.

After application of these criteria 158 identified publications remained, of which the abstracts and methods were read. The final exclusion criterion was studies without re-

peated measurements per subject, because such studies would not permit the evaluation of the four recovery terms. No more exclusion criteria were set because the purpose of this study was to give an overview of what assessments were made up to now, and acknowledging the fact that most studies in this field of research would not comply with the criteria of high methodological quality—such as case-control design. Finally, from the 158 studies, 77 studies that investigated neuroendocrine reactivity and recovery with repeated measurements per subject were taken into account for this systematic review.

Results

The neuroendocrine results from the 77 studies will be described in the four different categories of recovery, and subdivided into the nature of the work where measurements were made. Apart from these four paragraphs, the results from studies that examined reactivity, mesorecovery, and metarecovery will be presented separately, because this might give additional information about the neuroendocrine reactivity and recovery in time after certain tasks. As well as the descriptor “number of studies”, the results will be described in “number of assessments” because some studies assessed more than one task or evaluated their outcome variables at more than one point in time. The results in reactivity and recovery are described relative to the baseline concentrations. The term incomplete recovery is used to describe significantly higher or lower concentrations compared with baseline.

REACTIVITY, MICRORECOVERY, OR BOTH

The 51 studies that investigated reactivity or microrecovery, as defined for this review, are shown in table 1. From these 51 studies, 28 examined physical tasks,^{14-18 21 22 25-29 35-37 40 43-46 49 52 53 55 59-61 64} 11 studies examined tasks that contain physical as well as mental exposures,^{14 19 20 34 38 39 41 47 51 57 63} and 16 studies examined mental tasks.^{18 23 24 30-33 42 48 50 54 56 58 62 65 66} From the 51 studies, eight examined microrecovery,^{15 16 28 43 48 54 61 64} six examined reactivity and microrecovery,^{14 35 36 53 55 57} and 37 examined only reactivity during some kind of exertion.^{14 17-27 29-34 37-42 44-47 49-52 56 59 60 63 66}

None of the studies that examined physical tasks were performed in occupational settings (all were sports studies or experiments with healthy people) and none of the studies that examined mental tasks were performed in sport settings. Three of the 11 studies that examined combined physical and mental tasks concerned occupations—namely, nurses^{19 34} and lorry drivers.⁶³ Seven of the 15 studies that examined mental tasks concerned field occupational settings investigating aircraft crew or aircraft traffic controllers^{31 32 56 65 66} or bus and coach drivers.^{50 58}

Reactivity or microrecovery in adrenaline and noradrenaline were both measured in 29 assessments originating from 24 studies and cortisol in 43 assessments originating from 36 studies. Microrecovery of adrenaline and noradrenaline was measured in five studies and

Table 3 Summary of research concerning mesorecovery

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Bonifazi 1995 ¹⁷	8 M	I Swimmers	Monitoring of winter training season: 15x200 m freestyle. Three tests after (1) 6 Weeks (2) 12 Weeks (3) 24 Weeks	a	C	B	1 h After	↑	Food and drink intake
Carstensen 1994 ¹⁸	8	III Students	Cold pressure study (5 min hand immersion in ice water)	a	A NA	B: (a) Plasma (b) Platelets S	30, 60 Min after test	A: ≡ NA: ↑ a : ≡ b	
Filaire 1996 ²²	31 F	I Handball players Swimmers	In 24 h (a training day), 6 samples of saliva cortisol were measured. Three groups were compared.	a	C	S	0.5 h After training	≡	
Gerra 1996 ²⁴	20 F	III Sedentary women	(1) An emotional/violent 45 min film (2) A neutral (Walt Disney) 45 min film	a	A NA C	B	15 Min after test	A: ↑ 1 NA: ≡ C: ↑ 1 A/NA ≡	Time of day (morning), menstrual phase, food intake Time of day
Gillberg 1986 ²³	9 M	I Different activities: Lying, sitting, standing, walking, bicycling, running	Activities lasting for 1 h (except running: 45 min), with pre- and after testing of 1 h sitting	a	A NA	U	1 h After		
Häkkinen 1993 ²⁷	10 M	I Power lifters, body builders, weight lifters	Heavy resistance training leg extensors: (A) Maximal (20x1RMx100%) (B) Submaximal (10x10x70%)	a d	C	B	1 h After	A: ≡ B: ↑	Time of day
Heikamp 1996 ²⁸	10 F	I Marathon runners	(A) Maximal test treadmill (B) Non-competitive marathon run	a b	C	B	A: 30, 60 min after B: 30, 60 min after	A: 30 min ↑ 60 min ↑ B: 30 min ↑ A: after Tai Chi more ↓	Food intake, time of day
Jun 1992 ³⁰	48 F 48 M	III Laboratory stress test	A mental and emotional 1 h stress test: 1 h recovery by Tai Chi, brisk walking, Tai Chi meditation, or reading	a	A NA C	U U S	1 h	NA: ≡ in all groups C: ↓ in all groups A: ↑ Co-pilots or flight engineers NA: ≡	Caffeine and alcohol intake, time of day
Kakimoto 1988 ³¹ Nakamura 1989 ³²	17 M	III Transport aircraft cockpit personnel	Day of flying compared to day of ground work; 3 groups: pilots, co-pilots, and flight engineers	d (Ground work)	A NA	U	Every 2 h		Time of day
Kirschbaum 1995 ³³	20 M	III Students	Subjects were exposed to the trier social stress test five times. High responders (H) were compared to low responders (L)	a	C	S	10, 20, 30 Min after test	10: ↑ day 1 to 5 (H), day 1 (L) 20,30: ↑ day 1 to 5 (H), day 1 (L)	Time of day, alcohol and nicotine intake, diseases
Kirschbaum 1995 ³⁰	I: 12 F II: 45 F	III Students	Women who did or did not use oral contraceptives were compared to men during the trier social stress test	a	C	S	30 Min after test	LI: ↑ (M>F->F+)	Time of day (late afternoon)
Kirschbaum 1996 ³⁸	19 M 53 F	I Students	Subjects with or without using oral contraceptives were exposed to bicycle ergometry to subjective exhaustion	a	C	S	10, 20, 30 Min after test	10,20: ≡ 30: ↑ Both groups (OC- > OC+)	Time of day (around noon)
Lac 1997 ³⁶	5 M 4 F 10 M	I Sports students III Military pilots	Laboratory 30 min submaximal cycle ergometer test. Comparison between simulator flight and real flight	d a	C NA	S B	30 Minutes after flight 10 Min after flight	A/NA/C: ≡	Time of day (1000) Time of day (1200-1600)
Lundberg 1990 ¹⁰	29 M 29 F	III Managers v clerical workers	Mental laboratory tests, male v female and managers v clerical workers	a	A NA C	U	1 h After test	A: ↑ during stress NA: ↑ M (managers) C: ↑ during stress	Time of day (0900-1100)
Lundberg 1993 ³⁰	30 M	III Students	Two laboratory VDT tests: a stimulating self paces learning task v machine paced repetitive data entry task	a	A NA	U	1 h After test	A: data entry ↑ Learning NA, C: ≡	Time of day (started at 0830)
Mathur 1986 ⁴⁰	12 M	I Long distance runners	Long distance runners were compared with control non-athletes during bicycle ergometer maximal test	a	C	B	1 h After test	C: ≡ runners ↑ Non-runners	Time of day (started at 0730 after 30 min rest)

Table 3 Continued

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Nieman 1989 ⁴⁵	20 M	I Marathon runners	Marathon runners were compared with control non-athletes during a graded maximal treadmill test	a	A NA C	B	10, 15, 30, 45 Min after test	A: ≡ NA: ≡ C: ↑ after 15, 30 min	Time of day
O'Connor 1987 ⁴⁴	8 M	I Non-athletes	30 Min cycling at 75% of their VO _{2max}	a	C	B	15 Min after test	C: ↑ in B and S	Time of day (1800-1920)
Oberbeck 1998 ⁴⁷	8 M	II Students	A first time tandem parachute jump	a (4 h Before test)	A NA C	B	1 h After jump	A, NA: ≡ C: ↓	Time of day: All baseline measurements made at 0800.
Obminsky 1997 ⁴⁸	48 M	III Parachute jumpers	A routine acceleration test on a centrifuge (radius length=11 m, linear acceleration gradient of 0.2 G/s) for 30-40 s	a	C	S	15 Min after test	C: ↑ (blood) ↑ (Saliva)	Time of day (1100-1200)
Richter 1996 ⁵¹	43 M	II Students military aviation college	Measurements before, during, and after a parachute jump were performed	a	A NA C	B	Until 1 h after jump	A: ↑ (5-20 min) ≡ (20-60 min) NA: ↑ (5-20 min) ≡ (20-60 min) C: ↑	Time of day (1000-1200) Blood sampled continuously
Rudolph 1998 ⁵²	26 M	I University cross country runners (1) and control students (2)	30 Min treadmill run at 60% VO _{2max}	a	C	S	10, 30 Min after test	≡ 1, 2	Time of day (1500-1700), food intake
Sagnol 1989 ⁷¹	6 M	I Long distance runners	Ultralong run (24 h)	d	A NA	B	10 Min after test	A: ≡ NA: ↑	Time of day (1000)
Sagnol 1990 ⁷²	6 M	I Triathlon athletes	Triathlon	d	A NA	B	10 Min after test	A: ↑ NA: ↑ C: ≡	Time of day (1000)
Schnabel 1984 ⁵³	10 M	I Students	An exhaustive short term supramaximal treadmill exercise was performed	a	C	B	C: 15, 30 Min after test	A: ↑ NA: ↑ C: ≡	Time of day (0800-1030)
Schwartz 1990 ⁵⁵	12 M	III Non-specifically trained subjects	An exhausting incremental graded septest and a 1 min anaerobic cycle ergometer exercise were performed	a	A NA C	B	10/20 Min after test	A: ↑ NA: ↑ C: ≡ 10, ↑ 20	Time of day (morning)
Sluiter 1998 ⁵⁸	10 M	III Long distance coach drivers	A long distance trip of three (1,2,3) workdays/nights and one consecutive day off were compared with a (2nd day off) baseline day. Overall means (M) and separate samples were compared with baseline	d	A NA C	U	After work day 2 (11 h), and day 3 (14 h)	A: ↑ (2: 11) ≡ (3:14) NA: ≡ C: ≡	Alcohol, caffeine, nicotine intake
Strobel 1993 ⁵⁹	28 M	I Long distance runners (R) Triathletes (T) Controls (C)	An incremental treadmill test to exhaustion was assessed. Besides plasma free catecholamines, sulfated catecholamines were measured	a	A NA	B	30 Min after test	A: ≡ A: ↑ T NA: ≡ NA: ↑ R C T	Food, alcohol, and caffeine intake, time of day

Footnotes as for table 1.

Table 4 Summary of findings from 29 studies that assessed mesorecovery (relative frequency (number of subjects))

Mesorecovery (n=75)	Studies that assessed mesorecovery				Total
	Mental task	Mental/ physical tasks	Physical tasks		
			Aerobic	Anaerobic	
Adrenaline (n=20):					
Increase	5/9 (135)	1/3 (43)	3/7 (46)	1/1 (12)	10/20 (236)
No change	3/9 (38)	2/3 (51)	4/7 (54)	0/1 (—)	9/20 (143)
Decrease	1/9 (96)	0/3 (—)	0/7 (—)	0/1 (—)	1/20 (96)
Noradrenaline (n=20):					
Increase	2/9 (66)	1/3 (43)	4/7 (53)	1/1 (12)	8/20 (174)
No change	7/9 (203)	2/3 (51)	3/7 (47)	0/1 (—)	12/20 (301)
Decrease	0/9 (—)	0/3 (—)	0/7 (—)	0/1 (—)	0/20 (—)
Cortisol (n=35):					
Increase	6/11 (242)	2/3 (86)	10/18 (136)	1/3 (10)	19/35 (474)
No change	4/11 (70)	0/3 (—)	8/18 (147)	2/3 (10)	14/35 (227)
Decrease	1/11 (104)	1/3 (8)	0/18 (—)	0/3 (—)	2/35 (112)

Some studies performed several measurements at one time. The 75 assessments are categorised by nature of the task and the effect found for the different hormones.

cortisol in 12 studies. Seven of the 51 studies measured all three hormones in blood and two of the 51 measured all three hormones in urine.

In table 2 a summary of the findings of the 51 studies is given by categorising the effects per hormone, nature of tasks, and number of subjects involved. In the studies, a total of 101 assessments were presented.

Table 2 shows that for neuroendocrine reactivity or microrecovery after mental tasks the adrenaline results remained inconclusive, whereas noradrenaline and cortisol showed an increase in most assessments. After mental and physical tasks, most assessments showed a significant increase in both the catecholamines and cortisol. After physical tasks, most or all of the assessments showed a significant increase in the catecholamines as well. Inconclusive effects were found in cortisol excretion after anaerobic physical tasks.

MESORECOVERY

Mesorecovery was investigated in 29 studies, which are shown in table 3. From these 29 studies, 16 examined physical tasks,^{16 17 22 25 27 28 36 40 44 52 53 55 59 68 71 72} two studies examined tasks that contained physical as well as mental exposure,^{47 51} and 11 examined mental tasks.^{10 18 24 30-33 48 58 67 69 70}

No studies that examined physical tasks were performed in occupational settings (all were sports studies or experiments with healthy people) nor were any of the studies that examined only mental tasks performed in sport settings. Both studies that examined combined physical and mental tasks concerned parachute jumpers,^{47 51} and five out of the 11 studies that examined mental tasks investigated workers—such as aircraft cockpit personnel,^{31 32} military pilots,⁶⁹ managers and clerical workers,¹⁰ and coach drivers.⁵⁸

Mesorecovery of both adrenaline and noradrenaline was measured in 20 assessments originating from 16 studies and cortisol was measured in 35 assessments originating from 23 studies. Five out of 29 studies measured all three hormones in blood, and three out of 29 studies measured all three hormones in urine. In table 4 a summary of the findings of the 29 studies is given by categorising the effects per hormone, nature of tasks, and number of sub-

jects involved. In the studies, the results of a total of 75 assessments were presented.

Table 4 shows that mesorecovery after mental tasks was complete in noradrenaline excretion in most subjects, whereas adrenaline and cortisol show an increase in most assessments. After mental and physical tasks, recovery is either incomplete (increase) or complete (no change). Most assessments show incomplete recovery (increase) in cortisol after combined mental and physical tasks. Only one of the six studies that assessed mental and physical tasks was performed in an occupational setting—namely in managers and clerical workers.⁷¹ Although cortisol excretion decreased in two studies 1 hour after testing (after Tai Chi, brisk walking, and reading³⁰; and after a tandem parachute jump⁴⁷), the time of measurement, and therefore the influence of circadian rhythmicity could not be ruled out in either studies. After aerobic physical tasks, recovery was incomplete (increase) or complete (no change) in about half of the assessments for all three hormones. The catecholamines were examined after an anaerobic physical task in one study only. This study showed incomplete recovery (increase) in 12 subjects. No conclusive effects were found in cortisol excretion after anaerobic physical tasks.

METARECOVERY

In table 5, the studies that investigated metarecovery are shown. From these 22 studies, 10 examined physical tasks,^{14 15 22 27 28 36 49 59 71 72} six studies examined tasks that contained physical as well as mental demands,^{63 75-77 79 81} and seven studies examined mental tasks.^{18 30 58 70 73 74 78 80}

Again, none of the studies that examined physical tasks were performed in occupational settings (all were sports studies or experiments with healthy people) and no studies that examined only mental tasks were performed in sports settings. All six studies that examined a combination of physical and mental tasks concerned occupations—namely nurses,^{76 77} lorry drivers,^{63 79} assembly line workers,⁸¹ and cabin crew.⁷⁵ Five of the seven studies that examined mental tasks were in field occupational settings involving insurance employees,^{73 74} managers and clerical workers,^{78 80} and coach drivers.⁵⁸

Metarecovery in both adrenaline and noradrenaline was measured after 17 assessments originating from 14 studies and cortisol in 17 assessments originating from 13 studies. Five out of 22 studies measured all three hormones in urine. In table 6 a summary of the findings of the 22 studies that assessed metarecovery is given by categorising the effects per hormone, nature of tasks, and number of subjects involved. In the studies, the results of a total of 51 assessments were presented.

Table 6 shows that metarecovery after mental tasks was incomplete (increase or decrease) in both catecholamines and cortisol excretion in most assessments depending on the time of measurement. Short term metarecovery (1.5–3 hours after the test) showed an increase most often, and longer term metarecovery (>12 hours after the test) a decrease most often. Only one study examined 32 subjects with a

Table 5 Summary of research concerning metarecovery

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Aronsson 1987 ⁷⁵ Johansson 1984 ⁷⁷	13 F III	Insurance employees	7 y Follow up of VDU workers: at T0: group high % VDU work (n=11) v group low % VDU group (n=10) T1: n=13, no difference	T0: d T1: —	A NA	U	Day time versus Evening after work	1977: A: day/evening ↑ And E ↑ C NA: workday ↓ Evening ≡ E ≡ C 1984: E ↑ C E ↑ C	Time of day
Bassett 1987 ⁷⁵	11 F 17 M II	E: Aircraft cabin crew	9 Days collection of urine during flight (Sydney > LA, rest, and return flight)	d	C	U	Rest days in LA	1.5 hr: A/NA ≡ 1.5 hr: C ↑ 6 / 21 hr: C ↓ A: ≡ NA: ↑ a : ≡ b Handball ↑	Dietary intake, time of day
Berk 1990 ¹⁵ Nieman 1989 ¹⁶ 1 F	9 M I	C: Other occupations	Marathon run in laboratory	a	A NA C	B	1.5 / 6 / 21 h After		
Carstensen 1994 ¹⁸ 8	I III	Marathon runners Students	Cold pressure study (5 min hand immersion in ice water)	a	A NA	B: (a) Plasma (b) Platelets	120 Min after test 12 h After training		
Filaire 1996 ²² 31 F	I	Handball players	In 24 h (a training day), 6 samples of saliva cortisol were measured. Three groups were compared.	a	C	S	2/3 h After work	↑	Time of day, caffeine intake
Fox 1995 ⁷⁶ 1995 ⁷⁷ 136 F	II	Swimmers + controls	2 Working days	b	C	S	Mean values workday + evening Day off	During work: A ↑ NA ≡ C M > F Evening: A/NA ↓ whole group NA ↑ in F managers A: ≡ B: ↑	Time of day, food intake
Frankenhaeuser 1989 ⁷⁸ 30 M 30 F	III I	Nurses Managers or clerical workers	1 Working day and consecutive evening 1 Day off; managers compared with clerical workers, men compared to women	c	A NA C	U	2 h After 12/36 h After	A/B: ≡ A/NA: ↑ solo driver	Time of day
Häkkinen 1993 ²⁷ 10 M	I	Power lifters, body builders, weight lifters	Heavy resistance training leg extensors: (A) Maximal (20×IRM×100%) (B) Submaximal (10×10×70%) Inward and outward trip (total 6 days); 2 up v solo driver	a d	C	B	24 h (Rest day between inward and outward journey) B: 120 Min after 24 h After Day off	B: 120 min ↑ 24 h ↓ A: W ≡ F NA: W ≡ F C: work morning ↑ ↑ 1 h 30 min ≡ 5 h ↑ A / NA ≡ C	Time of day, food intake
Hartley 1994 ⁷⁹ 3 M 2 M	II	Lorry drivers	(A) Maximal test treadmill (B) Non-competitive marathon run 3 Measurements of workday free day: before, during, and 1 y after implementation of new technologies	c	A NA C	U	1 h 30 min, 5 h After test Work day v Rest day		Time of day, food intake
Heitkamp 1996 ²⁸ 10 F	I	Marathon runners		a	C	B	Testday v rest day		Caffeine and nicotine intake, time of day
Kortunka 1996 ⁸⁰ 14 M	III	Office worker		d	C	S	One day after triathlon		Time of day (1000)
Lac 1997 ³⁶ 5 M 4 F	I II	Sports students	30 Min submaximal cycle ergometer test	d	C	U	Workday v rest day		Same 2 h during workdays and rest day
Lundberg 1989 ⁸¹ 20 M	II	Assembly line workers	During 2 h work on 2 days compared with rest day	d	A NA C	U	Time of day (0830)		Time of day, 2 days before test and one day after triathlon
Lundberg 1993 ³⁰ 30 M	III	Students	Two laboratory VDT tests (a stimulating self-paces learning task v machine-paced repetitive data entry task) v a day off	a	A NA C	U	24 h After test	A: ↑ learning ≡ Data entry NA ↑ both tests C: ≡ both tests ≡	Time of day (1000)
Odagiri 1996 ⁸⁹ 21 M	I	Triathlon athletes	Measurements before and after a triathlon were performed	d	C	B	24 h, 48 h After test	A: ↑ NA: ↑ A: ↑ 24 h, ↓ 48 h NA: ↑ 24 h, : ≡ 48 h	Time of day (1000)
Sagnol 1989 ⁷¹ 6 M 1 F	I	Long distance runners	Ultralong run (24 h)	d	A NA A	B	24 h, 48 h After test		Time of day (1000)
Sagnol 1990 ⁷² 6 M	I	Triathlon athletes	Triathlon	d	NA	B			Time of day (1000)

Table 5 Continued

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Sluiter 1998 ⁸⁸	10 M	III Long distance coach drivers	A long distance trip of three (1,2,3) workdays/nights and one consecutive day off (4) was compared to a (2nd day off) baseline day (5). Overall means (M) and separate samples were compared to baseline	d	A NA C	U	After work day 2 (14, 17 h), day 3 (17, 20, 23 h), And day 4	A: ↓ M4 to M5, (2: 14, 17; 3: 23) ≡ (3: 17, 20) NA: ↓ (2: 14) ≡ M4 C: ↓ M4 to M2, 3 A ≡ A ≡	Alcohol, caffeine, nicotine intake
Strobel 1993 ⁸⁹	28 M	I Long distance runners (R) Triathletes (T) Controls (C)	An incremental treadmill test to exhaustion was assessed. Plasma free catecholamines and sulphated catecholamines were measured	a	A NA	B	2 h After test R, C 24 h After test T	NA ≡ NA ↑ R C A: ↑ (1, 2) NA: ↑ (2)	Food, alcohol, and caffeine intake, time of day
Tanaka 1992 ⁸²	9 M 9 F	III Students	Three groups were compared: (1) VDT word search task with large print, (2) VDT word search task with small print, (3) Reference hard copy word search task One work day and evening were assessed	a	A NA	U	2 h After test	NA ≡ NA ↑ R C A: ↑ (1, 2) NA: ↑ (2)	Time of day (0900), lasted for 2 h followed by a rest period of 2 h
Van der Beek 1995 ⁹⁰	32 M	II Lorry drivers	One work day and evening were assessed	d	A NA	U	Sampled 20, 23 h	A ↑ NA ↑	Coffee, alcohol, and medication intake

Footnotes as for table 1.

mental and physical task, after which incomplete recovery (increase) was found in both adrenaline and noradrenaline excretion. Another study examined 136 subjects with a mental and physical task, after which incomplete recovery (increase) was found in cortisol excretion. After aerobic physical tasks, most assessments showed complete recovery in adrenaline and noradrenaline and the results were inconclusive in cortisol excretion. Recovery was incomplete (increase) in the 20 subjects in whom the catecholamines were examined after an aerobic physical task. One third of the assessments of cortisol excretion after an anaerobic physical task showed incomplete (increase) and two third showed complete recovery. Of the nine studies that found incomplete recovery of cortisol, six assessments were on mental or combined mental and physical demands in occupational settings of aircraft cabin crew,⁷⁵ nurses,^{76 77} managers,⁷⁸ and office workers.⁸⁰

MACRORECOVERY

The studies that investigated macrorecovery are shown in table 7. From these 17 studies, 10 examined physical tasks,^{8 29 35 37 64 72 82-86} three studies examined tasks that contained physical as well as mental exposure,^{38 39 57} and four studies examined mental tasks.^{56 80 87 88}

Once more, none of the studies that examined physical tasks were performed in occupational settings (all were sports studies or experiments with healthy people), and none of the studies that examined only mental tasks were performed in sport settings. One of the three studies that examined combined physical and mental demands was on ballet dancers during a performance season,^{38 39} and three of the four studies that examined mental tasks concerned occupational settings involving office workers^{80 88} and cockpit crew.⁵⁶

Macrorecovery of adrenaline was measured in seven assessments originating from six studies, noradrenaline in nine assessments originating from seven studies, and cortisol in 17 assessments originating from 12 studies. One of the 17 studies measured all three hormones in blood, and two of the 17 studies measured all three hormones in urine. No change in adrenaline was found in one study, and in one study a decrease was found in triathletes.⁷² Only two out of 14 measurements of cortisol were performed in urine, and no change was found in both occupational studies on office workers⁸⁰ and cockpit crew members.⁵⁶ In table 8 a summary of the findings of the 17 studies is given by categorising the effects per hormone, nature of tasks, and number of subjects that were involved. In the studies, a total of 33 assessments were presented.

Table 8 shows that macrorecovery after mental tasks is incomplete (increase) in both adrenaline and noradrenaline excretion in two out of three assessments. For cortisol, incomplete recovery was shown in most assessments but half of them showed an increase in the shorter term macrorecovery, and half a decrease (overshoot) in the longer term macrorecovery. Only one study examined 12 subjects

Table 6 Summary of findings from 22 studies that assessed metarecovery (relative frequency (number of subjects))

Metarecovery n=28	Studies that assessed metarecovery				Total
	Mental task	Mental/ physical tasks	Physical tasks		
			Aerobic	Anaerobic	
Adrenaline (n=17):					
Increase	4/10 (51)	1/1 (32)	1/5 (6)	1/1 (20)	7/17 (109)
No change	3/10 (37)	0/1 (—)	4/5 (51)	0/1 (—)	7/17 (88)
Decrease	3/10 (70)	0/1 (—)	0/5 (—)	0/1 (—)	3/17 (70)
Noradrenaline (n=17):					
Increase	6/10 (91)	1/1 (32)	2/5 (13)	1/1 (20)	10/17 (156)
No change	2/10 (27)	0/1 (—)	3/5 (44)	0/1 (—)	5/17 (71)
Decrease	2/10 (40)	0/1 (—)	0/5 (—)	0/1 (—)	2/17 (40)
Cortisol (n=17):					
Increase	2/5 (42)	1/1 (136)	4/8 (60)	1/3 (10)	8/17 (248)
No change	2/5 (30)	0/1 (—)	2/8 (50)	2/3 (10)	6/17 (90)
Decrease	1/5 (10)	0/1 (—)	2/8 (20)	0/3 (—)	3/17 (30)

Some studies performed several measurements at one time. The 51 assessments are categorised by nature of the task and the effect found for the different hormones.

with a mental and physical task, after which incomplete recovery was found in adrenaline excretion and complete recovery in noradrenaline. After aerobic physical tasks, an overshoot in recovery (decrease) was found in adrenaline and results were inconclusive in noradrenaline. Recovery was complete (no change) in most assessments, in which cortisol was examined after an aerobic physical task. Only one study (21 subjects) examined an anaerobic physical task and an overshoot in recovery (decrease) was found. Cortisol showed incomplete recovery with a significant increase in four studies. Only one of these four studies was performed in an occupational setting in office workers.⁸⁸ Probably because of circadian influences, and thus dependent of the time of measurements, a relative overshoot of recovery shown by a significant decrease of cortisol excretion was found in five studies.

REACTIVITY, MESORECOVERY, AND METARECOVERY

Seven of the 77 studies investigated reactivity, mesorecovery, and metarecovery.^{18 22 27 28 36 58 59} Only one study was performed in an occupational field setting on coach drivers.⁵⁸ The other six sports studies all examined physical tasks and one study also examined a mental task.¹⁸ One study measured all three hormones in urine,⁵⁸ two studies measured adrenaline and noradrenaline in blood,^{18 59} four studies measured cortisol of which two were in saliva^{22 36} and two in blood.^{27 28} Results from the occupational study showed significant reactivity and incomplete recovery indicated by an increase of adrenaline and noradrenaline during and immediately after work, and an overshoot of recovery indicated by a significant decrease in adrenaline and cortisol 24 hours after work. From the other six studies, differential results were shown ranging from significant reactivity and incomplete mesorecovery, and metarecovery in noradrenaline^{18 59} and cortisol^{22 27 28 36} to an overshoot in metarecovery in cortisol.²⁸ For adrenaline, metarecovery was complete, after significant reactivity^{18 59} and incomplete mesorecovery.⁵⁹

Discussion

The main purpose of this literature overview was to gain insight into the extent to which

neuroendocrine reactivity and recovery have been investigated, in terms of the definitions of the four recovery periods, in both work and sports. The categorisation in recovery time as it was defined for this review gave the opportunity to compare the outcomes of the different studies. Rationale for the choice of the cut off points in time was based on the way working life is organised in many countries and on the question of whether these schemes are sufficient to recover neuroendocrinologically from the occupational induced exertions. During a day of work, most people have of a maximum of 15 minute coffee or tea breaks in the morning and afternoon, and a lunch break of 30–60 minutes. Between two periods of work, in general a minimum of 12 hours (during the working week) and a maximum of 2 days (weekend) is given as time off work. Although the tasks in the different studies reviewed were not performed with the same amounts of time, both short term and long term tasks show useful information for work related neuroendocrine reactivity and recovery. We therefore included the duration of the tasks under study in the tables of the studies reviewed.

Many occupational neuroendocrine studies have been performed. Often, however, neuroendocrine data have been gathered without a proper baseline or without measuring data in a way that could assess reactivity and recovery.^{89–108} In sports research on the other hand, many neuroendocrine studies have been performed. Most of them investigated short term psychophysiological reactivity and micro-recovery or mesorecovery to some kind of physical exertion in the laboratory. These studies have good designs and are able to control several variables. The results from laboratory and sports research may be transferable to some occupations, but more research is needed on the course of recovery relative to health effects in occupational settings in which tasks are repetitive during the working week and cover more hours a day. Because the sports studies most often use blood as the bodily fluid for measurements, few of them monitor their subjects for much longer than a couple of hours. Therefore, not many results are found on metarecovery and macrorecovery.

In all, a respectable number of studies, especially in sports research, have been published on neuroendocrine reactivity, microrecovery and mesorecovery in the past 15 years. Fewer studies on metarecovery have been found, and only a few on macrorecovery probably due to the methodological problems and efforts those studies give rise to. During the selection procedure of the studies, it was decided not to add more qualitative exclusion criteria because high qualitative methodological designs have not been used often in the different studies. Furthermore, the diversity in populations tested in the different studies was high, and therefore, no overall effect size was calculated.

The first reason for the inclusion of sports research in this review was that the differentiation into mental, combined mental and physical, and physical tasks can be applied to both work and sports activities.

Table 7 Summary of research concerning macrorecovery

1st author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Filaire 1998 ⁸²	46 F	I Handball players Volleyball players	Before and after 16 weeks training one sample of saliva was taken. Volleyball players were compared with handball players and sedentary women	a	C	S	Before and after 16 weeks of training	≡	Time of day (0800)
Flyn 1997 ⁸³	11 M	I Distance runners	Training volume was increased twice for 10 days: one time only with running (200%), and one time more cross training like with additional bicycling (200%)	a	C	B	D0, D5, D10	≡	Time of day (morning)
Hoogveen 1996 ⁷⁹	10 M	I Professional cyclists	Maximal ergometer test before and after 3 months of extensive training.	a	C	B	Before test values before and after 3 months training	↑ After 3 months	Humidity, temperature, time of day
Hooper 1993, ⁸⁴ 1995 ⁸⁵	5 F 9 M	I Elite swimmers	During a 6 months training period, and subgroup analyses of overtrained swimmers v not overtrained swimmers: 5 samples in 6 months at same time a day	?	A NA C	B	After 2-4 weeks After 12-14 weeks 5-6 Weeks before trials During tapering (3-5 d before trials) After competition (1-3 d after trials)	A: 5 ↓ 1-4 NA: ≡ C: ≡ Overtrained: NA: 4 ↑ 1,2,3,5 Overtrained swimmers v not overtrained: NA: 4 ↑	Temperature, time of day, medication, caffeine, alcohol, dietary intake
Kraemer 1998 ⁸⁵	13 M 8 F	I Untrained subjects	8 Weeks short term heavy resistance training (lower limb, 3 muscle groups, 3/week) T1=week 1, T2=week 6, T3=week 8	a	C	B	T1=week 1, T2=week 6, T3=week 8	M,F: base T3 ↓ T1,2	Medication intake, endocrine disorders, time of day
Korunka 1996 ⁸⁰	14 M	III Office worker	3 Measurements of working day free day: before, during, and 1 y after implementation of new technologies	d	A NA C	U	Day off	A: ↑ during and after implement. NA: ↑ during and after implement. C: ≡	Caffeine and nicotine intake, time of day
Lehmann 1991 ³⁷	8 M	I Middle and long distance runners	Increase in volume of training during 4 weeks:	c	A NA C	U	A/NA: days 2,6,13,20,27,34 C: days 1,5,12,19,26,33	A: ↓ days 21, 28	Diseases, time of day
Liederbach 1992, ³⁸ 1994 ³⁹	6 F 6 M	II Ballet dancers	Dancers were followed up during a 5 week performance season: Once/week nocturnal urine sampling	c	A NA C	U	5 Weeks	NA: ↓ days 7, 27, 34 C: ↓ days 20, 27	Time of day
López Calbet 1993 ⁸⁵	7 M	I Cyclists	Cyclists were followed up for 6 months.	b	C	S	Beginning of season v end season, morning sample	NA: ≡	No eating before sampling
Mackinnon 1997 ⁸⁶	8 M 16 F	I Elite swimmers	During 4 weeks an increase in training volume with 3 measurements. Swimmers who showed overreaching (O) were compared with the well trained (W) group	b	NA C	B / U B	T1=week 0 T2=week 2 T3=week 4	NA (B): T3 O ↓ W NA (U): T1,3 O ↓ W C: T3 O ↓ W ↓ from T2 to T3	Time of day (0600-0800)
Malarkey 1995 ⁸⁷	55 M	III Medical students	In fall (F) and spring (S) three 24 h measurements before, during, and after medical examinations. Day(D) and night(N) means compared as was a group with high experienced stress (H) compared with a group with low experienced stress (L)	c	C	B	T1=3-4 weeks before examination T2=during examination T3=2 weeks after examination	F T1 > S T1 ↓ from F T1 to T2 ↑ H D from T1 to T2 compared to L	Nicotine and alcohol intake, time of day
Sagnol 1990 ⁷²	6 M	I Triathlon athletes	Triathlon	d	A NA C	B	60 h after test	NA: ≡ A, C: ↓ day 3, 4 (E>C)	Time of day (1000)
Shiota 1996 ⁸⁶	10 M	III Cockpit crew members	During 8 days of which 5 days off and two flights from Tokyo to Los Angeles (and vice versa) were measured. Two groups were compared: one outdoor exercise group (E) and one control group (C)	d	A NA C	U	Day 3,4,5,6,7,8	NA ↑ day 3, 4 E ↑ Day 4, 5 C C: ≡	Time of day
Sinyor 1988 ⁸⁷	6 M	II Sedentary men	The effect of 10 weeks of aerobic training on sympathoadrenal responses to a psychosocial stress was measured	a	A NA	B	2 Weeks before the training period	A,NA: ≡	Time of day

Table 7 Continued

Ist author and year	F/M (n)	Job nature (I, II, or III), + job title or sport	Experimental condition	Baseline value (a, b, c, or d)	Hormone (A, NA, or C)	Bodily fluid (B, U, or S)	Time of measurement	Outcome (↑=increase ↓=decrease ≡=no change)	Controlled variables
Theorell 1995 ⁸⁸	20 M 34 F	III Office workers	Before, during, and after a psychosocial job intervention: an active group was compared with a passive group, and men were compared with women	a	C	B	During 7 months 4 additional samples: 2 during intervention, 1 immediately after, and one 4 months after	C: Females ≡ Males: ↑ both groups begin intervention ↓ Active group samples 3, 4 ↑ Passive group samples 3, 4 ↑ s. 5 Both groups C: ↑ week 3 ≡ Week 6, 9	Time of day (0800–0900)
Verde 1992 ⁶⁴	10 M	I Distance runners	Five 30 min running evaluations were performed before, immediately after, and 3 weeks after the training volume was increased with 38% during the middle 3 weeks	a	C	B	Week 3, week 6, week 9	≡ Week 6, 9	Time of day (afternoon)

Footnotes as for table 1.

Secondly, and more importantly, neuroendocrine occupational research obviously lags behind the neuroendocrine sports research, and the similarity of complaints and symptoms between overtrained sportsmen and people with occupationally induced chronic fatigue is amazing. The symptoms accompanying overtraining are characterised by fatigue, sleeping problems, increased irritation or excitement, and emotional lability. These symptoms are supposed to be due to a lack of proper rest and recovery, and thus a lack of tapering within periods of training. Synonyms mentioned by Fry and Kraemer⁷ are: overtraining syndrome, staleness, burnout, chronic overwork, physical overstrain, overfatigue, chronic fatigue syndrome, and failure to adapt. To classify sportsmen as overtrained or not overtrained is often difficult because the process is seen as a continuum from well trained to overreached and eventually to overtrained.⁸ This idea is analogous to the development of chronic fatigue in occupational settings in which repeated lack of recovery is seen as the start of a vicious circle from acute to chronic fatigue. Reasons for the occurrence of overtraining, are: repeated insufficient recovery between workouts and increase in training volume, and thus monotony of training. For decades, two types of overtraining have been distinguished⁹: (type I) sympathetic, and (type II) parasympathetic. Sympathetic is characterised by increased sympathetic activity at rest reflected by increased catecholamine concentrations, an increased resting heart rate, decreased appetite, and weight loss. Type II parasympathetic overtraining shows decreased sympathetic activity with parasympathetic activity predominating at rest and with exercise. This is accompanied by low resting heart rate, rapid heart rate recovery after exercise, and decreased catecholamine concentrations. Symptoms associated with the parasympathetic overtraining, are: more hours sleeping, and a phlegmatic or depressive state. It is said that the sympathetic syndrome develops before the parasympathetic syndrome, and occurs more often in younger people who train for speed or power.⁷

Linking this knowledge to work shows several things. One assumed cause of work related health problems is a spillover of neuroendocrine reactivity that occurs when recovery after exertion is repeatedly incomplete. In the long term, this cumulative spillover will lead to chronic fatigue that in turn will lead to health problems. Thus, the vicious circle of spillover is compatible with the neuroendocrine reactivity found in a sympathetic overtraining syndrome. Also, the kind of recovery overshoot (the decrease in catecholamine and cortisol excretions) found by Sluiter *et al*⁵⁸ is compatible with the neuroendocrine reactivity found in parasympathetic overtraining syndrome, as described by Heitkamp *et al*²⁸ and Lehmann *et al*.³⁷

The second purpose of this review was to get insight into which bodily fluids these studies have been sampling. Therefore, some methodological issues have to be signalled in the investigation of neuroendocrine reactivity and

Table 8 Summary of findings from 17 studies that assessed macrorecovery (relative frequencies (number of subjects))

Macrorecovery n=21	Studies that assessed macrorecovery				Total
	Mental task	Mental/ physical tasks	Physical tasks		
			Aerobic	Anaerobic	
Adrenaline (n=7):					
Increase	2/3 (24)	1/1 (12)	0/3 (—)	—	3/7 (36)
No change	1/3 (6)	0/1 (—)	0/3 (—)	—	1/7 (6)
Decrease	0/3 (—)	0/1 (—)	3/3 (28)	—	3/7 (28)
Noradrenaline (n=9):					
Increase	2/3 (24)	0/1 (—)	1/5 (14)	—	3/9 (38)
No change	1/3 (6)	1/1 (12)	2/5 (32)	—	4/9 (50)
Decrease	0/3 (—)	0/1 (—)	2/5 (20)	—	2/9 (20)
Cortisol (n=17):					
Increase	2/6 (83)	—	2/10 (20)	0/1 (—)	4/17 (103)
No change	2/6 (24)	—	6/10 (134)	0/1 (—)	8/17 (158)
Decrease	2/6 (83)	—	2/10 (32)	1/1 (21)	5/17 (136)

Some studies performed several measurements at one time. The 33 assessments are categorised by nature of the task and the effect found for the different hormones.

recovery. Urinary measurements of free adrenaline and noradrenaline provide a reliable measure of the circulating concentrations of these hormones in blood.⁵ Also, salivary cortisol was found to be highly associated with the free cortisol fraction in blood.⁶ Thus, the outcomes of the different studies are comparable for the fluids in which the measurements were performed.

Firstly, because of the circadian rhythmicity in both catecholamines and cortisol, and the large variability between subjects in baseline concentrations and reactivity, studies should control within subjects. This should be done by repeated measurements controlled for time of day, and when possible, baseline measurements during 1 or more days off. Studies performed in this way more easily control for the use of nicotine, caffeine, and alcohol.

Secondly, the peripheral catecholamines are measurable in urine and blood (plasma and platelets) whereas cortisol is also measurable in saliva. As blood sampling is invasive, and thus might give additional stress to subjects, most studies on mental and psychological tasks prefer measurements in saliva or urine. However, microrecovery seems to be most measurable in blood or saliva, because acute hormonal excretions can be monitored. A good example of how blood sampling can be used to measure reactivity, microrecovery, mesorecovery, and metarecovery has been discussed.²⁷ Excretion of cortisol has been found to be in bursts. These may result in relatively large differences in concentrations especially early in the morning for two moments close in time. The outcomes of early morning studies that used blood plasma or saliva for cortisol in mesorecovery, metarecovery, and macrorecovery may, therefore, be criticised. Measurements in saliva are easy to perform and do not interrupt the activities of the subjects. In saliva, however, the reactivity of cortisol is said to be measurable at best 15 to 20 minutes after the test,²⁸ and the outcomes of salivary cortisol studies on microrecovery may therefore be questioned in tasks that do not last longer than 15 minutes. In urine, a buffer of hormonal excretion is measured, and the mean excretion rate of the hormones during a certain period is the

outcome. When more than 1 day is examined, the time of sampling ideally should be the same for each day to facilitate control for circadian influences. Also, it is important to register the activities performed in between two urinary sample times. For reactivity and microrecovery in urine, task duration should be relatively long and the sampling time has to be immediately before and within half an hour after performance of a task to measure as accurately as possible. Because urine provides a reliable measure of the circulating concentrations of the catecholamines in blood,⁵ in our opinion, metarecovery and macrorecovery ideally should be measured in urine in occupational environments.

The third and main purpose of this review was to find out what is known about the reactivity in stress hormones after the different and consecutive periods of recovery relative to the different natures of tasks at hand. The hypothesis of persistent neuroendocrine spillover as a cause in the development of chronic fatigue is the reason for paying more attention to the course of recovery in the different studies.

To assess this course of recovery, some examples from the seven studies which examined reactivity, microrecovery, mesorecovery, and metarecovery relative to mental, combined mental and physical, and physical tasks are discussed now. In the laboratory, Carstensen and Yudkin¹⁸ measured plasma and platelet catecholamines during an emotional stressor. In plasma noradrenaline concentrations, significant reactivity remained and incomplete recovery was found up to and including metarecovery, whereas platelet noradrenaline only showed significant reactivity. No differences were found in adrenaline concentrations. In an appropriate design, Häkkinen and Pakarinen²⁷ measured plasma cortisol in 10 male top level athletes (powerlifters, body builders, and weight lifters) after heavy resistance exercise for the leg extensors and no differences in cortisol concentrations were found after maximal exertion. The submaximal exercise showed significant reactivity and this remained up to and including the metarecovery level, because a significant increase in cortisol was found, and this increase did not return to baseline concentrations after 2 hours. Heitkamp *et al*²⁸ measured plasma cortisol in 14 female marathon runners in two longer term physical test occasions: (a) in the laboratory during a maximal test on a treadmill, and (b) during a non-competitive marathon run. After the maximal test, no reactivity in cortisol concentrations was found after 3 minutes, indicating sufficient microrecovery, but for mesorecovery, a significant increase in cortisol concentration after 30 minutes was found. The marathon test showed a significant increase in cortisol concentrations during the marathon (after 2 hours), and no metarecovery was found at 2 hours after the marathon. After 24 hours, however, an overshoot in metarecovery was shown, because the cortisol concentrations were significantly lower than at baseline. The only study in an occupational setting (mental task) that measured urinary reactivity, mesorecovery, and

metarecovery in catecholamines and cortisol was performed by Sluiter *et al.*⁸⁸ in 10 coach drivers during and after a 48 hours shuttle bus trip. For reactivity, a significant increase in adrenaline and to a lesser extent in noradrenaline during most of the trip was found. Mesorecovery was obviously incomplete. An overshoot in metarecovery was found for adrenaline and cortisol, with significantly lower excretion rates compared with baseline. This is labelled "fatigue debt" and, as was mentioned before, resembles the phenomenon found in parasympathetic overtraining syndrome in sports research.

Plasma concentrations of adrenaline and noradrenaline are said to increase during all types of physical activity, varying with the intensity and duration of the exertion.¹⁰⁹ This was confirmed in the outcomes of 10 of the 11 studies on reactivity or microrecovery that investigated physical tasks or combined physical and mental demands and measured both catecholamines in blood plasma.

Increases in adrenomedullary activity, as indicated by plasma adrenaline concentrations, often correlate more closely with increases in pituitary-adrenocortical activity, as indicated by plasma concentrations of corticotrophin, than with increases in sympathoneural activity, as indicated by plasma noradrenaline concentrations.³ Because the concentration of corticotrophin determines the concentration of cortisol, this statement could not be confirmed from the outcomes of the different studies in this review that investigated both catecholamines and cortisol in blood. In all but one of the 15 studies (all examining physical tasks), the outcomes in the catecholamines were the same. In seven of the same 15 studies, the outcomes in both the catecholamines and cortisol were the same, whereas in six studies different outcomes in cortisol compared with both catecholamines were found.

Recommendations for future research on recovery are twofold. Firstly, occupational neuroendocrine research should focus more on the methods used in monitoring the course of recovery and the nature of tasks that are assessed relative to health problems. Secondly, to link clinical presentations with neuroendocrine outcomes, repeated simultaneous measurements of health complaints and the working environment should be made. The overall goal is to gain knowledge about the (partly) assumed role of recovery as an aetiological factor of chronic fatigue relative to work demands, and thus possibly prevention of future cases of chronic fatigue.

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Vancouver style

All manuscripts submitted to *Occup Environ Med* should conform to the uniform requirements for manuscripts submitted to biomedical journals (known as the Vancouver style.)

Occup Environ Med, together with many other international biomedical journals, has agreed to accept articles prepared in accordance with the Vancouver style. The style (described in full in the *JAMA*[1]) is intended to standardise requirements for authors, and is the same as in this issue.

References should be numbered consecutively in the order in which they are first mentioned in the text by Arabic numerals on the line in square brackets on each occasion the reference is cited (Manson[1] confirmed other reports[2][3][4][5]). In future references to papers submitted to *Occup Environ Med* should include: the names of all

authors if there are three or less or, if there are more, the first three followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter. Titles not in *Index Medicus* should be given in full.

Examples of common forms of references are:

- 1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomed journals. *JAMA* 1993;269:2282-6.
- 2 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.
- 3 Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology, mechanisms of disease*. Philadelphia: W B Saunders, 1974:457-72.