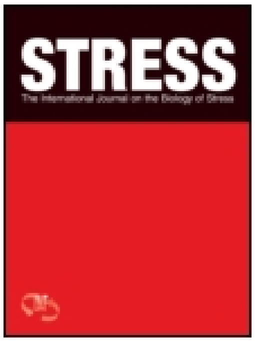

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ORIGINAL RESEARCH REPORT

Neuropsychological sequelae of work-stress-related exhaustion

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Abstract

The aim was to assess long-term cognitive performance after substantial recovery from work-stress-related exhaustion, in relation to subjective cognitive complaints and return to active work. In total, 54 patients previously diagnosed with work-stress-related exhaustion participated in a neuropsychological examination ~2 years after initial sick leave. Most participants were substantially recovered at follow-up, with only 13% still meeting the criteria for exhaustion disorder suggested by the Swedish National Board of Health and Welfare. When participants' scores on 14 neuropsychological tests were compared to a matched group of 50 controls, the former patient group showed lower performance mainly on attention tests of the reaction time type, but also slightly lower scores on visuo-spatial constructional ability. However, the former patient group performed better than controls on two memory tests and, in part, on a test of simultaneous capacity. Self-ratings of everyday cognitive problems remained significantly higher in the former patient group than among controls, but the extent of self-rated cognitive problems was generally unrelated to performance on the neuropsychological tests. No relationship between performance on these tests and the extent of work resumption was observed. In summary, persons with previous work-stress-related exhaustion showed persistent signs of a minor attention deficit, despite considerable general recovery and return to work.

Keywords

Attention, burnout, cognitive, executive functions, memory, mood, neuropsychological tests, work stress

History

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Introduction

It is well known from clinical settings that patients diagnosed with work-stress-related exhaustion disorder (burnout) present with substantial cognitive complaints. Several attempts have been made to objectively verify the nature and extent of cognitive decline associated with work-stress-related exhaustion (WSRE), and most studies suggest the presence of slight impairment as measured by neuropsychological tests of attention and declarative memory (Öhman et al., 2007; Rydmark et al., 2006; Sandström et al., 2005). More specifically, a few recent studies have shown disturbed executive functioning as the most prominent feature of the cognitive problems associated with stress-related exhaustion (Jonsdottir et al., 2013; Oosterholt et al., 2012).

While cognitive impairment in the acute phases of WSRE seems rather well documented, little is known about the long-term cognitive outcome. In most previous studies, patients with WSRE have been examined shortly after diagnosis and sick leave, and in only three studies have patients been followed up with repeated neuropsychological examinations after treatment and in conjunction with varying degrees of recovery. Oosterholt et al.'s (2012) study re-assessed patients with WSRE after a 10-week period of cognitive behavioral therapy, and did not reveal any improvement in neuropsychological test performance despite reduced subjective cognitive problems. On the other hand, Österberg et al. (2012) demonstrated widespread cognitive improvements in former WSRE patients at a 1.5-year follow-up as well as a marked decrease in subjective cognitive problems. One further study (Wahlberg et al., 2009) is hard to interpret as the disappearance of initial differences between a group with WSRE and a control group at a 1-year follow-up seems to depend mainly on worsened performance in the control group.

The scarcity of prospective long-term follow-up studies of patients with WSRE has led to an unsatisfactory situation, in that we do not know to what extent the cognitive problems characterizing the acute stages of WSRE will eventually abate. Although the outcome of one long-term follow-up study (Österberg et al., 2012) would seem to suggest optimistic outcomes concerning cognitive recovery, it is still unknown whether cognitive recovery was complete or partial, as only prospective within-group comparisons of patients' test scores were reported, i.e. without comparable data from healthy controls. Because neuropsychological sequelae may seriously affect patients' ability to regain their professional capacities both qualitatively and quantitatively, it would seem important to improve our knowledge of whether or not full cognitive recovery is to be expected in the aftermath of

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WSRE. Improved knowledge may be of vital importance to the prospects and ambitions set out in the rehabilitation process, including the prognosis conveyed by the doctor to the patient.

The purpose of the present study was to generate knowledge concerning the possible long-term cognitive sequelae of WSRE. The study presents the results of an extensive neuropsychological assessment carried out at a 1.5-year follow-up of former WSRE patients, and a comparison of patients' scores with those of a matched control group. The study supplements our previous report of within-group improvements on a limited set of neuropsychological tests in a smaller sample of former WSRE patients (Österberg et al., 2012). Our main hypothesis was that slight impairments in attention, declarative memory and executive functions would still be demonstrable after substantial recovery and return to work. A supplementary hypothesis was that better performance on neuropsychological tests would be related to more complete work resumption and to lower levels of subjective cognitive problems in everyday life.

Methods

Participants

Former WSRE patients

Participants in the present study included patients previously diagnosed with work-stress-related exhaustion who had participated in an earlier, large study focused on a workplace intervention to facilitate return to work (Karlson et al., 2010). Shortly after onset of sick leave, the patients were included in the intervention study after a baseline investigation of their health and well-being, to which was later added a neuropsychological examination (for details, see Österberg et al., 2009). Only patients whose work could be shown to include major and clearly identifiable stressors were included in the intervention study. A few years after the intervention, and in conjunction with a general follow-up of health and well-being, patients were offered a more comprehensive neuropsychological re-examination. In total, 75 former WSRE patients were invited to participate in this neuropsychological follow-up, comprising the original set of 65 patients participating in the baseline examination, 3 patients who had declined participation in the baseline examination, and a further 7 former WSRE patients who had completed their participation in the intervention study prior to the start of the baseline neuropsychological examinations. Of the 65 patients examined at baseline, 45 agreed to participate in the follow-up, together with 9 of the 10 patients not previously examined, resulting in 54 participants (72% women) with a mean age of 50 years (Table 1). The mean time lag from baseline to follow-up was 20 months (range 14–30). All participants were re-assessed by a physician and a social worker at the Occupational and Environmental Medicine department, Lund University Hospital, Lund, Sweden. This re-assessment showed generally good health status, although 30% had minor somatic disorders (Table 2). At follow-up, 13% still met the criteria for exhaustion disorder suggested by the Swedish National Board of Health and Welfare (Socialstyrelsen, 2003) compared to 83% at baseline. Screening with the Primary Care Evaluation of Mental Disorders (Prime-MD) (Spitzer et al., 1994) showed that, at follow-up, 48% met the criteria for a Prime-MD diagnosis, most commonly depression, anxiety disorder, somatoform syndrome NUD and somatization disorder, or in combination (Table 2), compared to 74% at baseline, thus revealing a markedly decreased prevalence of depression and anxiety disorder. Scores on standardized self-rating scales for depressive symptoms and anxiety, the Symptom Checklist-90 (SCL-90) (Derogatis, 1992) and Beck Depression Inventory (BDI) (Beck et al., 1988), also showed marked decreases compared to the baseline levels (SCL-90 means: depression: −0.72; anxiety: −0.61; BDI mean: −7.0, t test p's < 0.002, $n = 45$). Still, at follow-up, BDI and SCL-90 scores remained higher than those among matched controls, and a small proportion of participants reported considerable depressive symptoms (Table 2). Antidepressants, anxiolytic drugs or sleeping pills (or a combination of these) were used by 48%, and 22% had psychotherapy. Also at follow-up, 41% had returned to the same degree of employment as prior to the onset of WSRE, 30% were on part-time sick leave, in partial retirement or partial unemployment, or had settled for part-time work (without sickness benefit) in order to cope, 19% were on full-time sick leave and 11% were on parental leave or had been given severance pay awaiting retirement.

Table 1. Demographic characteristics of the participating former work-stress-related exhaustion patients ($n = 54$) and healthy controls ($n = 50$).

Characteristic	Patients	Controls
Age		
Mean (SD)	49.7 (9.4)	49.9 (8.3)
Range	32–64	31–63
	n (%)	
Gender		
Men	15 (28)	13 (26)
Women	39 (72)	37 (74)
Education		
Nine-year compulsory schooling	8 (15)	6 (12)
Upper secondary school	18 (33)	8 (16)
University studies	28 (52)	36 (72)
Supervisory position		
Preceding sick-leave due to exhaustion	16 (30)	–
At follow-up	7 (18)*	10 (20)
Employment		
Private sector	16 (30)	18 (36)
Public sector	38 (70)	32 (64)

*Figures based on those who had returned to work to any extent at follow-up ($n = 38$).

Control group

Healthy controls were recruited among participants in three previous studies (Arvidsson et al., 2008; Österberg et al., 2004; Persson & Ørbæk, 2003), which gave access to information on year of birth and gender. An invitation letter was sent out, and those with a major disease or taking medications were asked not to respond. Consecutive invitations were issued until a suitable set of healthy age- and gender-matched controls had been obtained. Invitations were sent to 108 persons, of whom 26 did not respond, and 19 declined. Among the 63 persons accepting participation,

Table 2. Medical characteristics of the participants.

	Patients ($n = 54$)	Controls ($n = 50$)
Characteristic	*n* (%)	
Somatic disorders, total	16 (30)	5 (10)
Hypertension (treated)	5 (9)	4 (8)
Type I diabetes	1 (2)	0
Type II diabetes	1 (2)	0
Other*	10 (19)	1(2)
Medication		
Antidepressants; SSRI, SNRI or NaSSA †	22 (41)	0
Anxiolytics or sleeping pills	5 (9)	0
Medication for somatic disorders ‡	24 (44)	6 (12)
Hormonal replacements/contraceptives	8 (15)	12 (24)
No medication	13 (24)	33 (66)
Psychotherapy	12 (22)	0
Alcohol consumption		
Low to moderate	53 (98)	50 (100)
High	1 (2)§	0
Prime-MD		
Major depression	4 (7)¶	–
Mild depression or dysthymia	3 (6)**	–
Anxiety disorder	3 (6)	–
Anxiety disorder + major depression	6 (11)††	–
Somatization disorder only	4 (7)	–
Somatoform syndrome NUD only	6 (11)	–
BDI		
Severe depression	7 (13)	0
Moderate depression	7 (13)	0
Slight depression	14 (26)	2 (4)
Minimal depression	26 (48)	48 (96)
	Mean (SD)	
BDI total score (sum of 21 items)	13.2 (10.9)	3.3 (3.2)
SCL-90 subscale means		
Anxiety (10 items)	1.1 (0.8)	0.4 (0.3)
Somatization (12 items)	1.0 (0.8)	0.3 (0.3)
Depression (13 items)	1.3 (0.9)	0.5 (0.5)

*Two patients had thyroid disorder (treated), and the other patients each had one of the following: airway allergy with sleep apnea (treated), ankylosing spondylitis, atrial fibrillation, endometriosis, gluten intolerance (treated), mineral deficiency (treated), recurrent diverticulitis and slight B12 deficiency (treated). One control had sleep apnea (treated).
†Selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI) or noradrenergic and specific serotonergic antidepressant (NaSSA).
‡Mostly antihypertensive and antihyperlipidemic drugs and vitamin or mineral supplements.
§Refers to previous consumption; at follow-up this patient received treatment with acamprosate.
¶One patient also met the criteria for somatization disorder.
**One patient also met the criteria for somatoform syndrome NUD.
††Patients also met the criteria for: somatoform syndrome NUD ($n = 2$), somatization disorder ($n = 2$; one in combination with obsessive–compulsive disorder) and obsessive–compulsive disorder combined with social phobia ($n = 1$).
Prime-MD, Primary Care Evaluation of Mental Disorders (Spitzer et al., 1994); SCL-90, Symptom Checklist 90 (Derogatis, 1992); BDI, Beck Depression Inventory (BDI) (Beck et al., 1988).

13 were excluded due to a disease or medication that might affect cognitive performance (e.g. epilepsy, hypothyroidism, previous WSRE or medication with psychopharmacological drugs). Recruitment was terminated after having obtained a group of 50 healthy controls with similar distributions of age and gender as the former WSRE patients (Table 1). A university education was more common among the controls than among the former WSRE patients (72% versus 52%), but holding a supervisory/managerial position was more common among the former WSRE patients (prior to sick leave) than among the controls (30% versus 20%). Employment within the private versus public sector was similarly distributed across groups (Table 1). The vast majority of controls (90%) were occupationally active, although three participants had recently retired, one was unemployed, and one was living off private resources.

Neuropsychological tests

Participants were tested individually in the afternoon by an experienced psychologist. All tests were administered according to the standard procedures given in the test manuals. All scoring done by hand was cross-checked by a colleague. Below is an annotated list of the tests used, grouped according to the skill area under investigation.

Verbal intellectual ability

SRB:1 vocabulary from the DS-battery (Dureman et al., 1971), a verbal knowledge or intelligence test containing 30 items of multiple-choice type.

WAIS-R information, a test of contemporary and historical knowledge from the Wechsler Adult Intelligence Scale – Revised (WAIS-R) (Wechsler, 1992).

F-A-S, a controlled oral word association task (verbal fluency), using F, A and S as word-initial letters (Benton et al., 1994).

Visuo-spatial constructional skills

Rey Complex Figure Test (RCFT) (Meyers & Meyers, 1995), which is essentially a test of visuo-spatial memory (detailed description below), but also includes an initial task of copying the stimulus figure, which is used to assess visuo-spatial constructional skills.

Episodic memory

Cronholm–Molander verbal memory (Cronholm & Molander, 1957), an associative learning task comprising immediate and delayed recall sections.

Austin Maze with the Milner pathway (Milner, 1965; Walsh, 1985), a test of spatial learning and strategy, in a computerized version (Österberg et al., 2000). Ten trials were used, and error and performance time refer to the nine memory recall trials.

WAIS-R NI incidental learning (Kaplan et al., 1991), a test of memory for the digit-symbol combinations used in the WAIS-R Digit Symbol test (see below). The modified version used showed only the stimulus key row with the symbols hidden (scoring range 0–9).

Rey Complex Figure Test (RCFT), a test of visuo-spatial memory (Meyers & Meyers, 1995). After having copied the stimulus figure, the task is redraw it from memory after 3 min (immediate recall) and after 30 min (delayed recall), and finally to complete a recognition trial in which correct parts of the stimulus figure are mixed with distractors.

Working memory

WAIS-R Digit Span, a test of working memory (Wechsler, 1992). Series of digits are read to the participant, whose task is to repeat the series correctly, either in the same order (forwards) or in reversed order (backwards).

Sustained attention, processing speed and simultaneous capacity

WAIS-R Digit Symbol, a test of perceptual and fine motor speed (Wechsler, 1992).

APT k-test from the Automated Psychological Test System (APT) (Levander & Elithorn, 1987), measuring sustained attention. The k-test requires visual scanning of computer screen images, containing a scatter of 10 letters, for the presence/absence of a critical stimulus (k). Around 100 stimulus sets are shown during 5 min. The task is to respond correctly and quickly to each stimulus set by pressing the corresponding keys (''*k*'' versus ''no *k*''). Results are expressed: (a) according to signal detection theory, as d' (accuracy) and β (the balance between missed hits to targets and false hits to non-targets; a negative β indicating that missed hits were more common than false hits); (b) as reaction time (RT) level in relation to stimulus laterality (the mean of single RT responses for correct hits, left-center-right); (c) as error ratio (proportion of missed and false hits) and (d) as search strategy (the RT ratio for correct yes/no responses with ''k'' present/absent on a scale from sequential (obsessive) to global (impulsive), a higher value indicating a more global strategy).

APT Two-way Reaction Time (RT-2), a computer test in which stimuli are presented on the left and right side of a computer screen, using corresponding dual response keys. Results are expressed in terms of *level* (the mean of the 50 single RT responses) and *variation* (the SD of the 50 single RT responses).

APT Inhibition (RT-Inhib), a computer test similar to RT-2 with the addition of a randomly appearing (ratio 0.50) auditory alarm presented simultaneously with the visual signal, whereupon the participant is required to inhibit the response. Results for correct hits are expressed as for RT-2, with the addition of an error ratio (the proportion of false hits).

APT Simultaneous Capacity (SimCap), a computer test of the ability to deal with two tasks simultaneously. One task (the background task) runs continuously, requiring the participant to identify three consecutive odd digits in a stream of digits (0–9), by pressing a button within 2 s. The other task (the foreground task) consists of responding to text messages, flashed at random but frequent intervals, within 2 s. The text messages are simple instructions or arithmetic (e.g. ''Press on 1'' or ''Press on 4 + 2''), responded to on a simplified keyboard with digits 0–9. Distracting messages that should not be responded to are also included, including performance feedback that should be over-looked. The level of difficulty (the complexity of messages) is process controlled; starting at the easiest level, if the participant manages the first one-third of the test well, difficulty is increased to the second level, and if this level too is handled well, the difficulty is raised to the third level during the final one-third of the test. The background task is evaluated according to signal detection theory, as d' and β (see *k*-test above), and the foreground task is expressed as the percentages of correctly serviced messages and spurious responses (any response outside the 2-s response window). The SimCap version used in the present study lasted 10 min.

Integrated Visual and Auditory Continuous Performance Test (IVA), a computer test of sustained attention and impulsivity (Sandford & Turner, 2004). Although IVA is intended mainly as a diagnostic tool for Attention Deficit Hyperactivity Disorder (ADHD), it has shown high sensitivity to other types of mild cognitive impairment (e.g. Tinius, 2003). In IVA, the numbers ''1'' (target) and ''2'' (foil) are presented on a computer either as auditory or visual stimuli, and the participant is instructed to click a mouse as rapidly as possible each time the target ''1'' appears, while avoiding the foil ''2''. Following a brief practice period, the test runs for 13 min, comprising 500 stimuli. The overall IVA results are expressed on two global scales: the Full Scale Attention Quotient (FSAQ) and the Full Scale Response Control Quotient (FSRQ). The FSAQ is based on three subscales: Speed (mean RT), Vigilance (missed targets) and Focus (outliers, i.e. sudden loss of attention). The FSRQ is based on the subscales Consistency (general variation in RTs, disregarding outliers), Prudence (responding to foils) and Stamina (fatigue effects; RT difference between the initial and final parts of the test). All scores are reported separately for the auditory and visual modalities. In the present study, IVA version 2006.20 was used, which provides results adjusted for age and education based on an unimpaired normative sample of 1700 persons (Sandford & Turner, 2004). Individual scores are presented in a traditional ''IQ-scale'' format (mean = 100; SD = 15).

Self-ratings of cognitive problems

The aim of the self-ratings of cognitive problems was to indicate patients' subjective perceptions of cognitive problems in everyday life. Two questionnaires were used.

Euroquest-9, comprising the Memory and Concentration subscale of the larger Euroquest (Chouanière et al., 1997), was used to provide information about subjective everyday cognitive problems during the past few months. Six items address memory problems, and three items problems with attention and concentration. The steps in the 4-point (1–4) response range are labeled ''seldom/never'', ''sometimes'', ''often'' and ''very often''. The scale has been validated as a sensitive indicator of cognitive impairment (Carter et al., 2002; Karlson et al., 2000).

The *5-item Questionnaire of everyday memory problems (5-QEMP)*, used in a previous study on patients with chronic stress (Öhman et al., 2007). The five questions of the 5-QEMP reflect various aspects of common subjective memory problems (see ''Results'' section for the phrasings of the questions). Answers are given on a five-point scale; For questions 1, 4 and 5, the scale steps are labeled (1) ''Never'', (2) ''Seldom'', (3) ''Sometimes'', (4) ''Quite often'' and (5) ''Very often''; for questions 2 and 3 the scale steps are labeled (1) ''Much better'', (2) ''Slightly better'', (3) ''Equal'', (4) ''Slightly worse'' and (5) ''Much worse''.

Data analysis

The statistical analyses were carried out using SPSS, version 20 (SPSS, Inc., Chicago, IL). Visual inspection showed that neuropsychological test scores and self-ratings were approximately normally distributed, except for skewed distributions for the variables WAIS-R NI incidental learning, the RCFT copy trial, APT *k*-test error ratio, the APT-SimCap percent spurious and the IVA subscales Vigilance and Prudence, necessitating ranking prior to statistical analysis.

Between-group comparisons of test and questionnaire data were carried out using univariate analysis of variance (UNIANOVA) in the general linear models module of SPSS, with Group (former WSRE patients versus Controls) as the main factor, together with the covariates age, gender, medication with psychopharmacological drugs and SCL-90 depression score. In addition, for neuropsychological test scores, education level was explored as a covariate. Initially all covariates were entered, and then removed one at a time (based on highest p value), until only covariates with $p < 0.20$ remained (Mickey & Greenland, 1989). In case a significantly lower test score among former WSRE patients was observed and gender or age remained a covariate in the final model, the interactions Group by Gender and Group by Age were added (one at a time) in order to explore possible differential effects of gender and/or age on the outcome. To explore whether test scores and self-ratings of cognitive problems were related to having resumed work, and to the degree of reduction in work hours at follow-up compared to before the onset of WSRE (from 0 to 100%, due to sick leave, voluntary reduction of work hours or other causes), Pearson's partial correlation was used, controlling for the same covariates as used in the UNIANOVA for each variable. The same method was used for analyzing relations between test scores, self-ratings of cognitive problems and SCL-90 depression scores.

In case of statistical significance for the factor Group, the effect size is given as partial eta square (η^2_P). Two-tailed p values <0.05 were considered statistically significant.

Ethics

All subjects gave their written informed consent to participate in the study. The study protocols were approved by the Lund University Ethics Committee (reg. no. 784-03) and the Regional Ethical Review Board in Lund (reg. no. 583/2006).

Results

Neuropsychological tests

Group differences

Compared to healthy controls, former WSRE patients showed lower performance mainly on tests of the reaction time type. Former WSRE patients had longer and more variable reaction times on the tests APT RT-2 and APT RT-Inhib (Table 3). On the IVA test, lower performance among former WSRE patients was found for both global measures: attention (FSAQ) and response control (FSRQ) (Table 4). An in-depth analysis of scores on the subscales underlying FSAQ indicated that poorer mean reaction time to visual stimuli (Speed, Visual) and a higher frequency of outliers (Focus, Visual) were the main determinants of lower FSAQ among former WSRE patients. Similarly, more variable reaction times for both visual and auditory stimuli (Consistency) and progressively slower reaction times for auditory stimuli toward the end of the test (Stamina) seemed to be the main determinants of lower FSRQ in former WSRE patients. The former WSRE patients also scored slightly lower than controls on visuo-spatial constructional ability (the copy section of the RCFT) (Table 3). A closer analysis revealed that rather low scores on the RCFT copy task (<17th percentile based on age-corrected norms from the manual) tended to be more common among former WSRE patients than among controls (30% versus 14%, $p = 0.055$; chi-squared test). The former WSRE patients also showed a somewhat more global search strategy in the APT *k*-test than controls did, as well as a trend toward more false hits and fewer missed targets (β) on the lowest complexity level (1) of the APT SimCap test, although the latter finding was not corroborated at higher complexity levels (Table 5). Generally, effect sizes for all observed differences were approximately medium (range 0.04–0.12).

On the other hand, former WSRE patients achieved higher scores than controls on the immediate recall section of the Cronholm–Molander verbal memory test and on the WAIS-NI Incidental Learning test. Also, the subset of former WSRE patients achieving the highest complexity level in SimCap had a higher accuracy (d') score than controls did. Significant group differences were not found on tests for verbal intellectual ability (SRB:1 vocabulary, WAIS-R Information, F-A-S Verbal Fluency), the memory tests Austin Maze, RCFT and WAIS-R Digit Span, or for the remaining variables of the APT *k*-test, APT SimCap and IVA.

Interactions with age and gender

The interaction Group by Gender, explored for APT *k*-test Search Strategy and RT-Inhib (level), and IVA FSRQ and Consistency (visual), showed a gender-related difference only in APT *k*-test Search Strategy ($p = 0.006$), indicating a stronger group difference among men (means 0.57 versus 0.52 for former WSRE patients and controls, respectively). The interaction Group by Age was explored for RCFT copy, the APT variables *k*-test Search Strategy, RT-2, RT-Inhib and SimCap (level 1, Beta), and the IVA variables FSAQ, FSRQ, and Consistency Visual and Auditory, which did not reveal any age-related group difference (all p values >0.28).

Self-ratings of cognitive problems

The former WSRE patients scored significantly higher than controls on both questionnaires targeting cognitive problems, when comparing raw data across groups. The effects sizes of these differences were generally large (range 0.13–0.30). For the Euroquest-9, higher scores were seen on the concentration and attention subscale as well as on the memory problems subscale, giving a distinctly higher total score among former WSRE patients (Table 6). For the 5-QEMP, the former WSRE patients had higher ratings on all items ($F[1,102] > 15$; $p < 0.001$ throughout), resulting in a markedly higher total score. The largest mean differences were seen on the items ''Do you forget appointments if not prompted by someone else or by a reminder such as a calendar or diary?'' and ''How is your memory today, in comparison with your memory 5 years ago?''.

Table 3. Neuropsychological test raw scores* for former work-stress-related exhaustion patients and healthy controls.

	Patients ($n = 54$)		Controls ($n = 50$)		ANOVA, Group		
Cognitive domain and test	Mean	SD	Mean	SD	F†	p‡	η_p^2
Verbal intellectual ability							
SRB:1 vocabulary	24.8	2.9	24.5	2.5	1.62	0.21^{A,E}	–
WAIS-R Information	22.6	3.5	22.2	3.2	2.30	0.13^{E,G}	–
F-A-S Verbal Fluency	44.5	10.2	47.5	10.6	2.68	0.11^{E,G,P}	–
Visuo-spatial constructional skills							
Rey Complex Figure Test, copy	33.3	2.1	34.5	2.1	13.55	<0.001^{A}	0.118
Episodic memory							
Cronholm–Molander verbal memory, immediate recall	24.6	4.0	23.4	4.3	4.77	0.031^{A,E,G}	0.046
-- delayed recall	19.7	6.2	18.5	5.0	3.07	0.08^{A,E,G}	–
Austin Maze§, total errors¶	29.8	17.2	29.9	14.3	<0.01	0.98^{A}	–
-- total performance time (s)¶	293	103	296	102	0.07	0.79^{A,E,G}	–
Incidental learning WAIS-R NI, number correct¶	6.6	2.1	5.7	2.4	5.34	0.023^{A,E}	0.051
Rey Complex Figure Test, immediate recall (3 min)	20.5	6.6	21.5	5.9	1.05	0.31^{A}	–
-- delayed recall (30 min)	20.2	6.6	21.5	5.9	1.51	0.22^{A}	–
-- recognition trial	20.7	1.7	20.4	2.1	1.30	0.26^{A,E,G}	–
Working memory							
WAIS-R Digit Span, forward	7.5	2.3	7.1	2.2	0.83	0.37	–
-- backward	7.2	2.2	7.5	2.3	0.18	0.67^{E,G}	–
Sustained attention and processing speed*							
WAIS-R Digit Symbol	54.9	11.5	60.5	9.5	2.92	0.091^{A,D,G}	–
APT *k*-test, d'	4.10	0.41	4.16	0.42	0.46	0.50	–
-- β **	−0.77	0.66	−0.56	0.57	2.90	0.09^{A,G}	–
-- RT level for correct responses, left part of screen (ms)¶	1100	225	1025	190	0.06	0.80^{A,D,E,G,P}	–
-- RT level for correct responses, center part of screen (ms)¶	944	215	901	192	1.36	0.25^{A}	–
-- RT level for correct responses, right part of screen (ms)¶	1141	213	1100	237	0.28	0.60^{A,D,G}	–
-- search strategy††	0.58	0.07	0.54	0.08	6.20	0.014^{A,G}	0.058
-- error ratio (%)¶	2.3	2.2	1.9	2.2	1.61	0.21	–
APT RT-2, level (ms)¶	348	72	308	38	5.50	0.021^{A,D}	0.052
-- variation (ms)¶	78	43	58	22	8.88	0.004^{A,D}	0.082
APT RT-Inhib, level (ms)¶	508	134	410	82	11.56	0.001^{A,D,G}	0.105
-- variation (ms)¶	128	62	94	38	4.69	0.033^{A,D}	0.045
-- error ratio (%)¶	6.7	6.2	7.4	5.8	0.61	0.44	–

*Scores for IVA and APT SimCap are presented in Tables 4 and 5, respectively.
†d*f* ranged from [1,97] to [1,102].
‡Univariate ANOVA p values for between-group comparisons, corrected for age (A), Symptom Checklist-90 depression score (D), level of education (E), gender (G) and medication with psychopharmacological drugs (P) in case $p < 0.20$ for each covariate.
§$n = 53$ in the patient group; for one case, the Austin Maze data were excluded due to incomplete data.
¶A lower score signifies better performance.
**Qualitative variable; a negative β indicates that false rejections (missed ‘‘k’’s) were relatively more common than false alarms (alarms when k not present).
††Qualitative variable; a lower value indicates a more sequential/obsessive search strategy, while a higher value indicates a more global/impulsive search strategy.

Table 4. IVA attention test scores for former work-stress-related exhaustion patients and healthy controls.

	Patients ($n = 54$)		Controls ($n = 50$)		ANOVA, Group		
Main scales and subscales	Mean	SD	Mean	SD	F*	p†	η_P^2
Attention							
Full Scale Attention Quotient	99.3	21.7	107.2	14.3	4.76	0.031^{A}	0.045
Speed, Auditory	120.8	13.8	126.4	12.9	1.32	0.25^{A,D,G}	–
-- Visual	102.4	12.3	109.1	8.8	3.47	0.065^{D,G}	–
Vigilance, Auditory	97.1	20.0	100.9	13.5	1.68	0.20^{A}	–
-- Visual	96.8	22.0	99.7	12.4	<0.01	0.99^{A}	–
Focus, Auditory	87.2	19.6	92.1	17.1	1.91	0.17^{A}	–
-- Visual	94.9	21.1	101.6	15.9	3.33	0.071^{A}	–
Response control							
Full Scale Response Control Quotient	88.9	22.0	97.4	18.2	4.83	0.030^{A,G}	0.046
Consistency, Auditory	85.3	20.8	94.9	15.3	5.75	0.018^{A,E}	0.054
-- Visual	95.5	22.1	103.7	17.3	4.57	0.035^{A,G}	0.044
Prudence, Auditory	99.5	20.8	103.1	19.5	1.09	0.30	–
-- Visual	93.8	23.4	92.9	21.2	0.57	0.45^{A}	–
Stamina, Auditory	96.4	19.8	100.9	19.3	4.33	0.040^{D}	0.041
-- Visual	92.7	13.8	95.4	14.3	<0.01	0.96^{P}	–

*d*f* ranged from [1,99] to [1,102].
†Univariate ANOVA p values for between-group comparisons, corrected for age (A), Symptom Checklist-90 depression score (D), level of education (E), gender (G) and medication with psychopharmacological drugs (P) in case $p < 0.20$ for each covariate.

Table 5. APT Simultaneous Capacity test raw scores for former work-stress-related exhaustion patients and healthy controls.

	Participants reaching level *n* (%)			Patients ($n=54$)		Controls ($n=50$)		ANOVA, Group		
Difficulty	Patients	Controls	Variable	Mean	SD	Mean	SD	F*	p†	η^2_p
Level 1	54 (100)	50 (100)	d'	3.43	0.76	3.48	0.61	0.51	$0.48^{A,D}$	–
			β‡	2.43	0.74	2.66	0.83	6.03	$0.016^{A,D}$	0.057
			Corr. serviced messages (%)	87.5	11.8	90.3	7.9	1.97	0.16^{A}	–
			Spurious responses (%)§	1.37	3.59	0.52	1.80	0.16	$0.69^{D,E,G}$	–
Level 2	50 (93)	48 (96)	d'	3.06	0.63	3.14	0.48	0.26	$0.61^{A,D}$	–
			β‡	2.81	0.81	2.89	0.70	0.21	$0.65^{A,D,G}$	–
			Corr. serviced messages (%)	91.4	8.1	95.0	6.9	1.14	$0.29^{A,P}$	–
			Spurious responses (%)§	3.10	4.88	0.85	2.71	1.41	$0.24^{D,G,P}$	–
Level 3	24 (44)	31 (62)	d'	3.02	0.57	2.71	0.51	8.68	$0.005^{A,D}$	0.145
			β‡	2.67	0.72	2.68	0.70	0.08	$0.78^{D,P}$	–
			Corr. serviced messages (%)	76.7	15.4	75.8	13.0	0.11	0.75^{A}	–
			Spurious responses (%)§	8.96	6.53	10.19	8.68	0.25	$0.62^{A,E}$	–

*d*f* ranged from [1,51] to [1,101].
†Univariate ANOVA p values for between-group comparisons, corrected for age (A), Symptom Checklist-90 depression score (D), level of education (E), gender (G) and medication with psychopharmacological drugs (P) in case $p<0.20$ for each covariate.
‡Qualitative variable; a positive β indicates that false rejections (missed targets) was relatively more common than false alarms (responding to distractors).
§A lower score signifies better performance.

Table 6. Self-rated cognitive problems for former work-stress-related exhaustion patients and healthy controls.

					ANOVA, Group					
	Patients ($n=54$)		Controls ($n=50$)		Unadjusted for covariates*			Adjusted for covariates*		
Main scales and subscales	Mean	SD	Mean	SD	F †	p	η^2_p	F ‡	p	η^2_p
Euroquest memory and concentration problems§										
Total mean score	2.43	0.67	1.80	0.47	29.7	<0.001	0.226	1.95	$0.17^{D,P}$	–
Concentration and attention problems subscale	2.29	0.71	1.61	0.53	30.3	<0.001	0.229	1.58	$0.21^{D,P}$	–
Memory problems subscale	2.49	0.72	1.90	0.49	24.3	<0.001	0.192	1.67	$0.20^{D,P}$	–
5-item questionnaire of everyday memory problems§										
Total mean score	3.52	0.75	2.69	0.49	44.1	<0.001	0.302	16.65	$<0.001^{D}$	0.142
1. Does anybody close to you (family, friends) think you have a poor memory?	2.98	1.06	2.24	0.87	15.1	<0.001	0.129	3.07	$0.083^{A,D,G}$	–
2. How is your memory today, in comparison with your memory 5 years ago?	4.22	0.74	3.52	0.50	31.3	<0.001	0.234	9.65	0.002^{D}	0.087
3. How do you perceive your memory in comparison with that of other persons your age?	3.69	0.80	3.04	0.60	21.4	<0.001	0.173	7.08	0.009^{D}	0.066
4. Do you forget appointments if not prompted by someone else or by a reminder such as a calendar or diary?	3.75	1.05	2.56	0.81	41.2	<0.001	0.289	18.79	$<0.001^{D,G}$	0.160
5. Does it occur that you do not remember things that have recently happened?	2.98	1.16	2.10	0.89	18.8	<0.001	0.156	13.39	0.032^{D}	0.045

*Univariate ANOVA p values for between-group comparisons, either unadjusted for covariates or adjusted for age (A), Symptom Checklist-90 depression score (D), gender (G) and medication with psychopharmacological drugs (P) in case $p<0.20$ for each covariate.
†d*f* = [1,102].
‡d*f* ranged from [1,99] to [1,101].
§Higher scores represent poorer ratings.

When the raw data were adjusted for potential covariates in the ANOVA (see ''Methods'' section and Table 6), the between-group differences found in Euroquest-9 scores were no longer statistically significant, apparently due to strong relations between Euroquest scores and SCL-90 depression scores (ANOVA covariate values: F's > 24; p's < 0.001 throughout). On the other hand, scores on all but one of the 5-QEMP items were still significantly higher among former WSRE patients after adjustment for SCL-90 depression score (ANOVA covariate values: F's > 5.3; p's < 0.03 throughout). Significant relationships between SCL-90 depression scores and scores on the questionnaires targeting subjective cognitive problems also occurred within the control group, although of a lower magnitude for the single 5-QEMP items (data not shown).

Relationships between neuropsychological test results and self-ratings of cognitive problems

To study whether subjective cognitive problems could predict the outcome of cognitive tests, possible relationships between neuropsychological test results and total Euroquest-9 and 5-QEMP scores were looked for, using partial correlations corrected for the same set of covariates included in the ANOVA models (Tables 3–5) for all 53 test variables (i.e. 106 correlations were carried out). Among former WSRE patients, a relationship between higher subjective cognitive problems and lower cognitive performance was observed only between 5-QEMP and the APT *k*-test d' ($r = -0.274$, $p = 0.045$), although a borderline significance was also observed between 5-QEMP and F-A-S verbal fluency ($r = 0.266$, $p = 0.059$). At the same time, significant correlations in the opposite direction (i.e. higher subjective problem level related to better performance) appeared between the Euroquest-9 total score and the variables WAIS-R Digit Symbol ($r = 0.278$, $p = 0.048$) and APT *k*-test RT level (right part of screen) ($r = -0.373$, $p = 0.007$). A corresponding analysis of the control group only showed a relationship between higher Euroquest-9 total score and lower score on the IVA Visual Vigilance variable ($r = -0.300$, $p = 0.036$), with the IVA Auditory Vigilance variable bordering on significance ($r = -0.273$, $p = 0.058$).

Because the SCL-90 depression score was observed to correlate with most of the subjective cognitive complaints variables, and because the SCL-90 depression score was adjusted for in several of the partial correlations between cognitive complaints and test performance (18 test variables), a separate analysis was carried out with SCL-90 depression deleted from the list of covariates for this subset of variables (i.e. 36 correlations explored). Within the group of former WSRE patients, this showed that a higher Euroquest-9 total score was related to a higher reaction time level in the APT RT-2 test ($r = 0.293$, $p = 0.030$) and that a higher 5-QEMP total score was related to a higher percentage of spurious responses in the APT SimCap test, level 1 ($r = 0.302$, $p = 0.030$). Another attempt to circumvent the relation between the scores on SCL-90 depression and subjective cognitive problems was made by using the question showing the least association with SCL-90 depression scores (''Do you forget appointments if not prompted by someone else or by a reminder such as a calendar or diary?''). However, within the group of former WSRE patients, the ratings in this question did not show any significant relationship with any score among the 53 test variables.

Relationship between cognitive parameters and work resumption

The extent of work resumption among former WSRE patients was not related to any of the neuropsychological test variable scores ($r \leq 0.23$ throughout; $p \geq 0.09$), or to any of the single-item or summary scores on self-ratings of cognitive problems ($r \leq 0.28$ throughout; $p \geq 0.16$).

Discussion

The present long-term follow-up study of patients previously diagnosed with work-stress-related exhaustion suggests the presence of a slight attention deficit despite substantial recovery and successful return to work. The study supplements our previous investigation (Österberg et al., 2012) in which we reported clear within-group improvements on several tests of attention and short-term memory from baseline to the 20-month follow-up, although our conclusions were incomplete due to the limited set of tests for which data were available on both occasions as well as the absence of parallel control group data. To address the issue whether the improvements at follow-up were complete or only partial, an extensive set of neuropsychological tests was used at follow-up, including parallel data from a matched group of healthy controls. The present outcome suggests that neuropsychological sequelae are present to some extent even after an ~2-year recovery period and (in most cases) successful return to work. That there was indeed general substantial recovery is illustrated by the fact that, at follow-up, only 13% still fulfilled the criteria for exhaustion disorder suggested by the Swedish National Board of Health and Welfare (versus 83% at baseline), that only 19% remained on full-time sick leave, and that marked decreases were found in self-ratings of depression, anxiety and cognitive problems.

The pattern of impairment observed in former WSRE patients was characterized by slower and more unstable responses in attention tests of the reaction time type. This was obvious for the APT RT-2 and RT-Inhib level and variation variables, while the error rate on the latter test did not exceed that of the control group. Similarly, on the attention test IVA, former WSRE patients showed normal error rates (Vigilance and Prudence variables), while impairments were apparent for basic speed and speed stability (Speed, Focus and Consistency variables). This suggests that the former WSRE patients managed to monitor their performance and maintain a response style of good quality (i.e. few errors), though at the expense of fluctuating reaction times. Moreover, a trend of progressively longer reaction times toward the end of the rather lengthy IVA test (the Stamina variable) suggests a fatigue effect that exceeds that of the control group. At the same time, it should be noted that the effect sizes of these discrepancies were medium, or slightly below, which indicates that the impairment is minor and probably difficult to detect on an individual level when using a typical clinical neuropsychological assessment.

Against this background it may not come as a surprise that the former WSRE patients maintained a high level of performance on the very demanding simultaneous capacity test, in which scores are based on the ability to attend to multiple commands but are unrelated to the speed of response (within a 2 s limit). Although a slightly lower proportion of former WSRE patients (44% versus 62% among controls) managed to reach the highest level of difficulty on this interactive test, the subgroup of former WSRE patients reaching that level ($n = 24$) actually outperformed the corresponding control subsample ($n = 31$) on the SimCap accuracy parameter (d').

In addition, the former WSRE patients performed slightly better than controls on two episodic memory tests (Cronholm–Molander and Incidental learning WAIS-R NI), and performed equally well as controls on all remaining tests of episodic memory and working memory. Thus, the present study gives no support for persistent impairment in episodic memory functioning after recovery from work-stress-related exhaustion. The memory impairments observed in previous studies of patients in the acute/early stages of exhaustion disorder – for example, concerning visuo-spatial episodic memory (RCFT test; Sandström et al., 2005), verbal episodic memory (Öhman et al., 2007) and working memory (WAIS-R Digit Span; Jonsdottir et al., 2013; Öhman et al., 2007) – were absent in the group of former WSRE patients at follow-up. This group also did not show lower performance than controls on the verbal fluency test (F-A-S), in sharp contrast to the striking impairment in verbal fluency observed by Öhman et al. (2007) among patients in the acute/early stages of WSRE. On the other hand, a lower visuo-spatial constructional ability was found among former WSRE patients compared to controls, seemingly reflecting a higher proportion of participants with quite low performance levels.

As mentioned, there are very few neuropsychological follow-up studies of former patients with WSRE. Oosterholt et al. (2012) were unable to show cognitive improvement at follow-up. However, their follow-up was carried out after only 10 weeks, and included only 16 patients and three cognitive tests, factors that may have contributed to the absence of improvement. Wahlberg et al. (2009, p. 744), who had a substantially longer, 12-month follow-up period and studied 29 patients using seven test parameters, reported that ''the impairments in attention (complex reaction time) and working memory found in the baseline study were no longer present''. However, the absence of previous group differences at follow-up seemed to have been caused by reduced performance among controls and not by actual improvements in the WSRE group (see Österberg et al., 2012 for details). Thus, to date only the study by Österberg et al. (2012) has documented clear cognitive improvements at a long-term follow-up of former patients with WSRE, although the outcome of the present study suggests that cognitive abilities are not fully restored even after a 2-year recovery period.

Given that a slight attention deficit persists despite substantial recovery, similar and possibly more pronounced deficits would be expected in the early/acute stages of WSRE. This also seems to be the case. In close parallel to the present, Oosterholt et al. (2012) described longer reaction times for a WSRE group compared to controls while the ability to inhibit erroneous responses was unimpaired. Moreover, Sandström et al. (2005) reported a pattern of results on the attention test IVA virtually identical to that found in the present study: slower and more variable reaction times but in other respects normal quality of performance (the Prudence and Vigilance variables). Widening the perspective from reaction time tests to attention tests in general, nearly all studies published on the topic thus far have reported some impairment in attention-related cognitive processes in the early/acute stages of stress-related exhaustion (Jonsdottir et al., 2013; Öhman et al., 2007; Österberg et al., 2009; Rydmark et al., 2006; Sandström et al., 2005; Van der Linden et al., 2005). Attention and several closely related cognitive functions (e.g. processing speed, mental tempo, working memory, creativity) can be subsumed under the major cognitive domain ''executive function'', although this cognitive dimension has been operationalized slightly differently in the individual studies, as it has in the neuropsychological literature in general. In a broad sense, the results of previous studies, seen as a whole, would seem to provide ample evidence for inferior executive functioning. Given that executive functioning is largely dependent on the integrity of the frontal lobes, it is of particular interest that a recent fMRI study of patients on stress-related long-term sick leave showed significantly lower prefrontal cortex activation during complex task load and a tendency toward slower reaction times compared to controls (Sandström et al., 2012). Taken together, previous studies in this area strongly suggest that cognitive problems in early/acute stages of WSRE are related to a disturbance in executive functioning. In addition, the present study suggests that a disturbance in executive functioning persists even after 2 years of recovery.

In contrast, the lower level of visuospatial constructional ability observed among the former WSRE patients in the present study is not supported by similar findings in the early/acute stages of stress related exhaustion. Öhman et al. (2007) neither found any impairment when employing the same visuospatial test parameter used in the present study (RCFT-copy), nor did Sandström et al. (2005) or Jonsdottir et al. (2013) see signs of impairment on other tests tapping the same cognitive domain. As visuospatial impairment has not been shown in the early/acute stages, we find it less likely that such impairment would be a genuine long-term sequela of WSRE.

A significant decrease in subjective ratings of everyday cognitive problems in the WSRE group was reported in our previous study of cognitive changes from baseline to follow-up (Österberg et al., 2012). The present study, however, does reveal that the level of subjective cognitive problems remained clearly elevated at follow-up compared to healthy controls. Moreover, the group differences had large effect sizes. An illustration of the significance of these problems is the responses given to the question ''*Do you forget appointments*...'' (5-QEMP item no. 4, Table 6), where the two highest scale steps (''Often'' or ''Very often'') were indicated by no less than 60% of participants in the group of former WSRE patients compared to 10% of the control group. Although the extent of subjective cognitive problems was strongly related to the degree of depressive symptoms, most of the 5-QEMP questions remained significantly elevated even after statistical correction for depressive symptoms, with large effect sizes observed for the 5-QEMP total score and the question ''*Do you forget appointments*...''. Thus, the marked discrepancy between profound subjective memory problems and normal objective performance on episodic memory tests can hardly be explained as merely one of the facets of depressed mood. Although it is conceivable that even a minor impairment in attention might give rise to considerable annoyances in everyday situations – possibly perceived as memory problems – an alternative explanation might be that persons who have experienced long-term sick leave due to

WSRE are particularly observant of any flaws they may have in cognitive functioning for a long period of time following recovery and return to work. Such enhanced self-monitoring fits well into the ''cognitive-emotional sensitization'' model that has been proposed to account for various medically unexplained symptoms (Brosschot, 2002). Whatever the true causes are of prolonged subjective cognitive problems after substantial recovery from WSRE, it is important to remember that no general relationship with objective test performance was found, which means that the level of subjective complaints is a poor indicator of actual cognitive functioning.

No relationship was found between scores on any of the neuropsychological test variables and the extent of work resumption. Nor was the extent of subjective cognitive problems related to work resumption. A similar absence of relationships was shown in our previous baseline and follow-up studies of essentially the same group of patients (Österberg et al., 2009, 2012). It is conceivable that a number of factors besides cognitive capacities determine the decision or ability to return to work (e.g. economic and social incentives).

One strength of the present study was the broad array of cognitive domains explored, using 14 neuropsychological tests, providing no fewer than 53 variables. Only the studies by Sandström et al. (2005) and Öhman et al. (2007) used test batteries of a similar size. We chose this comprehensive set of tests in order to examine as many aspects of cognitive functioning as possible and to facilitate a fine-grained analysis. The downside to this approach is of course the risk of mass significance, possibly introducing spurious group differences among the large number of analyses carried out. We recommend, therefore, that readers primarily consider the general pattern of statistically significant findings across cognitive domains. As mentioned, a clear pattern of inferior scores on attention test parameters of the reaction time type (APT RT-2, RT-Inhib and IVA) appeared in the group of former WSRE patients, though the effect sizes were, at best, moderate (medium). We consider this coherent pattern of slight deviations in attention tests to be the main outcome of the study, and not the presence/absence of group differences in isolated variables. Concerning the 5-item questionnaire on everyday memory problems, large group differences/effect sizes were observed, which would have remained statistically significant also after correction for mass significance using, for example, Bonferroni correction.

It might also be questioned whether it was appropriate to include the 13% of former WSRE patients who still met the exhaustion disorder criteria (Socialstyrelsen, 2003). We dealt with this issue in our previous follow-up paper (Österberg et al., 2012), showing that the general pattern of recovery also included this subset of participants. To avoid selection effects, we chose not to remove this subset from the study group.

An important reservation must also be made concerning the issue of causality in relation to our findings. It is possible that a slight deficit in executive functioning was present long before the patients developed WSRE, and that such a deficit can predispose individuals to develop WSRE (Bridger et al., 2011). However, in a previous paper (Österberg et al., 2012), we were able to show clear within-group improvements from baseline (acute WSRE) to follow-up on several tests of short-term memory and attention. This suggests that some degree of cognitive impairment was in fact present in the acute phases of WSRE, making it reasonable to assume that the present results actually do represent a minor neuropsychological sequela of WSRE.

Conclusions

With regard to some aspects of attention, former WSRE patients still performed at levels slightly lower than controls after a 2-year period, during which substantial recovery and – in most cases – successful return to work had been achieved. Although the initial impairment in early/acute stages of WSRE seems to be mainly reversible (Österberg et al., 2012), a minor attention deficit may persist for long periods, possibly having consequences for regaining full work capacity.

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Declaration of interest

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