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Will an early episode of career burnout have long term consequences on cognitive functions, emotions and depressive symptoms? A longitudinal study among newly graduated nurses

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Content

1 Abstract

A large body of evidence from preclinical studies suggests that chronic stress affects the structure of neurons, mainly the length of dendrites, in the prefrontal cortex (PFC), hippocampus and amygdala. In the PFC and the hippocampus chronic stress produces a retraction of dendrites whereas in the amygdala increases in dendritic length are observed. There is some evidence that such alterations in these brain regions would lead to impairment in cognition, memory and learning, and cause depressive symptoms and anxiety. When stress ceases these neurobiological changes appear to be partly reversed in the PFC, completely reversed in the hippocampus, but not reversed in the amygdala. Based on these studies we hypothesize that job burnout, which is a state of chronic stress, would cause future impairments in PFC-dependent cognitive functions, depressive symptoms and anxiety in humans.

In this study, data were taken from a prospective longitudinal study, named the Longitudinal Analysis of Nursing Education/Employment/Entry in working life (the LANE study) consisting of over 1000 nurses that were followed from their last year in nursing education into their first years of working life. One, two, three and five years after graduation they responded to a questionnaire comprising self-report instruments measuring psychological and physical health, social and psychological factors at work and professional efficacy, among other things. Job burnout was measured by the Oldenburg Burnout Inventory scale. At follow-up five years after graduation items measuring depressive symptoms, cognitive problems, negative emotions, general health and positive emotions were analysed.

We found that 13,5% of the nurses had had at least one episode of high symptoms of burnout, here referred to as *early career burnout* (ECB), one, two or three years after graduation. At follow-up, i.e. 2-4 years later we found that nurses with a history of ECB, but without ongoing symptoms of high burnout, had a higher prevalence of depressive symptoms, cognitive impairments such as attention and making decisions, anxiety, aggression and worry as well as lower prevalence of positive emotions compared to nurses without a history of ECB. In conclusion, our explorative analyses of nurses early in their career suggest that having had an episode of chronic stress, i.e. high symptoms of job burnout, can cause remaining cognitive problems, emotional and affective symptoms several years later when stress symptoms have

ceased. Finally, in agreement with the model of allostatic load for chronic stress, these symptoms can be related to possible neurobiological alterations in PFC, hippocampus and amygdala.

2 Introduction

2.1 Allostatic load as a model for job burnout

Job burnout is often a chronic state of stress that develops gradually over time as a consequence of prolonged stress at work. It is characterized by exhaustion, cynicism, reduced engagement and professional inefficacy (Maslach et al. 2001). In order to understand how burnout affects the individual's mental health a biological model of how chronic stress affects underlying neurobiological structures is needed. One model of chronic stress is the theory of *allostatic load* and *allostatic overload* (McEwen et al. 2015). In this model, the stress response, such as activation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, is designated *allostasis*. These responses are essential for adaptation and maintenance of the body's homeostasis in a challenging situation and are primarily mediated by the hormones noradrenaline, adrenaline and cortisol. However, if the stress response is activated repeatedly over a longer period of time without enough time for recovery, this will cause physiological changes, *allostatic load*. Thus, allostatic load refers to the cumulative effects of multiple stressors and the dysregulation of the physiological systems, for example changes in the production and release of cortisol, adrenaline and noradrenaline in response to a challenge. When such dysregulations produce pathophysiological changes, it is referred to as *allostatic overload* (McEwen et al. 2015). Examples of allostatic overload are hypertension and insulin resistance. These processes have been studied to a large extent in laboratory animals, mainly rats.

When rats are subjected to chronic stress neurobiological changes in certain brain regions develop. In the hippocampus chronic stress produces degeneration of dendrites and loss of synapses, as well as decreased formation of new neurons (neurogenesis) (Juster et al. 2010). Hippocampus is important for the formation of new memory and hence also for learning. Chronically stressed rats show both memory and learning impairments. A dysfynction of the hippocampus has also been implicated in depression (Juster et al. 2011). When stress ceases, these neurobiological changes will recover in the hippocampus region. Chronic stress also leads to shrinkage of dendrites and loss of dendritic spines of neurons in the prefrontal cortex (PFC) (McEwan and Morrison 2013). A well-functioning PFC have been suggested to be important for e.g. attention, working memory, cognitive

flexibility, goal-oriented behavior, regulation of impulses and decision making. With decreased connectivity in this brain region, impairment of these cognitive functions is likely to emerge. As PFC also play an important role in regulation of emotions, for instance in stressful situations, it is likely that stress-induced emotions such as fear and aggression will increase. In one specific part of the PFC, the orbitofrontal cortex, chronic stress appears to rather increase dendritic growth and branching. This cortical area has been suggested to be involved in e.g. reward, sensory integration, and in decision-making and expectation (Kringelbach 2005). A dysregulation of orbitofrontal cortex has been implicated in obsessive–compulsive disorder (Menzies 2008). The neuronal changes in the PFC due to stress do not appear to be permanent in young animals as the dendrites grow out again when the stress ceases. However, in middle aged animals only a minor recovery has been observed and in aged rats no recovery was found (McEwen and Morrison 2013).

The amygdala plays a crucial role in rapidly allocate emotional significance to environmental events, and adjust emotional and physiological responses to these events. In contrast to neurons in the hippocampus and the PFC, chronic stress induces growth of dendrites in the amygdala. An increase in neuronal connectivity in the amygdala appears to be linked to enhanced fear learning, and an increase in anxiety-like behavior (McEwen et al. 2015). Chronic stress in laboratory animals also increases aggression, an effect that could be due to this alteration in amygdala together with a dysfunction of PFC. In contrast to the neurons in hippocampus and PFC, the expanded dendritic branching of neurons in the amygdala do not appear to normalize after recovery from chronic stress, at least not after 3 weeks (Vyas et al. 2004). In addition, chronic stress-induced increase in anxiety-like behavior, which is thought to be a consequence of the neuronal changes in amygdala were still present in laboratory animals 3 weeks after recovery.

2.2 Aim

We have previously found that almost twenty percent of newly examined nurses showed high levels of burnout at some point during their first three years in the profession (Rudman and Gustavsson 2011). In this study we investigated in the same cohort if a previous episode of burnout affects cognitive functions, emotions and depressive symptoms at five year's postgraduation follow-up.

2.3 Hypothesis

Based on the model of allostatic load we predict that nursing professionals who have had an episode of job burnout early in their career will in the future suffer from cognitive and emotional dysfunctions, as well as depressive symptoms. We hypothesize that they have developed neuronal changes in the hippocampus, PFC and amygdala as a consequence of have being exposed to chronic stress at work. Neuronal changes in hippocampus would cause impairment in memory and learning, but may also cause depressive symptoms. Hence, our first hypothesis is that nurses who have had an episode of burnout will have higher probability for reporting depressive symptoms at follow-up. Moreover, changes in PFC would cause impairment in attention, working memory, cognitive flexibility, goal-oriented behavior, regulation of emotions and impulses and in decision making. This would negatively affect job assignments which require planning and organization as well as executive functions. Our second hypothesis is that nurses who have had an episode of burnout will at follow-up report more dysfunctions in these cognitive domains compared to those without an early episode. Our third hypothesis is that nurses who suffer from job burnout will report higher levels of negative emotions, mainly anxiety, but also irritability and aggression at follow-up several years later. Furthermore, all these impairments would influence everyday life negatively with a decrease in general well-being and quality of life and we hypothesize also that this also affect positive emotions negatively.

3 Method

3.1 Subjects

Data were taken from a prospective longitudinal study, named the Longitudinal Analysis of Nursing Education/Employment/Entry in working life (the LANE study). The LANE study comprises three national cohorts of newly graduated nurses who were followed from last year in nursing education into their first years of working life (Rudman et al., 2010). For the purposes of the present study, the LANE cohort, consisting of 1155 nursing students who graduated in the autumn of 2002, was used. The present article includes data from a follow-up five years after their graduation from higher education. On this occasion, 951 responded to a survey, resulting in an 82% response rate (see figure 1). Median age was 36 years (minimum 27 years, maximum 57 years) and 90% were women. Data on symptoms of job burnout was compiled from questionnaires that the nurses answered one, two and three years after graduation (see figure 1).

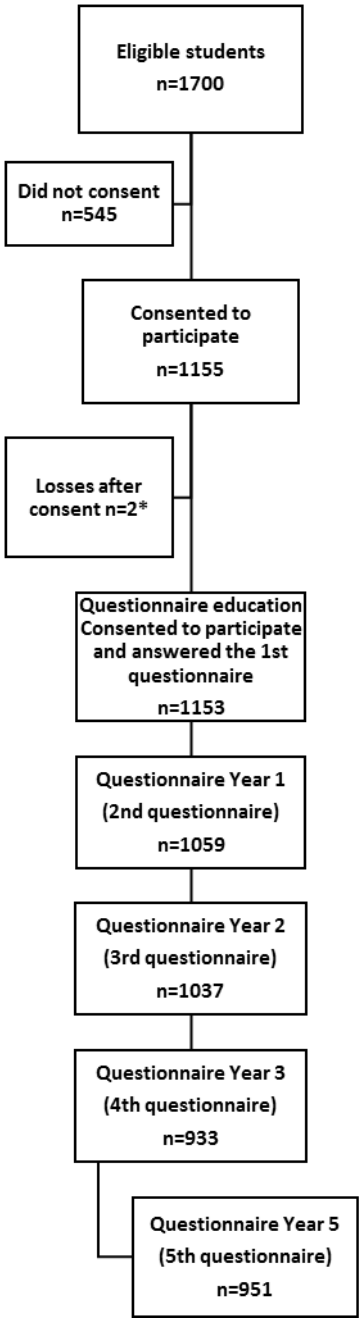

Figure 1. Description of the five data collections (i.e. sample selection, participant recruitment, consent, timing of follow-ups and the wave response). Education= last year of nursing education (in 2002), Year 1= one year after graduation (in 2004), Year 2=two years after graduation (in 2005), Year 3=three years after graduation (in 2006), Year 5=five years after graduation (in 2008). * Reason: consented but did not fill in the first questionnaire

3.2 Instruments

The LANE questionnaire comprises self-report instruments measuring background characteristics, psychological and physical health, social situation, healthcare utilization, sickness absence, social and psychological factors at work, as well as

professional efficacy and quality aspects of the healthcare system (Rudman et al., 2010).

The outcome variable, job burnout, was measured by the Oldenburg Burnout Inventory OLBI (Demerouti et al. 2001). The scale consists of two dimensions i.e. exhaustion (five items) and disengagement (five items). Exhaustion refers to the consequence of intensive physical, affective and cognitive strain and disengagement refers to the process of distancing oneself from one's work, resulting in negative attitudes towards the work in general. Answers are given on a four-point response scale ranging from "Totally disagree" to "Totally agree". In these analyses we have used a validated cutoff for high burnout symptoms (combining scores from exhaustion and disengagement items) according to Gustavsson et al. (2010).

Depressive symptoms were measured by the Major Depression Inventory (MDI; Bech et al. 2001). MDI measure depressive symptomatology, both according to the DSM-IV and ICD-10 with 12 items, as well as severity by summarizing 10 of the items. Two of the items on the scale have sub-items a and b, but only the highest score of either a or b is considered in score analysis (Bech et al., 2001). Items are measured in frequency and the relevant time frame is the last two weeks, as is the case for the DSM-IV diagnosis of major depression and the ICD-10 diagnosis of moderate to severe depression (Bech et al., 2001). The four-point frequency response scale range from 1 = All the time, 2 = Most of the time, 3= A minor part of the time and 4 = Not at all. The cut off for having high levels of symptoms were set at 1 and 2. In addition, we here use two items assessing degree of suffering from the depressive symptoms with a dichotomous response scale i.e. whether one or more of the symptoms caused substantial suffering a) during the last two weeks and b) for a two-week period during the last 12 months, or not.

Cognitive problems were measured by the Major Depression Inventory (Bech et al 2001) with the three items that assess difficulties in concentrating, making decisions and feelings of being "sluggish" and slow measured in frequency during the last two weeks, with the same four-point response scale (as described above) and the cut off for having high levels of symptoms were set at reporting symptoms "All the time" and "Most of the time".

Professional self-efficacy were measured by four items (i.e. *“Reorganize your work in unforeseen situations”, “Assess strength and weaknesses of your professional skills”, *“Assess patients’ needs of nursing interventions”, *“Execute nursing interventions”). Three of the items (*) were from the Core Competencies of Patient-Centered Care measure (Ehrenberg et al 2016). The respondents were asked to rate, on a scale from 0% (cannot) to 100 % (definitely can), how confident they were about performing the tasks defined in each item. Low professional self-efficacy was regarded when 70% or less was reported.

Occurrence of negative emotions was assessed on a dichotomous scale (yes/no last 12 months) in relation to four types of anxiety, panic, social, compulsive, and obsessive. Also, feelings of irritation, anger, restlessness and overexcitement (e.g. “Have you felt restless and overexcited?”) were measured in frequency by the Major Depression Inventory (Bech et al 2001) during the last two weeks, with the same four-point response scale (as described above) and the cut off for having high levels of symptoms were set at reporting symptoms “All the time” and “Most of the time”.

Frequency of worry about occupational risks were measured by seven items, i.e. worrying about physical injuries, making mistakes, being reported, get infected, be physically or psychologically overstrained and being exposed to violence, on a five-point response scale; 1 = Very often or always, 2 = Often, 3 = Sometimes, 4 = Seldom, 5 = Very seldom or never. Cut off for worry was set at responding 1 or 2 on the scale. In addition, three composite measures of general worry were generated 1) two worries or more about occupational risks, 2) three worries or more about occupational risks, 3) four worries or more about occupational risks.

General health (i.e. self-rated health; Fylkesnes et al 1992) and sleep quality (from The Karolinska Sleep Questionnaire; Akerstedt et al. 1994; 1997) during the past 4 weeks were measured on a 5-grade response scale with the answer alternatives: 1 = Good, 2 = Pretty good, 3 = Neither good nor poor, 4 = Pretty poor, 5 = Poor. The cut off for having poor health and sleep were set at 3 to 5. Poor recovery after sleep during the past 4 weeks was also measured on a 5-grade scale ranging from 1 = Almost every day, 2 = Many times per week, 3 = Some times per week, 4 = Seldom, 5 = Never. The cut off for having high levels of symptoms were set at 1 and 2. Finally, two items from MDI (Bech et al. 2001) that measured a need for more sleep

than usual and sleeping problems during the past two weeks on a four-point response scale range from 1 = All the time, 2 = Most of the time, 3 = A minor part of the time, to 4 = Not at all. The cut off for having high levels of symptoms were set at 1 and 2.

Positive emotions (Lindfors et al. 2014) were measured with seven items (happiness, generosity, strong love, inspiration, expectations, gratitude, optimism) on a four-point frequency response scale ranging from 1 = All the time, 2 = Most of the time to 3 = A minor part of the time and 4 = Not at all. The cut off for having low positive emotions were set at 3 and 4.

3.3 Data analysis

The prevalence of early career burnout (based on validated cut-off scores) was estimated for each data collection for the total cohort. Those reporting high levels on one or more occasion (during the first three years post-graduation) were defined as cases (called ECB below) and those not reporting high levels of burnout on any occasions (during the first three years post-graduation) were forming the control group (called Control below). The prevalence of symptoms or problems measured at follow-up, five years after graduation, were then compared between these two groups.

First, an estimate of the prevalence for a certain problem or symptom (five years post-graduation) was estimated for the total cohort. Secondly, estimates were calculated for the case and control groups. In a third step, an odds ratio was computed comparing the relative risk between the two groups of reporting a symptom at follow-up (OR crude). As a final step, an additional odds ratio was computed using logistic regression, now controlling for ongoing episodes of burnout at follow-up (OR adjusted).

4 Results

4.1 Burnout

In total, the prevalence of nurses that had had at least one episode of very high burnout symptoms, here called early career burnout (ECB), one, two or three years after graduation was 146 nurses (13.5% of the total cohort). The prevalence of ECB at year 1, 2 or 3 was between 6.2 and 7.2 percent of the total cohort (see table 1). Two years after graduation, 29% of those who had an ongoing episode of ECB had had an episode also one year earlier. Three years after graduation, 35% with an ongoing episode of ECB had had an episode one or two years earlier (table 1). At follow-up five years after graduation 4.2% have an ongoing episode of high burnout symptoms.

Table 1. Prevalence of early career burnout (ECB) one, two and three years after graduation.

Year		Early career burnout			
	Responders	Cases	Cohort %	New cases	ECB %
1	1008	64	6.4		
2	975	70	7.2	50	71
3	788	49	6.2	32	65

Cases = number of respondents with ECB; Cohort % = prevalence of ECB in the total sample; New cases = number of new cases without previous ECB; % ECB = prevalence of new cases.

4.2 Depressive symptoms

Nurses with a history of ECB had a significantly higher prevalence of depressive symptoms at follow-up five years after graduation (Table 2). When corrected for ongoing burnout, three of the symptoms, low in spirit or sad, lost interest and lacking energy and strength, were still more prevalent in nurses with a history of ECB. We also found that almost one fourth of the nurses with a history of ECB reported that one or more of the depressive symptoms had caused them substantial suffering during the last two weeks. In addition, almost 40% of them reported that one or more of the depressive symptoms had caused them considerable suffering for a two-week period during the last 12 months. This is about twice as many nurses compared to those without a history of job burnout. When correcting for ongoing job burnout, having had substantial suffering from one or more of depressive symptoms was still

more common in the nurse with a history of job burnout than in those without. These results show that some of the depressive symptoms had been severe and about twice as many nurses with a history of burnout compared to nurses without such history reported this.

Table 2. Prevalence and odds ratios of depressive symptoms.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Have you felt in low spirits or sad?	9.6	17.5	8.1	2.4	***.001***	1.9	***.028***
Have you lost interest in your daily activities?	7.1	15.0	5.9	2.8	***.001***	2.0	***.030***
Have you felt lacking in energy and strength?	15.1	25.2	13.7	2.1	***.001***	1.7	***.024***
Have you felt less self-confident?	9.1	14.3	8.3	1.8	***.032***	1.3	.396
Have you had a bad conscience or feelings of guilt?	9.4	16.5	8.2	2.2	***.003***	1.8	.052
Have you felt that life wasn't worth living?	6.7	11.0	6.0	2.0	***.033***	1.6	.160
Suicidal ideation	4.6	8.7	3.7	2.5	***.013***	2.1	.058
Has one or more of the symptoms listed above caused you substantial suffering during the last two weeks?	14.3	23.6	12.7	2.2	***.001***	1.7	***.029***
Has one or more of the symptoms listed above caused you substantial suffering for a two-week period during the last 12 months?	24.3	39.4	21.6	2.3	***.001***	1.9	***.002***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

4.3 Cognitive problems

Three items in the questionnaire indicate cognitive functions and are listed in table 3. In the whole cohort few nurses reported having problems with these functions, but

nurses with a history of job burnout reported having such problems much more often than nurses without such history (Table 3). After statistical adjustment for ongoing episode of burnout, our results show that nurses who have had an episode of job burnout two to four years earlier had significantly more problems with concentration and taking decisions, as well as feeling more lethargic and slow.

Table 3. Prevalence and odds ratios of cognitive impairments.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Concentrations difficulties	4.3	14.2	2.9	5.6	***.001***	4.0	***.001***
Difficulties taking decisions	6.2	16.5	4.5	4.2	***.001***	3.5	***.001***
Sluggish/slow	8.0	17.3	6.5	3.0	***.001***	2.3	***.006***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

In the questionnaire we also had several questions regarding professional assignments measuring self-efficacy. Four of these require higher cognitive functions and were therefore also analysed (see Table 4). About twice as many nurses that had had an episode of job burnout reported low confidence on all four tasks compared to nurses who had not had such an episode. After adjustment for ongoing job burnout, three of the assignments were still more prevalent in the nurses with a history of ECB.

Table 4. Prevalence and odds ratios of low professional self-efficacy. Work assignments that require higher cognitive functions in nurses with and without a history of early career burnout (ECB) at 5-years follow-up.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Organize work assignments	8.5	13.9	7.8	1.9	***.026***	1.7	.072
Analyze own competence	14.2	23.8	12.9	2.1	***.001***	2.1	***.003***
Evaluate independently	8.3	15.6	7.0	2.5	***.002***	2.3	***.005***
Execute independently	7.4	13.1	6.5	2.2	***.001***	2.0	***.030***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

4.4 Negative emotions

We had several items in the questionnaire that measure negative emotions. We included four questions regarding different types of anxiety (panic, social, compulsive and obsessive) and one question regarding aggression where we also included irritation which can be regarded as a milder form of aggression. One item also measured restlessness and overexcitment. All these negative emotions were much more prevalent in nurses with a history of ECB, also after correcting for ongoing symptoms of burnout (Table 5).

Table 5. Prevalence and odds ratios of negative emotions.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Panic anxiety	18.4	32.5	16.1	2.5	***.001***	2.2	***.001***
Social anxiety	24.3	33.1	22.6	1.7	***.011***	1.6	***.036***
Compulsive anxiety	10.8	21.3	8.8	2.8	***.001***	2.5	***.001***
Obsessive anxiety	6.3	15.0	4.8	3.5	***.001***	3.1	***.001***
Irritated and angry	8.6	16.5	7.5	2.4	***.001***	1.9	***.032***
Restless and overexcited	6.1	13.4	4.9	3.1	***.001***	2.7	***.003***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

Worry can be regarded as a milder form of anxiety and thus as a negative emotion. In our questionnaire we had included several questions regarding worry about occupational risks (Table 6). We found that nurses with a history of ECB worried much more about all the occupational risks we asked for compared to nurses who had not had an episode of job burnout. High levels of worry were still present in nurses with a previous episode of ECB, but who had not ongoing symptoms of job burnout. To get a more general measure of worry, we also calculated how many nurses that had answered that they worried very often or often about two or more occupational risks. Of the nurses with a history of ECB, we found that about half of them worried about two or more risks, one third about three or more risks and about 15% about four or more occupational risks. This is almost twice as many as those

with no history of burnout. An increased risk was still present after correcting for ongoing high symptoms of burnout.

Table 6. Prevalence and odds ratios for worry about occupational risks.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Physical injuries	18.2	26.2	16.5	1.8	***.008***	1.7	***.021***
Make mistakes	27.6	41.0	25.3	2.1	***.001***	1.8	***.003***
Get reported	11.2	20.5	9.8	2.4	***.001***	2.0	***.011***
Get infected	12.5	24.6	10.4	2.9	***.001***	2.7	***.001***
Get physical overstrained	11.8	20.7	10.6	2.2	***.001***	2.0	***.011***
Get psychologically overstrained	23.4	38.5	21.0	2.3	***.001***	1.8	***.009***
Exposed to violence	7.7	14.8	6.8	2.4	***.003***	2.1	***.014***
General worry; 2 worries or more about occupational risks	30.0	52.5	26.2	3.1	***.001***	2.7	***.001***
General worry; 3 worries or more about occupational risks	17.3	33.6	14.7	3.0	***.001***	2.4	***.001***
General worry; 4 worries or more about occupational risks	7.7	14.8	6.6	2.5	***.002***	2.0	***.027***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

4.5 General health, sleep and positive emotions

Of the nurses with a history of ECB about 20 percent answered that their general health was poor which is significantly more than those without such history (Table 7). However, after correcting for ongoing symptoms of burnout there was no difference between the groups.

Both depression and anxiety is well-known to affect sleep negatively. Thus, we also included four questions regarding different aspects of sleep; “How do you assess your sleep quality?”, “How often do you get sleep that make you feel recovered?”, “How often have you felt that you need more sleep than usual?” and “How often do you have sleeping problems during the night?”. Poor sleep quality, need for sleep and sleeping problems were more prevalent in nurses with a history of ECB compared to controls (Table 7). An increased prevalence was still present after correcting for ongoing high symptoms of burnout in those nurses.

Table 7. Prevalence and odds ratios for general health and sleep problems.

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Poor general health	12.7	19.7	11.6	1.9	***.012***	1.4	.208
Poor sleep quality	10.9	19.7	9.4	2.4	***.001***	2.2	***.003***
Poor recovery after sleep	19.6	26.2	18.6	1.6	.050	1.5	.078
Need for sleep	13.8	29.1	11.3	3.2	***.001***	2.8	***.001***
Sleeping problems	12.0	23.6	10.2	2.7	***.001***	2.7	***.001***

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

The prevalence of nurses that answered “A minor part of the time” or “Not at all” regarding how often they felt different positive emotions is listed in table 7. Nurses with a history of ECB felt lack of happiness, generosity, inspiration and optimism about twice as often as nurses without a history of ECB. After correcting for ongoing episode of burnout, they were still more likely to lack happiness, generosity and inspiration.

Table 7. **Prevalence and odds ratio for lack of positive emotions.**

	Estimates in the total sample			**Statistical control or control by design**			
	Cohort %	ECB %	Control %	OR crude	p	OR adjusted	p
Happiness	16.5	26.8	14.6	2.2	***.001***	1.7	***.026***
Generosity	19.0	28.6	17.2	2.0	***.001***	1.6	***.036***
Strong love	13.5	17.5	12.9	1.4	.148	1.4	.197
Inspiration	37.3	50.0	35.0	1.9	***.001***	1.6	***.020***
Expectations	36.8	38.9	36.2	1.1	.529	1.0	.899
Gratitude	41.3	44.1	41.2	1.1	.506	1.0	.971
Optimism	21.7	28.6	20.3	1.7	***.018***	1.4	.117

Cohort % = prevalence in the total sample; % ECB = prevalence in the subsample with a history of early career burnout (ECB); % control = prevalence in the subsample without a history of ECB. OR crude = without correction. OR adjusted = corrected for ongoing episode of job burnout.

5 Discussion

In the present longitudinal study of over 1000 nurses that were followed from the last year of nursing education to three years after graduation, 13.5% had had at least one episode of very high symptoms of job burnout, here called early career burnout (ECB). Thus, it should be emphasized that ECB is not equivalent to the diagnosis exhaustion disorder. We found that those who have had an episode of ECB had higher levels of several emotional, affective and cognitive problems five year after graduation, i.e. 2-4 years after the episode. In agreement with the allostatic load model of chronic stress, these problems can be related to tentative neurobiological changes in the hippocampus, PFC and amygdala.

Specifically, we found that nurses who had experience an episode of job burnout reported higher prevalence of several depressive symptoms, in particular low mood and loss of interest in daily activities (anhedonia), the core symptoms of depression (DSM-5). They were also more than twice as likely to report that one or more of the depressive symptoms had caused them substantial suffering for a two-week period indicating severe and long-lasting symptoms. A dysfunction of the hippocampus has been implicated in the development of depression (see e.g. Juster et al. 2010). Our results support the hypothesis that ECB, which can be regarded as a state of chronic stress, affects the hippocampus also in humans causing depressive symptoms. In laboratory animals these alterations, mainly a shortening of dendrites and decreased neurogenesis, are restored when stress ceases. Thus, we also calculated whether depressive symptoms were still present in nurses who have had an episode of ECB, but no ongoing symptoms at the time when they answered the questionnaire. We found that these nurses still had a higher prevalence of low mood, lost interest in daily activities and feelings of low energy and strength. This is in contrast to the animal studies, if these symptoms develop as a consequence of the neurobiological alterations in the hippocampus. Hence, this could indicate that stress-induced alterations in the hippocampus do not completely recover in humans. On the other hand, development of depressive symptoms is probably not only a consequence of alterations in the hippocampus, but most likely also other brain regions are involved, such as the PFC. In particular, a dysfunction of the middle frontal gyrus, within the dorsolateral PFC has been implicated in anhedonia (Heller et al 2009). Since chronic

stress causes loss of dendrites also in the PFC and hence reduced connectivity, this could contribute to the higher prevalence of loss of interest in daily activities reported in nurses with a history of ECB. Taken together, nurses who have had a previous episode of ECB two to four years earlier had a higher incidence of depressive symptoms even after recovery from high burnout symptoms, as compared to nurses who had not suffered from an episode of ECB.

Regarding cognitive functions, we found that nurses with a history of ECB were two to five times more likely to have impairments in concentration, taking decisions or feel lethargic and slow compared to nurses who had not suffered from high symptoms of job burnout. These nurses were also twice as likely to report low professional self-efficacy in assignments that require complex cognitive functioning. These findings are in agreement with the hypothesis that chronic stress produces neurobiological alterations in the PFC a brain region essential for these cognitive functions. Most of the cognitive impairments were still more prevalent in nurses with a history of ECB but without ongoing symptoms than in the nurses without such history. These finding suggest that the neurobiological alterations of PFC neurons had not recovered when job stress/strain were less pronounced 5 years after graduation. In laboratory animals a recovery was observed in young animals, a partly recover in middle aged animals and no recovery in old rats when stress ceased. The nurses in our cohort were between 27 and 57 years old when answering the questionnaire, and hence, some of them could be regarded as middle aged. However, the number of nurses in different ages was too small to perform valid statistics on. In a recent systematic review, job burnout was found to be associated with impairment in three main cognitive domains: executive functions, attention and memory (Deligkaris et al 2014). However, most of the included studies in this review were cross-sectional and the authors point out the need for longitudinal studies in order to establish a cause-effect relationship between job burnout and cognitive dysfunctions. Our longitudinal study of nurses in their early career suggests that even after recovery from an episode of high symptoms of job burnout some cognitive functions were still impaired, i.e. attention and taking decisions, and they also felt more lethargic as compared with nurses without an episode of ECB.

Significantly more nurses who have had an episode of job burnout than those who have not had such episode reported that they had symptoms of anxiety, in particular panic, obsessive and compulsive anxiety, five years after graduation. The prevalence of anxiety was still higher in nurses with a history of ECB even without high symptoms of ongoing job burnout. These results support our hypothesis that an episode of job burnout will lead to increased dendritic branching in the amygdala and hence increased anxiety. Since higher anxiety was reported also in nurses with a history of ECB but without present symptoms of high burnout, our results imply that the increased dendritic branching in the amygdala do not retract to normal after an episode of ECB. These findings are in agreement with preclinical studies in laboratory rats where increased dendritic length in amygdala as well as higher anxiety-like behavior is still observed after chronic stress ceased. However, since anxiety and other emotions are regulated by the PFC, loss of dendrites in this region may contribute to heighten anxiety. Indeed, it has previously been reported that people suffering from chronic occupational stress were less capable of down-regulating negative emotions (Golkar et al. 2014). This appears to have been linked to an altered functional connection between the amygdala and one part of the PFC, the anterior cingulate cortex. Nurses who had experienced an episode of ECB also reported more often that they were irritated and angry and also worried significantly more over occupational risks. Increased aggression and worry may also be related to increased connectivity in the amygdala as well as a dysfunctional cortical inhibition of emotional stress responses.

Chronic stress in rats appears to increase dendritic branching in one particular area of the PFC, the orbitofrontal cortex. As increased activity in this brain region has been implicated in obsessive compulsive disorder (Menzies 2008), the higher prevalence of obsessive and compulsive anxiety found in nurses with a history of ECB, could imply that the orbitofrontal cortex may be affected in these nurses as observed in laboratory animals. If so, our results also suggest that these alterations in the orbitofrontal cortex do not normalize after recovery from job burnout.

Nurses with a history of ECB rated their overall health as poorer compared to nurses who had not had ECB. However, when high symptoms of job burnout were not present, they did not rate their health differently from nurses without a history of

ECB, suggesting that high symptoms of burnout probably contributed to their low rating of overall health. Sleep problems were also more prevalent in nurses with a history of ECB, and poor sleep quality, need for sleep and sleeping problems persisted when high symptoms of job burnout were no longer present. Finally, nurses who had had an episode of ECB, but had no ongoing symptoms, reported that they felt less happiness, were less generous towards others and felt less inspiration in everyday life. Less happiness could be related to that the nurses with a history of ECB also reported more negative emotions and depressive symptoms. Thus, our results suggest that a previous episode of ECB negatively affected positive emotions 2 to 4 years later.

Taken together, these explorative analyses of nurses with a history of an episode of high symptoms of early career burnout clearly give support to our theoretical hypothesizes. However, the results need to be replicated and should also include questions that better measures cognitive functions, in particular attention and memory. In addition, it would be of great interest to investigate if the problems persist years later and do a new data collection at about 10 years after graduation.

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7 Previous reports

Petter Gustavssons forskargrupp samlas under namnet ”Motivation, kompetens och hälsa” (inkludernade de så kallade LUST- och LÄST-projekten) och är en del av avdelningen för psykologi, Institutionen för Klinisk Neurovetenskap, Karolinska Institutet. Som en del av verksamheten utges rapporter sammanställda i tre olika skriftserier. Skriftserierna benämns:

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