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Brief communication

Psychosocial and biological predictors of resident physician burnout.

Running title: Incident burnout in residents: psychosocial-biological risk factors

V. Olivé. [1]Department of Medicine, Psychiatry Functional Unit, Institute of Neuroscience, University of Barcelona (UB), Barcelona, Spain. [2]Department of Occupational Health and Prevention, Hospital Clinic, Barcelona, Spain. Email: volive@clinic.cat

R. Navinés. [3]Department of Psychiatry and Psychology, Hospital Clinic, UB, Institut d' Investigació Biomèdica August Pi i Sunyer (IDIBAPS), CIBERSAM, Barcelona, Spain. Email: rnavines@clinic.cat

L. Macías. [4]Department of Biochemistry and molecular Genetics, Center of Biomedic Diagnosis (CDB), Hospital Clinic, UB, IDIBAPS, Barcelona, Spain. Email: lamacias@clinic.cat

J.A. López. [2]Department of Occupational Health and Prevention, Hospital Clinic, Barcelona, Spain. Email:jlopezm@clinic.cat

J. Ariz. [2]Department of Occupational Health and Prevention, Hospital Clinic, Barcelona, Spain. Email: jariz@clinic.cat

S. Quesada. [2]Department of Occupational Health and Prevention, Hospital Clinic, Barcelona, Spain. Email: squesada@clinic.cat

S. Barroso. [2]Department of Occupational Health and Prevention, Hospital Clinic, Barcelona, Spain. Email:sbarroso@clinic.cat

X. Filella. [4]Department of Biochemistry and Molecular Genetics, Center of Biomedic Diagnosis (CDB), Hospital Clinic, UB, IDIBAPS, Barcelona, Spain. Email: xfilella@clinic.cat

K. Langohr. [5]Department of Statistics and Operations Research, Universitat Politècnica de Catalunya/ Barcelonatech (UPC), Barcelona, Spain. Email: klaus.langohr@upc.edu

R. Martin-Santos* [1]Department of Medicine, Psychiatry Functional Unit, Institute of Neuroscience, UB, Barcelona, Spain. [3]Department of Psychiatry and Psychology, Hospital Clinic, UB, IDIBAPS, CIBERSAM, Villarroel 170, 08036-Barcelona, Spain. Phone (34) 932272754. Email: msantos@clinic.cat

* Corresponding author

Highlights

-Burnout and psychosocial risk factors in residents have been extensively studied, but most of the evidence comes from cross-sectional studies; few studies have included biological markers related to stress and immunity.

-This exploratory study showed an incidence of burnout after one year of residence of 22%; burnout may be predicted by high work demand and decreased cortisol levels.

-The results support early detection of both psychosocial work conditions and biological risk factors in order to design strategies for preventing resident burnout

Abstract: (N = 200)

Background: A high proportion of health professionals in training suffer from work-related stress and may develop a burnout syndrome.

Objectives: To study the incidence of burnout after the first year of residence in a teaching hospital and to identify baseline psychological, psychosocial work conditions, and biological risk factors.

Methodology: We assessed the following in a prospective cohort of residents at baseline (first month residence) and after 1 year: background factors (socio-demographics, psychiatric history), perceived stress score (Perceived Stress Scale), Maslach Burnout Inventory score, and psychosocial factors (Job Content Questionnaire). Blood samples were obtained to study serum cortisol, IL-6, and TNF-α concentrations. The cumulative incidence was modelled by multivariate log-binomial regression analysis.

Results: We included 71 participants with a female majority (64.8%), age 26.4 (2.65) years, psychiatric history in 20%, and burnout in 13%. Among those without burnout initially (N= 59), it had developed by 1 year in 22% of residents. Increased job demand (RR=1.259, 95%CI=1.019–1.556, p=0.033) and decreased cortisol levels (RR=0.877, 95%CI=0.778–0.989, p=0.032) predicted burnout after 1 year of residency among medical trainees.

Conclusion: Burnout syndrome develops in 22% of residents by 1 year of training and can be predicted by increased work demands and decreased cortisol levels.

Key words: Burnout residents; cortisol; cytokines; incidence; job demand-control model; relative risk; stress.

1. Introduction

The workplace is one of the main potential sources of stress in Western society [1,2]. Various investigations carried out on burnout in resident physicians have shown that this group of professionals is especially vulnerable [3-5]. Burnout is described as having three dimensions (emotional exhaustion, depersonalization, and reduced personal accomplishment) [6]. Traditionally, it has been clinically diagnosed using the Maslach Burnout Inventory (MBI) [7].

The mechanisms by which stress affects health are mediated by the so-called stress response at various levels: emotional, cognitive, adoption of risk behaviours, and physiological responses [8]. A sustained hyperactivation of the hypothalamus-pituitary-adrenal axis has also been observed in these settings, with an increase in cortisol secretion accompanied by anti-inflammatory cytokine release [9], that protects against disease behaviour. However, when this response is prolonged, it becomes maladaptive and results in an increase in pro-inflammatory cytokine release (IL-1b, IL-6, TNF-α), the main mediators between the immune response and the brain [10]. Despite the general consensus around cortisol and its role in mediating responses to stress, research has produced inconsistent findings on its relationship with burnout [11,12].

We aimed to study the incidence of burnout in a sample of residents from the beginning to the end of their first year of residency training in a teaching hospital, and to identify the psychological, psychosocial (work), and biological risk factors at baseline.

2. Material and methods

This longitudinal exploratory pilot cohort study lasted 1-year and included all junior physicians who joined the residency programme of a university hospital during the 2017–

2018 period. The ethics committee approved the study. We collected socio-demographic, psychiatry history, use of medications or drugs, and type of speciality (medical, surgery and others). During the first month, all participants underwent a general health examination, and a clinical， psychological, psychosocial, and biological evaluation. After a 1-year follow-up period, they underwent reassessment with the same protocol (data not shown with the exception of the MBI data).

We used the validated Spanish version of the self-administered Cohen Perceived Stress Scale (PSS) [13]. The scale uses a five-point Likert response format from “never” to “very often” to give scores between 0 and 56. The validated Spanish version of the self-administered MBI [14] was used to assess burnout. The 22-item MBI has three subscales: emotional exhaustion (EE), depersonalization (D), and personal accomplishment (PA) assessed with a Likert-type scale ranging from “never” to “daily”. A person is considered to have burnout syndrome when: MBI-EE≥27, MBI-D≥10, or MBI-PA≤33 subscale. Finally, we used the Spanish validated version [15] of the self-administered Job Content Questionnaire (JCQ) [16] to assess psychosocial work factors. The 22-item JCQ has three dimensions: demand, control, and social support, each item scored using a Likert scale from “strongly disagree” to “strongly agree”.

A complete laboratory screening was performed at baseline and at 1 year together with serum cortisol and interleukin concentrations. Samples were collected at 09:00, on an empty stomach and after having slept for 8 hours. The serum cortisol concentration was determined by radioimmunoassay (Immunotech, France) with a 4% intra-assay and a 8% inter-assay coefficient of variation. Immunological parameters were determined by enzyme-linked immunosorbent assay (ELISA,Diasource), with coefficients of variation of 6% for TNF-α and 7% for IL-6. The minimum detectable concentrations for TNF-α and IL-6 were 0.7 pg/mL and 2 pg/mL, respectively.

We performed all statistical analyses using the R software package (v4.1.1) and set the statistical significance at 0.05. Univariate analysis of the baseline factors associated with prevalent burnout syndrome at baseline and the cumulative incidence of burnout after 1 year was performed using Fisher´s exact test for categorical variables and the exact Wilcoxon rank sum test for quantitative variables. The cumulative incidence was modelled by multivariate log-binomial regression, which included statistically significant variables from the univariate analyses. Contrasting with logistic regression modelling, the log-binomial model uses the relative risk to measure effect size. The statistical results were not adjusted for multiple comparisons.

3. Results

All 90 residents who started the residency programme were invited to participate. Of the 75 (83%) who provided signed informed consent, 4 did not complete the initial visit, giving a final baseline sample of 71 (78.9%). For the 1-year follow-up assessment, we excluded 9 (12.7%) with burnout at the baseline and 3 who were lost-to-follow-up. The final sample at the end of the first year comprised 59 (65.6%) residents. At 1 year, thirteen residents (22%) had developed new cases of burnout syndrome

Table 1 shows the comparative analysis between those with and without burnout both at baseline and 1 year. Analysis revealed a greater percentage of non-Spanish nationals (p=0.047) and non-medical residents (p=0.013) presented burnout at baseline. Any resident were taken medication or using alcohol more than occasionally both at baseline or first year residency. Three residents smoke at baseline and at first year follow-up. No differences were observed between those with and without burnout both at baseline (p=0.500) at 1 year (p=0.579). PSS was significantly higher among those with burnout at baseline (p=0.003).

JCQ revealed significant differences in work demands between residents with and without incident burnout (p=0.044). The serum TNF-α concentration was lower among residents with burnout at baseline (p=0.042), but there were not statistical differences in IL-6 concentration showedbetween groups. Finally, the baseline serum cortisol concentration was lower in residents who presented incident burnout after 1 year compared to those who did not (p=0.040).

Table 2 presents the log-binomial regression model and indicates that increased work demand score and cortisol concentrations at baseline predicted incident burnout at 1 year of residency. According to the model, a unit increase in the baseline demand score was associated with a relative risk of 1.26 (95%CI, 1.02-1.56; p=0.033), whereas a unit higher baseline cortisol level was associated with a lower risk of incident burnout by a factor of 0.88 (95%CI, 0.78-0.99; p=0.032). Adding sex (p=0.602), baseline MBI-EE score (p = 0.995), baseline MBI-D score (p=0.609), and baseline MBI-PA score (p=0.938), respectively, to the model did not yield substantial improvement of the model fit.

4. Discussion

Our results suggest that high work demands, regardless of control over work and social support, may predicted burnout after 1 year of residency. These data point to the importance of incorporating measures to improve work pressure during residency training to prevent burnout and improve wellbeing [17]. Coupled with these findings, our data showed that baseline cortisol levels predicted the appearance of burnout in residents in training. To our knowledge, no other study in the published academic literature has reported on the relationship between basal cortisol and the incidence of burnout in residents. The risk of incident burnout after 1 year of residency was higher in those with lower baseline cortisol

concentrations. Although baseline cortisol levels were within normal parameters, they may have been inadequate to cope with the demand of work, leading to vital exhaustion by 1 year of hospital residency. In line with our study results, the Dresden Burnout Study [18] suggested blunted cortisol secretion in response to long-term exposure to stressful work [19]. However, other research has found a positive correlation between burnout and long-term hypercortisolism [20].

Our finding that a noteworthy 13% of residents met the criteria for burnout in the first month of residency, as reported elsewhere [21], suggests that the syndrome can develop early and should be evaluated by occupational health services soon after residency begins. This group also reported greater levels of perceived stress compared with residents who did not have baseline burnout. Stressors not directly related to work, such as adapting to a new life stage after leaving university, could explain this association [22]. The lower levels of the pro-inflammatory cytokine TNF-α, suggested an early anti-inflammatory response of the body trying to protect by decreasing levels of this inflammatory cytokine [23].

The longitudinal design allowed us to obtain relevant preliminar results about the impact of burnout. Our study also benefitted from the use of surveys and face-to-face visits. However, there were several limitations. First, and most importantly, we had a small sample size. Second, we only included residents in their first year of hospital training, whereas it would be more informative to have included follow-up over the entire residency. Third, the results of this single-centre study may not be fully generalizable to others due to normal variations in working conditions. Fourth, we did not assess depressive symptomatology or personality traits that could play a role. Finally, we only studied a few biological variables, and among these, we measured blood cortisol levels at a fixed time without controlling for the time since awakening.

In conclusion, our results suggested that approximately one in four residents presented

a *de novo* burnout syndrome by 1 year of training in our sample, which was predicted by increased baseline work demand and lower cortisol levels. Of note, slightly more than one in ten residents already suffered from burnout within the first month of training and this was associated with high-perceived stress. However, future large and multicentric studies would be needed to confirm these preliminary results. Given the major consequences of burnout for residents in training, academic institutions need to develop specific protocols to monitor risk factors for, and offer strategies to prevent, burnout during this critical training period.

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Conflict of interest

None to declare.

Author contribution

VO, RN, and RMS designed the study. LM performed the biomarker analyses. VO, LM, JAL, SQ, and SB gathered data. KL, VO, and RMS performed the data analyses. VO, RN,

and RMS wrote the first version of the manuscript. All authors contributed to, and approved, the final manuscript.

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Table 1. Descriptive and comparative analysis of characteristics of the sample, perceived stress, job demand /control/support social aspects and biological variables at baseline and one-year follow-up between groups

	Initial burnout Baseline* N = 71		**Incident burnout** One-year follow-up N = 59		P**
Sample characteristics	(1) With N= 9 (12.7%)	(2) Without N= 62 (87.3%)	(3) With N= 13 (22.0%)	(4) Without N= 46 (78.0%)	a) 1 vs 2 b) 3 vs 4
Age, Mean (SD)	26.9 (2.7)	25.9 (2.6)	25.2 (1.2)	26.1 (2.9)	.206 (a) .240 (b)
Women, N (%)	5 (55.6%)	41 (66.1%)	8 (61.5%)	31 (67.4%)	.711 (a) .746 (b)
Single, N (%)	9 (100%)	61(98.4%)	13 (100%)	45 (97.8%)	---***
Nationality, N (%)					**.047** (a) .274 (b)
-Spanish	6 (66.7%)	46 (74.2%)	12 (92.3%)	31 (67.4%)	
-Others European	2 (22.2%)	1 (1.6%)	0 (0.0%)	1 (2.2%)	
-South American	1 (11.1%)	15 (24.2%)	1 (7.7%)	14 (30.4%)	
Ant. psychiatry disorders, N (%)	2 (22.2%)	12 (19.4%)	3 (23.1%)	9 (19.6%)	1.0 (a) .716 (b)
Type speciality, N (%) -Medical -Surgery -Others (RX, lab, etc.)	 3 (33.3%) 2 (22.2%) 4 (44.4%)	 47 (75.8%) 8 (12.9%) 7 (11.3%)	 9 (69.2%) 2 (15.4%) 2 (15.4%)	 36 (78.3%) 5 (10.9%) 5 (10.9%)	 **.013** (a) .645 (b)
Psychological and psychosocial variables	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Perceived stress score (PSS)	20.4 (10.1)	11.5 (6.77)	11.4 (4.33)	11.9 (7.34)	**.003** (a) .850 (b)
Job Content Questionnaire (JCQ)					
-Demand	18.67 (3.81)	16.87 (3.37)	18.69 (3.45)	16.36 (3.28)	.191 (a) **.044** (b)
-Control	20.56 (4.42)	21.64 (2.54)	21.85 (3.24)	21.60 (2.43)	.866 (a) .721 (b)
-SCC	16.44 (1.94)	17.16 (2.46)	17.15 (2.23)	17.09 (2.54)	.311 (a) .690 (b)
-SSS	12.56 (2.88)	12.90 (2.65)	12.67 (2.83)	12.89 (2.64)	.691 (a) .495 (b)
Biological variables	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
[Cortisol]	20.6 (7.89)	20.3 (6.67)	16.8 (5.86)	20.9 (6.29)	.894 (a) **.040** (b)
[IL-6]	4.67 (6.16)	15.0 (42.0)	7.38 (12.6)	17.8 (48.2)	.933 (a) .722 (b)
[TNF-α]	6.33 (1.50)	6.41 (9.80)	5.08 (1.44)	6.80 (11.4)	**.042** (a) .866 (b)

Abbreviation: IL-6, Interleukin 6; SSC, Social support from co-residents; SSS, Social support from supervisor; TNF-α, Tumour Necrosis Factor-alpha.
* First month of residency period.
** Fisher's exact and Wilcoxon test.
*** No tests applied since all but one resident are singles.

Table 2. Multivariate log-binomial regression model of burnout incidence

Parameter	Estimate	SE	Wald	p	RR* = Exp (B)	95% CI
Intercept	-2.781	2.061				
[Cortisol]	-0.131	0.061	4.580	0.032	0.877	[0.778–0.989]
Demand	0.230	0.108	4.538	0.033	1.259	[1.019–1.556]

*RR, Relative risk.