# **Biomarkers of Clinician Burnout**

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# INTRODUCTION

Professional burnout has adverse consequences for healthcare quality and safety and staff wellbeing.<sup>1</sup> Efforts to address burnout are hampered by challenges in conceptualizing and measuring burnout, in part because of inadequate understanding of its pathophysiology.<sup>2</sup> Because burnout and stress are conceptually linked, neuro-hormonal changes in response to stress (such as cortisol levels) may provide novel avenues for understanding the pathophysiology of burnout and for improving measurement using biomarkers. In addition to measuring salivary cortisol, which reflects acutely circulating hormone concentration with diurnal variation, hair cortisol represents a marker for long-term stress exposure.<sup>3</sup> Separately, the concept of connection and trust is emerging as a potential protective moderator of burnout. Oxytocin, known to increase in situations with high trust or bonding,<sup>4</sup> may therefore be a useful biomarker for protection against workplace stress. We aimed to examine associations of salivary and hair cortisol with emotional exhaustion (EE) and depersonalization (DP) (measures of burnout) and association of urinary oxytocin with connection and trust among clinicians.

# **METHODS**

Salivary and hair cortisol and urinary oxytocin were collected, and perceived burnout (two-item MBI),<sup>5</sup> engagement (Utrecht Work Engagement Scale<sup>6</sup>), connection ("I feel a strong sense of connection and community at work"), and trust ("I trust my obgyn colleagues and feel safe discussing concerns with them") were measured in 25 female clinicians in the ObGyn Department at MGH in May 2018 at the start of a series of monthly support groups designed as part of an ongoing study of strategies to reduce burnout. Hair cortisol concentrations were obtained from the 3 cm most proximal to the scalp reflecting prior three-month cortisol levels.<sup>3</sup> Because of this lag, an additional hair sample was collected three months after initial collection. Linear regression was used to assess the relationship between hormone levels and measures of wellbeing, focusing on association between cortisol and burnout and oxytocin and connection and trust.

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# RESULTS

Study population characteristics, including rates of completion of biomarker assessment, are reported in Table 1. EE was significantly associated with higher salivary cortisol levels  $(0.03 \mu g/dL \text{ increase with high vs low EE; } p=0.036)$  whereas DP was significantly associated with lower salivary cortisol levels (0.04 $\mu$ g/dL decrease with high vs low DP; p=0.018). When hair cortisol was analyzed as repeated measure, it positively associated with EE (coefficient 20.21, SE8.77, p=0.026) and trends toward inverse association with DP (coefficient - 20.18, SE10.42, p=0.06). These associations were not significant when adjusting standard errors for clustering within subject (p=0.19 for both). Oxytocin was significantly higher among participants reporting higher sense of connection (29.2 pg/mg/creatinine (16.2 pg/mg/creatinine) vs 17.3 pg/mg/creatinine (3.8 pg/mg/creatinine): p=0.028). There was a positive correlation between oxytocin and engagement (r=0.45; p=0.048). Oxytocin was higher among participants reporting higher trust in colleagues (29.4 pg/mg/creatinine

**Table 1 Participant Characteristics** 

	Respondents (N=25)			
	N	%	Mean	SD
Years in practice:				
<5	0	0	-	-
5-10	4	16	-	-
11–15	5	20	-	-
16–20	7	28	-	-
>20	9	36	-	-
Burnout*:				
Low emotional exhaustion	10	40	-	-
High emotional exhaustion	14	56	-	-
Low depersonalization	19	76	-	-
High depersonalization	5	20	-	-
Engagement				
Utrecht work engagement scale	24	96	38.9	6.5
Trust among colleagues <sup>†</sup> :				
Low trust	14	56	-	-
High trust	10	40	-	-
Connection <sup>‡</sup>				
Low sense of connection/community	12	48	-	-
High sense of connection/community	12	48	-	-
Biomarkers:				
Salivary cortisol (µg/dL)	21	84	0.056	0.02
Hair cortisol (time 1) (pg/mg)	16	64	8.14	13.3
Hair cortisol (time 2) (pg/mg)	20	80	24.8	30.1
Urinary oxytocin (pg/mg/creatinine)	22	88	24.98	34.9

\*Participants indicating that they experienced symptoms at least weekly were considered to meet the criteria for high EE or high  $DP^5$ 

†Responses for trust were reduced to high trust (strongly agree) and low trust (moderately agree, slightly agree, slightly disagree, moderately disagree, strongly disagree)

*‡Responses for connection were reduced to high sense of connection (strongly/moderately agree) and low sense of connection (slightly agree, slightly disagree, moderately disagree, strongly disagree)* 

(19.2 pg/mg/creatinine) vs 19.1 pg/mg/creatinine (4.5 pg/mg/ creatinine)), but this did not reach significance (*p*=0.076).

### DISCUSSION

At a time of limited understanding of the pathophysiology of burnout,<sup>2</sup> these results demonstrate opposing relationships between the two commonly identified burnout domains, EE and DP, and endogenous cortisol levels. We hypothesize EE may increase physiologic stress response while DP may result in dampened stress response, perhaps due to link with apathy and emotional disconnection, though as observational study cannot draw conclusions about causality. Oxytocin levels were associated with higher levels of connection and engagement. This biomarker may be a useful measure of workplace culture and relatedness, known to be critical for functioning of healthcare workers. Future studies will be important to confirm these novel findings in larger samples.

There is particular need for establishment of a biomarker that accurately measures stress over time. Although statistical significance was strongest for the association with salivary cortisol, hair cortisol levels may be easier to assess in faculty settings as they are not sensitive to transient fluctuations of hypothalamicpituitary-adrenal axis activity, do not require collection at same time of day, and are a measure of chronic cortisol exposure.

The study has several limitations. It included a small number of self-selected faculty in one department. Missing information on some biomarkers further limited statistical power. However, to our knowledge, this is the first study to demonstrate that biomarkers may provide valuable information in both measuring and understanding professional burnout. Additional research is needed to determine if these results hold in larger samples and to understand how best to incorporate biomarkers into ongoing efforts to understand and address clinician burnout.

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*Author's Contribution* ASB, SH, LB, FP, EAL, NE, and KA contributed significantly to the conception and design of the work. ASB, SH, and LB contributed to the acquisition of data for the work. ASB, SH, FP, LB, EAL, and KA contributed to analysis and interpretation of the work. All authors were involved in the drafting and revision of the work for important intellectual content and approved the final version of the manuscript before publication.

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#### Declarations:

**Ethics Approval:** The Institutional Review Board of the organizing hospital (Partners Healthcare, Protocol number: 2018P000415) approved the study. Written consent was obtained from all participants. All data used were strictly anonymized; only a research coordinator had access to the file linking responses to identifiers.

All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

**Conflict of Interest:** EAL is on the scientific advisory board and has a financial interest in OXT Therapeutics, a company developing an intranasal oxytocin and long-acting analogs of oxytocin to treat obesity and metabolic disease. EAL's interests were reviewed and are managed by Massachusetts General Hospital and Partners HealthCare in accordance with their conflict of interest policies. All other authors report no declarations of interest.

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