A new perspective on cancer-related fatigue: Negative affectivity and inflammation leading to increased effort expenditure

Tamara E Lacourt, E Vichaya, C Escalante, M Manzullo, B Gunn, C Heijnen, R Dantzer

Contact: Tlacourt@mdanderson.org

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Introduction

- Between 44% – 66% of cancer patients report moderate to severe fatigue during cancer therapy
- Fatigue becomes chronic in 22% - 39% of cancer survivors
- Inflammation and negative affectivity have both been associated with fatigue, but the mechanisms are unknown
- **Negative affectivity**: a tendency to experience negative emotions

We focused on incentive motivation as a possible link between fatigue, negative affectivity, and inflammation

- **Incentive motivation:** the amount of effort one is willing to engage in to obtain a reward

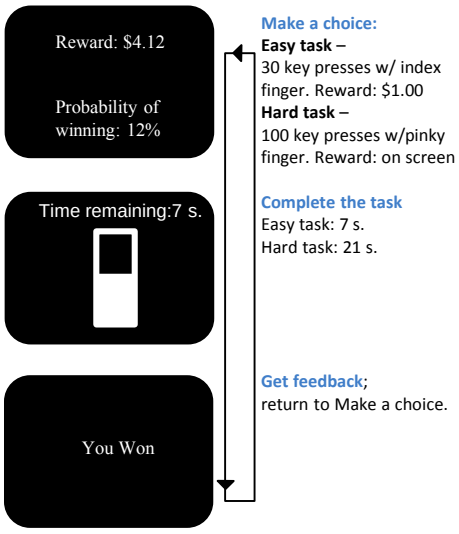
Methods

- Cancer patients and survivors (n = 47; 22 patients, 25 survivors) were recruited at MD Anderson Cancer Center
- Patient-reported **general fatigue** was assessed with subscale of the MFSI-SF.
- Patient-reported **negative affectivity** was assessed with the PANAS
- Plasma concentrations **of IL-1ra, TNF-α, sTNFRII, IL-6, and sIL-6r** were measured using ELISAs
- Motivational effort expenditure was assessed with the **Effort Expenditure for Reward Task (EEfRT) (see right).**

The EEfRT has been validated in depression, anhedonia, and neurological disorders.[1,2]

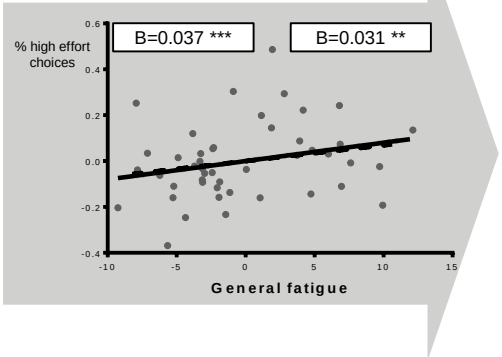
Primary outcome of the EEfRT: % hard task/high effort choices

EEfRT: an objective measure of incentive motivation



Results

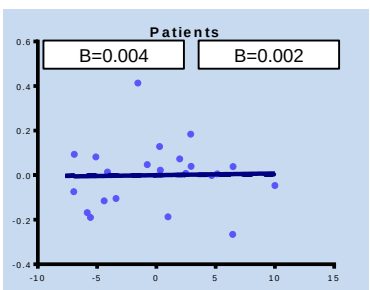
Greater fatigue is associated with more high effort choices. These associations are somewhat reduced when negative affectivity is added to the models.

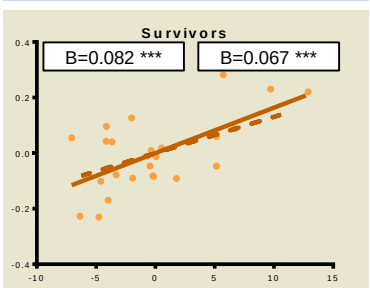


Fatigue alone
Fatigue controlled for NA

Plots display partial regression lines. Covariates: age, gender, use of anxiolytics.
B-values represent logodds for making high effort choices (Generalized Estimating Equations models)

Associations between fatigue and high effort choice **are apparent in survivors**, but **not in patients**





Summary

1. **Fatigue, negative affectivity, and inflammation are all associated with increased motivation to exert effort.**

2. The associations of fatigue and negative affectivity with effort expenditure are not independent.

3. **These findings are apparent in cancer survivors**, who were at least 3 months past any cancer treatment.

4. **In cancer patients**, actively undergoing any type of cancer treatment (including maintenance treatments), **fatigue was not associated with high effort choices**

Pro-inflammatory markers are also associated with more high effort choices. However, markers were not associated with fatigue

	High effort choices		Fatigue	
	B (logodds)	P	B	P
CRP	0.115	0.036	-1.42	0.15
IL-6	**0.252**	**<0.001**	0.05	0.96
sIL-6r	**0.232**	**<0.001**	-1.02	0.30
TNF-α	**0.201**	**0.001**	0.85	0.45
sTNFRII	**-0.198**	**0.010**	-0.94	0.48
IL-1ra	**-0.231**	**0.001**	-0.46	0.68

Conclusion

- **We propose that high negative affectivity is associated with a propensity for high effort choices, resulting in a high vulnerability for ongoing cancer-related fatigue during cancer survivorship**.
- In contrast, effort expenditure choices do not play a role in acute cancer-related fatigue experienced by cancer patients.
- Our observation that inflammation was associated with increased effort expenditure is in agreement with recently published results on experimentally induced inflammation in healthy volunteers[3].
- **Inflammation can contribute to fatigue through an effort investment pathway.**
- Longitudinal rather than cross-sectional studies are needed to better understand causality.

Acknowledgements

This research was supported by funds form the University Cancer Foundation and the Duncan Family Institute for Cancer Prevention and Risk Assessment via the **Cancer Survivorship Research Seed Money Grants** at the University of Texas MD Anderson Cancer Center.

References

1) Treadway et al. J Abnorm Psychol 2012;121:553-558
2) Treadway et al. Schizophr Res 2015;161:382-385
3) Lasselin et al. Neuropsychopharmacology 2017;42:801-810