Endurance exercise reduces cortisol in Parkinson's disease with mild cognitive impairment

Smyth, N., Skender, E., David, F.J., Munoz, M.J., Fantozzi, G., Clow, A., Goldman, J.G. and Corcos, D.M.

This is the peer reviewed version of the following article: Smyth, N., Skender, E., David, F.J., Munoz, M.J., Fantozzi, G., Clow, A., Goldman, J.G. and Corcos, D.M. (2019) Endurance exercise reduces cortisol in Parkinson's disease with mild cognitive impairment. Movement Disorders. 34 (8), pp. 1238-1239. doi:10.1002/mds.27719, which has been published in final form at:

https://dx.doi.org/10.1002/mds.27719.

Endurance Exercise Reduces Cortisol in Parkinson's Disease with Mild Cognitive Impairment

Nina Smyth, PhD[1]

Elizabeth Skender, MS[2]

Fabian J. David, PhD[2]

Miranda J. Munoz, BS[2]

Giamila Fantuzzi, PhD[3]

Angela Clow, PhD[1]

Jennifer G. Goldman, MD, MS[4]

Daniel M. Corcos, PhD[2]

[1] Department of Psychology

School of Social Sciences

University of Westminster

London

[2] Department of Physical Therapy and Human Movement Sciences

Feinberg School of Medicine

Northwestern University

Chicago

[3] Department of Kinesiology and Nutrition

University of Illinois at Chicago

Chicago

[4] Shirley Ryan AbilityLab and Departments of Physical Medicine and Rehabilitation and Neurology at Feinberg School of Medicine Northwestern University

Chicago

c) Corresponding Author:

Daniel M. Corcos, PhD
Department of Physical Therapy & Human Movement Sciences
Feinberg School of Medicine
Northwestern University
645 North Michigan Avenue (Suite 1100, room 1137)
Chicago
(312) 908- 6792 (Office)
(708)-214-5454 (Cell)
daniel.corcos@northwestern.edu

d) Word Count:

500 words

e) Running title:

Exercise lowers cortisol in Parkinson's disease

f) Key words

Endurance Exercise - cortisol - Parkinson's disease

g) Financial Disclosures/Conflict of Interest

Dr. Goldman and Dr. Corcos received funding support from the Consolidated Anti-Aging Foundation (J.G.G., D.M.C.). No others received funding or had potential conflicts of interest.

h) Funding sources for study

Consolidated Anti-Aging Foundation (J.G.G., D.M.C.).

Parkinson's disease (PD) is a multifactorial complex disorder associated with motor signs as well as diverse non-motor symptoms such as circadian disruption, depression, and cognitive decline. Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, evidenced by hypersecretion of cortisol, is implicated in such non-motor symptoms[1] and elevated levels of cortisol have been documented in PD, especially in the morning[2]. Participation in physical activity may reduce the risk and rate of progression of PD[3,4] and endurance exercise may reduce the rate at which the signs of PD progress[5]. Since physical fitness and long term physical activity is associated with attenuated cortisol secretion in healthy participants[6], we undertook a feasibility study to examine the effects of high intensity endurance exercise on diurnal salivary cortisol secretion (as well measures of cognition, structural and functional brain imaging and blood derived biomarkers) in patients with PD with mild cognitive impairment (PD-MCI). We predicted that 6-months of high intensity endurance treadmill exercise would generate a measurable decrease in salivary cortisol secretion from baseline levels.

Following ethical approval, eight patients with PD-MCI (5 males), as determined by clinical and cognitive assessment (mean MoCA 23.75±2.2), who were not exercising at high intensity participated in this study. Participants had mean (SD) age of 66.0±8.0 years (range 53-79 years); disease duration based on initial diagnosis of 5.6±5.4 years (range 1-13 years); Hoehn and Yahr stage 2±0.5 (range 1-3). Using best practice guidelines (1-1 instruction; written guidelines; electronic monitoring of awakening and saliva sampling collection times)[7] participants collected saliva samples at home on 2 typical consecutive weekdays before and after the intervention. Samples were collected during a post-awakening period (0, 0.25, 0.50,

0.75 hours after awakening) and a daytime period (3, 6, 9, 12 hours after awakening) and were assayed in duplicate (Salimetrics, intra and inter-assay variations <10%).

The intervention involved 6 months of high intensity treadmill exercise and included 5-10 min of warm up, 30 min of exercise at 80-85% maximum heart rate, followed by 5-10 min of cool down. Participants exercised an average of 2.5 days per week (average number of sessions completed: 75±7). During the first 8 weeks of training, exercise duration and intensity were gradually increased to target levels.

Distribution of cortisol data was normalized by square root transformation (raw data illustrated). Multi-level modelling compared 2 days pre- vs. 2 days post-intervention. Mean wake time was 6:03±1 hour 20 minutes and adherence to protocol was excellent (modal time of first sample = 3 min post-awakening and reported effects were consistent with non-adherent samples omitted). A trend for reduced cortisol secretion as averaged across all time points was observed with a 19% reduction; (p=0.07); this reached statistical significance for the post-awakening period (p=0.02), but not for the daytime period (p=0.14). Cortisol secretion in participants with PD post-intervention more closely resembled healthy reference data post-intervention (Figure 1).

These data support the need for further exploration of HPA axis dysregulation in PD, including its non-motor symptoms, to understand not only its potential role in the mechanisms underlying non-motor symptoms of PD, but also its responsiveness to intervention studies such as physical exercise that can improve non-motor symptoms.

Acknowledgment.

We thank the patients who took part in this study and the referring physicians at Rush University Medical Center, a Parkinson's Foundation Research Center of Excellence.

We also acknowledge funding support that was provided by Consolidated Anti-Aging Foundation (J.G.G., D.M.C.).

(8) Author's roles.

Nina Smyth

1. Research project: A. Conception, B. Organization,
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Elizabeth Skender

1. Research project: C. Execution;
2. Statistical Analysis: C. Review and Critique;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Fabian J. David

1. Research project: C. Execution;
2. Statistical Analysis: C. Review and Critique;
3. Manuscript Preparation: B. Review and Critique;

Miranda J. Munoz

1. Research project: B. Organization,
3. Manuscript Preparation: B. Review and Critique;

Giamila Fantuzzi

3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Angela Clow

1. Research project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Jennifer G. Goldman

1. Research project: A. Conception, B. Organization, C. Execution;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

Daniel M. Corcos

1. Research project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique;
3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

(9) Financial Disclosures of all authors (for preceding 12 months)

Nina Smyth

The British Academy
Challenge Fund – Department for Work and Pensions and Department for Health and Social Care
Sir Halley Stewart Trust

Elizabeth Skender

U01NS102038	09/01/2017-06/30/2020	NIH/NINDS

Fabian J. David, PhD

R01NS092950	07/01/2016-06/30/2021	NIH/NINDS

Miranda J. Munoz, BS

Northwestern University Integrated Neuroscience Program

Giamila Fantuzzi

Angela Clow

Jennifer G. Goldman

Acadia, CHDI
Michael J. Fox Foundation
NIH, Parkinson's Foundation
Consultant: Acadia, Aptinyx, Sunovion, Worldwide Med;
Honoraria - American Academy of Neurology, International Parkinson's Disease and Movement Disorders Society, Parkinson's Foundation

Daniel M. Corcos

R01NS100937	09/15/2017-06/30/2022	NIH/NINDS
R01NS092950	07/01/2016-06/30/2021	NIH/NINDS
U01NS102038	09/01/2017-06/30/2020	NIH/NINDS
R01AG060162	09/01/2018-05/31/2022	NIH/NIA
R01DK110669	02/01/2017-01/31/2021	NIH/NIDDK
R25HD074546	04/01/2018-03/31/2023	NCMRR

(10) References

1. McEwen B, Gianaros PJ. Stress- and allostasis-induced brain plasticity. Annu. Rev Med 2011;62:431–45.
2. Skogar Ö , Fall PA, Hallgren G, et al. Diurnal salivary cortisol concentrations in Parkinson’s disease: increased total secretion and morning cortisol concentrations. Int J Gen Med 2011;4:561–569.
3. Xu Q, Park Y, Huang X, et al. Physical activities and future risk of Parkinson disease. Neurology 2010;27:341-534, 2010.
4. Paul KC, Chuang Y, Shih I, et al. The association between lifestyle factors and Parkinson’s disease progression and mortality. Mov Disord 2019;34:58-66.
5. Schenkman M, Moore CG, Kohrt WM, et al. Effect of high-intensity treadmill exercise on motor symptoms in patients with DeNovo Parkinson disease: a phase 2 randomized clinical trial. JAMA Neurol 2018;75:219-226.
6. Wood CJ, Clow A, Hucklebridge F, Law R, Smyth N. Physical fitness and prior physical activity are both associated with less cortisol secretion during psychosocial stress. Anxiety Stress Copin 2018;31:135-14.
7. Smyth N, Thorn L, Hucklebridge F, Evans P, Clow A. Post awakening salivary cortisol secretion and trait well-being: the importance of sample timing accuracy. Psychoneuroendocrinolo 2015;58:141-151.

(12) Figure 1 Legend

Figure 1: Diurnal salivary cortisol concentrations (mean+SEM) pre (circles) and post (squares) exercise intervention. Laboratory reference data (triangles) from comparable healthy participants are provided for illustrative purposes: post-awakening period: n=55, 43F/13M, aged 68.3±8.5; daytime period: n=26, 15F/11M, aged 48.6±11.7 years.