International Journal of Psychophysiology 80 (2011) 157–160

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Short Communication

Short and long-term effects of smoking on cortisol in older adults

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ARTICLE INFO

Article history:
Received 27 October 2010
Received in revised form 31 January 2011
Accepted 9 February 2011
Available online 17 February 2011

Keywords:
Aging
Cortisol
HPA axis
Pack-years
Smoking

ABSTRACT

We investigated concurrent as well as long-term effects of smoking on cortisol. The population consisted of 2508 elderly adults. Current smokers, as opposed to former smokers, had higher basal cortisol levels and higher morning increases of cortisol. Overall, pack-years was related to morning cortisol rise, but this was accounted for by current smokers. Time since quitting was positively associated with a greater decline in daytime cortisol indicating that the effects of smoking remit. This suggests that smoking has short-term, rather than long-term, consequences on cortisol secretion patterns.

1. Introduction

Smoking is a commonly known risk factor for mental and physical health. However, the biological mechanisms for this are not always clear. Studies suggest that the effects on biological systems such, as the endocrine system, may play a role for many chronic disorders (Rohleder and Kirschbaum, 2006; Tziomalos and Charsoulis, 2004). Cortisol is a stress hormone within the hypothalamic–pituitary–adrenal (HPA) axis, which is influenced by smoking and related to chronic diseases (Lundberg, 2005; Steptoe and Ussher, 2006). Thus evaluating the association of smoking to cortisol may help elucidate the mechanism by which smoking influences disease.

Cortisol follows a diurnal pattern, first rising 30-minutes after awakening and then declining throughout the day. Smoking acutely increases cortisol levels and it has been shown that this stimulation is dose-dependent (Rohleder and Kirschbaum, 2006). Studies in large samples of younger adults demonstrated that, relative to non-smokers current smokers have higher overall basal cortisol levels, greater morning increases, and lesser declines in cortisol over the day (Kumari et al., 2010; Rohleder and Kirschbaum, 2006). Comparable results were reported in a middle age cohort study, in which current smokers had higher salivary cortisol levels and morning increases, when compared with former and never smokers, while there were no differences between former and never smokers (Badrick et al., 2007).

Many smoking-related health problems occur after a long history of smoking, but subsequently decrease after smoking cessation (Office of the Surgeon General Report, 2004). As cortisol may mediate chronic health consequences of smoking, it is important to explore the effects of long-term smoking on cortisol. Older adults generally have longer smoking history than younger adults. Additionally, the duration since quitting is longer for former smokers in older adults. Although there is evidence for a short-term effect of smoking on cortisol in older adults (Badrick et al., 2007), the long-term effects and the diurnal pattern have not been fully explored by examining long-term indicators of smoking. Therefore, the current study examined the association between short and long-term indicators of smoking and cortisol levels in older adults.

The current study was based within the Rotterdam study, a population-based cohort of adults aged over 55 years which focuses on the occurrences and determinants of common chronic diseases (Hofman et al., 2009). The data from the fourth follow-up round (2002–2004), in which salivary cortisol was sampled, was used in this cross-sectional study. The population consisted of 2508 participants (mean age 74.9 ± 5.8 years, 58% female) whose smoking status data was complete, and who had at least one saliva sample. There were 297 current smokers (11.8%), 1389 former smokers (55.4%), and 822 never smokers (32.8%).

Participants were asked about their smoking status, and current smokers were asked how many cigarettes they smoked daily and how long they had been smoking. Former smokers were asked about their smoking history with regard to the number of cigarettes they had

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doi:10.1016/j.ijpsycho.2011.02.007

Table 1
Participant characteristics by smoking status.

	Current smoker $n=297$	Former smoker $n=1389$	Never smoker $n=822$	p value[a]
Age (years), mean ± (SD)	73.4 ± (5.3)	74.9 ± (5.6)	75.4 ± (6.2)	<.001
Gender (female), n (%)	170 (57.2)	596 (42.9)	693 (84.3)	<.001
Marital status (married), n (%)	161 (54.2)	941 (67.7)	454 (55.2)	<.001
Education (primary school only), n (%)	48 (16.2)	159 (11.4)	135 (16.4)	<.001
Mini Mental State Examination, mean ± (SD)	27.5 ± (1.9)	27.6 ± (2.3)	27.4 ± (2.3)	.20
Body Mass Index (kg/m²), mean ± (SD)	26.1 ± (3.7)	27.6 ± (3.9)	27.6 ± (4.2)	<.001
Number of cigarettes smoked daily, mean ± (SD)	12.4 ± (7.4)	N/A	N/A	N/A
Pack-years, mean ± (SD)	33.6 ± (21.4)	25.4 ± (23.5)	N/A	<.001
Time since quitting (years), mean ± (SD)	N/A	28.2 ± (3.6)	N/A	N/A

[a] p values are overall values.

smoked per day and the time since they had quit. Pack-years, a combination of duration and intensity of smoking, was subsequently calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person had smoked. The number of cigarettes smoked daily provides an indication of whether there is a dose-response relationship. Time since quitting makes it possible to determine whether the effect of smoking on cortisol was permanent, and pack-years is an indicator of long-term exposure. The latter is particularly pertinent to the current study, where, given the older age of the population, a longer life history could be obtained.

Because the cortisol level increases 30 min after awakening and declines throughout the day, multiple measures of cortisol levels during the day provide more valid information about daily cortisol release (Pruessner et al., 1997). Saliva samples were therefore collected on awakening (C1), after 30 min (C2), at 5 pm (C3) and at bedtime (C4). HPA axis activity was evaluated by three summary measures. Total cortisol exposure throughout the day was tested by Area Under the Curve (AUC) given by the individual cortisol measurement on the y-axis and the time between the cortisol measurements on the x-axis. Cortisol Awakening Response (CAR) was used to investigate the morning increase 30 min after awakening. CAR was calculated as the difference between C2 and C1 over two (Pruessner et al., 2003). Diurnal decline was assessed by a slope, which was calculated by fitting a linear regression line for each participant, which predicted the cortisol values from time since awakening. A greater decline in daytime cortisol means that the slope of the regression line is steeper (higher or positive β), whereas a lesser decline means that the slope is flatter (lower or negative β).

Sex, age, and marital status were evaluated as covariates. The time between subsequent cortisol measurements within the same day was used as a covariate in the analysis of C2 and C3. Cognitive status was evaluated with the Mini Mental State Examination (Folstein et al., 1975) and used as a continuous variable. Education was scaled from primary education (1) to university level (7) and used as a continuous variable. Pharmacy records were used to collect data on systemic corticosteroid use.

The association between smoking and both the single and summary cortisol measures was evaluated. An ANOVA was conducted to determine whether smoking status (current, former, and never) was associated with cortisol. An ANCOVA was performed to test the association between smoking status and cortisol, adjusting for sex, age, marital status, cognitive status, education, corticosteroid use, and time between cortisol measures (for C2 and C3). The pair-wise comparisons between the three smoking groups were evaluated using a Bonferroni correction with an adjusted p value of .0167 (three tests were conducted; .05/3) for statistical significance. A series of adjusted linear regressions were conducted to examine the association between the number of daily cigarettes, pack-years, time since quitting and cortisol. All analyses were adjusted for sex, age, marital status, cognitive status, education, corticosteroid use, and time between cortisol measures. To enhance comparability across the results, missing values of covariates were imputed by using the Expectation–Maximization Algorithm. The maximum percent of missing values was 12% (corticosteroid use). Missing variables were imputed on the basis of the entire baseline population (n = 3539).

Participants' characteristics according to smoking status are presented in Table 1. Current smokers reported an average of 12.4 ± 7.4 daily cigarettes. Mean pack-years was 33.6 ± 21.4 in current smokers and 25.4 ± 23.5 in former smokers (p<.001). Mean time since quitting for former smokers was 28.2 ± 13.6 years.

Single cortisol levels and summary measures by smoking status were compared by ANCOVA. Results of descriptive and inferential analyses of cortisol among groups are presented in Table 2. Adjusted analyses demonstrated that smoking status significantly affects C2, C3, C4, AUC, and CAR. Post-hoc comparisons using a Bonferroni correction indicated that current smokers had higher mean C2, C3, C4, AUC, and CAR (p<.01) than former and never smokers. There were no significant differences in any cortisol measures between never and former smokers.

A series of adjusted linear regressions were conducted to examine the association between cortisol and: the number of daily cigarettes, pack-years, and time since quitting. Among those with a history of

Table 2
Descriptive and inferential analyses of saliva cortisol levels and three summary measures by smoking status.

	Descriptive analyses unadjusted mean ± (SD)			Inferential analyses					
				Unadjusted			Adjusted		
	Current smoker $n=297$	Former smoker $n=1389$	Never smoker $n=822$	df	F	p value	df	F	p value
Salivary cortisol (nmol/l)									
At awakening (C1)	14.5 ± (9.6)	14.9 ± (8.6)	14.2 ± (8.3)	2, 2297	1.7	.20	2, 2295	.3	.78
Awakening + 30 min (C2)	21.2 ± (11.6)	18.2 ± (10.2)	17.6 ± (9.8)	2, 2382	13.1	<.001	2, 2185	10.7	<.001
5 pm (C3)	5.1 ± (3.8)	4.3 ± (3.6)	4.2 ± (3.8)	2, 2417	7.2	.001	2, 2181	7.4	.001
Bedtime (C4)	2.7 ± (2.4)	2.3 ± (2.6)	2.4 ± (2.7)	2, 2307	2.5	.08	2, 2096	5.0	.009
Cortisol Awakening Response (nmol/l)	3.4 ± (6.0)	1.6 ± (5.4)	1.6 ± (5.0)	2, 2192	12.6	<.001	2, 2016	13.0	<.001
Area Under the Curve (nmol/l)	9.5 ± (4.2)	8.2 ± (3.8)	8.1 ± (3.7)	2, 2022	12.5	<.001	2, 2186	12.2	<.001
Slope (nmol/l/h)	−0.78 ± (0.64)	−0.82 ± (0.56)	−0.80 ± (0.55)	2, 2063	.6	.60	2, 2057	.6	.56