Preventive Medicine 94 (2017) 12–19

Contents lists available at ScienceDirect

Preventive Medicine

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

Influences of lifestyle factors on cardiac autonomic nervous system activity over time

Mandy Xian Hu, MD [a,*], Femke Lamers, PhD [a], Eco J.C. de Geus, PhD [b], Brenda W.J.H. Penninx, PhD [a]

[a] Department of Psychiatry and EMGO Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands
[b] Department of Biological Psychology and EMGO Institute for Health and Care Research, VU University, Amsterdam, The Netherlands

ARTICLE INFO

Article history:
Received 21 June 2016
Received in revised form 8 September 2016
Accepted 6 November 2016
Available online 9 November 2016

Keywords:
Autonomic nervous system
Lifestyle
Physical activity
Alcohol use
Smoking

ABSTRACT

Physical activity, alcohol use and smoking might affect cardiovascular disease through modifying autonomic nervous system (ANS) activity. We investigated: 1) whether there are consistent relationships between lifestyle factors and cardiac ANS activity over time, and 2) whether 2-year changes in lifestyle factors relate to 2-year changes in cardiac activity. Baseline ($n = 2618$) and 2-year follow-up ($n = 2010$) data of the Netherlands Study of Depression and Anxiety was combined. Baseline data was collected in the Netherlands from 2004–2007. Lifestyle factors were habitual physical activity, frequency of sport activities, alcohol use, and smoking. Indicators of cardiac activity were heart rate (HR), respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP) (100 min of registration). The results showed that high physical activity (−1.8 beats/min compared to low activity), high frequency of sport activities ('couple of times/week': −2.5 beats/min compared to 'almost never') and mild/moderate alcohol use (−1.2 beats/min compared to non-drinking) were related to low HR. Heavy smoking was related to high HR (>30 cigarettes/day: +5.1 beats/min compared to non-smoking). High frequency of sport activities was associated with high RSA ('couple of times/week':+1.7 ms compared to 'almost never') and moderate smoking with longer PEP (11–20 cigarettes/day: +2.8 ms compared to non-smoking). Associations were consistent across waves. Furthermore, 2-year change in frequency of sport activities and number of smoked cigarettes/day was accompanied by 2-year change in HR ($\beta = -0.076$ and $\beta = 0.101$, respectively) and RSA ($\beta = 0.046$ and $\beta = -0.040$, respectively). Our findings support consistent effects of lifestyle on HR and parasympathetic activity in the expected direction. Cardiac autonomic dysregulation may be partly mediating the relationship between lifestyle and subsequent cardiovascular health.

1. Introduction

Autonomic nervous system (ANS) dysfunction has been found to be prognostic for unfavorable health outcomes, such as the metabolic syndrome (MetS) (Vrijkotte et al., 2015; Koskinen et al., 2009; Brunner et al., 2002; Hu et al., 2016a) and cardiovascular disease (CVD) (Curtis and O'Keefe, 2002; Kop et al., 2010). Several lifestyle factors that are known risk factors for MetS and CVD have been hypothesized to affect these adverse health outcomes through modifying ANS activity. For instance, physical activity is suggested to be beneficial for cardiac ANS activity (Rosenwinkel et al., 2001; Joyner and Green, 2009; Carter et al., 2003; Mueller, 2007; Wichi et al., 2009; Goldsmith et al., 2000). Indeed, exercise was found to be associated with a favorable shift from sympathetic to parasympathetic cardiac activity (Ueno and Moritani, 2003; Grassi and Seravalle, 1994; Melo et al., 2005; Soares-Miranda et al., 2012; Rennie et al., 2003; Van Lien et al., 2011; Amano et al., 2001; Iwane et al., 2000; Killavuori et al., 1995; La Rovere et al., 1992). In contrast, alcohol use has been associated with unfavorable effects on cardiac ANS activity, illustrated by studies showing increased sympathetic and/or decreased parasympathetic activity with increased alcohol intake (Boschloo et al., 2011; Ohira et al., 2009; Ryan and Howes, 2002; Reed et al., 1999.; Vaschillo et al., 2008; Sagawa et al., 2011; Spaak et al., 2010). Similarly, data suggests that smoking has a detrimental effect on cardiac ANS activity (Middlekauff et al., 2014; Haass and Kubler, 1997; Dinas et al., 2013). This effect has been found after chronic (Hering et al., 2010; Lucini et al., 1996; Poulsen et al., 1998; Hayano et al., 1990) and acute (Hayano et al., 1990; Niedermaier et al., 1993; Sjoberg and Saint, 2011; Narkiewicz et al., 1998; Pope et al., 2001) exposure to tobacco smoke.

Studies on alcohol use and smoking have either investigated acute effects of these substances or effects of habitual drinking or smoking at one time point and studies on physical activity have often looked at effects of short-term exercise interventions on cardiac ANS activity. To our knowledge, only one study investigated the association between habitual physical activity and parasympathetic activity over a longer time period (Soares-Miranda et al., 2012), and found that physical

* Corresponding author at: AJ Ernststraat 1187, 1081 HL Amsterdam, The Netherlands.
E-mail address: m.hu@ggzingeest.nl (M.X. Hu).

http://dx.doi.org/10.1016/j.ypmed.2016.11.003
0091-7435/

activity predicted positive changes in heart rate variability (HRV), an often-used measure of cardiac parasympathetic activity. Otherwise, not much is known about the longitudinal relationships between habitual lifestyle factors and both sympathetic and parasympathetic activity, leaving important questions unanswered, such as how changes in lifestyle affect cardiac ANS activity. Finally, the relationship between habitual lifestyle factors and cardiac ANS activity may not be linear and it is important to understand at which threshold a certain behavior is likely to be detrimental or beneficial. Some studies have found decreased HR and increased HRV with increased amounts of regular exercise behavior (Rennie et al., 2003; Okazaki, 2005). In contrast, one study found that the effect of taking up regular exercise leveled off at a moderate dose, such that more prolonged and intense exercise training did not lead to more improvements in cardiac ANS activity (Iwasaki et al., 2003). Regarding alcohol use, one study demonstrated that increasing doses of habitual drinking were associated with increasing sympathetic activity (Ohira et al., 2009), while another study found that only heavy drinkers had significantly elevated sympathetic activity (Boschloo et al., 2011). As for smoking, one study implied that heavy smoking, but not moderate smoking, caused reduction in parasympathetic activity (Hayano et al., 1990). Most of these studies have used small, diverse samples and different methodology, which may have caused the discrepancies in results.

The aim of the current study was to investigate: 1) whether there are consistent relationships between physical activity, alcohol use and smoking with – both sympathetic and parasympathetic – cardiac activity over a 2-year follow-up, and 2) whether changes in these lifestyle factors are related to changes in cardiac ANS activity over 2 years. Indicators of cardiac ANS activity were heart rate (HR), controlled by both branches of the ANS (De Geus and Van Doornen, 1996), respiratory sinus arrhythmia (RSA) as an index of parasympathetic control (Neijts et al., 2014; De Geus et al., 1995), and pre-ejection period (PEP) as an index of sympathetic activity (De Geus and Van Doornen, 1996; Lien et al., 2015). Our large sample size allowed for the inclusion of many important confounding factors.

2. Methods

2.1. Subjects

Participants belonged to the Netherlands Study of Depression and Anxiety (NESDA), an ongoing longitudinal cohort including 2981 respondents aged 18–65 years consisting of persons with depressive/anxiety disorders and healthy controls. Respondents were recruited from the community, primary care and mental health care in the Netherlands. A four-hour baseline measurement, including demographic, psychiatric and physical assessments, was conducted between September 2004 and February 2007, and follow-up assessments took place after two, four and six years. Questions about lifestyle factors were incorporated in a self-report questionnaire filled out by the participants before every assessment. A detailed description of the rationale, objectives and methods of the NESDA study can be found elsewhere (Penninx et al., 2008). The research protocol was approved by the Ethical Review Board of each participating center, and written informed consent was provided by all participants.

Data for the present study were drawn from the baseline ($n = 2981$) and 2-year follow-up ($n = 2596$) assessment. Of the total baseline sample, 225 individuals were excluded because of missing questionnaire data on lifestyle factors, and an additional 138 individuals because of missing physiological data due to equipment failure or poor electrocardiogram quality. At 2-year follow-up 331 individuals were excluded because of missing data on lifestyle factors, and 255 individuals because of missing physiological data. Consequently, the analyses were conducted with 2618 participants at baseline and 2010 participants at 2-year follow-up.

2.2. Lifestyle factors

We investigated four self-reported lifestyle factors: physical activity, sport activities, alcohol use and smoking.

Physical activity was measured by the short IPAQ (Booth et al., 2003), a 7-item instrument assessing the amount of habitual vigorous activity, moderate and walking activities over the last 7 days. The continuous score is calculated in Metabolic Equivalent Total (MET)-minutes per week: MET level $*$ minutes of activity $*$ events per week (Booth et al., 2003). The categorical score indicates three levels of physical activity: low, moderate and high. Detailed information about the methodological development of the IPAQ can be found at the IPAQ website www.ipaq.ski.se.

Sport activities were determined by the question: 'How often do you engage in sport activities, such as swimming, cycling, playing soccer or other sports?' Participants were required to choose from the categories: 1) almost never, 2) a couple of times/year, 3) every month, 4) a couple of times/month, 5) every week, or 6) a couple of times/week.

Alcohol use was assessed by the Alcohol Use Disorder Identification Test questionnaire (Babor et al., 1992) from which we derived the number of alcoholic drinks per week. A drink was defined as follows: 1) a single small (8 oz) glass of beer, 2) a single shot/measure of liquor/spirits, 3) a single glass of wine. For the categorical score, this number was divided into three categories: non-drinker (<1 drink/week), mild/moderate drinker (men: 1–21 drinks/week, women: 1–14 drinks/week), and heavy drinker (men: >21 drinks/week, women: >14 drinks/week).

Smoking was indicated by the current number of cigarettes/day. For the categorical score, this number was divided into the following categories: 0 cigarettes, 1–10 cigarettes, 11–20 cigarettes, 21–30 cigarettes, and >30 cigarettes per day (Heatherton et al., 1989).

2.3. Physiological measurements

Cardiac ANS measures were recorded with the 'Vrije Universiteit Ambulatory Monitoring System' (VU-AMS). The VU-AMS records electrocardiograms (ECG) and changes in thorax impedance (ICG) from a six-electrode configuration (De Geus and Van Doornen, 1996). During the recording, an event marker was used to indicate the start and end of the different assessment conditions. Movement registration through vertical accelerometry indicated periods where the subjects were not stationary. These non-stationary periods were removed from the analyses, resulting in four conditions: a supine rest condition with blood pressure measurement, a psychiatric interview, a general interview and an Implicit Association (computer) Task. The recording of these four conditions lasted approximately 100 min and data from these conditions were averaged to create a single value of HR and RSA per individual. Since postural changes are the main source of change in preload (Houtveen et al., 2005), the supine condition was excluded when averaging PEP.

HR, controlled by both branches of the ANS, was derived from the interbeat interval (IBI) time series from the ICG signal (Neijts et al., 2014). The HRV measure of RSA was used as an index of cardiac parasympathetic activity, combined the ECG with the respiration signal obtained from ICG, and was obtained by subtracting the shortest IBI during HR acceleration at inhalation from the longest IBI during HR deceleration at exhalation for all breaths (Neijts et al., 2014; De Geus et al., 1995). PEP, an index of sympathetic activity, was ensemble averaged across one-minute periods time-locked to the R-waves in the ECG. PEP was defined as the interval between the Q-onset in the ECG, indicating onset of left ventricular electrical activity, and the upstroke (B-point) of the ICG signal, indicating the beginning of left ventricular ejection (De Geus and Van Doornen, 1996; Lien et al., 2015). Automated scoring of HR, RSA and PEP was checked by visual inspection and, where necessary, corrected or discarded.