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Improving the methodology for non-invasive autonomic nervous system recording and its implementation in behavioral research

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2014

document version

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citation for published version (APA)

van Lien, R. (2014). *Improving the methodology for non-invasive autonomic nervous system recording and its implementation in behavioral research.*

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Preface

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Recent years have witnessed an increase in the ambulatory assessment of the effects of psychological and behavioral factors (e.g. personality, stress, exercise) on the cardiovascular system. So far, the cardiovascular parameters measured in naturalistic settings have been largely limited to measures of heart rate (variability) and intermittent cuff-based blood pressure (BP) recordings.

In stress research, large clinical importance is given to separately assessing sympathetic versus parasympathetic nervous system activity (Berntson et al., 1994a; Berntson, Cacioppo, & Quigley, 1991; Berntson, Cacioppo, & Quigley, 1993a; Berntson, Cacioppo, & Quigley, 1994b; Berntson, Cacioppo, Quigley, & Fabro, 1994; Berntson, Norman, Hawkley, & Cacioppo, 2008; Nicholson, Kuper, & Hemingway, 2006). Parameters indexing both these branches of the autonomic nervous system (ANS) can be derived non-invasively from combined recording of the electrocardiogram (ECG) and the impedance cardiogram (ICG). The technology to measure these parameters in a naturalistic setting has been available for some time, and the VU University Ambulatory Monitoring System (VU-AMS) has been a pioneer device in this respect (de Geus, Willemsen, Klaver, & van Doornen, 1995; Willemsen, de Geus, Klaver, van Doornen, & Carroll, 1996). With over 300 devices sold to more than fifty departments worldwide, the VU-AMS has obtained a pole position in the field of ambulatory ANS recording and its application in the field of biobehavioral medicine.

A first major aim of my PhD project was to critically re-examine the validity of the current strategies for ambulatory assessment of parasympathetic nervous system (PNS) and sympathetic nervous system (SNS) activity using the VU-AMS. A second aim was to test new methods to detect SNS activity feasible for ambulatory assessment in naturalistic settings. A third and final aim was to help disseminate the knowledge gathered throughout the development of the VU-AMS device, and in particular to ensure a correct use of VU-AMS hardware and software by the growing community of VU-AMS users.

The organization of this thesis by and large reflects these three aims. In chapter one, a complete overview is given of the invasive and non-invasive assessments of the sympathetic and parasympathetic nervous system currently in use in human participants. The chapter ends by listing those assessment strategies that could potentially be used in an ambulatory recording setting. Current ambulatory studies predominantly use the preejection period (PEP) and respiratory sinus arrhythmia (RSA) as the indices of sympathetic and parasympathetic activity, with co-registration of posture and physical activity by accelerometers to ensure comparison of ANS activity across the same level of physical load. In laboratory situations the PEP and RSA measures seem to perform almost perfectly (de Geus, Kupper, Boomsma, & Snieder, 2007; Houtveen, Groot, & Geus, 2005; Krzeminski et al., 2000; Mezzacappa, Kelsey, & Katkin, 1999; Miyamoto et al., 1983a; Nelesen, Shaw, Ziegler, & Dimsdale, 1999; Newlin & Levenson, 1979; Richter & Gendolla, 2009; Schachinger, Weinbacher, Kiss, Ritz, & Langewitz, 2001; Sherwood, Allen, Obrist, & Langer, 1986; Smith et al., 1989a; Allen & Crowell, 1989; Hatfield et al., 1998; Houtveen et al., 2005; Houtveen, Rietveld, & de Geus, 2002; Kamphuis & Frowein, 1985; Langewitz & Ruddel, 1989; Mulder, 1992; Sakakibara, Takeuchi, & Hayano, 1994; Tulppo, Makikallio, Takala, Seppanen, & Huikuri, 1996), but in ambulatory studies additional challenges exist that have not been fully tackled. Validity of ambulatory RSA, for instance, may be compromised in participants with very low heart rates during nighttime recordings due to ceiling effects in the acetylcholinergic neurotransmission (Goldberger, Ahmed, Parker, & Kadish, 1994; Goldberger, Challapalli, Tung, Parker, & Kadish, 2001; Goldberger, Kim, Ahmed, & Kadish, 1996). Chapter two will deal with this issue and suggest solutions when relating ambulatory RSA to regular exercise behavior with its known bradycardiac effect.

Reliability of ambulatory PEP scoring is very sensitive to the selection of the correct landmarks in the ICG, particularly the B-point, and in the ECG, particularly the Q-onset. Chapter three will test whether the ISTI, based on the more easily detected Z-point, can be used to replace the PEP and whether estimation of the Q-onset based on a fixed interval from the ECG R-wave yields valid results. Detection of the B-point and Q-onset currently always needs to be verified by laborious visual inspection. Furthermore, validity of PEP may be compromised by changes in preload and afterload which are not yet optimally detected in many current ambulatory designs. Chapters four, five, and six test whether adding salivary alpha-amylase (sAA) or the T-wave amplitude could help deal with these imperfections and possibly develop a new and more robust multivariate ambulatory index of the SNS activity.

Chapter seven reports on the gradual build-up of ambulatory assessment expertise in the consecutive VU-AMS hardware and software versions over the past 20 years which was strongly fueled by the interaction with its international user community. To further enhance this productive interaction, I developed a series of tutorials, workshops and instruction video to help disseminate correct and optimal use of the VU-AMS in the growing community of VU-AMS users. The chapter briefly reports on these tools for dissemination, and because web-based instruction video's have a central role in the dissemination strategy, main distribution of this thesis was done through digital information carriers.

The thesis ends with a short summary of the main findings and a projection of expected (and needed) future developments in the ambulatory assessment of the ANS in the behavioral sciences.

