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Cardiovascular reactivity in real life settings: Measurement, mechanisms and meaning

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Abstract

Cardiovascular reactivity to stress is most commonly studied in the laboratory. Laboratory stressors may have limited ecological validity due to the many constraints, operating in controlled environments. This paper will focus on paradigms that involve the measurement of cardiovascular reactions to stress in real life using ambulatory monitors. Probably the most commonly used paradigm in this field is to measure the response to a specific real life stressor, such as sitting an exam or public speaking. A more general approach has been to derive a measure of CV variability testing the hypothesis that more reactive participants will have more variable heart rate or blood pressure. Alternatively, self-reports of the participants' perceived stress, emotion or demands may be linked to simultaneously collected ambulatory measures of cardiovascular parameters.

This paper examines the following four questions: (1) What is the form and what are the determinants of stress-induced CV reactivity in real life? (2) What are the psychophysiological processes underlying heart rate and blood pressure reactivity in real life? (3) Does CV reactivity determined in the laboratory predict CV reactivity in real life? (4) Are ambulatory cardiovascular measures predictive of cardiovascular disease?

It is concluded that the hemodynamic processes that underlie the blood pressure response can reliably be measured in real life and the psychophysiological relationships seen in the laboratory have been obtained in real life as well. Studies examining the effects of specific real life stressors show that responses obtained in real life are often larger than those obtained in the laboratory. Subjective ratings of stress, emotion and cognitive determinants of real life stress (e.g. demand, reward and control) also relate to real life CV responses. Surprisingly, ambulatory studies on real life cardiovascular reactivity to stress as a predictor of cardiovascular disease are rare. Measuring the CV response to stress in real life may provide a better measure of the stress-related process that are hypothesized to cause disease than is possible in the laboratory. In addressing these questions, below we review the studies that we believe are representative of the field. Therefore, this review is not comprehensive.

Keywords

Ambulatory; Cardiovascular reactivity; Real life stressors; Heart rate; Blood pressure

1. Introduction

The highly influential cardiovascular reactivity hypothesis states that individuals showing exaggerated cardiovascular reactivity (CVR) to stress are at higher risk of developing cardiovascular disease (CVD) (Krantz and Manuck, 1984; Treiber et al., 2003). Most studies of the cardiovascular response to stress are conducted under controlled laboratory conditions. There are excellent practical and scientific reasons for this, centered on issues of measurement, design and control but the laboratory is a particularly difficult environment in which to study stress. There are severe ethical constraints on the nature, severity and duration of the stresses that can be studied in the human laboratory. As a result, most investigations are limited to a rather limited range of predominantly cognitive stressors (reaction time, mental arithmetic, video games, vigilance tasks). Some of these laboratory stressors have a social component (e.g. public speaking). Finally, a commonly used stressor is the rather bizarre, psychologically and physiologically complex, cold pressor test. Participants in laboratory studies are volunteers often fulfilling course requirements and the extent to which the laboratory tasks are experienced as stressful depends to a large extent on how far the participant collaborates with the experimenter and treats the task (e.g. playing a video game) seriously and as personally important. This is perhaps task since the tasks seldom involve significant objective reward or punishment. Such constraints means that laboratory stress tasks may not faithfully represent the stressors that are encountered in real life, i.e. they may have limited ecological validity. Furthermore, cardiovascular (CV) responses obtained in the laboratory may not be representative of the responses seen in everyday life with respect to size, duration or even mechanism. This is different from other areas of psychological study where, for example, it seems likely that the processes of executive function studied in the laboratory represent in a pure form processes that also occur frequently in everyday life. These restrictions on laboratory-based studies of stress are potentially substantial and could severely restrict our understanding of the psychological and physiological processes that underpin CV reactivity and critically limit the potential of laboratory-based CV reactions to predict future disease.

In this paper we wish to consider the study of the CV response to stress in everyday life with respect to four questions (1) What is the form and what are the determinants of stress-induced CV reactivity in real life? (2) What are the psychophysiological processes underlying heart rate and blood pressure reactivity in real life? (3) Does CV reactivity determined in the laboratory predict CV reactivity in real life? (4) Are ambulatory cardiovascular measures predictive of cardiovascular disease?

2. What is the form and what are the determinants of stress-induced CV reactivity in real life?

2.1. Situational determinants

Stress reactions may be studied in relation to discrete, objectively stressful situations. The advantage of this approach is that it does not rely on the participant's own perceptions of stress or emotional arousal and therefore the measure of stress and the effects of stress are not confounded. It has many of the advantages of a laboratory stressor without some of the constraints. Below, such paradigms will be elaborated as well as their use in stress research.

Examples of such situations are giving a speech and oral examinations. Oral presentations are relatively common, useful and are still relatively controllable (Johnston et al., 2008). Classroom examinations and oral presentations may not be directly related to the etiology of cardiovascular disease, as these are infrequent stressors. In addition, they may only be relevant to a subgroup of the population and may only occur during a relatively short part of their life (e.g. academics, students). However, these situations are important because these

stressors represent a particular class of situations that are stressful and potentially harmful (interpersonal communication in an evaluative context). Matthews et al. (1986) measured blood pressure and heart rate in adolescents that were giving a speech in a high school English class. In addition to cardiovascular measures, they also obtained self-reports such as anxiety and hostility (these are discussed below). In addition the grades for the speeches that were assigned by their teacher were obtained and the speech was recorded. BP and HR were recorded before performance of the speech, just prior to giving the speech, immediately after the speech and during the next English class and these values were compared to a laboratory baseline. The authors comment that both the state anxiety and the CV reactivity data show that a naturally occurring stressor such as giving a speech is a particularly potent stressor and CV stress levels approached levels that are usually regarded as indicative of borderline hypertension (Matthews et al., 1986).

In a study aiming to compare laboratory and field measures of stress, Turner et al. (1990) measured ambulatory CV reactivity to a realistic speech stressor. Ambulatory blood pressure and heart rate were measured while participants presented their research in front of an audience in a situation that was meant to closely resemble a seminar. Presentations lasted for 10–15 min. The audience was gender balanced. Two members of the audience took notes during the presentation and talks were rated for clarity and organization. Ratings were used as the basis of monetary bonuses that were awarded to those giving the best speech (Turner et al., 1990).

Although the stressor in this study appears to be a naturalistic one, the situational characteristics have been controlled and the stressor resembles the speech stressor that has been generally used as part of the Trier Social Stress Test (Kirschbaum et al., 1993). Despite this “real world” reactivity scores were not correlated with laboratory reactivity scores, even though baseline values were correlated (Turner et al., 1990). Further analyses did suggest that the differential effects of posture explained part of the lack of association between laboratory and speech stressors but the associations did not reach significance, which may suggest that real world speech stressors are different from laboratory stressors. Judging by the baseline and task values that were reported for the laboratory stressor and the real life stressor, it would appear that, on average, participants were more reactive during the real world stressor. This would be in line with the assumption that ecological validity of the realistic speech stressor would be greater than that of the laboratory stressor, as the former may be expected to be a more potent stressor.

Kamarck et al. (2000) conducted a study involving ambulatory measurement of HR and BP during delivery of a classroom speech. Participants were students who were enrolled in a public speaking class. Participants’ CV measures were monitored before and during two speeches delivered in two different sessions. Additionally, two consecutive laboratory stress sessions were held, which included a Stroop task and a speech task. Within those laboratory sessions, test–retest reliability was highest for the speech task. Based on their reported generalizability coefficients, it would appear that reliability for the classroom speech measures are generally lower than those for the laboratory measures. Reliability of the classroom speech stressor was improved when ambulatory measures were aggregated over the anticipatory and the speech delivery stages (Kamarck et al., 2000).

Examinations are another example of a discrete, real life stressor. Hazlett et al. (1997) argue that examinations are a useful tool to measure CVR as these stressors have (1) a discrete start and end, (2) occur repeatedly, (3) situational characteristics are consistent across participants, (4) allow the measurement of a pre-stress baseline.

Sausen et al. (1992) conducted a study in which HR and BP were measured in students, before, during and after a written exam. In comparison to measures obtained during a nonstressful period, participants show significantly elevated BP and HR. Interestingly, CV levels were similar before and during the exam, suggesting anticipatory stress (Sausen et al., 1992).

Hazlett et al. (1997) obtained three baseline and three stressor measures of HR and BP. The exam was associated with significantly elevated CV levels. Temporal stability was examined by obtaining the same measures on a second occasion, about a month later. The authors concluded that test–retest reliability was ‘fairly high’, although it has to be noted that the reported correlations between measure 1 and measure 2 ranged between .23 and .67 for baseline and stressor BP and HR measures and correlations were only reported for absolute values, not for reactivity scores (Hazlett et al., 1997). Test–retest reliability tends to be higher for absolute values than for change scores (e.g. McKinney et al., 1985). Finally, judging by the HR and BP values reported, the exam only seemed to elicit a mild stress response; elevations of 5 mm Hg in diastolic and systolic blood pressure and 4 bpm for heart rate compared to baseline. Perhaps written examinations are not stressful enough to allow reliable measurement of CV reactivity. Similar values were reported by Warwick-Evans et al. (1988) in a study examining CV arousal levels before and after a written academic exam.

In contrast to written examinations, oral examinations seem to elicit strong stress responses. Van Doornen and Van Blokland (1989) measured real life stress in PhD students anticipating public defense of their PhD thesis. CV measures were obtained on the day of the defense and on a different day (baseline measure). Reactivity values were obtained by computing the difference between those two measures. All CVR measures were significantly different from zero, suggesting that this real life stressor is potent enough to cause significant elevations in HR, SBP and DBP and that these stress-related effects were observable even though CV were not measured during actual stressor exposure (Van Doornen and Van Blokland, 1989). More recently, Davig et al. (2000) conducted a study measuring ambulatory BP and HR during proposal or defense of a dissertation. Ambulatory HR was obtained during baseline, during the 4 min of anticipation preceding the stressor and during the first 4 min of the proposal or defense. Although it was not the focus of the analyses presented in this paper, the reported baseline values do suggest that participants were more stressed during the natural stressor than during the laboratory stressors. In addition, the CV arousal levels during the natural stressor are higher than CV levels during anticipation of the stressor (Davig et al., 2000).

Another example of high-frequency occurrence stressors that are ubiquitous, are interpersonal conflicts that occur in work and domestic situations. Brondolo et al. have examined to stress in New York traffic agents in a series of studies using ambulatory measures of CV reactivity (BP and HR). Traffic agents are routinely exposed to three negative interpersonal interactions per day, usually upon writing summonses. Traffic agents were given diaries in order to record the activities occupying them at the time of each CV measurement. Participating traffic agents received training to fill out the diaries. Brondolo et al. (1999) focused on differential effects of workday communication on CV reactivity. They examined the comparison of CV arousal in response to communication with the public, with colleagues, and supervisors, and non-communicative work tasks. As was hypothesized, talking to a coworker or supervisor was associated with lower BP levels than talking to the public. Effects were nonsignificant for HR (Brondolo et al., 1999).

It appears that psychosocial stressors, such as giving a speech, undergoing an oral examination, or negative interpersonal interactions can be used as part of a real life stress paradigm. Cardiovascular stress reactions to these stressors are substantial and generally

larger than those obtained in the laboratory. This underscores the ecological validity of these real life interpersonal stressors. Averaging anticipatory and stressor exposure measures may improve reliability of these measures.

2.2. Individual determinants

One of the most exciting developments in psychology in the last decade has been the renewed interest in measuring behavior, emotion and cognition in real life using Ecological Momentary Assessment (EMA). These methods allow the measurement of any behavior, thought or internal state that an individual can reliably report. In contrast to research focusing on situational determinants of stress-induced cardiovascular reactivity (see above) using infrequent real life stressors such as public speaking, EMA can study the relationship between the emotions aroused by diverse, possibly unspecified, stressors of differing potency. In addition, EMA allows the measurement of the effects of stress-related appraisals of the environment or of frequent events such as social interactions that may only occasionally be stressful. The range of situations that can be studied is much wider than what can be contrived in the laboratory, their validity is assured and the many real life moderators of the CV response to stress can be measured and modeled.

In most studies involving EMA and ambulatory CV assessment, participants are prompted by an electronic diary to rate their emotions on a variety of scales and this is related to simultaneously measured CV activity; this method is called experience sampling (Larson and Csikszentmihalyi, 1983). Usually these events are sampled on a quasi-random schedule so the participants cannot anticipate a diary entry and perhaps alter their behavior in anticipation. In some studies entries may be triggered by specific events (event sampling) but this is less common. Virtually all studies reported in the last decade have used multilevel or random effects modeling to analyze the resulting behavioral and physiological data. As will be discussed in further detail below, such methods provide a more sensitive and more defensible analysis of data that is measured repeatedly within an individual, handle variable numbers of data points well and can take account of the autocorrelated nature of much within participant behavioral and physiological data. Studies usually measure the direct effects of psychosocial factors on CV reactivity or the moderating effects of psychosocial factors on the CV response to stress.

2.3. Direct effects

Early studies that were conducted before good methods of statistical modeling were widely available indicated that periods of heightened emotion are associated with increases in BP (e.g. Anastasiades and Johnston, 1991). Later studies, using a more sophisticated statistical approach, have confirmed a link between emotion and CV reactivity (e.g. Kamarck et al., 2002; Räikkönen and Matthews, 2008). Important confounding variables in ambulatory CV research are physical activity and posture. Johnston et al. (2008), in a study of HR and tense arousal, assessed physical activity and posture objectively and demonstrated that psychological arousal related strongly to HR even after controlling for posture and activity. In a methodologically sophisticated study, Jain et al. (1998) assessed continuously measured BP, HR, as well as objectively measured activity and posture. A comparison of periods of high and low tense arousal showed that BP and HR was higher in periods of high tense arousal than that this was at least partially independent activity and posture (Jain et al., 1998).

As well as studies of the CV correlates of emotion, researchers have studied the theoretical determinants of stress. Kamarck et al. (2002) showed that variations in perceptions of demand and control (the critical determinants of strain in Karasek's influential model of work related stress; Karasek, 1979) were predictive of covariations in SBP and DBP (assessed frequently over 3 days). Interactions with others are associated with increases in

BP and HR but it appears that CV reactivity depended critically on the nature of the interaction (Kamarck et al., 2002). Gump and colleagues (2001) showed that SBP was lower when speaking to one's romantic partner than when not interacting, although the effects of interacting with other people were complex, perhaps because of the variety of possible interactions encompassed (Gump et al., 2001). In a fascinating study, Brondolo et al. (1999) highlighted the unique advantages of real life assessment by examining changes in BP in New York traffic agents. SBP and DBP were higher when agents were interacting with the public compared to when interacting with coworkers or supervisors. Traffic agents' mood was less negative/more positive when talking to colleagues or supervisors than during interactions with the public. Interestingly, happiness/satisfaction was negatively correlated to SBP, such that pressure was lower when participants were happy. However, mood did not appear to mediate the effects of situation (talking with supervisors, coworkers, or the public) on CV responding (Brondolo et al., 1999). In a follow up study of community volunteers, Brondolo et al. (2003) showed that the intensity of negative interactions related strongly to DBP and weakly to SBP. These associations were significant, even after controlling for mood (Brondolo et al., 2003).

2.4. Moderation effects

The richness of the data provided by ambulatory methods allows exploration of the possible moderators of the effects of stressful environments on CV activity. Such moderators can be enduring characteristics of the person or of the environment. Räikkönen et al. (1999) examined the moderating effect of hostility measures on the CV response to negative emotions. Participants low in potential for hostility (as measured by the Structured Interview) had heightened BP on occasions when they experienced periods of negative mood, whereas those with high potential for hostility had consistently high BP irrespective of their mood. Hostility as measured by the Cook–Medley did not moderate the link between negative emotion and CV reactivity. Brondolo et al. (2003) found that CV reactions to negative interactions were unrelated to hostility as measured by the Cook–Medley but they did find that hostility moderated the effect of the intensity of the negative interaction. DBP was elevated more in hostile individuals in the most negative interactions. This was particularly marked for the subcomponent of cynicism. In the same sample of traffic agents Karlin et al. (2003) showed that support from an immediate supervisor was associated with lower SBP in women but not men over the working day. Thus, in women, social support buffered the effects of stress on CVR. The buffering hypothesis was examined by comparing high and low stress periods during the day. SBP and HR were higher during high stress periods and immediate supervisor support moderated this, with the high support being associated with smaller elevations in SBP (Karlin et al., 2003). Vella et al. (2008) using the Cook–Medley Hostility as a moderator of the effects of the supportiveness and intimacy of social interactions on DBP. Highly hostile individuals showed increased DBP in interactions perceived as supportive and, unlike low hostile individuals, did not benefit (show lower DBP) from more intimate, personal interactions. HR and DBP were unrelated to hostility (Vella et al., 2008).

Holt-Lunstad et al. (2003) used event sampling to study the CV effects of social interactions with people with whom the participant had a generally positive, negative or ambivalent relationship. They confirmed earlier findings that interaction with family members was associated with lower BP. Interestingly, they found that interactions with people with whom one had an ambivalent relationship were associated with higher BP than interactions in primarily positively or negatively relationships. The actual characteristics of the interaction (for example, was it positive or negative), did not mediate these effects (Holt-Lunstad et al., 2003). Hawkey et al. (2003) examined the effects of loneliness on behavior and CV activity in the field using experience sampling. This study was unusual in the breadth of behavioral

and CV measures taken (Hawkey et al., 2003). Lonely people did not differ greatly in their daily activities but experienced more stress, demand and lacked belief in their ability to meet demands. However none of the diary measures of stress or appraisal related to any of the CV measures. This appears to contrast with other, broadly similar studies such as (Kamarck et al., 2002; Johnston et al., 2008) in which ratings of stress or associated processes strongly predicted CV activity assessed at the same time. However, it may be that the study by Hawkey et al. was underpowered to detect such effects since they analyzed only 6.3 data points in 70 participants while Johnston et al. (2008) measured 13.3 data points in 59 participants while Kamarck et al. (2002) obtained a highly impressive 106 observations in 340 people.

In summary, ambulatory studies have been used to examine CV effects of stressful, real life social interactions, and to examine how situational characteristics affect CV reactivity. After controlling for noise factors such as posture and activity, robust effects have been found for the effects of stress, stress-related emotions and stress determining processes on BP and HR. In addition to these direct effects of cognitive and emotional factors on CV responding, psychological variables such as hostility or the nature of an interpersonal relationship may moderate the CV response to stressful real life circumstances.

3. What are the psychophysiological processes underlying heart rate and blood pressure reactivity in real life?

It appears that real life stressors such as an examination or giving a speech may contain elements that resemble tasks that involve passive coping and dealing with fear-inducing or frustrating task characteristics as well as being required to actively cope with the task demands. Active and passive coping tasks are typically regarded as generating different hemodynamic response patterns. Blood pressure is regulated by two component parameters; the resistance of the blood vessels (vascular resistance) and the output of the heart (cardiac output). Obrist (1981) showed that physically undemanding active coping tasks generate a myocardial reaction pattern whereas passive coping tasks have been shown to generate vascular response patterns. It has been shown that when participants adopt a passive-like coping style in an active coping task, their reaction pattern will be relatively more vascular than for those who cope more actively (e.g. Tomaka et al., 1997, 1993). These vascular and myocardial reaction patterns are sympathetic response modes, which in addition to parasympathetic responding underlie blood pressure and heart rate patterns. This section provides a summary of studies that examine the psychophysiological processes underlying the CV response in a natural setting.

In a recent study (Zanstra et al., 2010) examined the hemodynamic response to a real life stressor. Participants in this study were students who wore a Portapres blood pressure monitor on the day they were scheduled to perform a classroom speech as part of their course requirements. Hemodynamic variables, such as vascular resistance and cardiac output, were derived from the blood pressure waveform that was measured continuously. In this way, vascular resistance and cardiac output can be computed (see Wesseling et al., 1993). Blood pressure data was collected before, during and after the presentation, as was ratings of stress appraisals. In this study, we examined changes in hemodynamic parameters during, and in anticipation of the stressor (public speaking). We found that both during anticipation and during the stressor, the (substantial) increases in blood pressure were mediated by increases in myocardial, rather than vascular parameters. Such a myocardial response pattern is consistent with an active coping response. It may be surprising that the anticipatory period was characterized by a myocardial response as well, since active coping with the stressor (i.e. public speaking) is limited during anticipation. Although it is possible

that participants were preparing themselves for the upcoming stressor, perhaps rehearsing their speech as a way to actively cope with the stressful situation.

Furthermore, in this study, it was shown that stressor appraisal is predictive of hemodynamic reactivity patterns (as was previously established in laboratory studies, c.f. Tomaka et al. (1993, 1997). As hypothesized, this study showed that the relationship between appraisal and hemodynamic reactivity seen in laboratory studies are also present during naturally occurring stress. Following the Tomaka et al. (1993, 1997) paradigm, stress appraisals were operationalised as the ratio of perceptions of demands and resources. A lower demand-to-resource ratio signifies relative challenge while the reverse indicates threat.

The anticipatory and stress periods were analyzed separately. During the anticipatory period, stressor appraisals were found to be predictive of both vascular and myocardial responding, such that increased threat predicted a relative vascular reaction pattern and increased challenge predicted a relative myocardial reaction pattern. Partial evidence for the association between appraisal and hemodynamic response patterning was also found for the stressor period; challenge appraisal predicted increased cardiac output although threat did not reliably predict vascular resistance.

In a study examining the association between loneliness and CV reactivity in real life, Hawkley et al. (2003) used an impedance cardiograph to measure CV parameters in combination with the use of diaries to obtain repeated measures of the behavioral and psychosocial variables of interest. It was hypothesized that lonely individuals adopt more passive coping strategies in their daily life and would therefore show a vascular reaction pattern, in comparison to non-lonely individuals who were expected to show cardiac reaction patterns. Confirmatory results had previously been obtained in the laboratory (Cacioppo et al., 2002). In order to examine differences in appraisals of daily events between lonely and non-lonely individuals, an experience sampling approach was used whereby CV measures were taken at regular intervals and participants were asked to enter or rate their activities, stress and cognitive appraisals, social context and interaction quality and health behaviors.

As hypothesized, loneliness was predictive of increased vascular resistance as measured by TPR and decreased myocardial activity as measured by lower SV and longer PEP. Interestingly, the effects of loneliness on CO and TPR remained, even after controlling for depression, neuroticism, and social support. However, in contrast to the study by Zanstra et al. (2010), stressor appraisals were not predictive of CV activity. The reason for this may be that appraisals are only predictive of CV reactivity patterns during stressful situations. Challenge and threat appraisals have been shown to be predictive of hemodynamic reaction patterns during stressful active coping tasks, but are not deemed to be predictive of CO and TPR during nonstressful episodes (Blascovich and Tomaka, 1996). The measures in Hawkley et al. (2003) were taken during an entire day, thereby including stressful and nonstressful episodes, and may not provide an adequate test of the theoretical model. Interestingly increased loneliness predicted a decrease in RSA, suggestive of decreased vagal tone in lonely individuals, although this did not survive controlling for social support (Hawkley et al., 2003).

In examining the effects of work stress, and an imbalance of work rewards and work effort on vagal tone, Vrijkotte et al. measured BP, HR and heart rate variability (assessed by root mean square successive difference (RMSSD). In addition, every 30 min, participants were asked to record their posture, activities and mood. Those who had a high imbalance between self-reported efforts and rewards had lower vagal tone (although this effect was only borderline significant) during three 24-h recordings (2 workdays and 1 non-workday),

Vrijkotte et al. (2000). Those with a high effort-reward imbalance also showed increased negative mood. It would have been interesting if the authors had examined whether negative mood mediated the effects of effort-reward imbalance on vagal tone, although since the latter effect was only borderline significant. In a more recent paper by the same authors, using data from the previously described study, the effects of effort-reward imbalance on sympathetic tone (as measured by PEP) were reported. Effort-reward imbalance was not predictive of sympathetic tone, however, overcommitment was associated with shortened PEP. Overcommitment is defined as a coping style characterized by the inability to disengage from work related activities (Vrijkotte et al., 2004).

Altogether, these findings suggest that the determinants of CV reactivity to chronic and acute stress can be reliably measured in real life. While few studies have been conducted, vagal and sympathetic (vascular and myocardial) parameters have been found to be associated with psychosocial variables such as loneliness, work stress, overcommitment, and challenge and threat appraisals. These results replicate and extend findings that were previously obtained in laboratory paradigms.

4. Does cardiovascular reactivity determined in the laboratory predict cardiovascular reactivity in real life?

The CV response to a laboratory stressor is at best a snapshot of an individual's habitual response to stress. If such responses are truly implicated in the aetiology of cardiovascular disease and the triggering of cardiac events then CV responses must occur in the same people with some force or considerable frequency. The relationship between laboratory and field measures of CVR has been studied for over 30 years. In an early review of 32 studies, Turner et al. (1994) concluded that the relationship between laboratory and field CVR (as distinct from levels of CV activity) was weak although some positive relationships were detected. Since then there have been a number of advances in our conceptualization of the measurement of laboratory and field reactivity and major advances in measurement and statistical analyses. As the Turner et al. (1994) review shows, initially most investigators simply correlated the CV response to a variety of stressors to some measure of reactivity in the field. Three other methods of characterising the laboratory responses while present in early studies are increasing used (Johnston et al., 2008). Laboratory tasks can be grouped on the basis of the psychophysiological processes involved, so Anastasiades and Johnston (1990) classified the tasks as involving either active or passive copying and argued that active coping tasks were associated with increases in cardiac output and such responses were predictive of CV reactions in the field. Kamarck et al. (2000) have argued for improving the validity and reliability of measures of laboratory reactivity by sampling tasks widely and aggregating responses over tasks and repetitions. A final, although rather less common, view emphasises the importance of the stressors invoking a particular physiological response. Van Doornen and Van Blokkland (1989), for example, emphasise the importance of provoking a noradrenergic response.

The methodological advances in ambulatory measurement have been in both physiological and behavioral measurement. A range of CV parameters can now be measured in ambulatory settings so that it is possible to measure blood pressure and its immediate determinants (cardiac output and total peripheral resistance continuously in ambulatory settings (e.g. Portapres; TNO, Amsterdam, The Netherlands). These methods have successfully been applied in studies of the CV response to real life stress (Jain et al., 1998; Zanstra et al., 2010). As well as such elaborate but rather bulky ambulatory systems there have been great advances in miniturisation so that it is now possible to measure and store the ECG and accelerometer measures of general activity on devices that are little bigger than ECG electrodes (e.g. Actiheart; Cambridge Neurotechnology, Cambridge, UK).

The second major advance is in the measurement of self-reported behavior by using various (electronic) diary methods, typically operationalised on handheld personal organisers (PDA) or smart phones (Kamarck et al., 2003). This approach is often referred to as Ecological Momentary Assessment (EMA, Stone and Shiffman, 1994).

The final important innovation has been in the analysis of ambulatory data. In the more interesting studies, ambulatory data collection usually involves sampling data repeatedly over periods of hours, days, or even weeks, resulting in highly autocorrelated measures. Until recently it was difficult to handle such data appropriately but the increasing understanding of the power and applicability of multilevel modelling (e.g. Hox, 2002) has transformed the analysis of such data and has provided a major boost to the study of the CV effects of stress in real life.

There are three distinct methods of assessing ambulatory CV reactivity. Probably the most common is to determine the response to a specific real life stressor, such as sitting an exam (Sausen et al., 1992; Davig et al., 2000) or public speaking (Matthews et al., 1986; Johnston et al., 2008). A more general approach has been to derive a measure of CV variability (Floras et al., 1987; Kamarck et al., 2003) perhaps after allowing for the effects of activity and posture (Anastasiades and Johnston, 1990; Jain et al., 1998) in the belief that more reactive participants will have more variable heart rate or blood pressure, all other things being equal. The final approach relates CV responses to self-reports of the participants' perceived stress, emotion or the demands they are under (Jain et al., 1998; Kamarck et al., 2003; Johnston et al., 2008).

Each of these approaches has its strengths and weaknesses. The use of a single, real life stressor is a clear-cut, objectively stressful situation, and the conditions under which the stressor occurred can be determined. However, such specific real life stressors are often very similar to the laboratory stressor being used as the predictor. Such studies, when positive, can therefore only provide modest evidence of laboratory-to-field generalization. Methods based on measures of CV variability have the great strength of being non-selective and incorporating much of the data from a participant's ambulatory record. The weakness of such measures is that CV variability reflects many processes that are not stress-related (e.g. changes in CV arousal due to metabolic demand). Furthermore, it is assumed that participants experience stress, but participants' stress is not measured. The final approach, which is becoming increasingly common, is to rely on self-reports from the participant of their emotions, the stressfulness of the situation or the demands or other stress-related features of their environment. Such ratings are then related to the CV activity measured at the same time. This approach is very attractive since it can sample a wide range of situations that differ in their stressfulness and can capture much of what occurs over an ambulatory measurement period (dependent, of course, on the frequency or form of sampling used). The downside is that the measures rely on the participant's self-report of the situation. Finally, it may be argued that the participants' perceptions and emotions may be affected by the very measures that are being proposed be a consequence of these perceptions and emotions, such as a pounding heart. Cause and effect may be blurred.

Johnston et al. (2008) attempted to test the relationship between stress reactivity in the laboratory and in real life using all of the approaches that have been identified above, in a study of heart rate. They found that average HR response to a variety of laboratory stressors (as advocated by Kamarck et al., 2000) did predict the increase in heart rate associated with public speaking (presenting a paper in a class as part of a course requirement in students). Heart rate was almost 13 bpm higher when speaking than in a carefully matched control period and this effect was nearly doubled in participants who were most reactive to the laboratory stressors (Johnston et al., 2008). This effect replicates findings from other similar

studies (Davig et al., 2000; Kamarck et al., 2000; Matthews et al., 1986; Turner et al., 1987) but not all (Turner et al., 1990). Johnston et al., did not find convincing relationships between the response to individual stressors and the CV response to public speaking. It is therefore tempting to conclude that aggregating across a wide range of laboratory stressors is important but Davig et al. (2000) did not find this to be helpful. While a summary measure of variability is attractive, this study and the six other earlier data sets collected by the same group that are reviewed by Johnston et al. (2008) fail to provide convincing evidence that the CV response to laboratory stressors (aggregated or otherwise) relates to CV variability in real life. Kamarck et al. (2003) also failed to find any link between laboratory CVR and the variability of CV responses in the field. Johnston et al. (2008) and the previous similar studies by this group did not obtain consistent support for Johnston et al. (1990) contention that the CV response to active coping tasks best predicts field reactivity. This hypothesis is probably not worth further study

The final issue examined by Johnston et al. (2008) was the relationship between laboratory reactivity and the HR response to self-reported negative emotions. Using multilevel modeling they showed that participants who were most responsive in the laboratory showed the largest heart rate increase to negative emotion even after allowing for activity and posture. Their HR was similar when they were not under stress. This was seen most clearly for the aggregated score of CV reactivity. Kamarck et al. (2003) using a similar design to Johnston et al. (2008) also showed that more reactive participants showed a greater increase in SBP when they were under high demand or had low control in real life. Using a rather less sophisticated method of analysis Jain et al. (1998) found HR and the product of HR and SBP was higher in reactive participants during periods of emotional stress.

This overview of the relationship between CV reactions in the laboratory and in the field suggests that the average CV response to a battery of laboratory stressors does relate to the CV response to stress in real life when that is assessed by examining the response to a objective stressor or by self-reported of experienced stress or the factors that cause stress. The CV response in real life is the product of two processes, a stressful situation and a hyper-reactive person.

5. Are ambulatory cardiovascular measures predictive of cardiovascular disease?

As was pointed out previously the cardiovascular reactivity hypothesis states that individuals showing exaggerated cardiovascular reactivity (CVR) to stress are at higher risk of developing cardiovascular disease (CVD) (Krantz and Manuck, 1984). A growing body of evidence shows that CVR, usually derived from laboratory measures, predicts a variety of preclinical and clinical states in prospective research designs (Treiber et al., 2003). Blood pressure responses to laboratory tasks have been linked to preclinical indices of CV disease risk such as changes in left ventricular mass (LVM; for a review, see Taylor et al., 2003) and carotid intima-media thickness; an index of carotid atherosclerosis (carotid IMT; Everson et al., 1997; Kamarck et al., 1997; Lynch et al., 1998; Matthews et al., 1998). However, results from longitudinal studies linking CVR with clinical endpoints have been mixed. It appears that the association between CVR and CVD is multifactorial (Treiber et al., 2003).

Since real life stressors have greater ecological validity than laboratory stressors, it can be hypothesized that ambulatory blood pressure reactivity to real life stress will be a better predictor of CVD than laboratory BP. The evidence from studies of average levels of ambulatory blood pressure encourage this view. In an early review it was concluded that ambulatory blood pressure (ABP) monitoring appears to be a better predictor of cardiovascular morbidity, as correlations between ABP and CVD indices tend to be stronger

than those between clinic BP and CVD indices (Pickering et al., 1985). More recently, studies have shown that ambulatory BP is a significant predictor of increased cardiovascular risk, even after controlling for blood pressure obtained in the clinic (Kamarck et al., 2002). Furthermore, in a subsequent paper, it was shown that ambulatory blood pressure mediated the relationship between self-reports of task demand and carotid intima-media thickness (IMT; an index of atherosclerosis in the carotid artery). Again, ABP was predictive of enhanced risk for CVD, over and above the effects of clinic BP (Kamarck et al., 2004). In 2007, a paper was published confirming these findings using a prospective paradigm (Kamarck et al., 2007).

Looking at the role of ambulatory blood pressure reactivity in the etiology of CVD from a developmental perspective, Belsha et al. showed that ambulatory SBP was positively correlated with LVM in adolescents using a cross sectional design (Belsha et al., 1998). In a longitudinal design Kapuku et al. (1999) examined the associations between ASBP and LVM, in youths. Results showed that ambulatory SBP was predictive of LVM over 2 years later (Kapuku et al., 1999).

Another area in which ambulatory blood pressure has been linked to cardiovascular disease risk, is chronic work stress. A demanding work environment has been shown to affect the association between CVR and subclinical cardiovascular disease (Treiber et al., 2003). Ambulatory blood pressure measured at the work place has been found to be associated with job strain and risk for cardiovascular disease (Schnall et al., 1990, 1998). Furthermore, the association between LVM and ambulatory blood pressure was strongest when measured on a working day (Devereux et al., 1983).

All in all, evidence suggests that ambulatory measures of BP and HR are a useful index of cardiovascular disease risk, over and above clinic or laboratory measures. Perhaps disappointingly there does not appear to be published evidence on the predictive power of measures of ambulatory reactivity. The mixed findings on the power of laboratory measures to predict CV disease suggests that predictive studies based on ambulatory measures of CVR are urgently required

6. Conclusion

The first question addressed in this paper was “What is the form and what are the determinants of stress-induced CV reactivity in real life?” We examined both the situational and the individual determinants of the ambulatory stress response. Studies examining the role of situational factors involve psychosocial stressors, such as giving a speech, undergoing an oral examination, or negative interpersonal interactions can be used as part of a real life stress paradigm. The effects of specific real life stressors can be studied and appear to produce responses that are often larger than those seen in the laboratory. Additionally, subjective ratings of stress, emotion and theoretically important processes that are believed to determine stress (such as demand, reward and control) also relate to real life CV responses. The second question addressed the psychophysiological processes underlying heart rate and blood pressure reactivity in real life. Initial studies examining the hemodynamic processes that determine blood pressure can be measured in real life and the psychophysiological relationships seen in the laboratory can also be seen in real life. The third question was; “Does CV reactivity determined in the laboratory predict CV reactivity in real life?” It appears that averaging over multiple laboratory stressors, due to the effects of both situational and individual factors, does relate to the CV response to stress in real life when that is assessed by examining the response to a objective stressor or by self-reported of experienced stress or the factors that cause stress.

Finally, we asked (4) “Are ambulatory cardiovascular measures predictive of cardiovascular disease?” The information that real life studies provide on the strength, mechanisms and frequency of the CVR in real life suggests that it should be a better predictor of future disease than laboratory measures but this is as yet an underexplored area.

6.1. Future directions

There has been great progress in the study of the CV effects of stress in real life in the last 30 years, but much remains to be done. Advances are likely to come in four areas; technical, theoretical, empirical and application. Technically there are continued advances in the miniaturization of physiological recording devices and the power of data handling devices such as PDAs and, increasingly smart phones (Morrison et al., 2009). It is now possible to use such phones to obtain self-report data as ratings, text, audio recordings and either store it or have it automatically phoned in. In addition the same devices can establish where the participant is using GPS and features of the environment using audio recordings.

The main theoretical question has perhaps remained the same over the years; to determine to what degree the CV response to stress is a product of the person, the situation or, most likely, the specifics of the interaction of these factors. The empirical question, which is closely tied to the theoretical issue of individual and situational factors, is to determine the critical personal characteristics such as race, gender, age and socioeconomic status.

The main applied question is, as we have indicated above, to determine if CV response to naturalistic stressors when assessed using the best methods actually predict future disease better than the CV response to laboratory stressors. If, as we hope this is the case, then this opens up new avenues for diagnosis and prevention. If it does not then it is a serious challenge to the reactivity hypothesis.

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