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► To cite this version:

Cédric T. Albinet, Cindie de Faria, Mickaël Causse. Cardiac pre-ejection period to index motivation and effort mobilization in cognitive studies: A critical narrative review. 2024. hal-04488295v1

HAL Id: hal-04488295

<https://hal.science/hal-04488295v1>

Preprint submitted on 4 Mar 2024 (v1), last revised 21 Jun 2024 (v2)

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Cardiac pre-ejection period to index motivation and effort mobilization in cognitive studies: A critical narrative review

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Abstract

This paper reviews studies on the cardiac pre-ejection period (PEP) in the field of cognitive psychophysiology. The main objective was to better understand the relationship between PEP and effort mobilization in cognitive functioning. We reported studies that have measured the PEP in various cognitive tasks and experimental paradigms and other additional works that have highlighted inter-individual variability affecting PEP during both resting and cognitive activities. The reported literature tends to confirm that PEP might be a useful tool to measure cardiac sympathetic control related to effort mobilization and task difficulty. Methodological aspects, influencing factors (importance of success, emotions, psychiatric condition...), and limitations of the PEP usefulness (e.g., high inter-individual variability, questionable relevance in within-subject design) are also emphasized. Finally, we raised some questions and offered directions for future research to further our understanding of PEP measures.

Keywords: Pre-ejection period; cognition; effort mobilization; cardiac reactivity

Funding

This article was initially part of the Ph.D. thesis project of the second author. This work was supported by a grant from the Région Occitanie Pyrénées-Méditerranée and by an ANR-ASTRID grant (ANR-19-ASMA-0009). The authors declare that they have no financial interest in the research. Reprint can be requested to C. Albinet (cedric.albinet@univ-jfc.fr).

1 Introduction

Mental effort generated by an intellectual activity (e.g., mental calculation) is known to stimulate the sympathetic branch of the autonomic nervous system (ANS) (e.g., Obrist, 1976; Richter et al., 2008). Traditionally, cardiovascular measures such as heart rate (HR), HR variability (HRV), or blood pressure (BP) have been used as indexes of ANS variations related to mental effort (e.g., Mandrick et al., 2016). However, since the early 2000s, a growing attention has been paid to the cardiac pre-ejection period (PEP), as an interesting and more direct indicator of mental effort because PEP is a measure of cardiac contractility that is regulated primarily by beta-adrenergic (sympathetic) influences on myocardial tissue. Indeed, under certain boundary conditions, PEP has been demonstrated to be a reliable estimate of the activity of the sympathetic nervous system (SNS) (Bernston et al., 1994; Cacioppo et al., 1994; Kelsey, 2012; Krohova et al., 2017; Mezzacappa et al., 1999). The rationale for linking, mental effort, motivation and PEP came first from the work of Wright (1996). Motivation can be broadly defined as the process that determines the direction and energization of behavior (Elliot, 2006). The direction stands for “what people do”, and energization stands for “how much effort people mobilize.” Brehm’s motivational intensity theory follows the principle of resource conservation (Brehm & Self, 1989). This theory predicts that effort investment will change with task difficulty as long as success is possible and worth the effort. When task difficulty rises, so does the effort invested in the task, but putting in effort needs to be justified. Minimizing the waste of energy is the principle of resource conservation. Integrating the work of Obrist (1976) on active coping and Brehm’s motivational intensity theory, Wright (1996) developed a systematic research program proposing that the rise in effort mobilization can be observed through changes in cardiovascular responses influenced by the SNS. This served as the basis for the subsequent studies to use PEP as a marker of effort mobilization.

The recent growing number of studies measuring cardiac PEP in cognitive experiments motivated this review to examine the utility of the PEP as a physiological correlate of mental effort

mobilization. In this paper, we first summarize the basic fundamental knowledge about ANS and cardiovascular activity. We then present the cardiovascular measures of autonomic activity, focusing on PEP and its estimation. Subsequently, we review the existing literature linking PEP to mental effort and motivation in cognitive studies, before discussing some important factors modulating or influencing PEP variability. Finally, we expose some important methodological issues, recommendations, and we propose future research directions to better understand this metric.

2 The autonomic nervous system and cardiovascular activity

The ANS is a component of the peripheral nervous system that regulates the “unconscious vegetative life”. It is involved in the homeostasis of the whole body by regulating physiological processes such as HR, BP, or digestion. It is divided into three distinct systems: sympathetic, parasympathetic and enteric. The SNS and the parasympathetic nervous system (PNS) jointly regulate cardiac activity (Karemaker, 2017) depending on the context (e.g., exercise, stress, work, rest) (Greenstein & Greenstein, 2000; Thomas, 2011). At rest, the heart is mainly controlled by the parasympathetic pathway, with a high vagal input discharge associated with a withdrawal of the sympathetic input, which reduces its rate to around 60-80 bpm (Martin et al., 1974; Jose & Collison, 1970, Thomas, 2011). During mental or physical activity, HR first rises following a withdrawal of parasympathetic input, and subsequently, the sympathetic input gradually takes over to further increase HR (Martin et al., 1974, Thomas, 2011). The interplay of these systems allows to rapidly adjust HR.

2.1 Cardiovascular measures of autonomic activity

Several cardiovascular measures are classically used in the literature to investigate ANS activity either invasively or non-invasively, by examining the electrical activity of the heart, cardiac

imaging, or BP (Berntson, Quigley, & Lozano, 2007). Beyond the recording of HR, measures of HRV have figured predominantly in cardiovascular psychophysiology. As stated above, both parasympathetic and sympathetic branches of the ANS influence HRV (Karemaker, 2017). High-frequency HRV, in the respiratory frequency range, has been shown to reflect variations in vagal sinoatrial control and can thus be seen as a selective index of PNS (Berntson et al., 1997; Berntson et al., 2007; Task Force, 1996). However, none of the HRV parameters reflects directly and selectively SNS activity (Kiyono et al., 2017). As such, HRV appears not well suited to directly examine the sympathetic activity associated with mental effort (Brehm & Self, 1989; Obrist, 1976; Richter, Gendolla, & Wright, 2016).

2.1.1 Pre-ejection period (PEP)

The PEP corresponds to one systolic time interval; more precisely it is the time interval between ventricular depolarization on the electrocardiogram (ECG), corresponding to the start of the QRS complex (Q wave, see *Figure 1*), and the opening of the aortic valve that provokes the blood ejection from the left ventricle (B point on the impedance cardiography: ICG, see *Figure 1*). There is an increase in left ventricular pressure during this period due to ventricular contraction triggered by the ventricular depolarization. This ventricular contraction is isovolumic because all valves are closed, which means that ventricular blood volume does not change (Krohova et al., 2017). The PEP is followed by the left ventricular ejection time (LVET), and together, these two parameters (PEP and LVET) correspond to the electro-mechanical systole (EMS): the total time of the electrical and mechanical components of the systole (see *Figure 1*).

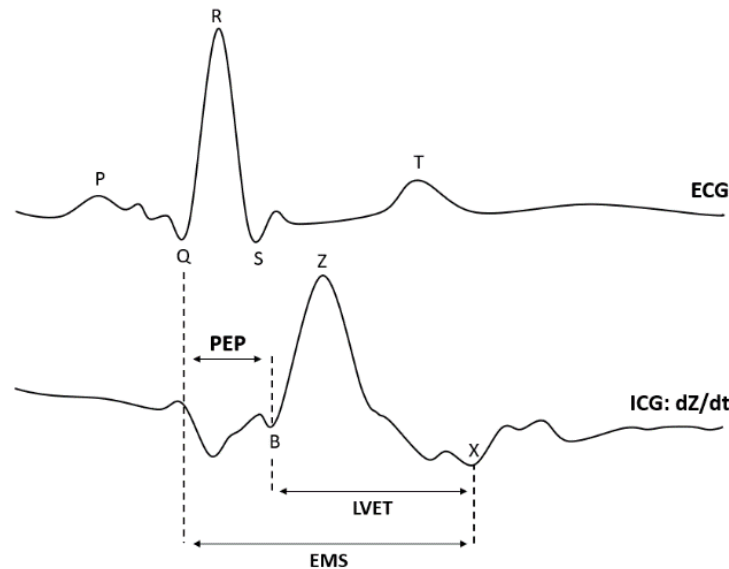


Figure 1: ECG and ICG signals are represented by different main waves and the PEP, LVET, and EMS intervals. ECG: electrocardiogram; ICG: impedance cardiography; PEP: pre-ejection period; LVET: left ventricular ejection time; EMS: electro-mechanical systole.

The PEP is primarily influenced by SNS activity, although muscarinic receptors on the atria can also change atrial contraction force and thus may influence the PEP period; but this effect is generally minor. The PEP depends on the preload (initial stretching of the cardiac myocytes before contraction), the afterload (the pressure that the heart must work against to eject blood during systole), and the cardiac contractility (Newlin & Levenson, 1979). Isovolumic contraction force depends on cardiac contractility and preload, which influences the duration of the PEP. An increase in the preload increases the force of contraction via the Frank-Starling mechanism, leading to a decrease in PEP (Krohova et al., 2017, Newlin & Levenson, 1979). Thus, as discussed more in detail in Section 5.1, these factors may limit the interpretation of PEP and must be taken into account. Normal values of PEP in adults generally range between 90 and 130 ms (see *Table 1*), but these values differ markedly in the literature, most likely due to the large inter-

individual variability of this biological mechanism, but also to discrepancies in methodological aspect of its computation (see Section 2.1.2). The left ventricle presents mainly β -adrenergic receptors for noradrenaline, a neurotransmitter used by the sympathetic system. It means that the stronger the sympathetic β -adrenergic stimulation on the myocardium, the stronger its contractility and the shorter the PEP (Bernston et al., 1994; Harris et al., 1967; Newlin & Levenson, 1979). In other words, PEP duration is inversely related to sympathetic activity.

| Mean PEP duration in ms | References |
|-------------------------|--|
| 90-95 | Bernston et al. 1994 |
| 95-100 | Brinkmann and Franzen, 2013; Chatelain et al. 2016; Chatelain and Gendolla, 2015; Chatelain and Gendolla, 2016; Framorando and Gendolla, 2019b; Franzen and Brinkmann, 2015; Gendolla and Silvestrini, 2011; Houtveen et al. 2005 (<i>lying down</i>); Lasauskaite et al. 2013; Lasaukaite et al. 2014; Mazeret et al. 2019; Richter et al. 2008; Silvestrini, 2018; Silvestrini and Gendolla, 2011b; Silvestrini and Gendolla, 2013 |
| 100-105 | Cancela and Silvestrini, 2021; Houtveen et al. 2005 (<i>sitting</i>); Framorando and Gendolla, 2018; Framorando and Gendolla, 2018b; Framorando and Gendolla, 2019; Franzen and Brinkmann, 2016; Freydefont et al. 2012; Gendolla and Silvestrini, 2010; Mazeret et al. 2021a; Mazeret et al. 2021b; Quigley and Stifter, 2006; Silvestrini, 2015; Silvestrini and Gendolla, 2011a |
| 105-110 | Franzen et al. 2019; Freydefont and Gendolla, 2012; Gurel et al. 2019; Houtveen et al. 2005 (<i>standing up</i>); Mallat et al. 2019; Mezzacappa et al. 2001; Richter and Gendolla (2009a) |
| 110-115 | Brenner et al. 2005 |
| 115-120 | Brinkmann et al. 2009 |
| 120-125 | Covassin et al. 2011; Duschek et al. 2016; Rahman et al. 2018; Silvia et al. 2014 |
| >130 | Bair et al. 2020; Zauner et al. 2020 |
| Unknown | Ahles et al. 2017; Annis et al. 2001; Cellini et al. 2013; Franzen and Brinkmann, 2016b; Montoya et al. 1997; Plain et al. 2020; Rattel et al. 2020 |

Table 1: Mean PEP duration in ms for normal healthy adults (in a sitting position except for Houtveen et al. (2005) for which the position is specified in italic), as reported by each article cited in this review.

In the literature, PEP reactivity is defined as the difference between PEP measured during the performance of a given task and PEP measured during baseline, in general during rest (PEP reactivity = task PEP – baseline PEP). A negative number indicates shortened PEP and increases SNS activity in response to the task. To prevent confusion, in this article, the raw measure is referred to as “PEP” and the difference (task-rest) as “PEP reactivity.” A “higher PEP reactivity” or a “stronger PEP reactivity”, or in other words, a “more negative PEP reactivity,” will indicate shorter PEP during a period of interest vs rest and increased sympathetic activity, for example, during a task compared to rest.

2.1.2 PEP measurements methods

Decades ago, a phonocardiogram, carotid blood pressure, and an ECG were the three sources used to quantify PEP. Currently, ECG and ICG are usually collected simultaneously to measure PEP and represent the most used method (see Figure 2).

ECG records the electrical activity of the muscles of the heart. It is generally recorded using electrodes with a conducting gel placed on the skin. While other configurations exist, the three-electrode arrangement is among the most widely used: one electrode is placed under each clavicle, and the third is placed at two fingers below the floating ribs on the left side (see green circles in *Figure 2*). The electrodes detect the electrical changes caused by cardiac muscle depolarization and repolarization during each cardiac cycle.

ICG is a technology that converts changes in thoracic impedance to volumetric changes that occur during the cardiac cycle. Thoracic impedance hinders the current flow carried by ions across the chest (Yu et al., 2005). It can be recorded for example by using four pairs of electrodes placed on the right and left side of the base of the participant’s neck and on the left and right middle axillary line at the height of the xiphoid. Each pair consists of two electrodes arranged in a vertical strip, four cm apart from each other. The electrodes located closest to the thorax, the voltage electrodes or the receiving electrodes (red squares in *Figure 2*), measure the surface

potential proportional to the impedance in the chest cavity. The electrodes farther from the thorax, the current electrodes or the sending electrodes (blue squares in *Figure 2*), transmit the current at high frequencies along the thorax (Lozano et al., 2007; Kelsey & Guethlein, 1990; Sherwood et al., 1990).

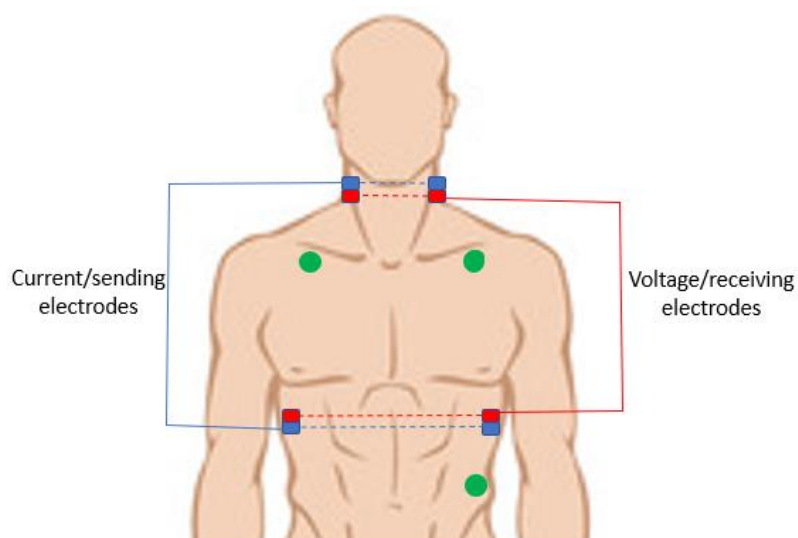


Figure 2: Representation of a possible configuration for the placement of ECG electrodes (green circles) and ICG electrodes (blue and red squares).

The ECG is used to identify the onset of the PEP, which corresponds to the lowest deflection of the Q-wave (the Q-point). As seen in *Figure 1*, the ICG is used to record the end of the PEP, the B point, which indicates the opening of the aortic valve. It is achieved by computing the first derivative of the change in thoracic impedance and thus finding the resulting dZ/dt signal. The dZ/dt signal corresponds to the velocity changes of the blood flow. The Z-point (dZ/dt_{max}) represents the maximal speed of the blood ejection, which is preceded by the B-point, since the opening of the valve results in a peak in aortic blood flow (Bernston et al., 2004; Lozano et al., 2007). Metshein et al. (2021) recently reported that while the ECG signal is reasonable for different electrodes placements, the ICG signal has quite varying quality as a function of electrodes placement, which can affect the positioning of the B point for example, among others.

As such, careful positioning of the electrodes as well as their formal description in the manuscripts' methodological section is required.

Different automatic methods to detect the Q-point have been suggested, including identifying the onset of the Q wave, the peak of the Q wave, the onset of the R wave, or using a fixed constant (e.g., 48 ms before R) (Berntson et al., 2004; Sherwood et al., 1990). Different methods have also been suggested to identify the B-point: using the first (dZ/dt), second (d^2Z/dt^2), or third derivatives (d^3Z/dt^3) of the dZ/dt signal; the dZ/dt zero-crossing point; or the primary rapid-rise in dZ/dt (Berntson et al., 2004; Sherwood et al., 1990; Gurel et al., 2019; Zauner et al., 2020). The B-point can be the minimum of d^3Z/dt^3 that occurs just before the maximum in dZ/dt . The interested reader can find a discussion on these aspects and a proposition for a new automatic algorithm in Forouzanfar et al.'s study (2018).

It has also been shown that PEP can be successfully approximated by the RZ interval (interval between R-peak and Z-point (dZ/dt)). R-peak and Z points are salient waveform points that are easily and reliably identified, contrary to the Q and B points. However, it's worth noting that this measure cues the PEP, without being a direct measure of the latter (Silvia et al., 2021). The use of RZ interval can be useful, for example, in single-trial studies. Indeed, Q and B points can be noisy and harder to pinpoint in comparison to a peak, such as R or Z. Without repetition, a good and reliable estimation of PEP can thus be complicated, and RZ interval could be a good alternative (Kuipers et al., 2016; Lozano et al., 2007; Sherwood et al., 1990, Silvia et al, 2020).

Nevertheless, PEP still has some longstanding assessment issues, and the signal has to be visually checked and corrected when necessary, as recommended by Sherwood et al. (1990). Indeed, as said above, both Q and B points are susceptible to distortion, noise, and factors that can degrade signals recorded through skin-electrodes (Bernston et al., 2004; Lozano et al., 2007; Sherwood et al., 1990). Individual differences in cardiac waveforms also affect points detection.

For all these reasons, algorithms might not always be able to pinpoint them correctly and time-consuming manual inspections are sometimes required.

All these differences in data collection and processing may explain in part differences in signal quality and differences in absolute PEP values found in the literature.

3 Review of studies using PEP to index motivation and mental effort mobilization in cognition

Although the present study is not a systematic review, we performed a comprehensive research of the pertinent work measuring cardiac PEP in cognitive studies. The literature search was conducted on Pubmed, Web of Science, and Google Scholar databases, using different combinations of the following keywords: “preejection period”, “pre-ejection period”, “cogn*”, “motivation”, and “effort”. A further search of articles was done on the institutional and personal websites of known authors who published on PEP in the cognitive field. The included studies were published in peer-reviewed journal at the end of 2021 at the latest. A two-step screening of the titles and abstracts permitted to exclude articles that were irrelevant (clinical studies, not related to PEP or cognition, PEP not recorded during a cognitive task, PEP results not presented in the article, not written in English or French, review papers, of no interest for this article) or duplicate. Afterward, all the articles were read and we selected all the publications in which the measure of PEP was performed during a cognitive task with a clear focus on motivation and/or mental effort. The final number of publications selected for this review was 52 articles. They all are summarized in *Table 2*.

| Authors | Population | Cognitive Task | Experimental design | Main PEP Results |
|-----------------------------|--|---|--|--|
| Ahles et al. 2017 | 76 Adolescents (mean age 13 y), with depressive symptoms. | Delayed-matching-to-sample-task. | 3 min baseline followed by the task. Reward incentive was presented during the task. | PEP reactivity to reward is associated with anhedonia symptoms but not with non-anhedonic depressive symptoms. |
| Annis et al. 2001 | 33 male psychology students (no age reported). | Recognition memory task. | 10 min baseline, then a performance feedback on practice run is displayed (moderate or low performance feedback). Six work periods were presented, where participants could earn chances to win prizes by attaining different performance standards. | With moderate performance feedback, PEP reactivity evolves directly with the assigned performance standard. With low performance feedback, PEP reactivity is first more and more negative, until the high-performance standard during which a task disengagement was observed. This shows that there is an effect of perceived ability on mental effort. |
| Bair et al. 2020 | 36 MDD patients (mean age 48 y) vs 39 healthy participants (mean age 47 y). | Number-letter task, Continuous performance test, N-back task and Stroop task. | 7 min baseline followed by the four tasks presented in a randomized order (each lasting 10 min). Within-subject design but with between-subjects analysis. | Blunted (less negative) PEP reactivity in MDD patients for every task, compared to the healthy participants, and longer reaction time. A correlation between performance and autonomic parameters was found. |
| Beauchaine et al. 2001 | 22 control (mean age 13,2 y), 17 ADHD (mean age 13,1 y) and 20 conduct disorder (CD/ADHD) (mean age 14 y). | Repetitive response task. | 5 min baseline. 7 task blocks of 2min, each separated with a 2,5 min rest. Block 1 is a practice block, blocks 2, 3, 4 and 6 have a reward condition. Block 5 starts with a reward condition then becomes an extinction of reward condition. Block 7 has an extinction condition. | CD/ADHD participants showed positive PEP reactivity and ADHD participants showed a blunted PEP reactivity compared to control. |
| Bernston et al. 1994 | 10 healthy women (mean age 22,5 y). | Speech stress, mental arithmetic, reaction time task. | 3 min baseline, then a pharmacological blockade of the autonomic system with infusion of saline, metoprolol or atropine sulfate, then 3 min baseline, 3 min recording seating and standing, the 3 tasks are then presented with a 3 min rest before each task. | Shorter PEP during stressful tasks. During the 3 tasks, a rise in sympathetic activity and a diminished parasympathetic activity were observed but without correlation between the two branches. PEP duration changed in accordance with the autonomic pharmacological blockades. |
| Brenner et al. 2005 | 50 students (age between 18 and 24 y). | Repetitive response task with reward and frustrative nonreward. | Six 2 min blocks separated by 2,5 min rest periods. The first 3 blocks were reward conditions, the fourth started as reward then switched to extinction, the fifth was reward, and the sixth started as extinction then switched to reward. | PEP was the only autonomic parameter to react to reward. A habituation of PEP reactivity to reward was observed with the strongest PEP reactivity during the first reward block. |
| Brinkmann and Franzen, 2013 | 88 students (41 dysphorics & 47 non-dysphorics) (mean age 21,39 y). | Sternberg type short memory task. | 2 (dysphoric vs nondysphoric) × 3 Incentives (0 vs 5 vs 15 SwissFrancs) between-persons design. 7,5 min habituation/baseline followed by the task (5 min, 29 trials). | A linear increase of PEP reactivity was found with an increase of incentive in non-dysphorics, while dysphorics showed a blunted and nonlinear PEP reactivity. |
| Brinkmann et al. 2009 | 1) 75 students (mean age 23 y). 2) 145 students (mean age 22 y). | 1)Mental concentration task. 2)Mental arithmetic task. | 1) Three between-person conditions (hedonic consequences: neutral vs reward vs punishment). 8 min baseline followed by the task (5 min, 50 trials). 2) 2 (dysphoric vs nondysphoric) × 2 (hedonic consequences: neutral vs reward) between-person design. 9 min baseline followed by the task (5 min, 20 trials). | The results of both studies show that dysphorics have a blunted PEP reactivity to both punishment and reward. They also show an insensitivity to hedonic consequences. |

| | | | | |
|--------------------------------|--|---|---|---|
| Cancela and Silvestrini, 2021 | 30 students (mean age 21,5 y). | Easy memory span task. | Within-subject design with 4 conditions: pain-alone, task-alone, task with nonpainful heat stimulations (task-warmth), and task with painful stimulations (task-pain). 8 min baseline followed by the task alone block, then the pain alone block, then the task-warmth block and the task-pain block. Each block is 3 min long. | Pain increases subjective task difficulty. PEP reactivity was stronger when painful stimulation occurred during the task. |
| Cellini et al. 2013 | 13 normal sleeper vs 13 primary insomniacs (mean age 24 y). | Easy letter memory task (ELMT) and N-back task. | 10 min of relaxation was followed by a 3 min baseline recording, then participants performed the ELMT and after a 15 min break the N-back task (3 blocks). Within-subject design. | Insomniacs showed hyperarousal at rest with a lower PEP and working memory impairment. But no relations between those two results were found. |
| Chatelain and Gendolla, 2015 | 1) 54 students (mean age 28 y). 2) 86 participants (mean age 26 y). | 1) Parity task. 2) Adaptation of the Brickenkamp d2 mental concentration task. | 1) Participants randomly assigned to anger, fear or happiness prime. 8 min baseline was followed the task. During the task, a fixation cross is presented, then a facial expression, then a noise picture, and finally a word flanked by 2 numbers (odd or even). 2) Fear, anger or sadness primes. Same order of presentation but with the mental concentration task. | Fear and sadness primes result in greater PEP reactivity than anger and happiness. Sympathetic impact of implicit fear and sadness on effort-related cardiac response, the emotions influencing the amount of effort put into a task. |
| Chatelain and Gendolla, 2016 | 82 students (mean age 24 y). | Difficult Sternberg type short memory task. | Prime (Fear vs Anger) x Incentive (High vs Low) between-persons design. 8 min habituation/baseline followed by the task (5 min, 36 trials). | Fear primes lead to a stronger PEP reactivity in the difficult task when incentive was high compared to anger primes. When incentive was low, anger primes showed the stronger PEP reactivity. |
| Chatelain et al. 2016 | 80 psychology students (mean age 21 y). | Mental arithmetic task. | Randomly assigned to a 2 (fear vs anger) x 2 (easy vs difficult) between-subjects design. 8min baseline followed by the task (5 min, 32 trials). | For the easy task, fear primes lead to stronger PEP reactivity than anger primes. For the difficult task, reverse effect, anger primes lead to stronger PEP reactivity. |
| Covassin et al. 2011 | 8 normal sleepers (mean age 24,8 y) vs 8 primary insomniacs (mean age 22,9 y). | Stop Signal Task. | Two sessions: before and after a night of polysomnographic recording. 5 blocks, each preceded by a 1 min baseline fixation cross. Within-subject study. | PEP is lower in insomniacs at rest, showing a constant sympathetic hyperarousal. There was no difference in PEP reactivity during the task and no correlation found between performance (inhibition deficit for insomniacs) and physiological data. |
| Duschek et al. 2016 | 40 hypotensive (mean age 24,7 y) vs 40 normotensive (mean age 24 y). | Number-letter task, continuous performance test, n-back task and flanker task. | 7 min rest period and the tasks were presented in a fixed order. Within-subjects study. | Hypotensive participants show higher PEP as well as increased error rates in n-back and flanker task with a positive correlation between the two. |
| Framorando and Gendolla, 2018a | 87 students (mean age 20,46 y). | Sternberg type short memory task. | 2 (prime: sadness vs anger) x 2 (visibility: suboptimal vs optimal) between-persons design. 8min habituation/baseline followed by the task (5min, 32 trials). | PEP reactivity was stronger with sadness primes in the suboptimal presentation of the primes condition compared to anger primes, but not in the optimal condition. |
| Framorando and Gendolla, 2018b | 124 students (mean age 24 y). | Parity task. | Prime (sadness vs anger) x prime visibility (suboptimal vs optimal) between-persons design. 8 min habituation/baseline followed by the task (5 min, 36 trials). | When primes are briefly flashed, sadness prime conditions showed stronger PEP reactivity than the anger prime condition. The opposite was observed when affect primes were clearly visible. However, these results only occurred for men. |
| Framorando and Gendolla, 2019a | 166 students (mean age 23,5 y). | Arithmetic task. | Prime (sadness vs anger) x warning (warning of the presence of primes vs no warning) x | Only when there was no warning about the presence of primes, PEP reactivity was stronger in |

| | | | | |
|--------------------------------|---|--|--|---|
| | | | gender between-persons design. 8 min baseline followed by the task (5 min, 30 trials). | the happiness prime condition than the sadness prime. This was also only significant for men. |
| Framorando and Gendolla, 2019b | 123 students (mean age 22,62 y). | Memory task or simply watching. | Prime (sadness vs happiness) about the pre-achievement vs watching) between-persons design. 10 min habituation/baseline followed by the task (5 min, 36 trials). | PEP reactivity was stronger with happiness primes than sadness primes during the achievement condition. During the watching condition, PEP reactivity was weaker without a difference between the 2 primes. |
| Franzen and Brinkmann, 2015 | 56 nondysphoric students (mean age 22,46 y) and 51 dysphoric students (mean age 23,51 y). | Recognition memory task. | 2 (dysphorics vs nondysphorics) × 3 (neutral vs reward vs punishment) between-persons design. After a baseline recording, a memorization phase of 5 min is presented (presentation of 30 non-words), followed by a recognition phase (90 trials, 30 target non-words and 60 distractors non-words). | For non-dysphorics, PEP reactivity was stronger for both incentive conditions compared to the neutral condition, while for dysphorics, it was blunted across conditions. |
| Franzen and Brinkmann, 2016 | 1) 35 students (mean age 22,11 y). 2) 30 students (mean age 21,37 y). | Adaptation of the Brickenkamp d2 mental concentration task | 1) 2 between-person conditions (dysphorics vs nondysphorics) and 2 within-person conditions (reward anticipation vs consumption). 8 min habituation/baseline followed by the task (5 min, 51 trials). 2) 2 between-person conditions (dysphorics vs nondysphorics) and 2 within-person conditions (punishment anticipation vs consumption). 8 min habituation/baseline followed by the task (5 min, 51 trials). | Dysphorics showed a blunted PEP reactivity for both reward and punishment conditions, but a blunted self-reported wanting during reward condition and a normal wanting during punishment. |
| Franzen and Brinkmann, 2016b | 42 students (men age 24,64 y). | Sternberg type short memory task. | 2 wanting vs liking. 8 min habituation/baseline followed by 5 min task (21 trials). | Highly anhedonic participants showed a reduced PEP reactivity and self-reported wanting. |
| Franzen et al. 2019 | 20 participants with MDD and 20 controls (mean age 42,65 y). | Sternberg type short memory task. | First a neutral 8 min long movie is presented and used to record baseline. Followed by two blocks of 2,8 min of the same task. With either a reward incentive then a punishment incentive in the 2 nd one, or the reverse. | With reward incentive, MDD participants showed a blunted PEP reactivity and self-reported wanting. While with a punishment incentive, MDD participants showed a blunted PEP reactivity but an unchanged self-reported avoidance motivation. |
| Freydefont and Gendolla, 2012 | 62 students (mean age 22 y). | Sternberg type short memory task. | 2 (affect prime: anger vs sadness) × 2 (incentive: low vs high) between-person design. 8 min habituation/baseline followed by the task. | PEP reactivity was stronger with high incentive when sadness prime are used than with low incentive. With low incentive, PEP reactivity was stronger with the anger primes than with the sadness primes. |
| Freydefont et al. 2012 | 75 students (mean age 21 y). | Sternberg type short memory task. | 2 (affect prime: anger vs sadness) × 2 (difficulty: low vs high) between-person design. 8 min habituation/baseline followed by the task (32 trials). | For the easy task, sadness primes lead to stronger PEP reactivity than anger primes. For the difficult task, reverse effect, anger primes lead to stronger PEP reactivity. |
| Gendolla and Silvestrini, 2010 | 48 students (mean age 23 y). | Sternberg type short memory task. | 3 primes (action vs neutral vs inaction). 8 min habituation/baseline followed by the task (32 trials). | PEP reactivity was stronger with action primes than with neutral primes, which was stronger than inaction primes. Task performance followed the same pattern. |
| Gendolla and Silvestrini, 2011 | 1) 45 students (mean age 22 y). 2) 42 students (mean age 21 y). | 1) Attention task. 2) Sternberg type short memory task. | Participants are randomly assigned to one prime condition (sadness vs happiness vs anger). 8 min habituation/baseline followed by the task (5 min, 36 trials). | For both experiments sadness-primes resulted in a stronger PEP reactivity than happiness and anger primes. |

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| Gurel et al. 2019 | 25 Healthy young (mean age 25,5 y) vs 25 older subjects with coronary artery disease (mean age 64,8 y). | Arithmetic stress. | 15 min rest followed by 1 min of mental arithmetic tests. | Mean PEP lower in elderly population than young population and PEP is reduced during task for both groups but more strongly in the young group. |
| Kelsey et al, 2000 | 162 students (age between 18 and 33 y). | Mental arithmetic. | 3 groups: no evaluative videotaping, videotaped during the second task, or videotaped during the third task. Each group started with, respectively a 8, 24 or 16 min baseline followed 3 task blocs, separated by 4 min baseline periods. | PEP reactivity was higher during task blocs which were videotaped. |
| Kelsey et al, 2004 | 224 students (mean age 19,2 y). | Mental arithmetic. | 2 (evaluative observation or not) x 2 (8 min or 16 min baseline). 4 task blocks (4 min) with 4 min baseline between each blocks, except before the 3 rd block where baseline was 12 or 4 min depending on the group, and during the 3 rd block evaluative observation occurred or not. | Habituation was observed across tasks blocks with a decrease of PEP reactivity, except when evaluative observation occurred during the 3 rd block, where an increase of PEP reactivity was observed. |
| Kelsey et al, 2007 | 1) 326 students (mean age 19,3 y). 2) 136 adolescents (mean age 14,7 y). 3) 142 adolescents and young adults (mean age 17,8 y). | 1) mental arithmetics. 2) video game and cold pressor. 3) mathematics, video game, and cold pressor. | 1) 8, 16 or 24 min baseline followed by three mental arithmetic tasks (4 min) separated by 4min baseline. 2) 10 min baseline before each task, 3 min video game and 3 min cold pressor. 3) 10 min baseline before each task, two mental arithmetic tasks (5 min), 3 min video game and 3 min cold pressor. | PEP reactivity was significant for all tasks except the cold pressor task. A high reliability within tasks was found while lower reliability was found across tasks. |
| Lasaukaite et al. 2013 | 52 healthy students (mean age 20,5 y). | Adaptation of the Brickenkamp d2 mental concentration task. | Participants were randomly assigned to a 2 (prime: happy/sad) x 2 (cue/no cue) between-persons design. Pictures of neutral, sad and happy faces. Baseline taken during a neutral film is watched. | Sadness primes had stronger PEP reactivity than happiness primes, and use of cue showed stronger PEP reactivity than no cue for both primes. With sadness prime, task demand and mental effort are higher, higher cognitive demand. Effect of emotional feelings on mental effort. |
| Lasaukaite et al. 2014 | 134 students (mean age 21 y). | Arithmetic task. | Prime (sadness vs happiness) x prime visibility (suboptimal vs optimal) x difficulty (easy vs difficult) between-persons design. 8 min habituation/baseline followed by the task (5 min, 36 trials). | When primes are briefly flashed, sadness prime conditions showed stronger PEP reactivity than the happiness prime condition when the task was easy. The opposite was observed when the task was difficult. These effects were reversed when the primes were clearly visible. |
| Mallat et al. 2020 | 110 healthy right-handed students (age between 18 -30 y). | Modified Fitt's Task with 5 levels of shrinking targets. | 8 min rest followed by 75 training trials then the experimental task. Between-subject design. | Curvilinear relationship of PEP with task difficulty. Negative PEP reactivity for the first two levels, then "intermediate" level has a more negative PEP reactivity. For the "very difficult" level, PEP reactivity stayed negative but diminished, showing a slight disengagement. For the "impossible level" it was positive, showing a total disengagement. |
| Mazeres et al. 2019 | 68 students (mean age 20,82 y). | Mental arithmetic task. | 2 (easy vs difficult) x 2 (low nAch vs high nAch) 8 min habituation/baseline followed by the task. | PEP reactivity was stronger in the difficult task condition, and stronger for the high nAch group. |

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| Mazeres et al. 2021a | 78 students (mean age 23,72 y). | Mental arithmetic task. | Task difficulty clear vs unclear. 8 min habituation/baseline followed by the task (6 min 40 s). | PEP reactivity was stronger in the high implicit achievement motive group when the task was difficult or unclear. |
| Mazeres et al. 2021b | 1) 88 students (mean age 20,68 y). 2) 88 students (mean age 20,92 y). | 1) Memory task. 2) Mental arithmetic task. | 1) 2 difficulty (easy vs difficult) x 2 groups (low nAch vs high nAch). 8 min habituation/baseline followed by the task (5 min). 2) 2 difficulty (easy vs unclear) x 2 groups (low nAch vs high nAch). 8 min habituation/baseline followed by the task (5 min). | PEP reactivity is stronger with high implicit achievement motive (nAch) when the task is either difficult or when difficulty is unclear. |
| Mezzacappa et al. 2001 | 1) 27 participants (mean age 25,4 y). 2) 31 participants (mean age 34 y). | Cold pressor. Mental arithmetic task. Stroop task. | 1) 10 min baseline, then 1 min arithmetic and cold pressor in random order, with 5 min baseline between the two tasks, and 1 min recovery recorded after each task. 2) 5 min baseline, 5 min Stroop task, 5 min recovery, 5 min arithmetic task and finally 5 min recovery. Within-subject study. | Cold pressor did not show a decrease in PEP but the mental arithmetic task did. No PEP results for experiment 2. Cardiovascular recovery from stress is associated with increased vagal modulation despite residual sympathetic activation. |
| Montoya et al. 1997 | 22 healthy adults (mean age 22,7 y). | Mental arithmetic. Cold pressor. | 5 min baseline then 5 min mental arithmetic task, 5 min baseline, 3 min hand cold pressor and another 5 min baseline. Within-subject study. | No effect of cold pressor on PEP but a significant decrease in PEP is observed during mental arithmetic. It suggests that cardiovascular responses to psychological challenge depend on the level of cognitive processing required for the task. |
| Plain et al. 2020 | 31 participants (mean age 22,22 y). | Speech in-noise test. | 5 min baseline, 6 x 2 within-subject design. Two reward levels (0,20€ or 5€) and six speeches in noise ratios. | No reward effect and PEP reactivity varied linearly with task demand. |
| Quigley et al. 2006 | 38 children (mean age 5,25 y); 20 adults (age 21 y). | Emotionally evocative video, interview, reaction time task and cold pressor. | 2 min baseline (4 min for adults) then 12 min video, then interview, then reaction time task and finally 1 min cold forehead pressor. Inter-task rest of 2 min for adults but not children. Within-subject design. | PEP reactivity is similar for children and young adults. The consistency of the reactivity across tasks within individuals and consistency of reactivity across children and young adults suggests that pre-ejection period is a reasonable estimate of sympathetic activity in children. |
| Rahman et al. 2018 | 46 students (mean age 19,2 y). | Stroop Color-Word Conflict Test. | 5 min baseline, 5 min Stroop test and 5 min recovery. | PEP was reduced during task and came back to baseline during recovery. |
| Richter et al. 2008 | 64 university students (mean age 24 y). | Sternberg type short memory task. | Participants are randomly divided into 4 groups Each group was assigned a difficulty level. The task consisted of 72 trials (each lasting 4000ms). Baseline time isn't given in the article. | PEP reactivity was more and more negative with task difficulty until the task became impossible, at which point PEP reactivity was positive. |
| Richter and Gendolla, 2009 | 31 psychology students (mean age 28 y). | Delayed-matching to-sample task. | 10 min habituation followed by 28 trials. Task instructions only explained the general procedure of the task to create task with unclear difficulty and they learned they could win a prize for successful task performance. Within-subject study, participants were randomly assigned to 1 condition. | PEP reactivity increased with incentive value. |
| Silvetrini, 2015 | 1) 61 students (mean age 24 y). | Difficult Sternberg type short memory task. | 1) 2 (prime: pain, neutral) x 2 (incentive: moderate, high) between-persons design. 8 min habituation/baseline followed by the task (5 min, 32 trials). | PEP reactivity was stronger in the pain-prime/high incentive condition compared to the other conditions. However, task performance was lower with pain primes compared to neutral primes. |

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| Silvestrini, 2018 | 1) 96 students (mean age 22 y). 2) 82 students (mean age 22 y). | Sternberg type short memory task. | 1) 2 (prime: pain, neutral) × 2 (difficulty: easy, difficult) between-persons design. 2) 2 (prime: pain, anger) × 2 (difficulty: easy, difficult) between-persons design. 8 min habituation/baseline followed by the task (5 min, 32 trials). | Pain primes resulted in a stronger PEP reactivity compared to both neutral and anger primes when the task difficulty was easy but was weaker than them when the task was difficult. Pain primes also resulted in the increase of self-reported perceived difficulty. |
| Silvestrini and Gendolla., 2011a | 40 students (mean age 21 y). | Adaptation of the Brickenkamp d2 mental concentration task. | 8 min baseline followed by mood manipulation with 8 min film presentation (funny or depressing movie clips). Before the attention task, there was an instrumentality manipulation (high/low hedonic instrumentality), then they performed the 5 min task. | PEP reactivity was stronger in participants with the positive mood induction than negative mood. But the strongest PEP reactivity was observed in participants who had the negative mood induction and the high instrumentality. The high instrumentality justified a higher effort in a negative mood. |
| Silvestrini and Gendolla, 2011b | 56 students (mean age 23 y). | Modified Brickenkamp d2 mental concentration task. | Participants are randomly assigned to a 2 (prime: sad vs happy facial expression) × 2 (difficulty: low vs high) between-persons design. 8 min habituation/baseline followed by the task (5 min, 36 trials) | PEP reactivity was the strongest for the sadness-prime/easy task condition and the happiness-prime/difficult task condition. |
| Silvestrini and Gendolla, 2013 | 75 healthy students (mean age 22 y). | Sternberg type short memory task. | 2 (prime: action, inaction) × 3 (difficulty) between person design. 8 min baseline followed by the task (either a nonword series of letters or a priming word was presented). | Stronger effort-related cardiovascular response with action primes than inaction primes, as long as success is possible: disengagement when the difficulty is "extremely difficult". No significant difference between PEP reactivity for the "easy" task vs "difficult". |
| Silvia et al. 2014 | 131 Adults (mean age 19,37 y). | Parity task. | 5 min baseline followed by 5 min task. | Longer PEP at baseline in people with higher depressive symptoms, as well as a smaller PEP shortening during task. |
| Tanenbaum et al. 2018 | 91 healthy children vs 75 children with ADHD (mean age 8,32 y). | Emotional Go/No-Go task. | 60 facial stimuli presented. Neutral Go/No-Go (control condition): calm faces. Female faces were the Go stimuli and male for No-Go. Emotional Go-No-Go: fearful faces were Go trials and No-Go for any other faces. | PEP reactivity was positive in both neutral and fear conditions while control participants showed negative results for both. ADHD children were less motivated to engage in the task. |
| Zauner et al. 2020 | 27 young healthy adults (mean age 26.2 y). | Sternberg task. | Morning sessions started at 07:00 am, before dawn, late-afternoon sessions at 5:00 pm, after dusk. Three different lighting scenarios were tested. Correlated color temperature set at 7000K (241lux), 4000K (128lux) or 2700K (54lux). After the ten-minute baseline, they performed the computerized cognitive task. Within-subject test. | The highest change (sympathetic activation) occurred for the medium one of the three stimuli (128 lux) during the late-afternoon session. Performance scores did not change with the light scene. Participants reached the same performance most efficiently at both the highest and lowest melanopic setting, and during the morning session. |

Table 2: Summary of the studies presented in this review. They all include PEP measures during a cognitive task.

Brehm's theory on effort investment has been extensively studied in relation to different cardiovascular responses (see Gendolla & Wright, 2012; Richter et al., 2016 for detailed reviews). *Table 2* reports the description and main results of the reviewed studies specifically on PEP and PEP reactivity across a great variety of experimental paradigms evaluating cognitive performance. In this section, we briefly review and discuss the most important results of these studies.

As a typical example of study conducted in this domain, Richter et al. (2008) used a modified version of the Sternberg task: a memory task using nonsense letter series in which participants had to report whether a single target letter was present in the previous series. The task had four different levels of difficulty, depending on the time of presentation of the nonsense letter series. The highest difficulty level was impossible because the presentation time was too short (15 ms) to consciously process the stimulus. In this between-subject study, each level of difficulty was performed by an independent group of participants. The results showed that PEP reactivity increased proportionally with task difficulty until the task became impossible (see *Figure 3*). PEP reactivity became more negative with increasing task difficulty. A task disengagement was then observed for the "Impossible" condition because the task became too difficult: the participants stopped putting effort into the task, and PEP reactivity became positive (task PEP was higher than baseline PEP in this condition). According to the authors, PEP duration is inversely proportional to an individual's task engagement, and energy mobilization is mediated by changes in β -adrenergic activity, supporting Brehm's theory.

Following this study, numerous works from this research group and others have examined more systematically the conditions under which such a relationship between PEP reactivity, indexing SNS control, and effort mobilization is demonstrated and the shape of this relationship.

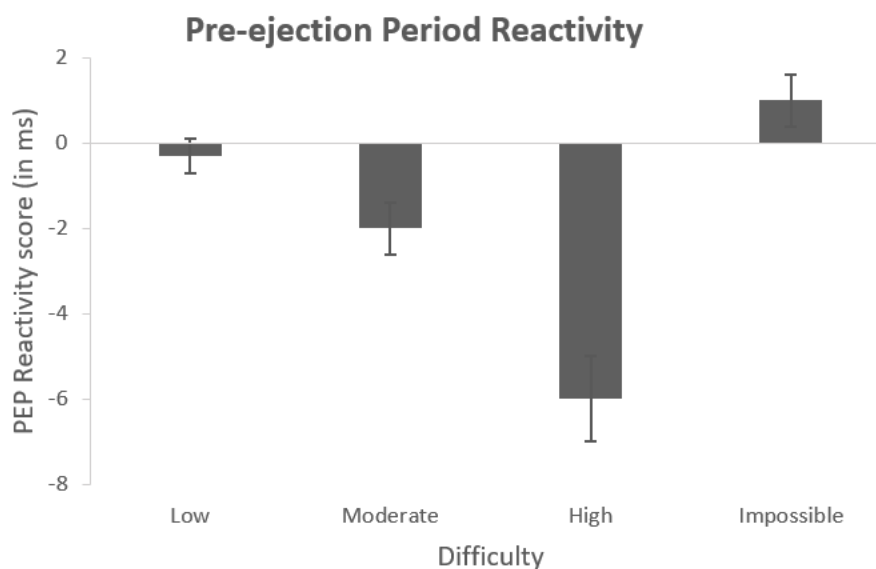


Figure 3: Reproduction of the results reported by Richter et al. (2008) for pre-ejection period (PEP) reactivity during the performance of a memory task across different levels of difficulty. Bars represent standard errors.

In the same kind of task as Richter et al. (2008), it has been shown that using action primes instead of nonsense letters elicited a stronger effort-related cardiovascular response (higher PEP reactivity) than using inaction primes (Gendolla & Silvestrini, 2010; Silvestrini & Gendolla, 2013). However, the linear relationship between PEP reactivity and task difficulty was not always demonstrated (e.g., Silvestrini & Gendolla, 2013) and some studies failed to find a sudden disengagement when the study becomes too difficult. For instance, using a modified Fitts' task (speed-accuracy sensorimotor task) with five difficulty levels, Mallat et al. (2020) showed that the relation between PEP reactivity and task difficulty was curvilinear and thus more consistent with Hancock and Szalma's model (2006) that proposes a curvilinear effect of stress level or task difficulty on behavioral and physiological adaptability. When task difficulty increases to a point where it becomes too difficult for the individual, mental effort investment is reduced and not stopped, and the behavioral strategy changes.

Important factors related to the relationship between cardiac PEP reactivity and effort mobilization in cognitive tasks concern mood, emotion and pain. For example, the mood has been shown to affect mental effort intensity, as indexed by PEP reactivity, during task performance due to its effects on task appraisal (Silvestrini & Gendolla, 2011a). Similarly, research from this Geneva Motivation Lab reported that using affect primes (sadness, fear) during a cognitive task can influence perceived difficulty and thus effort mobilization as measured by PEP reactivity (Chatelain & Gendolla, 2015; Framorando & Gendolla, 2019b; Lasauskaite et al., 2013). Several studies also found that the emotional effect on PEP reactivity is not linear and can be modulated by the objective difficulty of the parallel task (Chatelain et al., 2016; Framorando & Gendolla, 2018a; Framorando & Gendolla, 2018b; Framorando & Gendolla, 2019a; Freydefont & Gendolla, 2012; Freydefont et al., 2012; Gendolla & Silvestrini, 2011; Lasaukaite et al., 2014; Silvestrini & Gendolla 2011b). More detailed reviews of the effect of affect primes on effort mobilization can be found in Gendolla (2012) and Silvestrini and Gendolla (2019). Finally, in addition to sadness and fear, pain was also shown to affect perceived task difficulty and the resulting cardiovascular reactivity to effort mobilization (Cancela & Silvestrini 2021; Silvestrini, 2015; Silvestrini, 2018).

Some studies directly related PEP reactivity to mental stress. Berntson et al. (1994), Kelsey et al. (2007), Mezzacappa et al. (2001), Montoya et al. (1997), and Rahman et al. (2018) showed that, except for the cold stressor, mental stress inductions by reaction time tasks, speech stress tasks, mental arithmetic tasks or video game, elicited significant changes in cardiovascular functioning, with a shortening of PEP. This PEP sensitivity to mental stress is most likely due to the stronger sympathetic activity responsible for fight or flight behaviors in response to danger and stressful environment/situations. Moreover, studies reported that an evaluative observation condition resulted in an increase of PEP reactivity, indicating a resurgence of β -adrenergic cardiac reactivity, but that repeated similar stress tasks resulted in attenuated PEP reactivity, showing a possible form of habituation (Kelsey et al.; 2000; 2004).

Taken together, the results of the studies reviewed in this section and detailed in *Table 2* reported that manipulations of task difficulty, mental stress or incentive value, as well as mood and emotions elicit direct and measurable changes in cardiac PEP and PEP reactivity. Although not a direct measure, PEP is currently accepted as the most reliable index of SNS activity in controlled conditions (Kelsey, 2012; Krohova et al., 2017; Mezzacappa et al., 1999; Richter et al., 2008), and as such can be an efficient physiological metric of mental effort mobilization. Nevertheless, the relationship between task difficulty and PEP reactivity was not always shown to be clearly linear, and was also often curvilinear. Also, complete disengagement or sudden disengagement when the task became impossible was not systematically reported neither. These discrepancies could be related to the definition and manipulation of task difficulty that can diverge between studies. They also could be explained by the numerous moderators involved in the task difficulty and PEP relationship. The physiological processes behind effort mobilization may thus need further investigation. As reported above, emotions and mood influence PEP, but other important factors also deserve future consideration. These factors are reviewed in the next sections.

4 Inter-individual variability of PEP

Numerous factors independent from the experimental manipulation appear to influence PEP values in the literature. It is important to consider this variability when using PEP in psychophysiological and cognitive experimentations. The most important sources of inter-individual variability, described below, are age, sex, and psychological pathologies. Other sources of variability not reviewed here can be linked to diseases such as heart failure, aortic valve diseases, or chronic hypotension (see Duschek et al., 2016; Krohova et al., 2017; van Lien et al., 2013).

4.1 Age

According to Quigley and Stifter (2006), the mean resting PEP is shorter in young children (mean age = 5 years and 3 months) than in adults, with values ranging from 70 to 75. The authors also reported that children have a smaller sympathetic reactivity compared to adults. PEP reactivity was more important in adults than in children during four different tasks: watching a video of the *Wizard of Oz*, an interview, a go/no-go task, and a cold pressor task. However, in another study, Tanenbaum et al. (2018) reported a mean resting PEP ranging from 95 to 105 ms in 166 children aged 5-13 years, indicating that children may not always show a shorter PEP at rest compared to adults (see Table 1). The literature also investigated whether PEP differs in older adults compared to younger ones. Cybulski (1996) did not find any significant effect of age on the mean resting state PEP among adults aged 22 to 59 years. Steptoe et al. (2005) did not find a significant difference in mean resting PEP between adults (27-42 years) and older adults (65-80 years), but did find a stronger PEP reactivity in younger adults than in the older adult group in response to a cognitive task, as well as a better PEP recovery from task. Gurel et al. (2019) showed a shorter mean resting PEP and a lower PEP reactivity in older participants (age = 64.8 y \pm 5.9 y; resting PEP = 80 ms \pm 4.3 ms; PEP reactivity = -6.4 ms) than in healthy younger ones (age = 25.4 y \pm 4.4 y; resting PEP = 109.3 ms \pm 3.9ms; PEP reactivity = -9.6ms) during a mental arithmetic task. However, in this study, older participants showed higher mean BP and lower mean HR compared to younger participants, which could explain the apparent lower mean resting PEP of the older participants. As mentioned above, an important inter-individual variability in the mean resting PEP was observed in adults (see Table 1). It is thus difficult to evaluate the actual effect of age on PEP. This needs to be further studied in conjunction with the confounding factors mentioned in this article (e.g., HR, BP, sex, etc.).

4.2 Sex

Little research has examined the question of the potential moderating effect of sex. Among those studies, Rattel et al. (2020) used 15 neutral, threat, loss, achievement, and recreation-related

movies clips to assess affective differences between men and women. Emotion response estimates were measured for each clip using facial corrugator and zygomatic electromyography (EMG). EMG results were related to self-reported measures of emotional experiences taken at the end of each film. Arousal (excited/calm) and valence (pleasant/unpleasant) ratings were taken into account to characterize the emotional experience. The results showed that women have a more negative PEP reactivity compared to men and higher arousal and valence. Moreover, they also showed that women have higher concordance between arousal physiology and performance, as revealed by PEP reactivity.

4.3 Pathologies

The effect of different pathologies on PEP has also been studied. Beauchaine et al. (2001) showed a blunted PEP reactivity in attention-deficit hyperactivity disorder (ADHD) children compared to control children in a repetitive motor task in which rewards were given or removed across trials. Tanenbaum et al. (2018) explored the effect of ADHD on PEP reactivity during a Go/No-Go task. This study showed that compared to the control group that demonstrated a negative PEP reactivity during the cognitive task, ADHD children showed a reduced and positive PEP reactivity, possibly because they mobilized proportionally less effort, or lack the motivation to engage appropriately in the task.

Cellini et al. (2013) and Covassin et al. (2010) explored the effect of primary insomnia on cardiovascular changes and cognitive performance. These studies found sympathetic hyperarousal (e.g., HR increasing and PEP decreasing) at rest and during the tasks evaluating inhibition and working memory along with cognitive deficits in insomniacs compared to good sleepers. However, while evidence of both cognitive impairments and cardiovascular hyperarousal were shown in both studies, a clear relationship between the two phenomena is lacking. Indeed, no significant correlation was found between performance and physiological data, suggesting that different pathways might be at play.

Finally, several studies were interested in the effects of major depressive disorder (MDD) and dysphoria on sympathetic activity and cardiac reactivity (Ahles et al., 2017; Bair et al., 2020; Brinkmann & Franzen, 2013; Brinkmann et al., 2009, Franzen & Brinkmann, 2015; Franzen & Brinkmann, 2016, Franzen & Brinkmann, 2016b; Franzen et al., 2019; Silvia et al., 2014). MDD patients showed dysfunctional motivation and affective dynamics associated with anhedonia. In this population, PEP reactivity was positively associated with task performance, with smaller PEP reactivity during cognitive tasks in depressive compared to a healthy control group. Brinkmann and Franzen (2013), Brinkmann et al. (2009), and Franzen and Brinkmann (2015) showed that while for non-dysphoric adults there was a linear relation between PEP reactivity and reward, for dysphoric patients, the relation was not linear and PEP reactivity was blunted. In addition to reward, punishment also resulted in a reduced PEP reactivity, but while self-reported reward wanting (the motivation to obtain a reward) was blunted with reward (Franzen & Brinkmann, 2016; Franzen & Brinkmann, 2016b; Franzen et al., 2019), it was normal with punishment (Franzen & Brinkmann, 2016). Hence, it seems that these patients show a blunted effort-related sympathetic activity. Following Brehm's theory (Brehm & Self, 1989), depression could affect effort through changes in appraised task difficulty and/or changes in appraised goal importance.

All the studies reported in this section showed different sources of PEP inter-individual variability, such as ADHD and MDD which reduce effort-related sympathetic activity. Mental stress and insomnia were reported to be responsible for sympathetic and cardiovascular hyperarousal. Age and sex may also affect resting PEP and PEP reactivity. However, their actual and direct causal influences need to be carefully tested in controlled studies. All this variability in raw PEP and PEP reactivity values calls for carefully controlling studies' settings (e.g., same recording position, lighting of the room, see below) and participants' characteristics (e.g., age, sex, health condition, etc.).

Moreover, if inter-individual variability influences PEP value, between-subject designs might not be the best way to study PEP, especially if the groups of participants are heterogeneous in age, sex, physical and psychiatric condition, health history, and other variables. As such, the reliability of other designs examining variations of PEP as a function of effort mobilization, like the within-subject design, must be studied, as reviewed in section 5.2 of this article.

5 Methodological limits

5.1 Confounding factors

Several physiological parameters that can affect PEP measures must be considered when preparing experiments. First, it has been shown that the dissipation of catecholamines concentration (adrenaline and noradrenaline) lasts for about 9 seconds, affecting β -adrenergic receptors during this period (Kuipers et al., 2016; Mokrane & Nadeau, 1998). As it has been said, PEP is largely influenced by the sympathetic activity, acting via catecholamines and β -adrenergic receptors. The sympathetic reaction to an event could thus last up to 9 s. Therefore, to study the action of the sympathetic activity during a task, it might be preferable to use a long enough inter-trial interval to ensure that the influence of sympathetic activation on those receptors is over before the subsequent trial is administered. An inter-trial interval of at least approximately 10 s should thus be recommended when studying PEP during an event-related design.

Second, sympathetic activity is not the only parameter influencing the duration of the PEP. Indeed, as mentioned above, the Frank-Starling mechanism shows that HR changes can occur without sympathetic control, and this change in HR can modulate the PEP. A decrease in HR will increase the volume of blood that has more time to accumulate in the ventricle, which puts more pressure on the walls (preload). This pressure is likely to increase the contractility of the ventricle, decreasing the PEP (Krohova et al., 2017; Newlin & Levenson, 1979; Sherwood et al., 1990).

Similarly, decreasing diastolic blood pressure (DBP) reduces the ventricular pressure required to open the aortic valve (afterload). This results in the valve opening more quickly after

depolarization, and thus PEP will decrease accordingly. It is thus highly recommended to record and to report HR and BP during experimentation to verify that the effects observed on PEP are only due to sympathetic activity changes. PEP reflects increases in beta-adrenergic activity only when HR and BP are stable or increase (Krohova et al., 2017; Newlin & Levenson, 1979; Sherwood et al., 1990). Importantly, factors such as chronological age or pathology (e.g. Parkinson's disease, diabetes, Lyme disease) independently affect HR and BP and thus must be considered. Also, some behavioral or experimental factors could potentially affect HR and BP, and thus could indirectly impact PEP. For instance, at the start of an experiment, if a participant is strongly stressed about the experimentation, he/she could have a high HR, which will reduce during the experiment when he/she relaxes despite the cognitive stimulation and thus PEP could change not only because of mental effort but because of simple relaxation.

Third, body position significantly affects PEP values (Houtveen et al., 2005), with the largest PEP when standing, followed by sitting and subsequently lying down (see *Table 1*). Keeping the same position during the entire recording period is thus important to avoid confounding variations of PEP values coming from different positions and from the task. In the same vein, standing for a prolonged period of time could decrease DBP, and thus decrease PEP, which is a reason why sitting might be preferable when possible. Furthermore, daytime and lighting conditions also affect cardiovascular reactivity (Adan & Sánchez, 1996; Rüger *et al.* 2006) by affecting for example sleepiness and alertness, which can affect performance, concentration or the amount of mental effort participant invests into a task. For example, Zauner et al. (2020) showed the impact of these parameters on PEP reactivity, which was shown to be stronger during late afternoon and with medium luminosity. Additionally, colder light resulted in less effort mobilization and a smaller sympathetic activation with the same performance. These parameters may thus need to be constant in experiments and be specified in the methods of published studies.

5.2 PEP in within-subject studies

A lot of PEP studies in cognitive psychophysiology have used either between-subject design or a single task (e.g., Rahman et al., 2018; Silvia et al., 2014) without repetition. This implies that the intra-individual evolution of PEP as a function of experimental conditions when conducting repeated measures of the same task is poorly known. To use PEP as a physiological index of mental effort, it is important to know the reliability of this measure over time within the same subject. From an applied perspective, if one wants to use PEP and/or PEP reactivity to anticipate or prevent overload or incapacitation at work or in challenging situations, it is essential to disentangle the effects of time on task and the effects of task difficulty as well as the effects of recovery period within the same subject. For example, would the same results be observed in a study where PEP reactivity would be investigated at different levels of difficulty using a within-subject design (i.e., every participant would perform all levels in a row) compared to a study using a between-subject design (i.e., every participant would perform only one particular level of difficulty)? Could there be a habituation effect on PEP after a while? Would there be a clear disengagement with sudden positive PEP reactivity when the task becomes impossible? After a thorough search of the existing literature, no definite answers to these questions were found, partly because of the lack of information in the published studies and because these questions were never directly addressed. Although some published articles have used PEP in a within-subject design (18 out of 52 articles cited in this review, see *Table 2*), most of these articles did not address these questions.

Some responses can be inferred by examining the existing literature. For example, Kelsey et al. (2007) studied the reliability of cardiovascular reactivity. Using three combinations of different stress inducing tasks (and analyzing the Cronbach's α coefficient of internal consistency), they found that there was a high within task reliability for all tasks, but test-retest and across tasks reliability was high only with mental arithmetic tasks. Indeed, reliability declined

when video game and cold pressor tasks were added to the task list. Which suggest that across task consistency of cardiovascular reactivity could be limited.

Regarding possible habituation effects, some studies have started to tackle these questions such as the ones from Kelsey et al. (2000 and 2003) (see above, Section 3) that showed a habituation of PEP reactivity across repeated presentation of the same stress task. In addition, Plain et al. (2020) studied effort mobilization using a speech-in-noise task. Participants were asked to repeat a sentence they heard with lower and higher frequencies masking (from -1 to -21 dB) covering the speech, and with either a high or low reward (5€ vs 0.20€). The signal-to-noise ratio (SNR) was manipulated with a within subject design. The researchers found that effort investment during listening varied as a function of task demand and motivation (manipulated by reward). More precisely, the relationship between task demands during the speech-in-noise task and PEP reactivity was somewhat linear. PEP reactivity was the most negative at the lowest signal-to-noise ratio (-21 dB), indicating greater effort investment compared to higher SNRs. The behavioral results, which showed that the percentage of correct responses was higher for the lower ratio of -1 dB (91.6%) than for the higher ratio of -21 (2.7%), supported these physiological results. No effect of reward on PEP reactivity was observed. The results of Plain et al. showed no visible sign of habituation or physiological drift during the experiment (see *Figure 4-A*) because the six ratio levels were presented in either descending or ascending order. However, only PEP reactivity, calculated as the difference between PEP during each speech-in-noise task condition and resting PEP just before the task, was reported in the results. In other words, the six experimental conditions were each preceded by a 5-min resting condition. Unfortunately, the study did not report the mean absolute PEP values for the experimental or resting conditions, preventing the possibility to examine the dynamic of raw PEP values. Interestingly, in addition to the classic block wise analysis method to study PEP reactivity, this study used also an event-related analysis method. For this method, instead of averaging all the PEP data in a block, they selected the PEP

that occurred only during the presentation of a target sentence and then averaged these specific PEP for each block (see *Figure 4-B*). With this event-related method, as for the block-design one, no significant effect of reward was found, but a linear contrast revealed a significant effect of SNR, with a stronger PEP reactivity at the lower SNRs. This method also showed that while most of the PEP reactivity values found with the block wise analysis were positive (indicating that PEP during task was actually longer than PEP during rest), in the event-related analysis, most of the PEP reactivity values were negative. These results, although showing a small effect size of task difficulty on PEP reactivity in a within-subject design, suggest that an event-related analysis of PEP might be possible and sensitive to task demand.

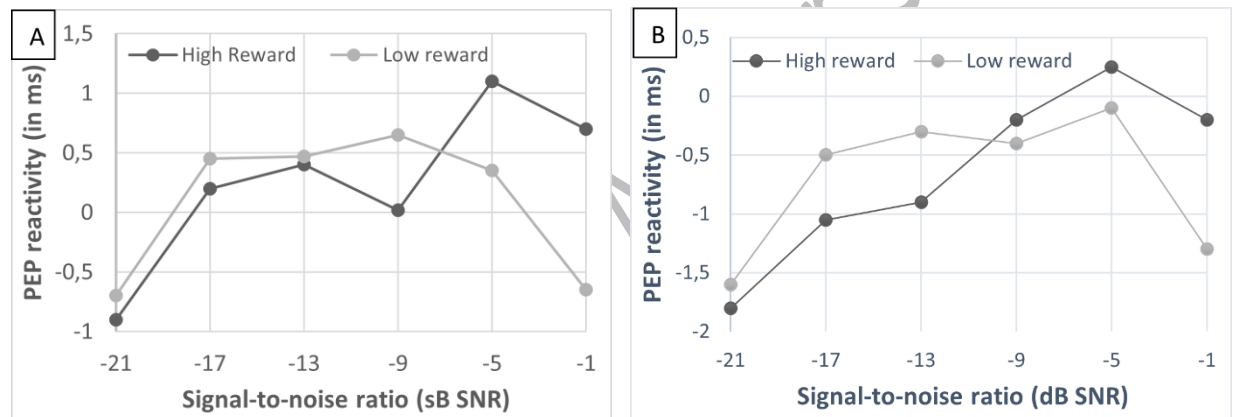


Figure 4: Reproduction of Plain et al.'s (2020) results for PEP reactivity (in ms) during a speech-in-noise task performed by two groups of participants (high reward vs low reward). The authors performed a block-wise analysis (A) or a target stimuli (event-related) analysis method (B).

Another study that used a within-subject design is from Brenner et al. (2005). The authors used six blocks of a 2-min repetitive simple decision task, each separated by 2.5 min of rest. Reward and extinction of reward conditions were manipulated within and between blocks. Results showed that PEP reactivity was significant during reward but not during extinction, and a linear trend analysis indicated that there was a significant habituation effect on PEP reactivity across

reward conditions. The first reward block had the strongest PEP reactivity and the last reward block had the weakest PEP reactivity (see Figure 5). Thus, contrary to Plain et al. (2020), this study showed a possible form of habituation of PEP reactivity across conditions in a within-subject design.

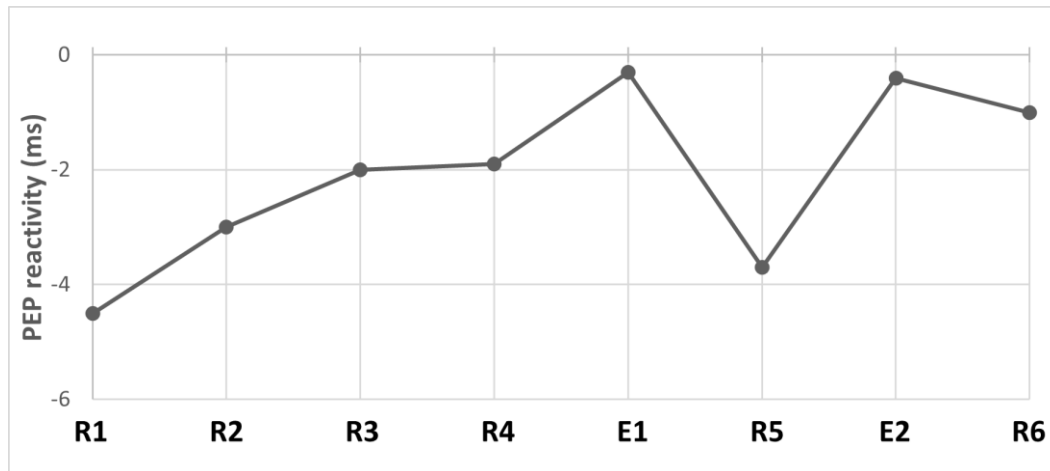


Figure 5: Reproduction of Brenne et al.'s (2005) results for PEP reactivity (in ms) during a repetitive response task across conditions of reward (R) or extinction of reward (E).

One aspect of the evolution of PEP as a function of time-on-task that has been studied in a within-subject design is the recovery time after a simulated rescue operation in virtual reality. Czarnek et al. (2021) showed that it takes about one to two minutes for PEP to return to baseline after the task completion. Their findings suggest that task-related sympathetic activity dissipates rather quickly. An inter-task interval no shorter than one minute is thus necessary to avoid the effect of the previous task on subsequent measurements. However, this study was conducted only on white fit males of the same age. Replication studies using different cognitive/physical challenging tasks and populations would be necessary to increase the generalizability of these results.

Finally, some studies, like the one by Mezzacappa et al. (2001), measured PEP over time in the same participants during different tasks but did not report the PEP evolution over time. Such missing information prevents us from finding definite answers about the PEP evolution over time

during cognitive tasks from the few within-subject studies literature. Moreover, the lack of information is critical for understanding how resting PEP and PEP reactivity are operationalized in within-subject studies. It is often not clear or not mentioned whether resting PEP is based on a single period at the start of the experiment or based on the successive resting periods between the challenging tasks. Knowing the evolution of both resting PEP and task PEP as a function of time is critical in this context because the results and their interpretation would potentially greatly differ. The articles reviewed here reported contradictory results on a possible habituation of PEP over time. Lastly, very recent studies reported that PEP reactivity appears stronger or significant only during the very first minute of task activity, going back to baseline level afterward, whatever it was demonstrated using a between-subject design (Framorando & Gendolla, 2018a; Framorando et al., 2023) or a within-subject design (Albinet et al., 2023). More work is needed using within-subject design to better understand this dynamics and how PEP reacts over time during and after a series of challenging tasks, task repetitions, or tasks difficulty levels.

Nevertheless, one must notice that the within-subject design is not without methodological limitations. Having the same participants administered with all task conditions significantly increases the length of the study time, not to mention the need to have individual baseline periods before each new task condition. Also, the benefit of lowering the number of participants (because they each perform all the task conditions) may be at the cost of an increased need of participants to counterbalance the condition order between participants. However, although requiring methodological assumptions, within-subjects design when correctly controlled, offers greater statistical efficiency (Geenwood, 1976; Howell, 2012).

6 Recommendations:

Some of the articles cited in this review present some issues or lack information about the mentioned concerns. For example, several articles did not present raw data, such as mean resting PEP (e.g., Annis et al., 2001; Cellini et al., 2013; Montoya et al., 1997; Rattel et al., 2020; see

Table 1). They only presented their results in the form of PEP reactivity, standard deviation, or log-transformed data. As discussed in the preceding section, the results presented in most of these articles did not specify how absolute PEP evolves as a function of experimental conditions or time. Knowing the mean resting PEP is important for understanding better the high variability of PEP values found in the literature. A careful look at the PEP measurement methods in the published papers does not show much difference in the literature that could explain this high variability. Research articles should describe their data collection method as clearly and precisely as possible to increase access to this valuable information.

Some factors that need to be controlled during an experiment and reported in the article include the homogeneity of participants (age, sex, existing condition, physical health), participants' position, lighting of the room, as well as the time of the day. Resting periods also need to be recorded, such as their length and when they are recorded during the experiment, as it is recommended to have a resting period between each task or block to allow PEP to return to baseline without influencing the subsequent task. Resting periods, inter-stimuli intervals, the method used to identify the Q and B points, and the placement of the electrodes on the body should also be reported. HR and DBP should be recorded and reported because of their potential confounding role in measuring PEP variations.

Moreover, while the mean PEP is important, so is PEP reactivity, as it shows the evolution of sympathetic activity between resting and task periods; thus, both need to be reported in articles. Finally, in within-subject designs, the important question of baseline or resting periods needs to be addressed. It is argued here that a resting period needs to be present between each task to calculate PEP reactivity from the resting period right before the task and not just from a delayed baseline measure. Indeed, although PEP recovery appears to be rather quick after one task (see Czarnek et al., 2021), little is known about its evolution on repeated measures. Comparing PEP values during a particular task with resting PEP values, taken just before that task, should allow

us to measure PEP reactivity more accurately by assessing the exact effect of the task, and not the effect of accumulating time, when the resting is taken only once at the beginning of the experiment.

A final recommendation concerns the necessary reflection on the interpretation of the physiological measure of PEP as an indicator of effort in mental activities. As first introduced by Cacioppo and Tassinari (1990) and thoroughly discussed in the context of motivation, by Richter and Slade (2017), and in the context of mental workload by Backs (2000), the relationship between a psychological state and a physiological response is not always unique and specific (e.g., a one-to-one relation), nor context-free (i.e., generality). To be considered as a marker of an individual's effort mobilization, PEP must show that it has a direct one-to-one relation with the mental state; that is, it is affected only by this mental state and not by changes in any other psychological variable, within a given context or for a given category of individuals (Cacioppo & Tassinari, 1990). If this marker is general, that is, unspecific to a situation, it is called an invariant. As reviewed by Richter and Slade (2017), those conditions are very difficult to be fully studied and validated. However, elucidating whether or not PEP is a marker or an invariant of mental effort is of critical importance, particularly in the context of within-subject studies, where the researcher generally wants to demonstrate that changes in mental effort directly lead to changes in PEP value, or inversely, that a modulation of PEP value directly predicts the level of mental effort once invests in a task. One must note that if this specificity is not demonstrated, the physiological measure can be described as an outcome (context-limited one-to-many relationship) or a concomitant (general one-to-many relationship) of the psychological phenomenon. This does not preclude the demonstration of a true valid relationship between the two phenomena, but this reduces the uniqueness of the relationship and hence the possible interpretation of the relationship. As such, other variables that may have direct effect on PEP value for example (see Section 5.1) must be controlled for before a valid conclusion can be done.

7 Conclusion:

This article presented the cardiac PEP, its relationship with the ANS, the methods used to record it, and its utilization in past studies in the cognitive psychophysiology field. PEP is an indicator of myocardial contraction that is considered the most reliable noninvasive measures of β -adrenergic sympathetic activity on the heart. A decrease in PEP indicates an increase in sympathetic activity.

PEP responds somewhat proportionally to an individual's task engagement, meaning that a β -adrenergic effect on the heart mediates energy mobilization in active coping. This energy is thought to be proportional to difficulty as long as success is possible. When mental workload increases, behavioral and physiological adaptability increases to reduce the decrement in performance, but when the required effort exceeds the individual capacity (or when motivation disappears), there is a task disengagement, and PEP returns to baseline levels. Indeed, the principle of resource conservation moderates and limits automaticity effects on effort mobilization. Brehm's motivational intensity theory (Brehm & Self, 1989), which follows the principle of resource conservation, has been proposed as a good model for the physiological response involved in effort mobilization. Numerous findings support Brehm's theory; however, much work is still needed as other studies have reported results inconsistent with that theory (e.g., Mallat et al., 2020; Silvestrini & Gendolla, 2013). Furthermore, this theory deserves to be tested more fully using a within-subject design.

Mental state, emotions, or even some psychological and psychiatric pathologies can influence PEP. Several confounding factors, such as HR, afterload, preload, cardiovascular issues, or BP, should also be considered and deserve future systematic examination in this field. If PEP becomes validated in within-subject studies, more applied research should then be conducted to examine the pertinence of this physiological index as an individual measure of mental workload, overload, and prevention of incapacitation in more ecological settings.

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