

Stress-Induced Alterations of Left-Right Electrodermal Activity Coupling Indexed by Pointwise Transinformation

M. SVĚTLÁK^{1,2}, P. BOB^{2,5}, R. ROMAN^{1,5}, S. JEŽEK³, A. DAMBORSKÁ^{1,5}, J. CHLÁDEK^{4,5}, D. J. SHAW⁵, M. KUKLETA^{2,5}

¹Department of Physiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic,

²Department of Psychiatry, First Faculty of Medicine, Charles University, Prague, Czech Republic,

³Department of Psychology, Faculty of Social Studies, Masaryk University, Brno, Czech Republic,

⁴Institute of Scientific Instruments, Academy of Sciences of the Czech Republic, Brno, Czech

Republic, ⁵CEITEC – Central European Institute of Technology, Masaryk University, Brno, Czech Republic

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Summary

In this study, we tested the hypothesis that experimental stress induces a specific change of left-right electrodermal activity (EDA) coupling pattern, as indexed by pointwise transinformation (PTI). Further, we hypothesized that this change is associated with scores on psychometric measures of the chronic stress-related psychopathology. Ninety-nine university students underwent bilateral measurement of EDA during rest and stress-inducing Stroop test and completed a battery of self-report measures of chronic stress-related psychopathology. A significant decrease in the mean PTI value was the prevalent response to the stress conditions. No association between chronic stress and PTI was found. Raw scores of psychometric measures of stress-related psychopathology had no effect on either the resting levels of PTI or the amount of stress-induced PTI change. In summary, acute stress alters the level of coupling pattern of cortico-autonomic influences on the left and right sympathetic pathways to the palmar sweat glands. Different results obtained using the PTI, EDA laterality coefficient, and skin conductance level also show that the PTI algorithm represents a new analytical approach to EDA asymmetry description.

Key words

Electrodermal activity • Pointwise transinformation • Autonomic nervous system • Asymmetry • Stress

Corresponding author

R. Roman, Department of Physiology, Faculty of Medicine, Masaryk University, Kamenice 5, 625 00 Brno, Czech Republic.

Fax: +420 549496338. E-mail: roman@med.muni.cz

Introduction

The integration of visceromotor, neuroendocrine, and behavioral responses to environmental demands is necessary for adaptive stress responses. The part of the complex network of brain systems involved in this integration, which controls autonomic regulatory mechanisms, is conceptualized as the central autonomic network (Benarroch 1993, Hagemann *et al.* 2003). Recent data show that repeated stress exceeding the adaptive capacity of the subject, especially in early childhood, may result in functional and/or structural changes at various levels of this network (Teicher *et al.* 2003, Bremner 2006). An increasing number of studies demonstrate different regulatory influences of the left and right cortical hemispheres on autonomic nervous system (ANS) functions. This may explain why cerebral lateralisation is an important feature in the regulation of the somatic stress response, including its psychosomatic consequences (Wittling 1995, Papousek and Schulter 2001, Coan and Allen 2003, Davidson 2004).

In this context it is interesting that stress can alter or even reverse measures of functional hemispheric specialization during cognitive processing in healthy subjects (Gruzelier and Phelan 1991, Asbjörnsen *et al.* 1992, Grillon and Davis 1995). The results of studies

obtained in patients exposed to severe stress also describe similar findings (Shalev *et al.* 1988, Schiffer *et al.* 1995). One possible explanation for the reversal of hemispheric asymmetries under stress is that the efficiency of a hemisphere is best when overall arousal is intermediate. It is hypothesized that if the arousal of the specialized hemisphere passes a critical limit, the other hemisphere predominates and asymmetries will reverse (Bradshaw 1989, Gruzelić 1993, Papousek and Schulter 2006). Decreased interhemispheric communication during anxiety represents another potential explanation (Compton 2008). From these findings it has been suggested that stress-induced changes of functional hemispheric specialization can lead to hemispheric imbalances in ANS, thus representing a link between psychological factors and autonomic regulation/dysregulation (Mayer 2000, Papousek and Schulter 2002).

An effective approach to laterality research is the analysis of electrodermal activity (EDA), providing bilateral measurement of two parallel outputs of the ANS. So far, investigations in this area have focused on the relationship between EDA asymmetry and hemisphere activation by various stimuli, and between EDA asymmetry and psychopathology. To date, the results of a vast number of studies are contradictory and do not suggest a unifying neuropsychological model for EDA asymmetry and its relation to stress and stress-related psychopathology (Freixa i Baqué *et al.* 1984, Hugdahl 1988).

A different and relatively new approach to the analysis of EDA asymmetry is represented by the method of pointwise transinformation (PTI), which was derived from time-series analysis (Lambertz 2000, Stam 2005). The method of PTI is a complement to the classical linear correlation analysis. The correlation analysis measures only linear dependencies, and the coefficient of laterality designed by Schulter and Papousek (1998) measures only differences in amplitude. In contrast, PTI can measure nonlinear as well as linear dependencies between two coupled time series (e.g. bilateral EDA measurements of the left and right hand). PTI enables the detection of changes in the coupling of two interacting systems. It tells us how much information (represented by bits) of one signal is predicted by another; i.e. to which extent they are dependent on each other. High PTI indicates a large coupling, and PTI close to zero means that the two investigated variables are independent entirely. PTI analysis applied on bilateral measurement of

electrodermal activity indexes the level of left and right EDA coupling, i.e. the left-right EDA coupling pattern. The suitability of nonlinear coupling analysis applied on bilateral EDA has been verified (Kettunen and Ravaja 2000, Rachow *et al.* 2011).

Recently, the superiority of PTI over linear analysis of EDA asymmetry was demonstrated in distinguishing attentional states (Bob 2013). Furthermore, PTI has been found to index psychosensory symptoms, revealing its utility for assessing epileptiform changes in alcohol-dependent patients (Bob 2011). Although PTI seems to be a beneficial and promising approach, providing additional information in EDA asymmetry research, only recently has it been applied in this manner. We propose that this relatively new analytical approach could shed more light on the so far contradictory results emerging from research into EDA asymmetry vis-à-vis stress and stress-related psychopathology.

In the present study we applied the PTI calculation to bilateral EDA recordings in order to measure the following: (1) Whether or not acute mild experimental stress (Stroop Colour-Word Test) induces specific changes in electrodermal activity asymmetry, specifically, changes in the left-right EDA coupling pattern indexed by PTI; (2) Whether these changes are associated with psychometric measures of chronic stress, i.e. with raw scores of psychometric measures of stress-related psychopathology; (3) Whether PTI is associated with the level of arousal.

Methods

Participants

Ninety-nine healthy university students participated in the study (69 males and 30 females; mean age 23.6 ± 1.3). The exclusion criteria were organic diseases of the CNS, any form of epilepsy, psychiatric disorders, alcohol dependence, drug abuse, sensory disorders and medical syndromes related to the skin, endocrine and metabolic disorders, cardiovascular diseases, and other internal diseases. All participants were right-handed according to the Waterloo Handedness Questionnaire (Elias *et al.* 1998). The study was approved by the University's ethical committee and all participants gave their written informed consent.

EDA measurement and Stroop word-colour test

Electrodermal activity (EDA) was recorded bilaterally using Psylab data acquisition system (Contact

Precision Instruments). With respect to nonlinear data analysis (Kantz and Schreiber 1997), recordings were sampled at 1000 Hz. Measurements were performed in a quiet room with a temperature of approximately 23 °C, using two pairs of Ag/AgCl electrodes with 8 mm active area diameter filled with electroconductive paste. The electrodes were attached to the medial phalanges of the index and middle finger of each hand.

Subjects were seated comfortably in a chair in front of a monitor situated approximately 100 cm from their eyes. After a five-minute rest period, during which subjects sat quietly with their eyes closed, EDA was recorded in four experimental conditions: (1) 120 s of the first rest state with eyes closed; (2) 40 s of a non-conflict Stroop task; (3) 40 s of a conflict Stroop task; (4) 120 s of the second rest state with eyes closed. The non-conflict and conflict Stroop tasks were discontinued by a rest period with eyes closed. This rest period was ended and the conflict Stroop task started when the EDA signal decreased to values obtained during the first rest state. In each Stroop task condition (Stroop 1935) four coloured visual stimuli were presented on a computer screen for 3 s with 7 s inter-stimulus interval. The stimuli were colour words naming the colour of the ink in the non-conflict task condition (e.g. GREEN written in green ink) and a different colour in the conflict task condition (e.g. GREEN written in red ink). The participants were asked to name the colour of the stimuli.

Psychometric measurement

For screening general distress and traumatic stress symptoms, we employed revised version of the Trauma Symptom Checklist (TSC-40; Briere and Runtz 1989). The inventory has 40 questions and the subjects indicate the degree of their experience on a 4-point Likert scale. The TSC-40 was developed to assess the adult symptom patterns associated with a history of victimizations, especially childhood sexual abuse, but it is also suitable for measuring general chronic stress symptoms (scores range from 0 to 120; Cronbach's alpha: 0.91, test-retest reliability after one week: 0.88).

For screening of depression, the self-reported Beck Depression Inventory (BDI-II; Beck *et al.* 1996) was utilised. The inventory has 21 items on a 4-point Likert scale (scores range from 0 to 63; Cronbach's alpha: 0.89, test-retest reliability after one week: 0.85).

The anxiety symptoms were measured using a Self-reported Anxiety Scale (SAS; Zung 1971). The inventory has 20 items on a 4-point Likert scale (scores

range from 20 to 80; Cronbach's alpha: 0.81, test-retest reliability after one week: 0.82). All the questionnaires were administered before EDA measurement in a quiet room with the help of a clinical psychologist.

Data analysis

We applied both linear and nonlinear analyses to EDA measurements. The traditional linear analysis of electrodermal activity in each experimental condition included the calculation of mean and standard deviation of EDA signal (skin conductance level; SCL). In assessing the level of arousal induced with the Stroop task, we chose as our parameter SCL expressed with respect to the first rest condition. To assess the degree of EDA asymmetry with a linear analysis approach, we calculated for every time-point within the recording period comprising each condition the difference in EDA signal between the right and left side, divided by their sum. The statistical mean of these values, multiplied by 100, was then used as the laterality coefficient (LC) for that condition. This is analogous to the measure employed by Schuster and Papousek (1998), except that it was applied to every time-point rather than just the peak of the skin conductance response. LC ranged from +100 to -100, with positive or negative values indicating higher EDA on the right or left hand, respectively.

The nonlinear analysis was performed using the software package Dataplore®, which analyses signals and time-series data using the algorithm for pointwise transformation (PTI). The PTI of two observable quantities was derived from Shannon's information concept and is calculated from the probability densities of the observables in the phase space (Lambertz *et al.* 2000, Liang *et al.* 2001). PTI provides information about a random variable being stochastically dependent on a second variable (the output unit is "bit").

For statistical analysis we used SPSS (version 19.0). We conducted a repeated-measures analysis of variance (ANOVA) with Huynh-Feldt correction to examine the effect of the within-subject manipulation of stress level with one between-subject factor of sex. To describe the influence of our predictors (rest and Stroop task, and stress-related psychopathology) on the changes in PTI, we used a multilevel regression model (Singer and Willett 2003). This permitted a statistically more powerful test of the influence of our predictors on the change in PTI. Using the MIXED procedure in SPSS 19 with full ML estimation we regressed individual PTI measurements (Level 1) on the level of stress, coded 0 for

Table 1. Mean PTI, LC, and SCL values during all conditions.

		Rest I	Non-Conflict Stroop	Conflict Stroop	Rest II
PTI	<i>Males</i>	1.77 (±0.53)	1.36 (±0.39)	1.45 (±0.37)	1.97 (±0.52)
	<i>Females</i>	2.07 (±0.35)	1.69 (±0.33)	1.72 (±0.31)	1.96 (±0.65)
	<i>Total</i>	1.86 (±0.50)	1.46 (±0.40)	1.53 (±0.37)	1.96 (±0.56)
	<i>Min</i>	0.29	0.55	0.38	0.94
	<i>Max</i>	2.41	2.36	2.33	2.41
LC	<i>Males</i>	1.92 (±14.91)	1.80 (±15.76)	1.92 (±15.62)	1.90 (±14.87)
	<i>Females</i>	0.02 (±13.39)	-0.05 (±11.75)	0.62 (±11.54)	0.03 (±13.20)
	<i>Total</i>	1.35 (±14.43)	1.24 (±14.63)	1.52 (±14.46)	1.30 (±14.33)
	<i>Min</i>	-35.30	-33.67	-32.26	-36.10
	<i>Max</i>	46.53	47.30	47.99	45.98
<i>SCL_{left}</i>	<i>Males</i>	2.62 (±1.63)	3.06 (±1.88)	3.03 (±1.80)	2.97 (±1.67)
	<i>females</i>	1.99 (±1.57)	2.47 (±2.04)	2.40 (±1.97)	2.28 (±1.86)
	<i>Total</i>	2.43 (±1.63)	2.88 (±1.93)	2.84 (±1.86)	2.76 (±1.74)
	<i>Min</i>	0.54	0.53	0.49	0.58
	<i>Max</i>	9.04	9.63	9.14	8.68
<i>SCL_{right}</i>	<i>Males</i>	2.75 (±1.78)	3.18 (±2.08)	3.16 (±2.04)	3.11 (±1.83)
	<i>Females</i>	1.97 (±1.30)	2.28 (±1.49)	2.24 (±1.42)	2.17 (±1.42)
	<i>Total</i>	2.52 (±1.68)	2.91 (±1.96)	2.89 (±1.92)	2.83 (±1.76)
	<i>Min</i>	0.52	0.53	0.49	0.74
	<i>Max</i>	9.47	12.90	12.61	11.0

PTI – pointwise transinformation (in bits); LC – laterality coefficient; SCL – skin conductance level (μS). Values are means (\pm SD).

resting and 1 for the stressing conditions (unconditional growth model). We then added the raw scores of psychometric measures of stress-related psychopathology to this model.

Results

Mean PTI values for both sexes within the experimental conditions are presented in Table 1. The results indicate that PTI was affected by experimentally induced stress [$F_{\text{corr}}(2.6; 250.2)=24.01$; $p<0.001$, $\eta^2=0.20$]. Specifically, mean PTI values decreased under the non-conflict and conflict Stroop tasks relative to the rest conditions (Fig. 1). Custom non-orthogonal contrast analysis of PTI values revealed that the rest conditions pooled together differed significantly from the task conditions pooled together [$F(1; 97)=63.61$, $p<0.001$, $\eta^2=0.40$], but the two task conditions did not differ from one another [$F(1; 97)=1.59$, $p=0.21$, $\eta^2=0.02$]. No difference between the two rest conditions was found, either [$F(1; 97)=0.34$, $p=0.56$, $\eta^2=0.003$]. Females achieved consistently higher levels of PTI in all experimental conditions by approximately 0.3 points [$F(1; 97)=14.73$, $p<0.001$, $\eta^2=0.23$], with the exception

of the second rest condition at the end of the protocol where the sex difference disappeared making the interaction between sex and stress statistically significant [$F_{\text{corr}}(2.6; 250.2)=3.06$, $p=0.036$, $\eta^2=0.03$].

The application of a multilevel regression model did not reveal any association between raw scores of TSC-40 (mean score: 24.5 ± 12.1 ; min 3, max 62), SAS (mean score: 33.4 ± 6.5 ; min 22, max 58), BDI-II (mean score: 8.0 ± 5.8 ; min 0, max 29) and the resting level of PTI or the amount of stress-induced PTI change.

To evaluate the relationship between LC and experimental stress we followed the same analytic procedure as described above with the PTI. The results indicated that LC is not affected by the non-conflict and conflict Stroop tasks [$F_{\text{corr}}(2.5; 251.5)=0.87$, $p=0.39$, $\eta^2=0.009$]. The analysis also revealed no significant differences in LC values between males and females within any task condition [$F(1; 97)=0.61$, $p=0.39$, $\eta^2=0.006$], nor did it show any interaction between sex and experimentally induced stress [$F_{\text{corr}}(2.5; 251.5)=0.28$, $p=0.59$, $\eta^2=0.003$]. The multilevel regression model did not reveal any association between the stress-related psychopathology (raw scores of TSC-40, SAS and BDI-II), and the resting LC values or the amount of stress-

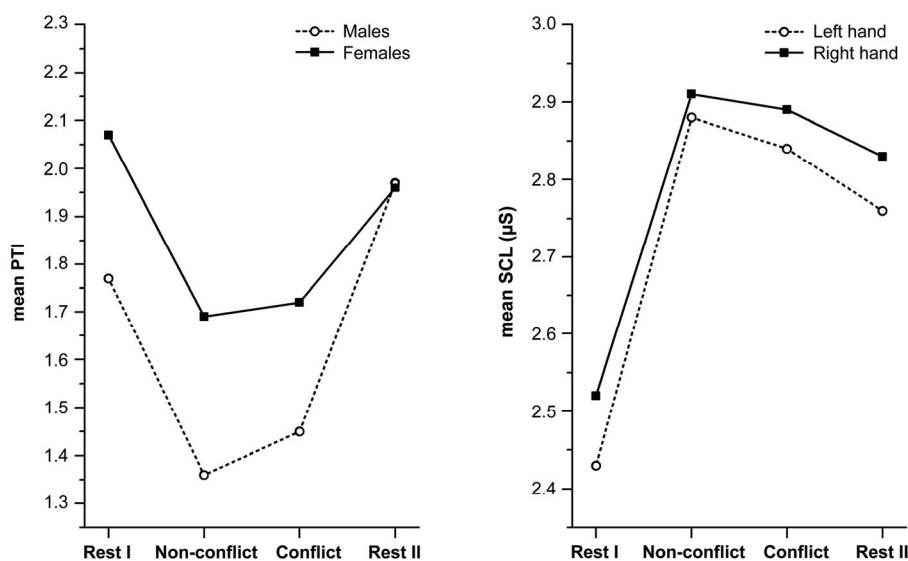


Fig. 1. Mean pointwise transformation (PTI) and skin conductance level (SCL) values during experimental conditions.

induced LC change.

EDA data were also analyzed separately for each hand (left/right). Mean SCL values for both sexes within the experimental conditions are presented in Table 1. The results indicated that EDA is affected by the level of stress on both sides of measurement: left hand [$F_{\text{corr}}(1.8; 162.0)=28.29$, $p<0.001$, $\eta^2=0.24$], right hand [$F_{\text{corr}}(2.1; 197.2)=29.02$, $p<0.001$, $\eta^2=0.24$]. The mean SCL increased significantly under the non-conflict and conflict Stroop tasks (Fig. 1). Custom non-orthogonal contrasts analysis revealed that the rest conditions pooled together differed significantly from the task conditions pooled together [$F(1; 97)=32.20/28.21$, $p<0.001$, $\eta^2=0.26/0.24$]. A significant difference between the non-conflict and conflict condition was identified for the left [$F(1; 97)=4.54$, $p<0.04$, $\eta^2=0.05$] but not the right hand [$F(1; 97)=2.07$, $p=0.15$, $\eta^2=0.02$]. A strong difference between the first and second rest conditions was also observed for both sides of measurement [$F(1; 97)=26.55/35.53$, $p<0.001$, $\eta^2=0.22/0.28$]. A gender comparison of the mean SCL revealed that females had significantly lower values than males [$F(1; 97)=7.5/9.3$, $p<0.01$, $\eta^2=0.07/0.08$]. No interaction between sex and the level of stress on either side of measurement was found: left hand [$F_{\text{corr}}(1.8; 162.0)=0.23$, $p=0.29$, $\eta^2=0.003$], right hand [$F_{\text{corr}}(2.1; 197.6)=1.29$, $p=0.29$, $\eta^2=0.02$].

A relationship between the left-right EDA coupling pattern and the level of arousal was not found in any Stroop task condition. Pearson correlation coefficients calculated between the mean PTI values and percent SCL increase ranged from 0.05 to 0.14 ($p>0.05$).

Discussion

The results of our study reveal lower PTI values during the task compared to rest conditions, which could be conceived as a demonstration of independent regulation of EDA during the stress and rest state. Since the PTI values obtained during the rest states before and after the Stroop tasks did not differ significantly, we attribute the PTI change to the acute mild stress condition itself and not to the time course of the experiment. Our results are in accordance with the findings of Gruzelier and co-workers (1981), who argue that hemispheric influences on EDA response are independent of the influences on the EDA level. The existence of different cortico-autonomic patterns in EDA regulation during the rest and stress conditions is supported also by Lacroix and Comper (1979), who failed to find EDA level lateralization while observing clearly asymmetric responses. Interestingly, the earlier study by Galbrecht and co-workers (1965) showed the opposite.

Recently, other studies have analyzed coupling between physiological systems related less obviously; Moertl *et al.* (2013) and Lackner *et al.* (2011), for example, utilised the phase synchronization index as an indicator of coupling between hemodynamic variables and respiration. Lackner *et al.* (2011) observed a decrease in this index between the respiratory and cardiovascular system during mental stress in comparison to a rest condition. This converges nicely with our results, thereby validating PTI as a useful method for investigating the nature of coupling between physiological systems.

Papousek and Schultze (2001) reported that EDA regulation is associated with anxiety and depression

symptoms. The authors showed that higher right hemisphere activity at the orbitofrontal locations in more anxious individuals is associated with a higher number of nonspecific EDA responses. In more depressive subjects such changes were associated with a higher activity in the left dorsolateral prefrontal regions. One might suppose that the possible higher rate of nonspecific EDA responses on the left or the right hand associated with psychopathology would be reflected in lower PTI values. Nevertheless, we observed no significant association between the level of stress-related psychopathology and left-right EDA coupling pattern indexed by PTI. One possible reason is that the students in our sample with higher rates of psychopathology symptoms probably represented a very heterogeneous group. They likely differed in terms of etiology of the clinical picture which could lead to variable degrees of EDA asymmetry. Moreover, only a few students scored within the clinically significant range.

Obrist (1963) put forward the idea that EDA asymmetry is related to arousal level, arguing that lower levels facilitate asymmetry while higher levels are conducive to symmetry. Contrary to this finding, our results showed no relationship in either task conditions between the left-right EDA coupling pattern indexed by PTI and the level of arousal indexed by SCL percent increase. Also, we did not observe any evidence of decreased EDA asymmetry indexed by LC. Unfortunately, any interpretation of LC is complicated by the fact that contralateral cortical inhibition of EDA cannot clearly be distinguished from ipsilateral excitation (Venables 1983). So far, evidence has been reported both for contralateral cortical inhibition (e.g. Lacroix and Comper 1979) and excitation of EDA (e.g. Myslobodsky and Rattok 1977). Some studies, however, failed to support such results (e.g. Fedora and Schopflocher 1984).

The gender of the participants is an important factor to be controlled in EDA asymmetry research (Boucsein 2012). The results are inconsistent, however; evidence has been reported for smaller lateralization effects both for male (Ketterer and Smith 1977, Boyd and Maltzman 1983) and female participants (Bryden 1979, Rippon 1990). In our study a gender comparison showed that females had significantly higher mean values of PTI during rest and this difference was maintained throughout both Stroop test conditions. This means that the degree to which EDA signals from the left and the right hands were coupled was constantly higher in females compared with men. Our results are in agreement with the findings of

numerous studies dealing with gender differences in hemispheric interactions. For instance, Duffy *et al.* (1996) demonstrated a higher interhemispheric EEG coherence in females relative to males. In their re-evaluation of sexual dimorphism in the human corpus callosum, Oka *et al.* (1999) observed that females have a larger corpus callosum relative to the size of their cortex than have males. It was proposed that the larger corpus callosum enables more interhemispheric communication with regard to language (Bloom and Hynd 2005). Studies using functional neuroimaging during language processing have showed that specific neuronal activity in both hemispheres is higher in females compared with males (e.g. Shaywitz *et al.* 1995, Kansaku *et al.* 2000). Due to the fact that the Stroop conditions in our study involved substantial language processing, the detected gender difference in PTI might also be influenced by these gender differences in hemispheric interactions.

The colour-word interference of the conflict condition has been shown consistently to increase stress relative to the non-conflict condition (e.g. Renaud and Blondin 1997). In the present study, however, no such effect was observed. We speculate that this resulted from a complex interaction of variables that rendered our conflict and non-conflict conditions less contrasting. In particular, during both the conflict and non-conflict tasks, subjects' stress states likely resulted from a complex interaction of many psychosocial variables, such as threat to social status (the subject underwent the experiment in the presence of two experimenters) and a loss of control (the subjects were unfamiliar with the experimental procedure or the task that they would be asked to perform). These overlapping psychosocial variables were probably so strong that the stressfulness of colour-word interference *per se* was attenuated.

In our experimental design the participants were required to speak during the task conditions but not during the rest conditions. It is important to acknowledge that speech activity is assumed to increase the number of nonspecific EDA responses. These artefacts cannot be easily determined, however, since the relationship of speaking to single EDA responses is not clearly detectable (Boucsein 2012). Moreover, the period of speaking was very short in comparison to the duration of the task condition. As such, the degree to which speaking contributes to our results is questionable. Future studies should investigate this further.

In summary, we conclude that acute stress alters the level of coupling pattern of cortico-autonomic

influences on the left and right sympathetic pathways to the palmar sweat glands. The different results obtained using the PTI, EDA laterality coefficient, and skin conductance level also show that the PTI algorithm represents a novel analytic approach to EDA asymmetry description.

Conflict of Interest

There is no conflict of interest.

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