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INTERLINKED POSITIVE AND NEGATIVE FEEDBACK LOOPS DESIGN EMOTIONAL SWEATING

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SUMMARY

Background: *The stereotyped nature of the skin conductance response (SCR) waveform has recently inspired several dynamic modeling approaches to the process of SCR. The suggested models differ: (i) in the order of the linear differential equation representing the process, and (ii) the neurobiological interpretation of the system parameters. While several research groups consider the sympathetic sudomotor nerve activity as the input signal in their models of the SCR, we assume that the initial neural event and feedback regulatory mechanisms that we can comprise with our models take place in the central brain structures. Here we demonstrate a refinement of the system identification procedure with skin conductance response signal, in order to test the thesis of the central meaning of the model's parameters.*

Subjects and methods: *The method consists in the application of the system identification procedure in the MATLAB® software environment in analyzing the SCR. Eleven short stories have been used to elicit emotional arousal in 27 healthy participants.*

Results: *The method for mathematical modeling of the SCR here proposed provides not only the best fitting with empirical SCR signals that has ever been reported, but also insight into the unique underlying control process and the hidden neural input to the SCR system. Through the system identification procedure we showed that there are two interlinked positive and a negative feedback loop which shape the SCR. The control process of SCR showed a linear and a within stimulus-type time invariant.*

Conclusion: *The findings argue in favor of the central nervous system interpretation of the parameters in the presented dynamic model of the SCR response. This encourages the idea of developing a method that could enable estimation of the central nervous system regulatory processes relying on the psychophysiological data.*

Key words: *skin conductance response - electrodermal activity - system identification - mathematical modeling - dynamic model - positive feedback - negative feedback*

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INTRODUCTION

Previous interpretations of dynamic models of skin conductance response

The skin conductance response (SCR) is a component of the output of arousal processing in the central nervous system. The stereotyped nature of the SCR waveform has recently inspired several dynamic modeling approaches to the process of SCR. The published mathematical models differ: (i) in the order of the linear differential equation representing the process (second and third order models have been proposed), and (ii) the neurobiological interpretation of the system's parameters.

While several research groups consider the peripheral sympathetic sudomotor nerve activity as the impulse input in their models of the SCR (Alexander et al. 2005, Bach et al. 2009, Bach et al. 2010a, Bach et al. 2010b, Bach et al. 2010c, Benedek & Kaernbach 2010), we assume that the initial neural event and feedback regulatory mechanisms that we can comprise with our models take place in central brain structures (Branković 2008). In the last case we would be able to derive much more information about the central neural processing from SCR than we used to do, and, what is even more important, to infer about the brain mechanisms in a way that is not achievable by any other available method including invasive ones – to probe the regulation (neurochemistry) of the limbic system (Branković 2008). In agreement with the thesis that the impulse input signal can adequately represent the central neural event in the genesis of SCR stands the observation that one or a few neurons may be responsible for the behavioral output (Lestienne 2001). The position has been already exploited in modeling the brain's transient electrical responses to discrete stimuli – evoked potentials (Rennie et al. 2002).

System identification method in neuroscience

The essence of our approach is to regard the SCR from the control system theory point of view, relying on the well developed system identification theory and technique (Ljung 1999). System identification as a method for the detection of feedback in the central nervous system has been suggested two decades ago (Schnider et al. 1989). The estimation of feedback regulation itself could enable an insight into the interactions among brain structures and neurotransmitter systems (Branković 2008). In that way, system identification could be considered as a potential solution to the task for neuroscience posed by Charney, Bremner, and Redmond (1995): "models which postulate too little or too much of a single neurotransmitter are not consistent with the complex regulation of neurotransmitter systems… there are major functional interactions among different neurotransmitter and neuropeptide systems which make single neurotransmitter theories simplistic… A task for future investigations… is to develop clinically applicable biological tests that can assess the functional interactions among different neurotransmitter and neuropeptide systems and specific brain structures. Successful development of such paradigms could result in improved diagnostic classification and prediction of treatment response…''.

The system identification approach enables us to look into the process of generation and regulation of SCR in a neurophysiologically meaningful way. Thus, through this method we approximate the whole arousal process (from the central initial neural event to the SCR output) as a series of integrators, with the integration constant (e.g. 100 ms), that corresponds to the temporal scale of brain operation (Varela et al., 2001). Relying on the results of the present study we expose further arguments in favor of the thesis that our dynamic models of SCR quantitatively describe the processing of central brain structures.

The "hidden input" problem in SCR modeling

Beside the problem of the neurobiological interpretation of the mathematical models of SCR, there is a methodological obstacle in the field. While the output signal of the SCR system is observable and measurable, the input signal is not directly measurable. Therefore, a separate scientific task is to find an appropriate mathematical representation of the driving input to the SCR system, i.e. to solve the "hidden input" problem (Figure 1). Previously suggested solutions have been to join the impulse function (Alexander et al. 2005, Bach et al. 2009, Bach et al. 2010a, Bach et al. 2010b, Benedek & Kaernbach 2010, Branković 2008) or Gaussian bump function (Bach et al. 2010c) as an input signal temporally located at the beginning of the correspondent SCR. Here, we suggest a new data informed solution for the hidden-input problem. The innovation happened to be crucial in the refinement of our modeling method enabling us to easily achieve almost perfect fit between any measured SCR and the simulated output of structurally the very same model.

The aims of the study are: (i) a further refinement of the system identification procedure with the skin conductance response signal (Branković 2008), and (ii) to test the thesis about the central meaning of the model's parameters (Branković 2008).

SUBJECTS AND METHODS

Participants

Twenty seven healthy volunteers (11 men and 16 women with mean age ± SD of 36.2 ± 7.9 and an average of 14.7 years of education) with no history of psychiatric and neurological treatment took part in the study. The participants were drawn largely from the hospital staff (nurses and medical technicians), but one third had non-medical occupations. All the subjects were right-handed.

Experimental procedure

Eleven short stories from the contemporary literature (without erotic and aversive content) have been chosen to elicit pleasant excitement in subjects. The stories have been chosen in a way to cover a wide spectrum of life situations and experiences (observing a landscape, meeting a parent or friend, parting, etc.). In the pilot-study fifteen healthy subjects reported that they had experienced pleasant excitement while reading the stories. The stories have been divided into meaningful fragments (1-4 sentences), and the number of fragments per story was 4-13. The total number of the fragments obtained in that way is 90. The fragments have been presented to the subjects as slide-presentations on a 15'' monitor. The subjects were instructed to read the stories as they usually do during leisure time and to switch to the next slide by their own clicking a computer mouse. During the slide-presentation skin conductance, heart rate, and respiration of subjects were recorded. The psychophysiological measurement has been performed using the PowerLab® 4/25, GSR Amp, and the software for digital data acquisition Chart 5 for Windows® with the sampling rate of 10 Hz. The slide-presentation and psychophysiological recording started after a five minutes adaptation period to experimental room and equipment. All subjects were tested during afternoons (2-8 P.M.). The room temperature was held between 20 and 22°C. The subjects washed their hands with soap and warm water before the montage of electrodes for skin conductance on the middle phalanges of the second and fourth finger on the left hand.

Data processing

To avoid distortion of SCR shape and amplitude we used raw non-filtered SCR signal as output signal in the system identification procedure. In order to avoid the effect of initial value of skin conductance level (SCL) on the SCR magnitude we divided the raw SCR signal of each subject by the initial value of SCL.

System identification has been performed using the System Identification Toolbox v. 6.0 included in the mathematical software MATLAB® v.7.0 (R14). We defined the state-space model structure and set the fixed parameters and nominal (initial) values of free parameters that enabled successful system identification for every single SCR of each subject in the sample.

The nominal values of the parameters were the following: A=[0 1 0; 0 0 1; -0.3; 0.3 0.5], B=[0; 0; 0.05], C=[1 0 0], D=0, and K=[0]. The structure matrices define the fixed and freely adjustable parameters during the identification process and were the following: A=[0 1 0; 0 0 1; NaN NaN NaN], B=[0; 0; NaN], C=[1 0 0], D=0, and K=[0], whereby NaN denotes unknown parameters to be estimated. The initial state vector was estimated from data, starting from zero values.

Finally, since the experimental signal (SCR) was discrete with the sampling interval of 0.1 s, the sought model was also discrete with the same sampling interval. The total count of modelled SCR in our dataset is 1639.

A difference in the obtained system parameters between the SCR types have been tested by the one-way multivariate analysis of variance (MANOVA). We performed the analysis by stimuli (N=1639), not by subjects (Table 2). The MANOVA was followed by univariate analyses of variance.

Spectral analysis of the SCR signal and its first three derivatives has been performed using the software Chart 5 for Windows®.

RESULTS

Mathematical modeling of the SCR process has been performed using the system identification method in the MATLAB® computing environment[10]. The purpose of the method is creating mathematical models of dynamic systems based on measured input and output data of the system. In contrast to directly measurable SCR signal, the input neural signal to SCR system is unknown (Figure 1). Here we deal in a brand-new fashion with this problem.

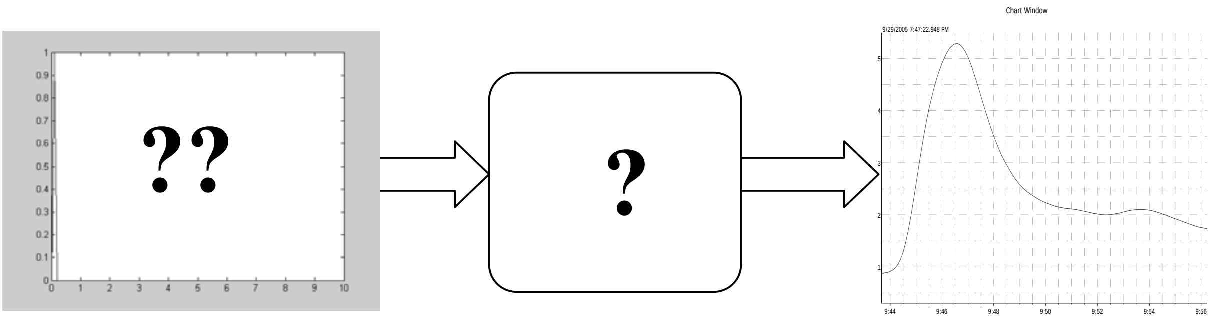

Figure 1. The system identification problem of skin conductance response (?) and the “hidden input“ problem (??)

Relying on our previous results (Branković 2008) in modeling of SCR to pleasant emotional textual stimuli (reading short stories from the contemporary literature) here we pursue with a linear third-order state-space model (Figure 2) whose equivalent linear differential equation is: y’’’+ay’’+by’+cy=mu(t).

SCR signal and its first three derivatives jointly reveal the initial neural event – a solution of the hidden-input problem

A hint to visualize the initial forcing event in the SCR signal came from mathematical dealing with differential equations with discontinuous forcing functions: the highest derivative of the solution appearing in the differential equation has jump discontinuities at the same points as the forcing function, but the solution itself and its lower derivatives are continuous even at those points (Boyce & DiPrima 2001). Considering the SCR as an output (solution) of a serial integration (in both mathematical and neurophysiological meaning of the word) and having in mind this simple mathematical rule we assumed that a hidden neural input leaves its trace on the highest derivative of the SCR system.

Indeed, an inspection of the SCR signal and its derivatives reveals that while the SCR signal and its first two derivates appear to be continuous, jump discontinuities features the third derivative of the SCR signal. This observation suggested that we could be able to read the traces of the discontinuous forcing function (the hidden input) in the third derivative of the SCR signal. The task is to determine an approximation of the unmeasured input signal looking at its prints on the third

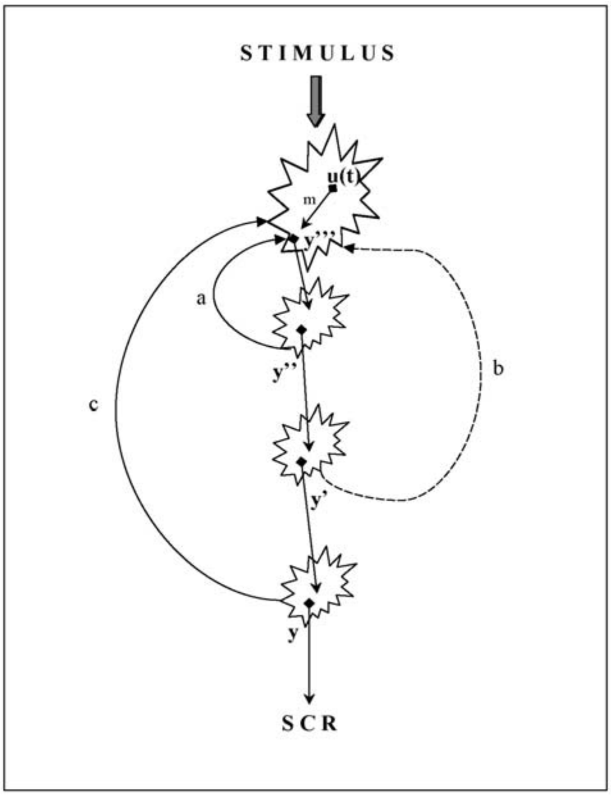

Figure 2. State-diagram for the mathematical model of the skin conductance response: y’’’+ay’’+by’+cy=mu(t). y=SCR

derivative of the SCR (Figure 3). We approximated the hidden inputs with series of impulses and square pulses. The timing and duration of the pulses have been determined according to the jump discontinuities of the third derivative of the SCR signal. We also exploited the possibility to quantify the strength of the hidden input through measuring the magnitudes of these jump discontinuities. The height of the putative input pulses (the strength of the hidden-input approximations) has been determined according to the height of the jump discontinuities of the third derivative of the SCR signal.

The method proved to be simple to be performed and happened to be crucial for the feasibility and accuracy of the system identification approach to SCR. It enables the easily obtaining of an almost perfect fit (>97%) between any measured SCR and the corresponding simulated model's output (Figure 4).

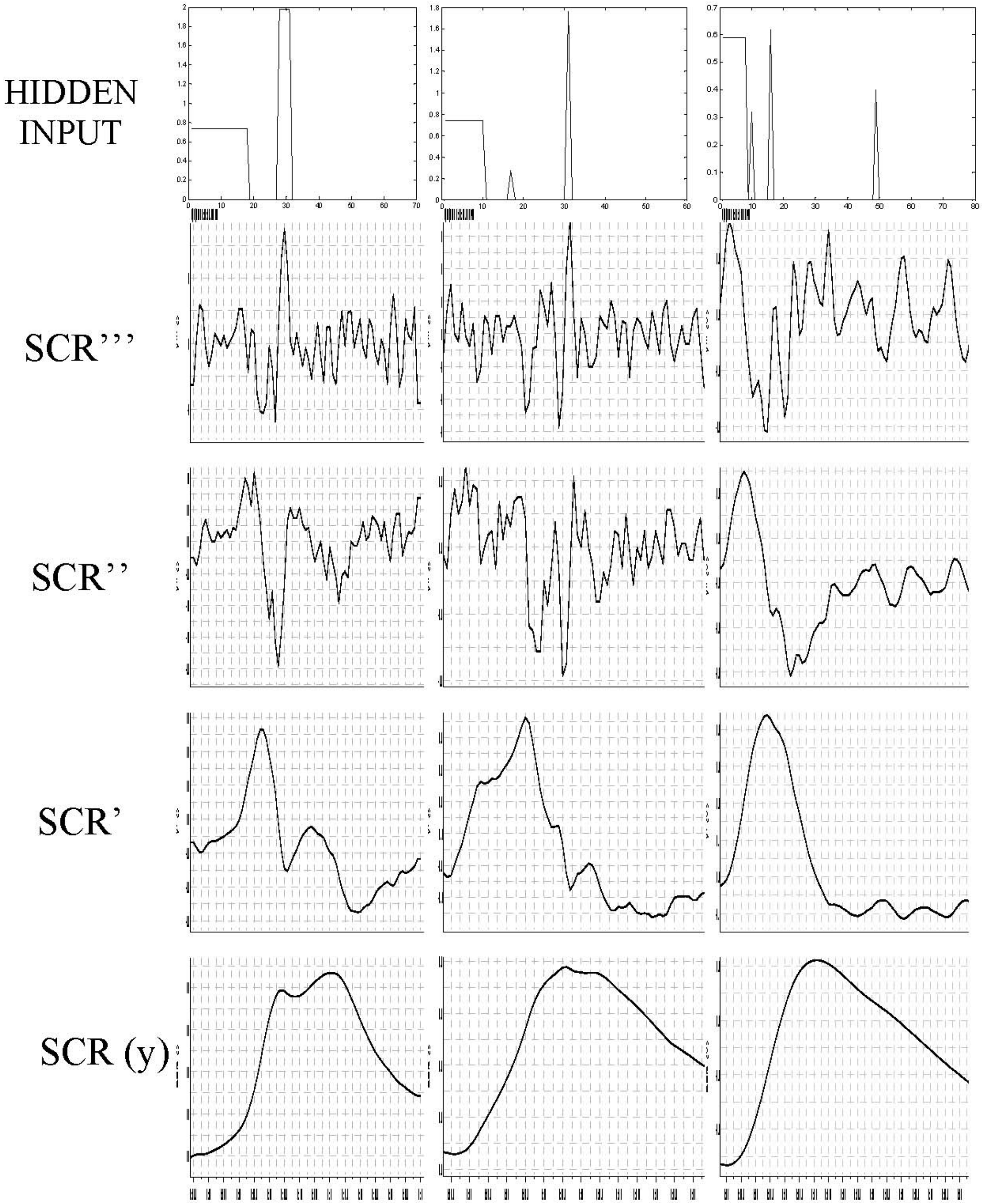

Figure 3. Hidden-inputs to the SCR system determined observing the jump discontinuities in the third derivative of SCR signal (SCR'''). Left column: the hidden-input consisting of two pulses of different strength and duration. Middle column: the input consisting of initial pulse and two impulses of different strength. Right column: the input consisting of initial pulse and three impulses

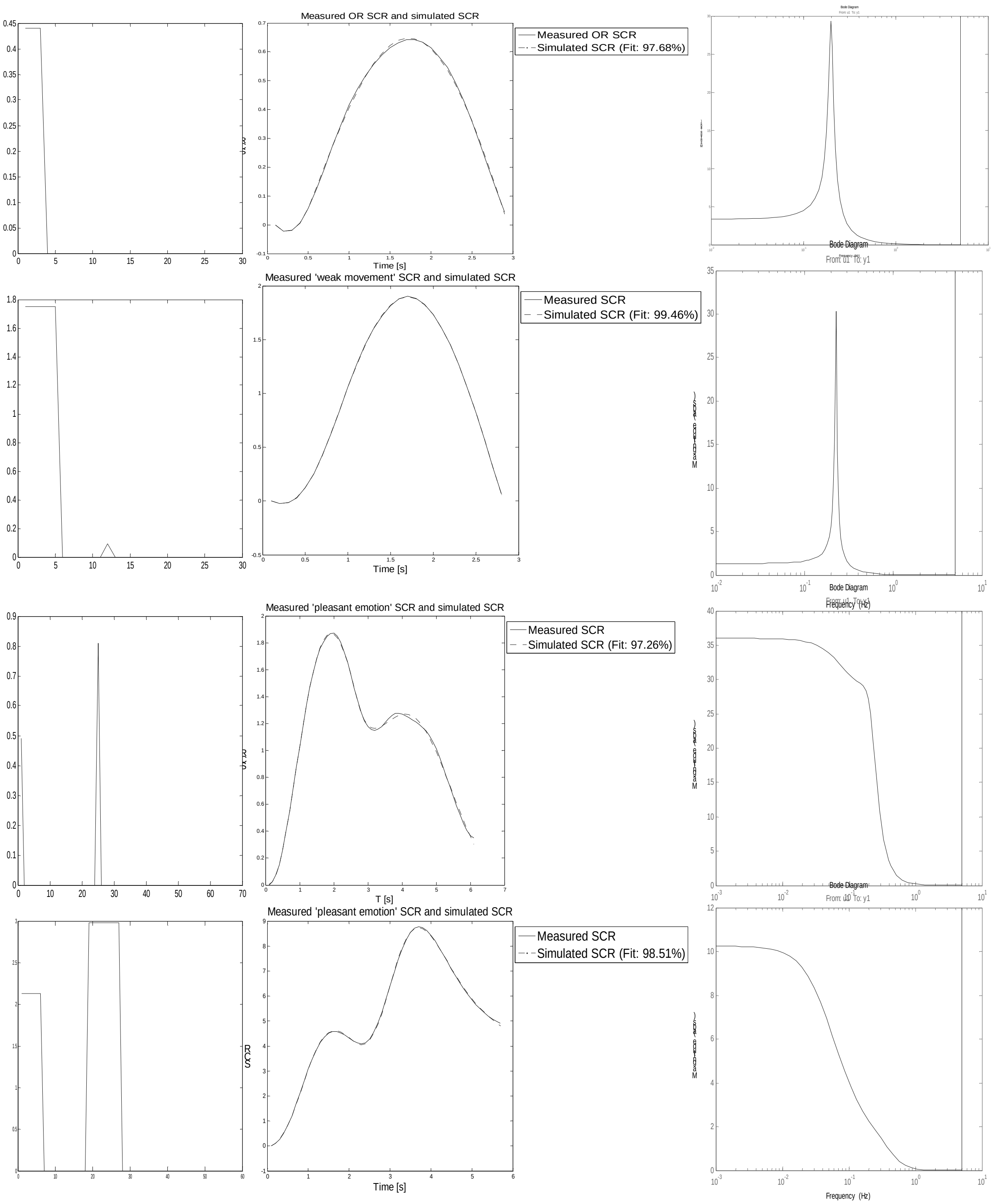

Figure 4. Examples of estimated hidden inputs and SCR models of different kind. Left column: the hidden inputs. Middle column: comparison of the measured and simulated SCRs. Right column: corresponding Bode diagrams of the SCR models (resonance found in 73% of the orienting response (OR) SCRs, 33% of SCRs associated with weak hand movements, 9% of SCRs elicited by pleasant emotional stimuli, and 2% of SCRs evoked by deep respiration).

Interlinked fast and slow positive and a negative feedback loop drive the SCR to pleasant emotional stimuli

System identification of the skin conductance response has been performed using the *System Identification Toolbox v. 6.0* included in the mathematical software MATLAB® v.7.0 (R14). We defined the model structure and set the fixed parameters and nominal (initial) values of the free parameters that enabled successful system identification of every single SCR to pleasant emotional stimulus for each subject in the sample (see Methods). The third-order state-space model appeared to be appropriate for two reasons. First, it yields accurate mathematical modeling of SCR providing high fit (>97%) between measured and simulated outputs, and second, it does it in a reliable, robust way, guarantying solution, convergence of the software algorithm dealing with the great variety of SCR input-output data (the total count of modeled SCR to pleasant emotional stimuli in our dataset is 1,002)

Through the system identification procedure we estimate the parameters of the state-space models, that correspond to the coefficients in the equivalent linear differential equation of the system: y''' + ay'' + by' + cy = mu(t). That enables us to regard the process of emotional arousal as an interaction among the following signals: 1) neural input to the SCR system, i.e. u(t), 2) the third derivative of the SCR signal (y'''), 3) the second derivative of the SCR signal (y''), 4) the first derivative of the SCR signal (y'), and 4) the SCR signal itself (y=SCR). Graphical representation of the interactions is shown in Figure 2.

Through modelling of over thousand SCR we were consistently encountering the same resulting feedback structure: the fast positive feedback loop (occurring early in the feedback scheme), the negative (in the middle), and the slow positive feedback loop (originating at the peripheral end of the regulatory chain in the SCR process).

The following six variables (parameters) have been chosen to characterize the SCR system: 1) input gain, 2) fast positive feedback loop gain, 3), negative feedback loop gain, 4) slow positive feedback loop gain, 5) overall static system gain, and 6) $\text{period}_{50\%}$.

Input gain. This parameter corresponds to the constant "m" in the differential equation of the system. It reflects the initial step in the process of the regulation of emotional arousal.

Fast positive feedback loop gain. Of the three feedback loops in the model (Figure 2) the first is proportional to the second derivative of the SCR signal (y'') and it is positive. We denote the parameter that characterizes this feedback loop as fast positive feedback loop gain. It equals the constant "-a" in the differential equation of the system.

Negative feedback loop gain. The second feedback loop in our model is proportional to the rate of change of the emotional arousal (y') and it is negative. It reflects a feedback inhibition in the arousal process. The parameter that characterizes this feedback inhibition equals the constant "-b" in the differential equation of the system.

Slow positive feedback loop gain. The third feedback loop in the model is proportional to the actual level of the emotional arousal, actual value of the SCR signal (y) and it is positive. The parameter that characterizes this feedback enhancement equals the constant "-c" in the differential equation of the system.

Static system gain. The value of low frequency or static system gain of linear time-invariant system can be obtained as a direct result of the MATLAB® function "dcgain".

$\text{Period}_{50\%}$. Some but not all models of SCR to pleasant emotional stimuli in our sample showed potential for resonance. That is why we could not use resonant frequency as a parameter to characterize the all obtained SCR models in our sample. Instead, using the Bode plots of the obtained individual models we determined for each SCR the time period when the amplitude of response would drop to a half value of that that appears responding to a single stimulus. Expressed in seconds, $\textit{period}_{50\%}$ has a psychological meaning and face validity. Namely, with a further shortening of the inter-stimulus period in comparison with the $\textit{period}_{50\%}$ the amplitude of SCR is rapidly diminishing.

Exploration of the within-subject distribution of values of the described system parameters revealed normal distribution of the three feedback loop gains and log-normal distribution of input gain, overall static system gain, and $\text{period}_{50\%}$ (as confirmed by the Shapiro-Wilk test). Description of the six variables chosen to characterize the system of SCR to pleasant emotional stimuli in healthy participants is presented in Table 1.

Control process of SCR is linear and within stimulus-type time invariant

Beside the SCRs elicited by pleasant emotional stimuli (the textual fragments of the short stories), from our psychophysiological records we were also able to

Table 1. Parameters of the system of SCR to pleasant emotional stimuli*

Parameter	Within-subject distribution	Within-subject coefficient of variation (%) range	Sample mean (sd)	Median	Range
Fast positive feedback loop gain	normal	0.97 – 1.51%	2.774 (0.029)	2.776	2.726 – 2.827
Negative feedback loop gain	normal	1.62 – 3.28%	- 2.577 (0.047)	- 2.557	(-2. 506) – (-2. 664)
Slow positive feedback loop gain	normal	1.96 – 5.37%	0.803 (0.020)	0.792	0.777 – 0.836
Input gain	log-normal	N/A	N/A	0.062	0.014 – 0.363
Static system gain	log-normal	N/A	N/A	97.788	22.39 – 840.57
$\text{Period}_{50\%}$ [s]	log-normal	N/A	N/A	11.996 s	4.357 – 35.336 s

* N/A: not applicable due to non-normal distribution

detect three other types of SCR. Between the series of textual slides of single stories there were break, empty slides. The SCRs occurring during exposition to these empty, break-slides have been considered as orienting responses (OR). The experimental situation also enabled us to recognize the SCR associated with small finger and hand movements while clicking a computer mouse. We were also able to detect the SCRs evoked by deep respirations, as visible from the records of respiratory movements.

The same system identification procedure with the same model structure and setting of the fixed and free parameters has been efficient in mathematical modeling of the three additional types of SCR. The six already defined system parameters used to characterize the system of SCR to pleasant emotional stimuli have been also determined for SCR systems associated with: orienting response, weak movement, and deep respiration (Table 2). Again, we revealed normal distribution of the three feedback loop gains and log-normal distribution of input gain, static system gain, and $period_{50\%}$ (as confirmed by the Shapiro-Wilk test). We obtained Gaussianity of the last three variables by logarithm transformation of the raw values.

A difference among the four types of identified SCR systems was tested by the multivariate analysis of variance (MANOVA) for the six dependent variables (the three feedback loop gains and the logarithm transformation of input gain, static system gain, and $period_{50\%}$). We performed the analysis by stimuli (N=1639), not by subjects (Table 2). The significant difference on the overall model between the SCR types was found ($F[18, 4610.821]=274.192$; $p<0.001$, Wilks' Lambda=0.128, eta-squared=0.496). The univariate analyses of variance among the SCR types revealed significant differences between the SCR types regarding the six system parameters. Considering effect size we can infer about a very strong association of SCR type with negative and slow positive feedback loop gain (eta-squared 0.815 and 0.806 respectively), and strong association of SCR type with fast positive feedback loop gain, static system gain, and $period_{50\%}$ (eta-squared 0.258, 0.236, and 0.231 respectively). On the other hand, we realize that the difference among SCR types in input gain is confounded with the large sample size (eta-squared=0.061).

Pairwise comparisons revealed increasing of strength of the three feedback loops' gains and duration of $period_{50\%}$ in the following rank: OR, weak movement, emotional, and deep respiration SCR. On the other hand, static system gain and input gain do not follow this rank. Moreover, system gain is about tenfold stronger in pleasant emotional SCR than in other types of SCR.

Relying on the found differences in control system parameters of the examined SCR types we can conclude that control process of SCR is linear and only within stimulus-type time invariant.

Table 2. Description of system parameters for different types of SCR*

Parameter	Orienting response (n=264)	Weak movement (n=224)	Pleasant emotional stimulus (n=1002)	Deep respiration (n=149)
Fast positive feedback loop gain (mean, sd)	2.236 (0.021)	2.624 (0.025)	2.774 (0.029)	2.914 (0.077)
Negative feedback loop gain (mean, sd)	- 1.886 (0.276)	- 2.301 (0.079)	- 2.577 (0.047)	- 2.858 (0.064)
Slow positive feedback loop gain (mean, sd)	0.469 (0.138)	0.673 (0.0476)	0.803 (0.020)	0.944 (0.068)
Input gain (median, range)	0.040 (0.064 – 0.253)	0.017 (0.003 – 0.257)	0.062 (0.014 – 0.363)	0.027 (0.003 – 0.045)
System gain (median, range)	11.248 (0.467 – 199.815)	8.178 (0.730 – 128.347)	97.788 (22.39 – 840.57)	8.870 (7.682 – 634.52)
$Period_{50\%}$ [s] (median, range)	3.484 (2.058 – 28.090)	4.975 (2.463 – 14.577)	11.996 s (4.357 s – 35.336 s)	14.444 (4.830 – 62.112)

*N: number of analyzed SCRs. Due to log-normal distribution of input gain, static system gain, and $period_{50\%}$, for these variables median and range are presented.

According to the frequency response Bode diagrams of the identified models in the sample (Fig. 4), the phenomenon of resonance (a case that at certain frequencies of occurring the stimuli system responds stronger than when encountered with isolated stimuli) characterizes 73% of the orienting response SCRs, 33% of SCRs associated with weak hand movements, 9% of SCRs elicited by pleasant emotional stimuli, and 2 % of the SCRs evoked by deep respiration. Fisher's exact test revealed a significant difference in the presence of the resonance among the SCR types (p=0.0002). Pairwise SCR type comparisons revealed that the overall significance of difference stems from more frequently occurrence of resonance in both orienting response and weak movement SCRs in comparison with the other two SCR types.

Periodicity of the hidden input and spectral characteristics of the SCR signal and its first three derivatives

The derivatives of the SCR signal are derived empiric signals. The same holds to certain extent also for the hidden input since it is defined by the third derivative of the SCR signal. In order to test the assumptions about the neurobiological reality of the dynamic models of SCR we performed the spectral analyses of the whole SCR recordings and their first three derivatives. The spectral analyses revealed: 0.01-0.55 Hz frequency range for the SCR signal, 0.01-1.5 Hz for SCR', 0.1-5 Hz for SCR'', and 0.2-5 Hz frequency range for the SCR''' signal.

Since approximations of the hidden input consist of series of square pulses we are able to measure intervals between the centers of the pulses. This reveals periodicity of the hidden input that can be characterized by the time period of occurrence of pulses (hypothetic neural bursts) in input. The range of periods of occurrence of pulses in hidden input was 0.5-10 s. The values of these periods in the data-set were non-normal distributed. Log-normal distribution has been achieved (as confirmed by the Shapiro-Wilk test) after the division of the data-set according to sex. T-test revealed significantly longer period between occurrence of hidden input pulses in women than in men ($p<0.001$).

DISCUSSION

A new method for the estimation of the input signal to the SCR system enabled accurate identifying of the linear dynamic models for every single SCR with the level of fit between the measured and simulated response that has been never reported before. We identified the unique model structure that involves two positive and one negative feedback loop in the system. We found that this model structure holds for SCR elicited not only by pleasant emotional stimuli but also for the SCR associated with deep respiratory movements, weak motor activity, and the orienting response. However, the parameters that characterize the feedback loops' gains appeared to be different in differently elicited SCR. This observation has never been reported before and challenges for explanation.

The results suggest that through the system identification technique we can derive more information about the underlying arousal process from the SCR recordings than we used to do: how much more depends on the true neurobiological meaning of the mathematical parameters that quantitatively describe the feedback regulation of the SCR system. This raises the question of the verity of our neurobiological interpretations of the dynamic models of the skin conductance response. Here we expose two arguments in favor of the thesis that these mathematical models comprise the whole arousal process – from the initial neural event in the brain to the sweat glands' activity.

Distinct regulation of different types of SCRs – evidence for the brain mechanisms involvement in the SCR models

Distinct regulation of different types of SCRs that we found through the system identification approach (revealing the differences in the control system parameters) raises the question of adequacy of the assumption that mathematical models of the SCR process describe the sudomotor nerve and sweat gland activity (Alexander et al. 2005, Bach et al. 2009, Bach et al. 2010a, Bach et al. 2010b, Bach et al. 2010c, Benedek & Kaernbach 2010). The doubt has been recently expressed by Bach and colleagues (2010b) who found a difference of SCRs evoked by aversive pictures in comparison with other applied stimulus classes: "There is no reason why the peripheral output system should exhibit a different response to one stimulus class than to any other... The twist is that it might be possible to estimate characteristics of central nervous function by deconvolving the observed signal." Yet, the spark of this view we can trace back in the Edelberg's work on the so-called recovery limb of the SCR four decades ago. Edelberg (1970) proposed that rapid- and slow-recovery SCRs reflect qualitatively different psychological processes as a result of distinct neural control.

The shift from peripheral to central interpretation of the mathematical models of SCR challenges our understanding of the physiological nature of the SCR. Does the phasic electrodermal response reflect sweat secretion, passive diffusion, and reabsorption process? It would be difficult to explain precise influence and transmission of the central neural events on the distinct SCR form (as found in this research) if it would be realized through sluggish processes such as secretion, diffusion, and reabsorption. But there is evidence that formation of SCR could be better explained as determined by constriction of myoepithelial cells of ducts of the sweat glands (associated with vasomotor activity) on activation of the sympathetic nervous system than by long-time secretion, spreading and reabsorption of secretion (Dementienko et al. 2000).

Comparability of spectral characteristics of the SCR signal, its derivatives, and hidden input with oscillatory activity of brain structures engaged in the arousal process

As a further argument in favor of the thesis that identified control process of SCR comprises the whole arousal process starting from initial neural event in the brain up to the skin surface conductance output we point to a comparability of spectral characteristics of the SCR signal, its derivatives, and periodicity of the estimated hidden input to the SCR system on the one side, with dominant oscillatory activity of certain brain structures engaged in the arousal process on the other side. In other words, we look for the brain spectral analogues of the SCR signal and its derivatives (Table 3). Our working hypothesis is that the nodes in our mathematical model (Figure 2) could be realized as principal points on the path of integration and feedback regulation of the neural signal conveying the information for central control of emotional sweating.

As a confirmatory evidence for our thesis can serve observation that the gradient of spectral domains of hidden input, SCR''', SCR'', SCR', and SCR parallels the frequency gradient of neuronal activity of the brain sites engaged in the arousal process, in the direction amygdala – brain stem. Thus, while the proximal parts of our model (hidden input, SCR''', and SCR'') manifest delta oscillatory activity (which itself characterizes activity of amygdala, dopaminergic neurons, activity of brain systems engaged in motivation, salience detection, recognition of a loved person, sexual arousal, and orgasm), spectral characteristics of the distal components (SCR' and SCR itself) correspond to infraslow oscillatory activity of brain stem structures (e.g. reticular formation, locus coeruleus, dorsal raphe nucleus).

Both distinct regulation of different types of SCR and the spectral comparability of SCR signals with brain structures lend support for the central interpretation of the identified model of the SCR process. This view has potentially significant implications for the perspective of SCR research. According to this view it follows that metrics of hidden-input and feedback loops in the SCR process could refer to the brain neurocircuitry and neurochemistry rather than to the biophysical properties of the sweat glands.

Positive and negative feedback loops in the arousal process assure correct responses in a noisy environment

Interlinked positive and negative feedback loops have been identified in many biological systems as the key regulatory scheme in the process of creation of output (Tsai et al. 2008, Brandman et al. 2005,

Table 3. Comparability of spectral characteristics of hidden input, SCR signal, SCR signal's derivatives, and oscillatory activity of brain structures engaged in arousal process

Frequency range [hz]	Period range [s]	Spectral characteristics of hidden input, scr and scr's derivatives	Brain site and functional correlates
0.1 – 5 Hz	0.2 – 10 s	HIDDEN INPUT Frequency range: 0.1 – 2 Hz Period range: 0.5 – 10 s SCR''' Frequency range: 0.2 – 5 Hz Period range: 0.2 – 5 s SCR'' Frequency range: 0.1 – 5 Hz Period range: 0.2 – 10 s	- Firing frequency of projection neurons of basolateral amygdala: 1.3 Hz (Likhtik et al. 2006). - Firing frequency in basolateral amygdala of behaving rat: 0.38 Hz (Ponomarenko et al. 2003). - Slow neuronal oscillations in the lateral amygdala: 0.9 Hz (Collins et al. 2001). - Intrinsic oscillations in neurons of lateral and basolateral nuclei of the amygdala: 1-6 Hz (Pape et al. 1998). - Phasic dopamine reward activation: 2-5 Hz (Schultz 2002). - Activity of motivational systems, sexual arousal and orgasm, salience detection – delta brain oscillations (Knyazev 2007). - Recognition of a loved person is pure delta (0.5-3 Hz) brain oscillatory process (Başar et al. 2008).
0.01 – 2 Hz	0.5 – 100 s	SCR' Frequency range: 0.01 – 1.5 Hz Period range: 0.67 – 100 s SCR Frequency range: 0.01 – 0.55 Hz Period range: 1.8 – 100 s	- Locus coeruleus slow frequency (0.02-0.25Hz) potential response to stress (Filippov et al. 2002). - Locus coeruleus and dorsal raphe nucleus slow frequency (0.02-0.04Hz) potential response to stress (Filippov et al. 2004). - Rhythms of the reticular neurons in the brainstem: 0.05-0.5 Hz (Lambertz and Langhorst, 1998). - Reticular formation of the brainstem 0.15 Hz cardiovascular rhythm (Perlitz et al. 2004). - Brainstem 0.4-0.7 Hz cardiac related oscillations (Barman & Kenney 2007). - Locus coeruleus 1.3 Hz tonic neuronal activity and 33-63% phasic increase in response to reward (Bouret & Sara 2004). - Slow-firing serotonergic neurons in the rat dorsal raphe nucleus: 1.7Hz (Allers & Sharp 2003). - Stereotypic burst-firing serotonergic neurons: 1.4 Hz (Hajós et al. 2007).

Brandman & Meyer 2008). The wide occurrence of dual-time (fast and slow) positive feedback loops combined with a negative feedback loop (the regulatory structure that we revealed in the SCR process) has motivated investigations of properties and functions of that regulatory motif during the last decade. Mathematical simulations revealed that such coupled feedback circuits enable systems in a noisy environment to produce perfect responses with respect to signal duration and amplitude. Thus, the foremost activated positive feedback rapidly induces the "on" state transition of the signaling system, the delayed positive feedback robustly maintains this "on" state, while the negative feedback reinstates the system in the original "off" state, prevents excessive response due to multiple positive feedback loops, and suppresses noise effects (Kim et al. 2006, Pfeuty & Kaneko 2009). This behavior is advantageous when it is desirable to limit the time that the system spends in the "on" state (Mitrophanov & Groisman 2008).

The dual-time switch, consisting of interconnected fast and slow positive feedback loops, found both sensitive to stimuli and resistant to fluctuations in stimulus, has been suggested as a ubiquitous regulatory motif performing sensitive robustness in biological systems (Zhang et al. 2007). It is a mechanism which is able to assure both "quick onset" and "brief duration" as fundamental and adaptive characteristics of emotions (Ekman 1992).

But why should it be important for the "emotional sweating" process to be regulated in such a way? Beside the appropriate responsiveness in rapidly changing circumstances (Ekman 1992) we reason that sensitive robustness of the SCR (and the peripheral sympathetic function in general) is required to provide proper memory processing. Namely, abundant evidence indicates that heightened arousal enhances memory encoding of both emotional (Strange & Dolan 2004, Phelps 2004) and non-emotional information (Lemon et al. 2009, Kemp & Manahan-Vaughan 2008). Our reasoning is more directly supported by the recent finding that arousal and increased sympathetic activity enhances memory consolidation through mechanisms initiated in the periphery and transmitted centrally via the vagus (King & Wiliams 2009). A common mechanism – determination of filter properties of the sympathetic arousal system through interlinked positive and negative feedback loops – could be responsible for setting the cutoff in signal-to-noise discrimination in both emotional responding and memory encoding. Here obtained values of $period_{50\%}$ for the pleasant emotional type of SCR (4-35s) correspond to the time-scale of physiological and behavioral emotional responding (Ekman 1992), and hence render the thesis about the filter function of the arousal system plausible from psychological point of view.

CONCLUSION

A new method for the mathematical modeling of the SCR has been proposed. It provides not only the best fitting with empirical SCR signals that has ever been reported, but also insight into the hidden neural input for the SCR system. Through the system identification procedure we have shown that there are two interlinked positive and a negative feedback loop which shape the SCR. The control process of the SCR showed linear and within stimulus-type time invariant. The last finding argues for the central nervous system interpretation of the dynamic models of the SCR. Future studies are needed to test the inter-trial reliability of the system parameters that here showed high intra-trial reliability. Also, the thesis about the central nervous system interpretation of the obtained system parameters could be further tested by conducting pharmacological intervention studies altering certain brain neurotransmitter systems (e.g. detecting the SCR system parameters' change in the psychiatric population receiving medication).

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