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Finger Thermoregulatory Model Assessing Functional Impairment in Raynaud's Phenomenon

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Abstract

Raynaud's Phenomenon (RP) is a paroxysmal vasospastic disorder of small arteries, pre-capillary and arteries of the extremities, typically induced by cold exposure and emotional stress. We used Control System Theory to model finger thermoregulatory processes in response to a standardized cold-stress for differential diagnosis in RP. The proposed model describes how the control mechanisms are activated and maintained. Thermal infrared imaging data from 14 systemic sclerosis subjects (SSc), 14 primary RP (PRP), and 16 healthy control subjects (HCS) were processed. The estimated model parameters elucidated the level of functional impairment expressed in the various forms of this disease.

Introduction

RP can be classified as primary (PRP), with no identifiable underlying pathological disorder [1], and secondary, usually associated with a connective tissue disease, use of certain drugs, or exposition to toxic agents [2]. Secondary RP is frequently associated with systemic sclerosis. In this case, RP typically may precede the onset of other symptoms and signs of disease by several years [3]. Thermal infrared (IR) imaging has been widely used in medicine to evaluate cutaneous temperature [4]. Since the cutaneous temperature depends on the local blood perfusion and thermal tissue properties, IR imaging provides important indirect information concerning circulation, thermal properties, and thermoregulatory functionality of the cutaneous tissue. Several IR imaging studies have been performed to differentiate primary from secondary RP, often in combination with the monitoring of the finger response to a controlled cold challenge. In fact, SSc, healthy controls (HCS), and PRP show different thermal recovery in consequence of the same standardized functional stimulation [5, 6, 7, 8]. In this paper, we used a Control System Theory approach to model finger thermoregulatory processes in response to a standardized cold challenge, to evaluate how the patho-physiological differe

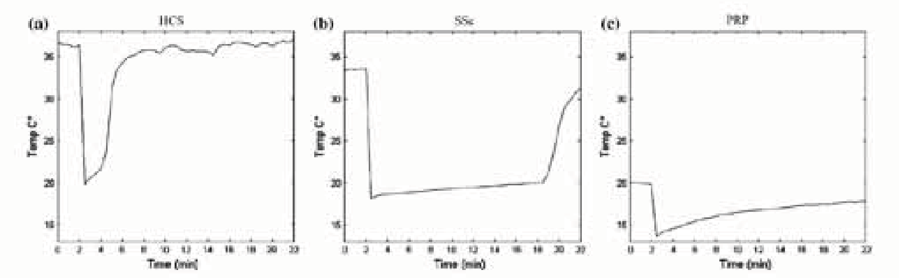

Figure 1. Temperature vs. time curves obtained from thermal imaging data during cold stress test in a) HCS, b) SSc, and c) PRP

Finger thermoregulatory model

Cutaneous circulation is a major effector of human thermoregulation. Exposure to cold stress elicits generalized cutaneous vasoconstriction, which may be extremely pronounced at the fingertip surface. The temperature time-evolution, before and after cold stress, can be recorded by means of thermal IR imaging [4], (Fig. 1). According to Control System Theory, differences in the temperature recovery curves depend on the efficacy of the finger thermoregulatory system, which in turn can be represented by the actual values of a given set of functional modeling parameters. The homeostatic process can be seen as a feedback controlled system. This kind of system considers a reference signal to produce the desired output. The reference signal indicates the value that the output has to assume. The reference value is represented by superficial basal temperature that can be considered steady during the experiment, while the output is the superficial finger temperature. A cold challenge induces a finger temperature (plant controlled output) change from the basal value (reference value). The cold challenge test activates specific responses of the thermoregulatory system, which operate at both local (i.e., peripheral) and systemic (i.e., central) levels attempting to restore the basal temperature [9]. Here we propose to model these two levels of the thermoregulatory system through two hierarchical control units: a higher level unit (supervisor), and a feedback lower level executor [10] driven by the supervisor [11]. The supervisor sets the reference signal on the basis of the basal pre-stress temperature and the onset time. The overall performance of the thermoregulatory system depends on the activity of both the supervisor and the executor. Besides the contribution of the thermoregulatory system, the finger temperature (i.e., system output) is also influenced by the thermal exchange between the finger and the surrounding environment. This thermal exchange depends on the temperature difference, which constitutes the external input to the thermoregulatory system [9,12].

Materials and Method

Fourteen SSc, 14 PRP and 16 HCS participated in this study, which was authorized by the Ethical Committee of the School of Medicine of the University of Chieti-Pescara. For each subject, the functional response to a mild cold challenge of hands in water was assessed by fIR imaging. Thermal IR imaging was performed by means of a digital thermal camera (FLIR SC3000, FlirSystems, Sweden), with a 320X240 QWIP FPA, capable of collecting the thermal radiation in the 8–9 μm band, with a 0.02-s time resolution and 0.02 K temperature sensitivity. Cutaneous emissivity was estimated as 0.98. The cold stress was achieved by immersing the hands (protected from getting wet by thin, disposable latex gloves) for 2 min in a 3-L water bath maintained at 10 °C. The control model was implemented using the Matlab Simulink Graphical User Interface©. The model parameters were computed and optimized through the Matlab Simulink Parameter Estimation Toolbox©, by using Non-Linear Least Square algorithm. Figure 2 shows an example of the comparison between the identified response and the experimental temperature curves for three representative subjects randomly chosen, frc

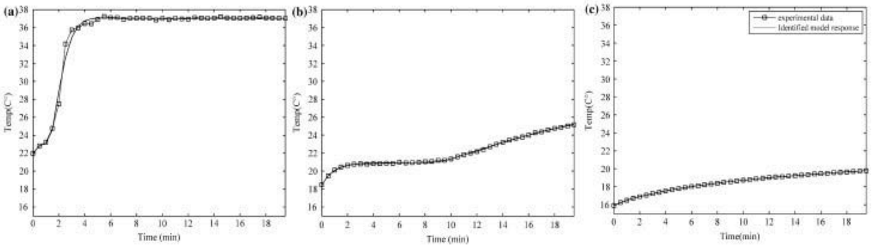

Figure 2. Comparison between experimental data and identified model response, for a) HCS; b) SSc and c) PRP.

Our model is univocally identified by a set of functional parameters (a, k, d, LT, and r). k and a determine the position of the poles in the closed loop and, therefore, the dynamics of the thermoregulatory system and its efficiency. The reciprocal of the plant time constant a represents the velocity of the response of the thermal process to external and internal stimuli. k refers to the control action and determines the efficiency of the feedback control system in achieving the steady state and restoring the reference basal conditions. d, which is one of the fitted parameters, represents passive heat exchange with the environment, and, therefore, depends on room temperature and actual finger temperature. LT is the time interval between the end of the cold stress and the onset of re-warming process. During this time, the thermal variations are mostly attributable to the passive heat exchange with the environment. r is the reference temperature measured in pre-stress conditions. From parameters analysis, HCS presented the fastest active recovery, with the highest gain. PRP presented the slowest and weakest recovery, mostly due to passive heat exchange with the environment and SSc presented an intermediate behavior, with the longest delay of response onset. The statistical analysis and the classification algorithms permitted to achieve an excellent differential diagnosis of primary vs. secondary RP. The application of such a model would play a fundamental role in the differential diagnosis and treatment of SSc and primary RP.

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