Body temperature fluctuation analysis in cirrhosis

Ali R. Mani[1], Roham Mazloom[2], Zahra Haddadian[2], Sara Montagnese[3]

[1] *Division of Medicine, University College London, London, UK*

[2] *Department of Physiology, Alborz University of Medical Sciences, Alborz, Iran*

[3] *Department of Medicine, University of Padua, Padua, Italy.*

To the Editor:

We recently reported that patients with cirrhosis exhibit an abnormal pattern in their skin temperature variability, with complexity analysis of skin temperature fluctuations distinguishing inpatients from outpatients, despite similar mean temperature values [1]. Patients with cirrhosis also exhibit abnormalities in circadian rhythmicity, part of which are of central origin [2]. Therefore, we wondered if abnormalities in skin temperature fluctuations may reflect abnormalities in core body temperature (CBT) regulation in these patients. To test this hypothesis, we analysed CBT data that we had previously recorded in control rats and rats with cirrhosis [3].

Cirrhosis was induced by bile duct ligation and CBT was measured for six hours using an implanted telemetric probe [3]. The complexity of CBT fluctuations was quantified by multiscale entropy (MSE) analysis [4]. This technique allows to assess the entropy (structural richness) of physiological fluctuations across a range of time scales that mirror the temporal dynamics of the system [4]. The concept of entropy is linked with information content in a time-series. Thus, higher MSE in CBT fluctuations can be interpreted as higher degree of information processing within the thermoregulatory system.

Cirrhotic rats exhibited a significant increase in MSE of CBT compared to control animals at baseline (Figure). In both groups, entropy measure for CBT signals increased in higher scales, indicating that CBT fluctuation is not a random process and carries information [4]. Increased MSE in CBT fluctuations can be interpreted as more engagement of the thermoregulatory system in cirrhosis. The underlying mechanism is unknown but it may be associated with higher energy expenditure or hyperdynamic circulation.

Body temperature fluctuation analysis can be used to assess the integrity of the thermoregulatory system. In patients with multiorgan failure, such integrity is lost and patients show a significant drop in entropy of CBT fluctuations [5]. When we injected low dose (1 mg/kg) of bacterial lipopolysaccharide into cirrhotic rats, they all developed multiorgan failure and died within 6 hours, while all control rats survived without organ failure. Complexity analysis of CBT showed a significant drop in MSE soon after LPS challenge in cirrhotic rats while MSE did not change in the control group (Figure). Thus LPS injection determined an abrupt transition from a heightened engagement to very low engagement of the thermoregulatory system in cirrhotic rats. These dynamics may underlie/contribute to the transition from a compensated to a decompensated/multiorgan failure state which is often observed in infected patients with cirrhosis.

Conflict of Interest: None

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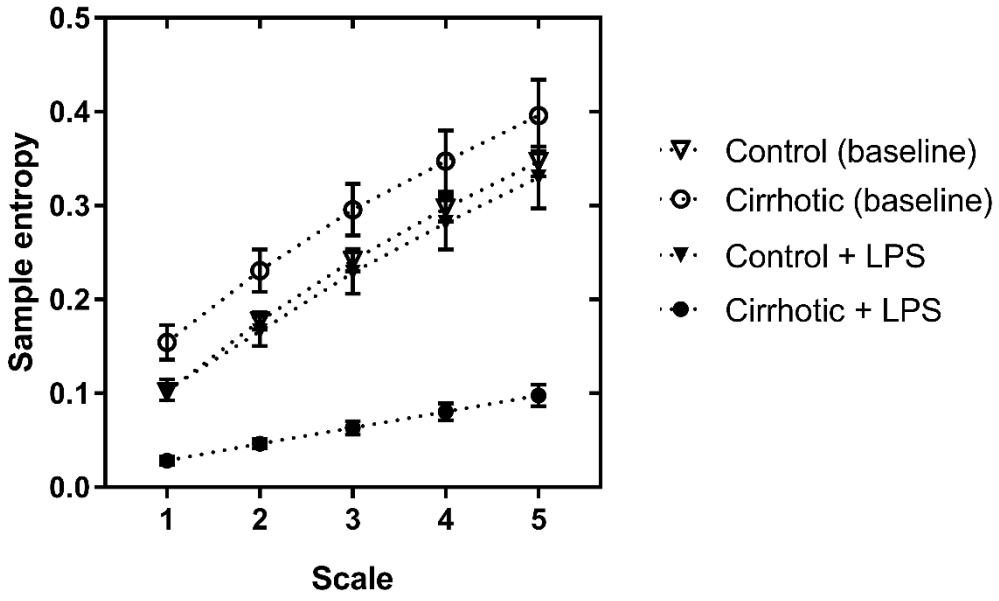

Figure Legend. Multiscale entropy (MSE) analysis of CBT in control and cirrhotic rats at baseline and after intraperitoneal injection of lipopolysaccharide (LPS, 1 mg/kg). CBT was measured using a telemetric probe implanted into experimental animals (sampling rate of 0.1 Hz). MSE measured estimated entropy of temperature time-series (Sample entropy) at different scales. All recordings were started at 8 AM and were continued for six hours. At least 6 rats were used in each group. Data is shown as mean ± SEM. Two-way analysis of variance showed that control and cirrhotic rats have a significant difference in MSE at baseline ($P<0.0001$). Acute LPS challenge was associated with a significant reduction in MSE in cirrhotic rats ($P<0.0001$) but not in controls.