論文の要旨

題　目　A Study on the Evaluation of Sympathetic Responsiveness of the Cardiovascular System and Related Applications
（心血管系の交感神経反応性の評価とその応用に関する研究）

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The sympathetic nervous system (SNS), one of the two antagonistic branches of the autonomic nervous system, plays an essential role in unconsciously regulating the responses of stimuli and keeping homeostasis in the body. The SNS can be activated by stimuli such as emotional stress, motion, or pain, acting on the cardiovascular system, sweat glands, pupil, etc. Therefore, the evaluation of SNS activity (SNSA) can serve to objectively quantify such stimuli and provide health information, such as pain intensity and mental health, to further promote quality healthcare in daily life. In particular, numerous evaluation methods based on the response of the cardiovascular system to SNSA have been proposed and applied in practice. However, different types of stimuli and different structures of the cardiovascular system make it possible for the cardiovascular system to respond differently to the innervation of the SNS, which remains a challenge for the applicability of these evaluation methods. Therefore, it would be of interest to evaluate the sympathetic responsiveness of the cardiovascular system for a more applicable method of SNSA evaluation.

The purpose of this dissertation is to outline the proposal and development of a quantitative method to evaluate changes in SNSA using cardiovascular biomarkers. The proposed method involves the hypothesis that there are regional differences in sympathetic responsiveness of the cardiovascular system depending on the type of stimulus. Centering on a piezoelectric sensor, the author constructs a system to measure and evaluate the sympathetic responsiveness of the cardiovascular system and attempts to extend it to wearables for health monitoring. The exploration and validation of the heterogeneity of sympathetic responsiveness also give rise to a robust method for estimating respiratory rate (RR). The outline of this dissertation is organized as follows.

In Chapter 2, the author proposes a method to evaluate the sympathetic responsiveness of the cardiovascular system under respiratory modulation. In the proposed method, heart rate (HR) and pulse wave amplitude are extracted beat-by-beat from multiple pulse waves measured at different sites of the body using a piezoelectric sensor. Then, RR is extracted from periodic fluctuations in HR and pulse wave amplitude, and the consistency between RR extraction results from multiple sites and the reference RR is evaluated. This evaluation can

further indicate the sympathetic responsiveness of their measurement sites under respiratory modulation involving SNS innervation. In addition, the validity and accuracy of the piezoelectric sensor in biosignal measurements are verified by comparing the extraction results with those of other commercially available medical devices. The measurement system can also be extended to wearables for health monitoring in daily life.

In Chapter 3, the author proposes a method to evaluate regional differences in RR estimates under painful stimuli to further evaluate the sympathetic responsiveness of the cardiovascular system. Based on the consistency of the RR estimation results in Chapter 2, short-term painful stimuli are invoked to evoke another SNSA and further modulate the cardiovascular system along with respiratory modulation. In the proposed method, electrocardiogram, fingertip photoplethysmogram, and arterial pulse waves near the elbow and wrist are measured simultaneously in a multi-intensity stimulus experiment. Six biomarkers are extracted from the measurements and their responses to SNSA are quantified and evaluated by frequency domain analysis and two evaluation indices of respiratory wave quality. The evaluation results can indicate whether there are regional differences in their robustness to pain, in other words, in their sympathetic responsiveness. This can also translate our evaluation results into a robust system for health monitoring in daily life. In addition, the proposed method tends to add to an appreciation that the choice of measurement location can help wearables enrich their functionality.

In Chapter 4, the author proposes a quantitative method to evaluate functional changes in peripheral arterial stiffness and SNSA using local pulse wave velocity (LPWV) measured from the artery near the wrist to the artery near the forefinger. The proposed method incorporates the hypothesis, already demonstrated in Chapter 3, that there is heterogeneity in sympathetic responsiveness of the cardiovascular system. Therefore, the sympathetic responsivity of the peripheral arterial segment can be further quantified by using LPWV to estimate functional changes in its arterial stiffness. The relationship between LPWV, simultaneously measured peripheral arterial stiffness index, and self-reported pain intensity is quantified in a multi-intensity stimulus experiment to examine the validity of the proposed method. The proposed method establishes LPWV as a quantitative biomarker for SNSA evaluation and demonstrates the optionality of using arterial pressure correction in SNSA evaluation depending on the application scenario. Therefore, quantitative evaluation of the sympathetic responsiveness of the cardiovascular system will not only grow a non-invasive neurosensing method using cardiovascular biomarkers but also contribute to the development of wearables for health monitoring.

Finally, Chapter 5 concludes the dissertation and outlines related challenges and future work.