CHAPTER 6

FUTURE WORK

This work was primarily a pilot study. The most important consideration for future work is the expansion of the data sets employed in these analyses. The analyses had some significant results with the small sample size. It is hypothesized that with larger data sets, more significant relationships can be established between central and peripheral autonomics, as well as between healthy and diseased populations.

6.1 Cardio-Pulmonary Coupling Model

The model can be expanded for testing the adaptability of the analysis in quantifying activity of signals which contain frequency content that is not harmonic. First the phase matching must be performed. Then, the analysis must be performed in small windows to capture the changes accurately. This may prove a valuable way to assess methods of implementing adaptive windowing of the signal for correlations.

6.2 Wavelet Entropy

The wavelet entropy analysis was performed on both the COPD and presbyopic subject populations. Both groups showed trends, but the sample size was quite small, yielding a large variance, and did not yield significant results.

The subjects in the presbyope group displayed some interesting, and in some cases significant, trends in the WavS methods, although the sample size must be larger to accurately assess the results obtained. In addition, it would be of interest to assess entropy levels after the influence of the respiration is removed. This would address questions regarding the influence of respiration in the level of variability in cardiac oscillations. It is hypothesized that the levels of entropy would be greatly reduces after removal of the respiration. However, the variance in the series would also be reduced and would likely yield significant results regarding the vagal modulation of HRV.

6.3 Wavelet Source Separation

The main intent of this aspect of the research was to determine if the respiration effect could be removed from the IIBI signal. The model results indicate that this can be done. However, what clinical implications for diagnosis does this method possess? The two subject populations yielded some striking results, but again, the research was a pilot study by design, and the sample sizes were not robust enough to form any statistical determinations. However, interesting trends exist and should be further investigated via the use of a larger sample size.

What was seen in the model, as well as in both subject populations, is that even for spread respiration spectra, the analysis was able to separate the signals fairly well. The respiration spectra were illustrated in Chapter 4, including the standard Fourier content measures as numerical validation, and it is clear that the overlap was removed for small and large band peaks in the spectra. Of particular interest is the fact that some frequency activity is still evident at specific frequencies that must be attributed to the cardiac cycle, as the bulk of the respiration spectral activity is removed from the IIBI spectra. Further investigation should be performed in the assessment of changes in the ratio, as the values for each group are now much closer together. The algorithm performed in essentially a normalizing capacity. With a smaller variance, smaller changes in mean value can be detected and therefore, a smaller sample size can be used for analysis.

The COPD population was characterized by a significant difference in values of HF and LF between the two groups. The minimum correlation threshold necessary to separate the signals varied according to subject population. As a result, the lower end of the correlation range was used for both sets of data. The correlation for the COPD subjects often went as low as 0.6 and the healthy subjects were able to employ an average separation threshold of least 0.8. Specifically, the larger removal of LF content in the control population than in the COPD population leads to questions of whether sympathetic stimulation occurs in COPD patients with each breath, as opposed to the LF content being an artifact of the noise. Interestingly, Min et al. found that acute hypoxia in fetal lambs increased low-frequency and LF/HF ratio content, suggesting an increased sympathetic activation compared with baseline in hypoxia [105]. The effects of hypercapnia were not discussed in that study. The results of this research indicate that the LF content may represent true sympathetic content in the COPD population, where it may be more driven by sinus arrhythmia in controls.

The WavS method showed some interesting trends in terms of the Presbyope population data. Of significance is the change in each of the cardiac response parameters. Although the samples size was not large enough for statistical significance, there are some notable results. It is of significance that the separation algorithm employed a correlation value of 0.85 for each subject as it was assumed that they were all ostensibly of the same general level of health. There were different levels of signal separation for each group based upon the level of correlation, which is evident in the varying degree of change in frequency content values from one breathing rate to another. It may also be appropriate to investigate non-linear correlation measures to more fully capture trends over larger windows of time.

In addition, the onset adjustment varied from population to population, suggesting the existence of some intrinsic factor that differs among populations, which resulted in a delay the cardiac loop. The same differences in both onset time and level of correlation were seen for both presbyopic and COPD populations. Although a certain degree of that is due to the change in signals from ECG to IIBI, there is a certain degree that is unaccounted for. Alterations in the cardio-pulmonary tissue may account for the change in onset time as the system ages or is diseased and should be investigated as a possible source for the variation.

There are points within the signals of both populations during which the respiration and ECG lose coordination, even during steady state. Although the signals typically return to the coordinated state, there are significant points during which control and subject populations have a decrease in the level of correlation of their cardio-pulmonary dynamics. Perhaps the threshold must be adaptive to account for this.

It is also evidenced that if the signals are out of phase with each other, the signals are not separated in the WavS algorithm, although the program performs well for respiration signals that are 180 degrees out of phase. This occurs even if there is a significant peak in the HRV spectrum that correlates with the respiration peak in the Fourier domain. When the signals are aligned, the separation accuracy increases. It is possible that a wavelet spectral alignment occurring before the analysis would improve the robustness of this analysis.