Exp Physiol. Author manuscript; available in PMC 2017 March 20.

Published in final edited form as:

Exp Physiol. 2014 February ; 99(2): 466–467. doi:10.1113/expphysiol.2013.076539.

Analysis of fetal heart rate variability in frequency domain: methodical considerations

Daniela Casati[1] and **Martin G. Frasch**[2,3]

[1]Department of Woman, Mother and Newborn, Children's Hospital V. Buzzi; Biomedical and Clinical Sciences School of Medicine, University of Milan, Italy

[2]Department of Obstetrics and Gynaecology, CHU Ste-Justine Research Centre, Faculty of Medicine, Université de Montréal, Montréal, Québec, Canada

[3]Animal Reproduction Research Centre (CRRA), Faculty of Veterinary Medicine, Université de Montréal, Montréal, Québec, Canada

Koome *et al.* (2014) investigated the possibility of inferring the status of fetal autonomic nervous system activity from heart rate (FHR) variability (fHRV) analysis in frequency domain. The authors provide evidence that this is not possible. However, a number of crucial methodological issues need to be resolved before this conclusion can be drawn.

First, information on the fetal ECG sampling rate is not provided, but it is crucial for a correct estimation and analysis of HRV (1996; Karin *et al.* 1993). The time scale of subtle fHRV events requires the temporal resolution of R peak detection in the QRS complex to be within <1 ms (Karin *et al.* 1993).

Second, the low-frequency to high-frequency ratio (LF/HF) of fHRV spectral power is presented and used as the measure of autonomic balance. This mathematical approach has been challenged because it does not reflect the underlying autonomic nervous system physiology (Eckberg, 1997). The authors themselves discuss this as an explanation for why the measure failed. Low-frequency spectral power reflects both sympathetic and parasympathetic influences, while HF spectral power reflects parasympathetic influences; consequently, changes in the ratio do not purely reflect the balance between sympathetic and parasympathetic activity. To assess autonomic balance, one would need to use direct measurements of sympathetic activity, such as muscle or renal sympathetic nerve activity, and relate these to changes in the HF power spectrum.

Lastly, there are a number of concerns with the authors' approach to frequency domain analysis, as follows. First, the adult HF band range was taken (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996) rather than the fetal one (Karin *et al.* 1993, 1996; Van Leeuwen *et al.* 2003). Thus, the conclusion that no developmental change in HF frequency band was present is premature, as

Call for comments

Readers are invited to give their opinion on this article. To submit a comment, go to: http://ep.physoc.org/letters/submit/expphysiol;99/2/466.

it was probably low-pass filtered above the 0.4 Hz cut-off chosen by the authors. Second, the fHRV intervals of 120 s may not have captured well the intermittent respiratory activity contributing to the higher frequency spectral power of fHRV and the LF and very LF band contributions (Karin *et al.* 1993, 1996). It is not clear how the authors validated these stationarity and physiological aspects. Third, while Van Leeuwen *et al.* (2003) likewise defined HF as <0.4 Hz, they did look at higher frequencies and reported a developmental increase of spectral power in those frequencies. Fourth, were the frequency domain measures normalized in relationship to the integration band width prior to statistical analysis? This is crucial for the assessment of developmental effects when the overall variability and spectral power change (Karin *et al.* 1993, 1996). Fifth, David *et al.* (2007) have shown in human fetuses that if mean FHR drops below 130 beats min^{-1}, aliasing of the respiratory frequency contained in the FHR signal will occur; breathing faster than 50% of mean FHR will exceed the Nyquist critical value of ~1.2 Hz and result in aliasing when estimating the HF component of fHRV. To rule this out, the authors need to assess the fetal respiratory frequency spectrum and FHR range in 0.8 gestation group.

The above critique demonstrates why fHRV analysis in the frequency domain has a low appeal for animal model-based or human fHRV monitoring. The expertise required to dissect modulatory contributions of the parasympathetic branch of the autonomic nervous system to fHRV *versus* the sympathetic modulatory contributions restricts the physiological applicability and dissemination of this approach. For these reasons, the time domain fHRV measures should be preferred, because they have been widely validated for detection of physiological and pathophysiological phenomena and are safer to use (Garzoni *et al.* 2013). Adherence to a fetal equivalent of the adult HRV Task Force is needed (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996) to promote and maintain a gold standard in validation of fHRV methodology at the fetal stage of development in animal and human studies. This is a *conditio sine qua non* to foster the development of objective and reliable fetal monitoring technologies relying on estimation of sympathetic and parasympathetic modulation of fHRV.

Acknowledgments

Funding

This work was supported by grants from the Canadian Institute of Health Research (CIHR) and Fonds de la recherche en santé du Québec (FRSQ).

References

David M, Hirsch M, Karin J, Toledo E, Akselrod S. An estimate of fetal autonomic state by time-frequency analysis of fetal heart rate variability. J Appl Physiol. 2007; 102:1057–1064. [PubMed: 17095644]

Eckberg DL. Sympathovagal balance: a critical appraisal. Circulation. 1997; 96:3224–3232. [PubMed: 9386196]

Garzoni L, Faure C, Frasch MG. Fetal cholinergic anti-inflammatory pathway and necrotizing enterocolitis: the brain-gut connection begins *in utero*. Front Integr Neurosci. 2013; 7:57. [PubMed: 23964209]

Karin J, Hirsch M, Akselrod S. An estimate of fetal autonomic state by spectral analysis of fetal heart rate fluctuations. Pediatr Res. 1993; 34:134–138. [PubMed: 8233713]

Koome ME, Bennet L, Booth LC, Davidson JO, Wassink G, Gunn AJ. Ontogeny and control of the heart rate power spectrum in the last third of gestation in fetal sheep. Exp Physiol. 2014; doi: 10.1113/expphysiol.2013.074567

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996; 93:1043–1065. [PubMed: 8598068]

Van Leeuwen P, Geue D, Lange S, Hatzmann W, Grönemeyer D. Changes in the frequency power spectrum of fetal heart rate in the course of pregnancy. Prenat Diagn. 2003; 23:909–916. [PubMed: 14634977]