Fetal heart rate variability: an ocean of meanings beyond ups and downs

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Running title: HRV - beyond ups and downs

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A commentary

I read with interest the review by Tarvonen et al. entitled "Increased variability of fetal heart rate during labour: a review of preclinical and clinical studies".[1]

The authors seek to clarify how physiologists and obstetricians use heart rate variability (HRV) terminology differently. This gap in mutual understanding has been one of the key reasons why fetal heart rate (FHR) monitoring intrapartum has failed so far to reduce the rate of fetal brain injury.[2] I suggest that this gap can only be closed if the mathematical understanding of the HRV is incorporated into the multidisciplinary bridge we are building.

Despite a thorough literature review, I missed this key component in the article. Consequently, the very notion of the HRV is not captured in the review. Rather, the article perpetuates the stereotypical misunderstanding of HRV as a simplistic “up or down” metric.

While the term “variability” does elicit an intuitive notion of increases and decreases, the underlying complexity has turned out to be far richer. In the following account, I attempt to explain this mathematical complexity. I focus on its relevance to the goal of preventing perinatal brain injury using intrapartum FHR monitoring.

HRV is multidimensional

Descriptions of HRV pattern in terms of “ups” and “downs” discard most predictive information.[3] The mathematical properties of HRV - when assessed over, say, five minute intervals - are changing over time as a function of behavioral states and other endogenous and exogenous factors, i.e., these patterns are dynamic. In addition to this time component, complex patterns of HRV emerge from measuring its properties over five signal-analytical domains, i.e., there are five complementary ways to express aspects of HRV: statistical, complexity/entropy, scale invariance/fractality, spectral power in certain frequency bands/energy, and geometric.[4] Observing these dynamic changes over the five signal-analytical domains results in multi-dimensional patterns. We observe many instances of fetal physiological behavior where these patterns appear to form a unique signature of a given behavior, e.g., systemic or organ-specific response to an inflammatory stimulus or the memory of chronic hypoxia.[5]

HRV is amenable to feature engineering

A related reason for the persistent failure of FHR monitoring intrapartum to live up to expectations is the limited or absent ‘feature engineering’ (automatic extraction of the five domains described above) of HRV. In addition to capturing the multi-dimensional properties of HRV, feature engineering makes allowances for the noisy, low sampling rate nature of the signal, to ensure that these properties are captured with the highest possible fidelity.[6,7] The limitations of the low sampling rate of beat-to-beat variability typically resulting from an ultrasound-based FHR computation are discussed elsewhere.[6]

’Feature engineering’ is standard data science/machine learning term. In the present context, it means identifying and reproducibly extracting certain mathematical properties of the input signal, such as HRV’s dynamic multi-dimensional patterns, and using these properties in a model to predict a clinical outcome of interest. A hands-on example of such an approach has been open-sourced recently.[4]

Among the HRV feature engineering approaches, there are promising developments in the detection of accelerative and decelerative FHR patterns using computerized HRV analyses.[8] Their clinical potential needs to be studied.

The difficulty in defining an individual FHR baseline may be overcome by the recent developments in HRV analysis which rely on individualized anomaly detection.[9] In such an approach, the computer algorithm learns to distinguish the individual baseline, e.g., FHR on admission to labour, from a later ensuing anomaly, e.g., during the second stage. The obvious caveat is the possibility of anomalies as early as on admission. That is the reason why a more comprehensive solution to this challenge is sought within the framework of “whole-pregnancy” FHR monitoring, i.e., by including antepartum FHR information into the analytical framework.[7]

It is chastening to realise that according to a recent NHS report, 70% of intrapartum brain injuries could be prevented if only someone had responded to abnormalities in labour – consistent vigilance appears to be humanly impossible.[10] A feature engineering approach to fetal HRV monitoring obviates the reliance on the human eye and can highlight patterns below the common human threshold of detection, e.g., beyond the sinusoidal patterns or variability below 5 bpm. In addition to an explicitly defined mathematical approach to feature engineering as outlined above, “black-box” deep learning approaches have been tested on intrapartum FHR and cardiotocography data.[11] These techniques rely on computer pattern recognition, an artificial intelligence approach used broadly in medical research and in other domains, e.g., to enable self-driving cars. It entails teaching the computers to “see” the cardiotocography patterns that humans could see if they could watch it at all times.[11] This approach is in its infancy but the importance of feature engineering on FHR/HRV was emphasized in the recent 3rd and 4th workshops on Signal Processing and Monitoring in Labor (SPaM).[7]

HRV and prediction of health outcomes

What we aim to predict or detect using HRV must be clearly defined before undertaking preclinical and clinical studies. In addition to the relevant studies on the prediction of hypotension mentioned by Tarvonen et al.,[9] other outcomes that are possible to predict or detect should be considered. These outcomes include the fetal inflammatory response syndromes (FIRS) or memory of past inflammation (predisposing to ‘second hit’ vulnerabilities, as is relevant for Zika virus infection), and of hypoxia (e.g., later manifesting as fetal growth restriction).[5,12]

Conclusions

When attempting to explain HRV, it may help to think of the ripples on the surface of an ocean. It is difficult to see them all at once and all the time or to grasp how the pattern originated. HRV comprises complex, but not random, patterns of interference and communication. A suite of mathematical tools that also account for uterine activity, maternal temperature, fetal movements and behavioral states, to name some factors that influence HRV, could decode HRV to detect and predict salient clinical events. AI and well-informed feature engineering are poised to enable development of clinical decision support tools for managing labor. Validation and adoption of such tools could reduce the incidence and severity of perinatal brain injury.

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Contribution to Authorship
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