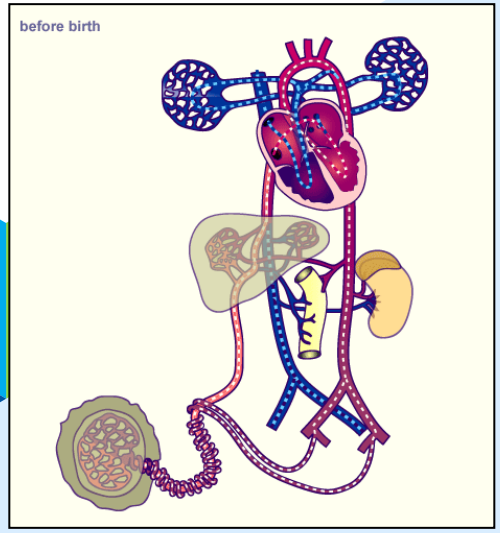
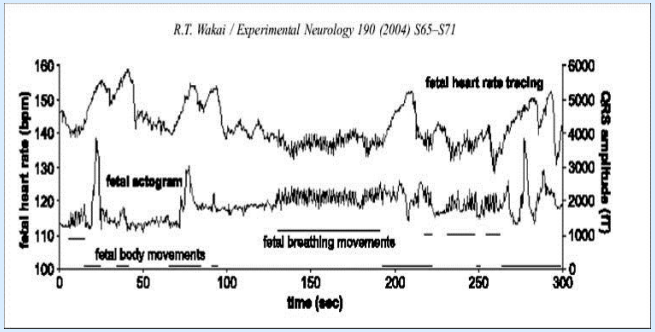
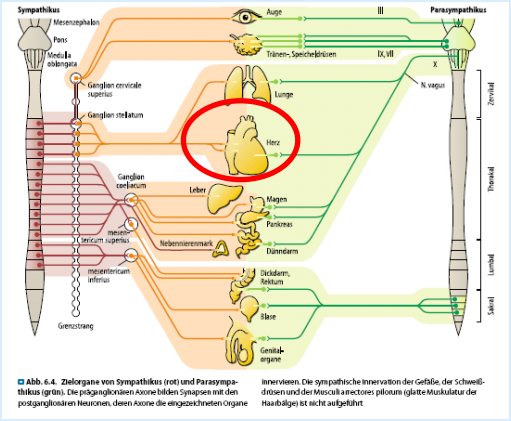
UNIVERSITÄTS KLINIKUM jena

Fetal heart rate regulation reflecting autonomic maturation







Listening comprehension in the communication with the unborn child

ESGCO, Lancaster/UK, 15. April 2016

Prof. Dr. med. U. Schneider

Uwe Schneider, Alexander Schmidt, Eva-Maria Dölcker, Susann Jaekel, Samuel Nowack and Dirk Hoyer for the *Study Group 'Prenatal Monitoring of Autonomic Maturation'*

Prenatal Monitoring of Autonomic Maturation

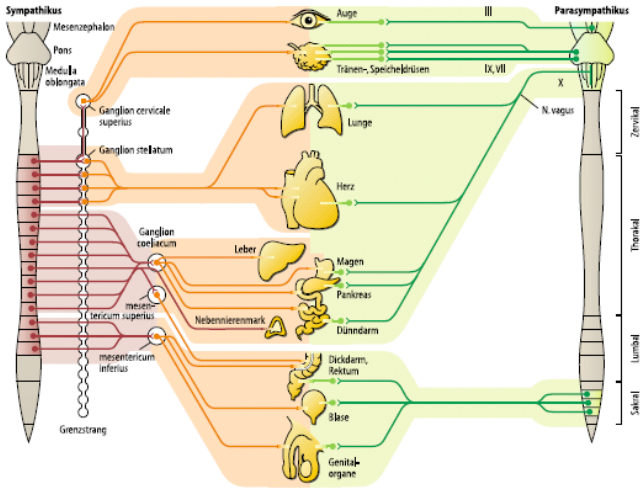
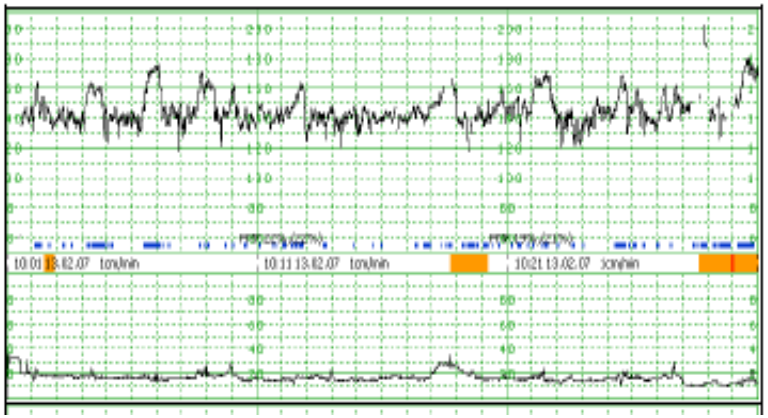


Abb. 6.4. Zielorgane von Sympathikus (rot) und Parasympathikus (grün). Die präganglionären Axone bilden Synapsen mit den postganglionären Neuronen, deren Axone die eingezeichneten Organe innervieren. Die sympathische Innervation der Gefäße, der Schweißdrüsen und der Musculi arrectores pilorum (glatte Muskulatur der Haarbälge) ist nicht aufgeführt

Key necessity for extrauterine life:
Developing autonomic ability to adapt to varying amounts of supply and demand

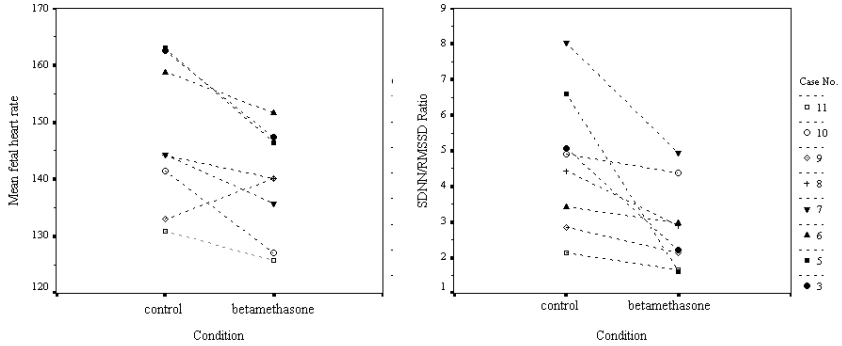
maturational process with a pace never to be observed again later in life

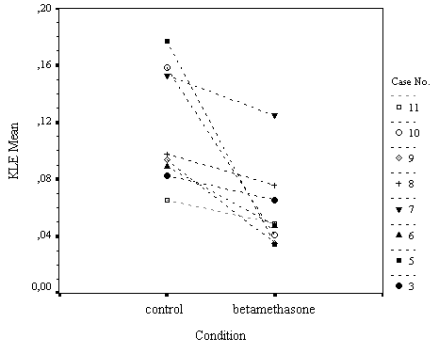


Fetal Heart Rate Pattern (+ movements) easiest to access non-invasively for continuous monitoring

representing direct effect of autonomic regulation (and some more …)

Prenatal Monitoring of Autonomic Maturation





Schneider U, EHD, 2010

Key necessity for extrauterine life:
Developing autonomic ability to adapt to varying amounts of supply and demand

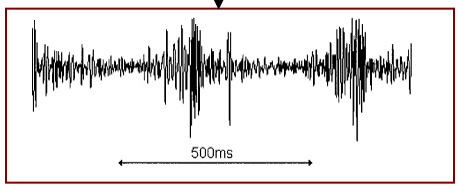
Adequate functioning representing a marker of fetal maturation

Disturbances of intra-uterine maturation or milieu causes changes in autonomic regulatory capacitiies

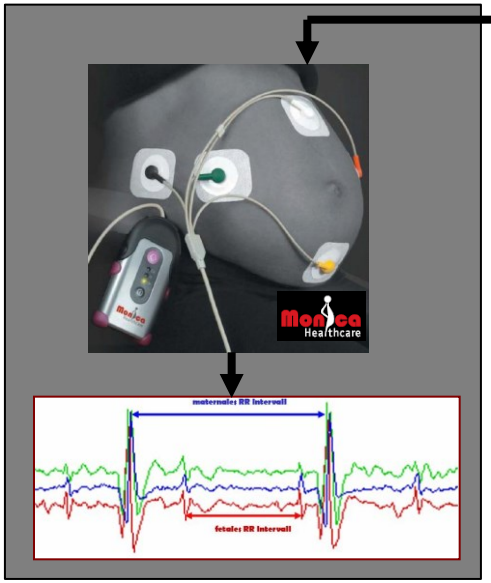
Acute suppression of sympathetic function after in utero exposition to synthetic steroids during pharmaceutical induction of fetal lung maturation, parasympathetic modulation not influenced

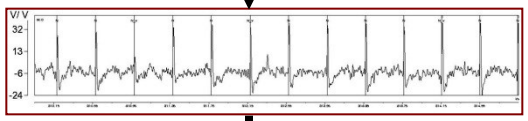
Non-invasive continuous antenatal monitoring of fetal heart rate

Doppler US based

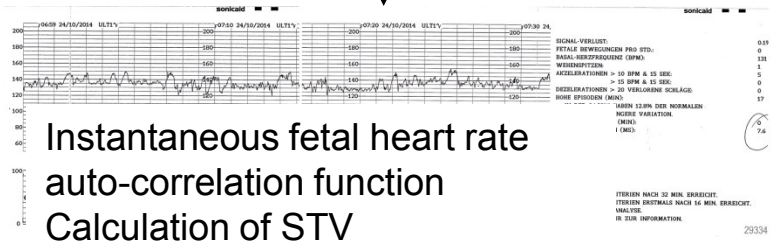


electrophysiologic





Result



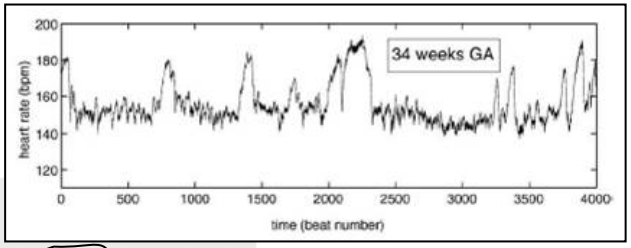
Instantaneous fetal heart rate
auto-correlation function
Calculation of STV

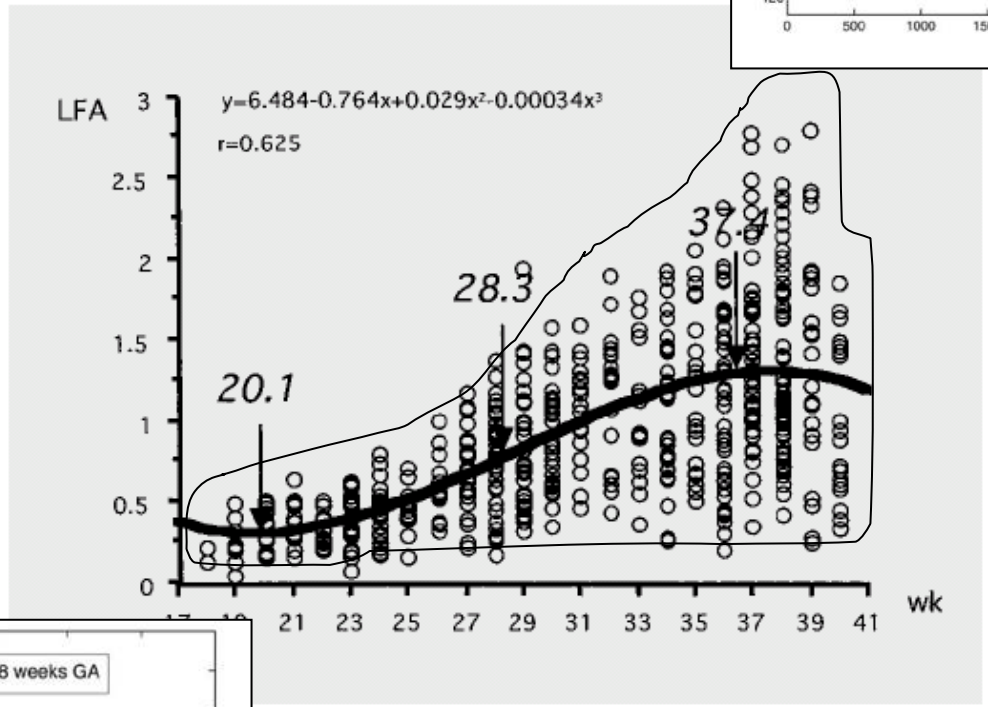
Beat – to – Beat detection of fetal heart rate
120 – 160 discrete time points, acuity +/- 1 ms
fHRV: fetal heart rate variability

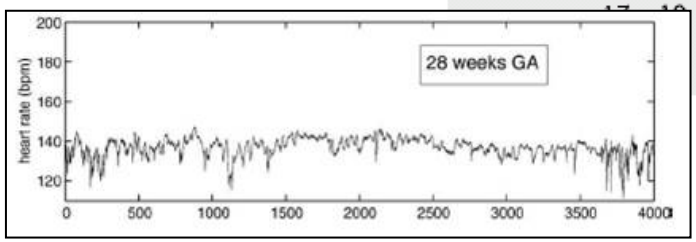
Physiology of fetal heart rate regulation I

Heart rate pattern and gestational age

Ohta et al., Fet Diagn. Ther 1999



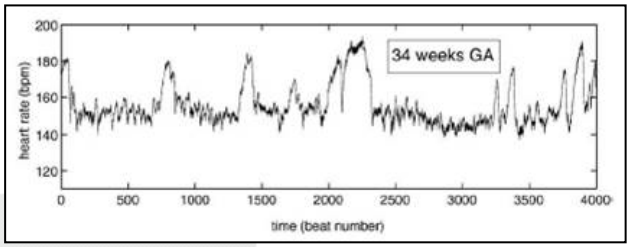


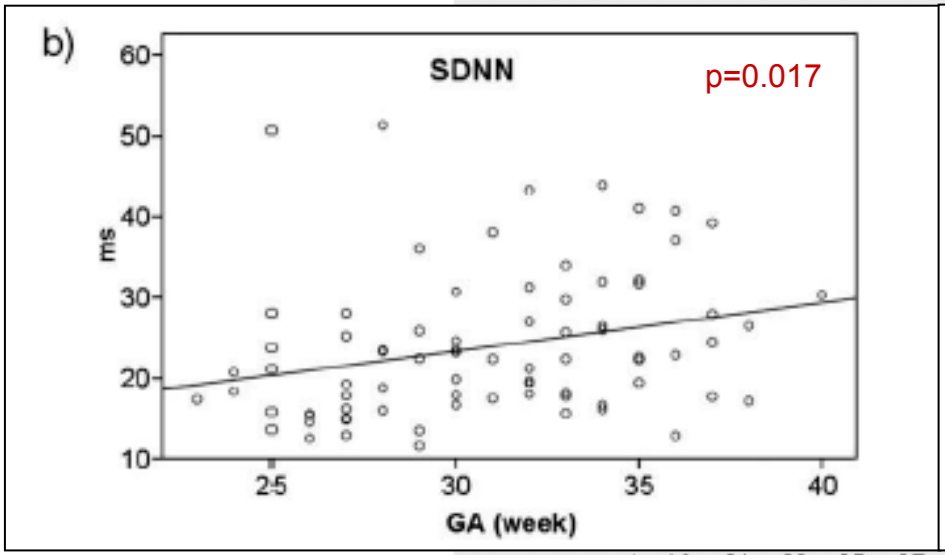


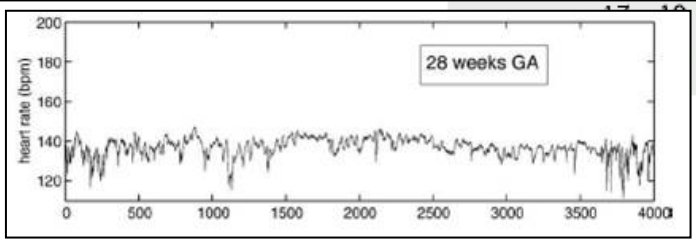
Physiology of fetal heart rate regulation I

Heart rate pattern and gestational age

Ohta et al., Fet Diagn. Ther 1999



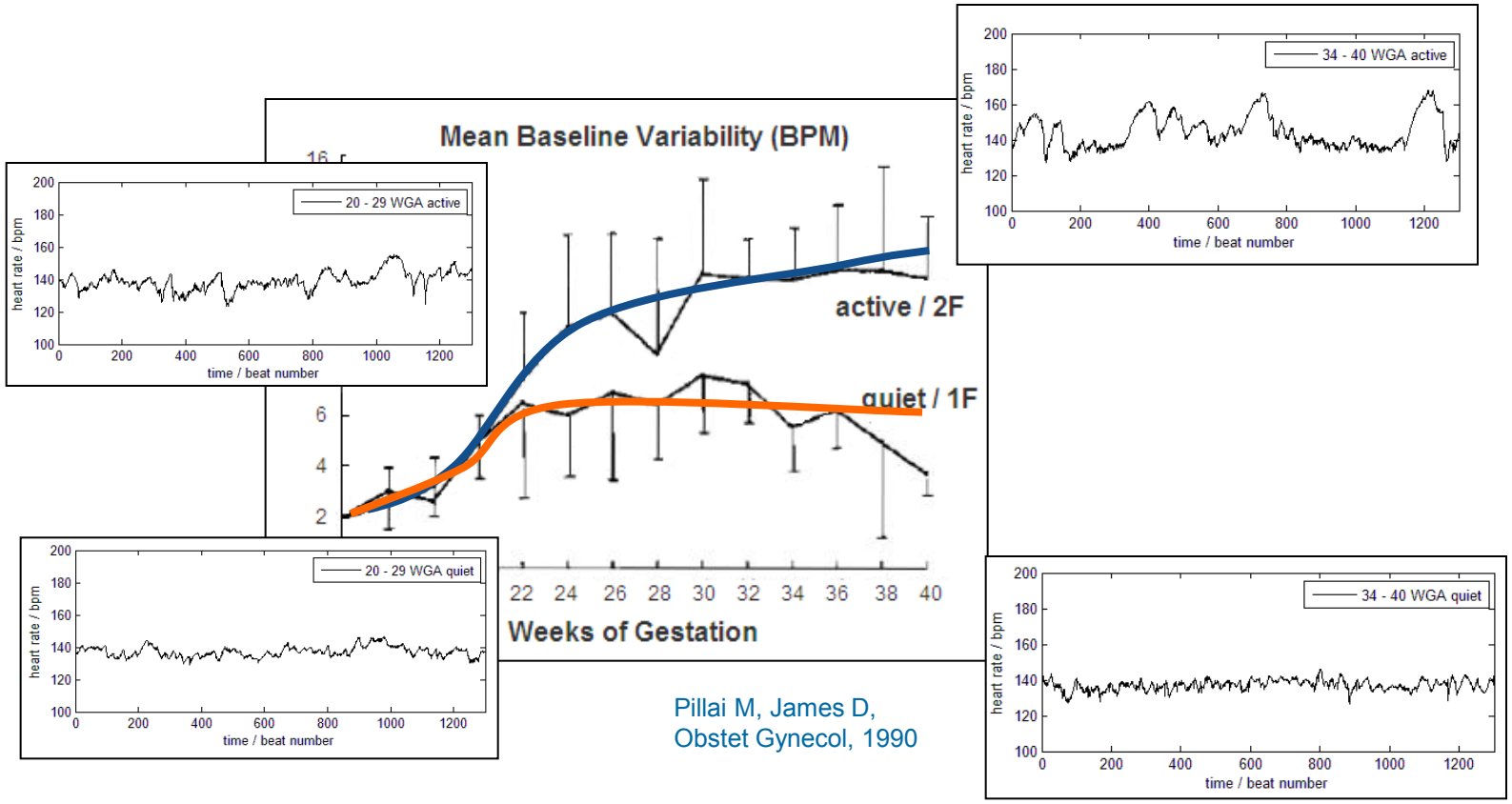




Hoyer et al., EHD, 2009

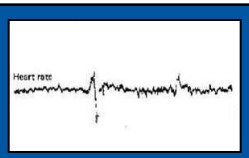
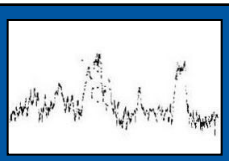
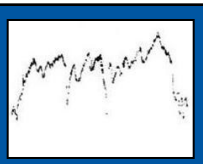
Physiology of fetal heart rate regulation II

Heart rate pattern and gestational age and neurobehavioural fetal state



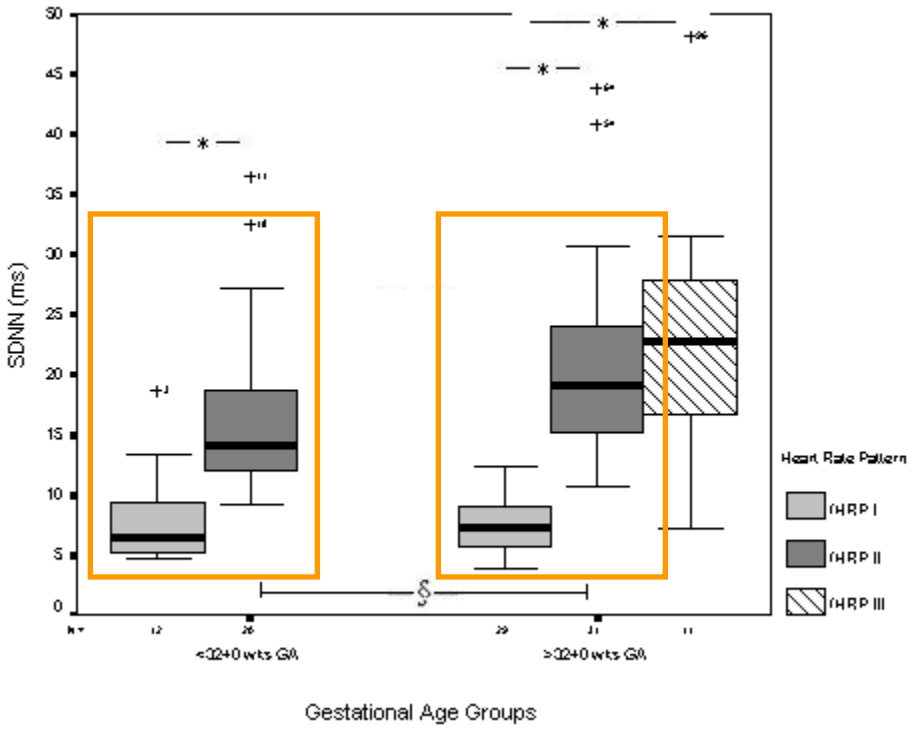
Pillai M, James D,
Obstet Gynecol, 1990

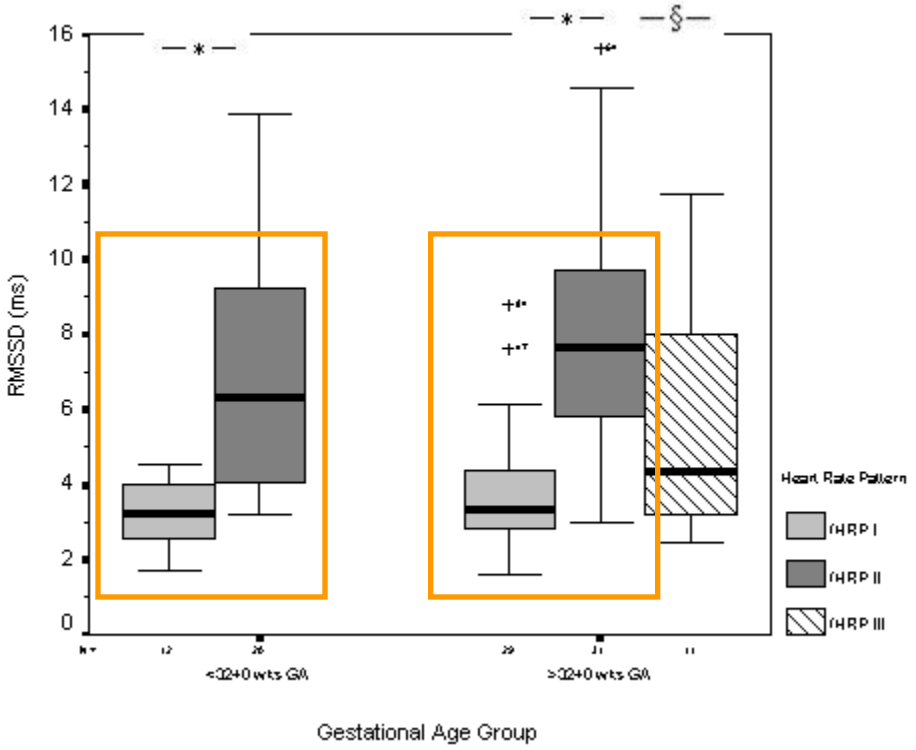
Nijhuis J, et al., EHD, 1982

Neurobehavioural fetal state	quiet / 1F	active / 2F	(3F)	Active awake / 4F
Heart rate pattern	Type A	Type B		Type D
Charakteristics				
Basal heart rate (bpm)	115 - 150	115 -153	k.A.	155 - 172
Oscillation bandwidth	narrow	normal	normal	non-determined
accelerations	rare, singular	frequent	keine	long-lasting
Body movements	rare, ‘startles’	intermittend - continuously	no	continuously
Rapid eye movements	no	continuously	continously	continuously
Time share at term	25 – 30 %	60 – 70 %	< 1%	ca. 10 %
Duration (min)	3 - 38	3 - 94	k.A.	4-137

Distribution of linear fHRV according to heart rate pattern

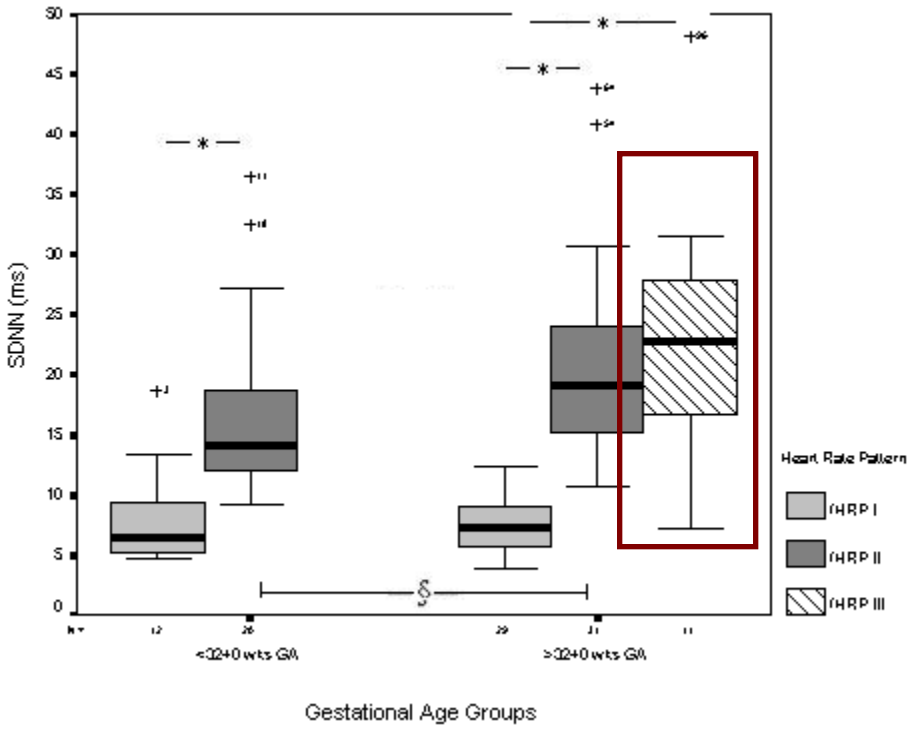
(Frank et al., 2006, Schneider et al. 2008, 2009)

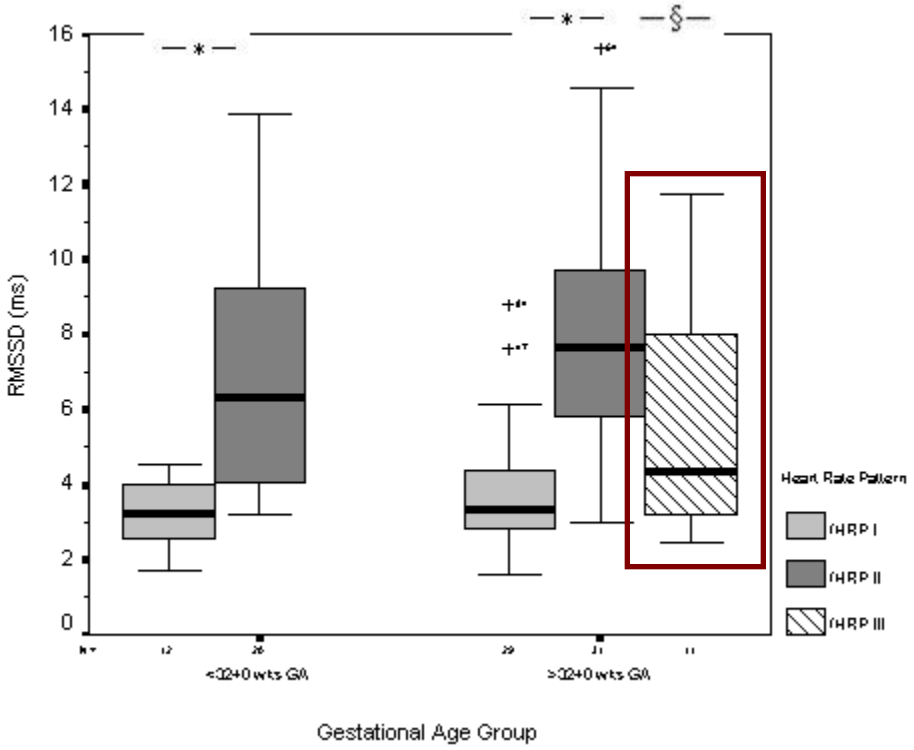




Distribution of linear fHRV according to heart rate pattern

(Frank et al., 2006, Schneider et al. 2008, 2009)





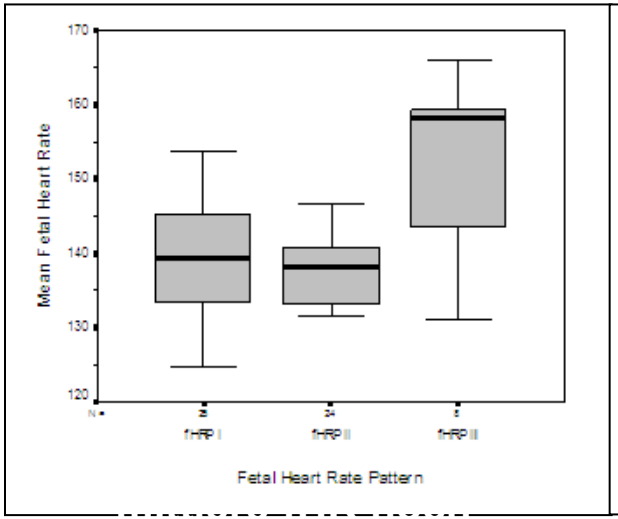
Sympathetic Triad

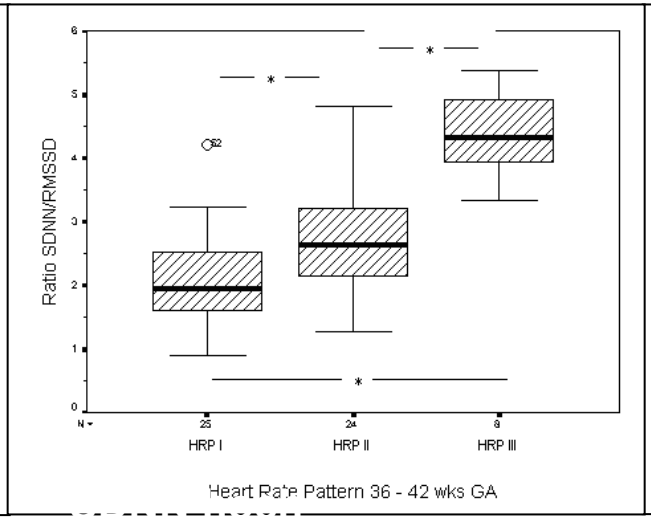
(mature fetal neurobehavioural states > 35 wksGA)

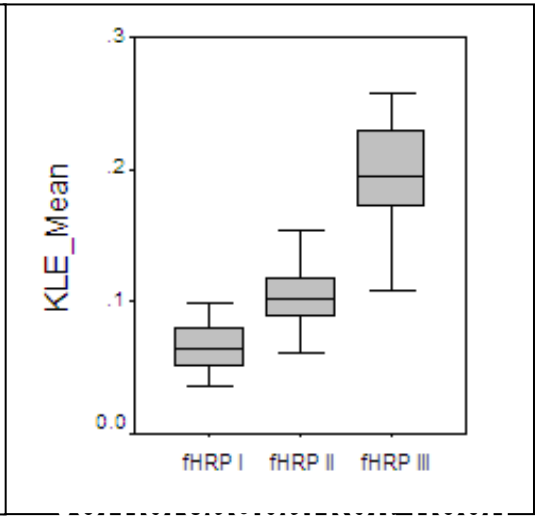
Basal heart rate

Sympathovagal Balance

Predictability

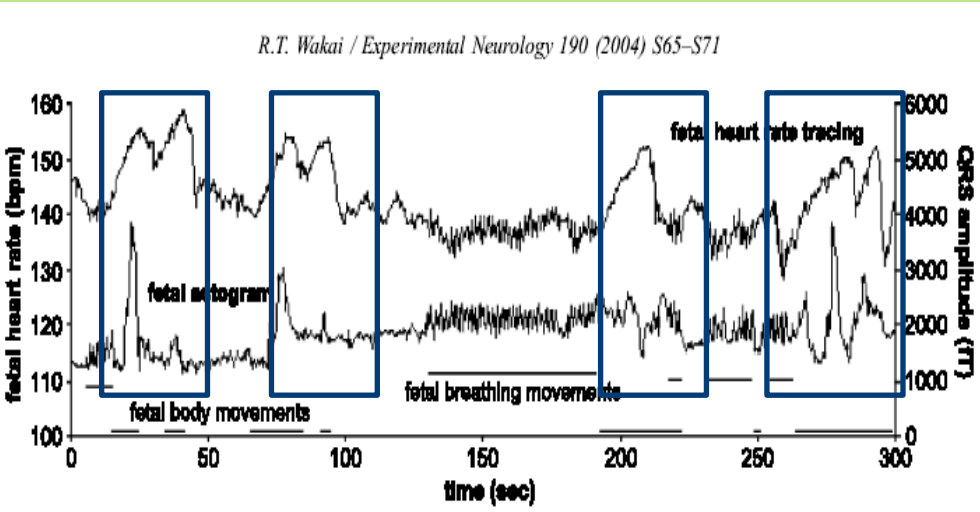






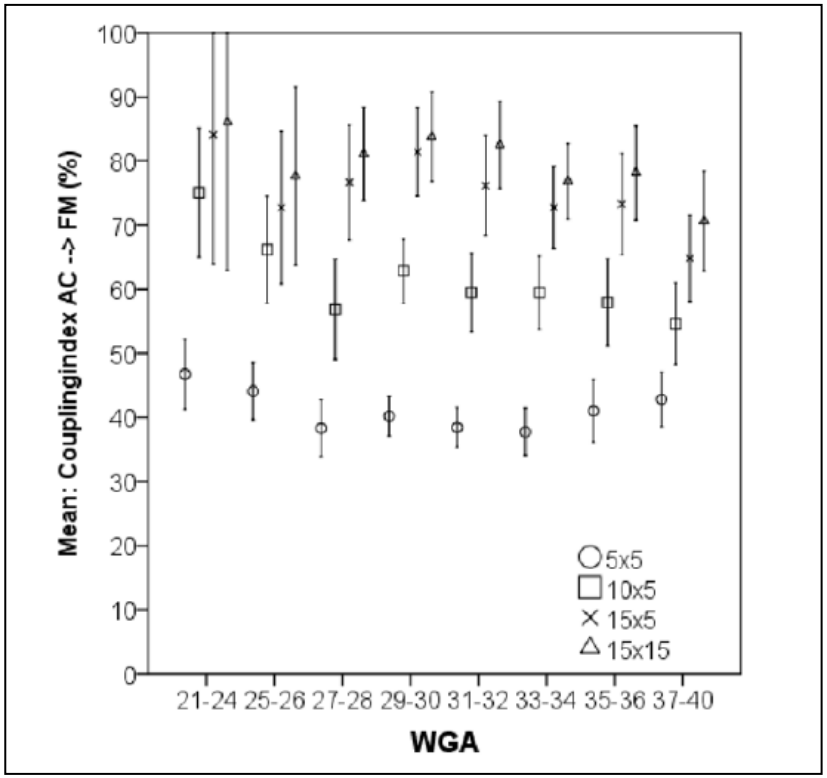
Schneider U et al., JPM, 2008

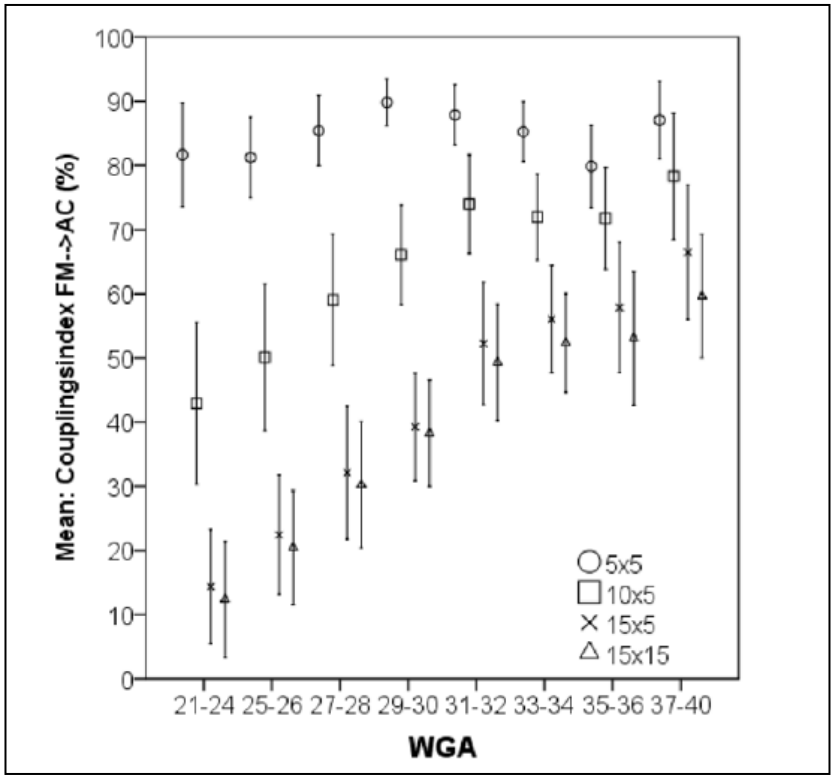
Synchronization of behavioral patterns



Schmidt A et al., Phys Meas, 2014

Association between FM and heart rate accelerations



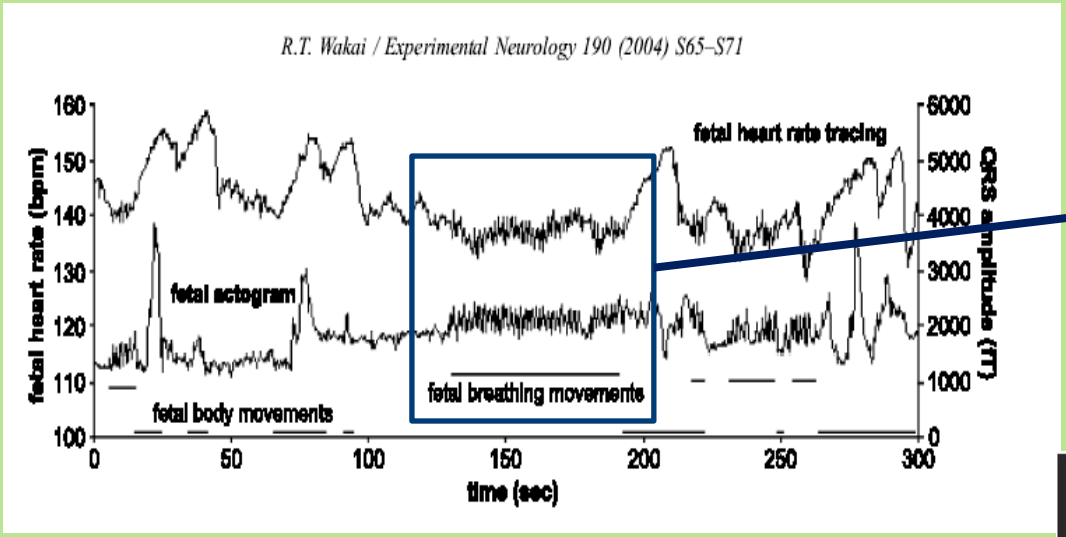


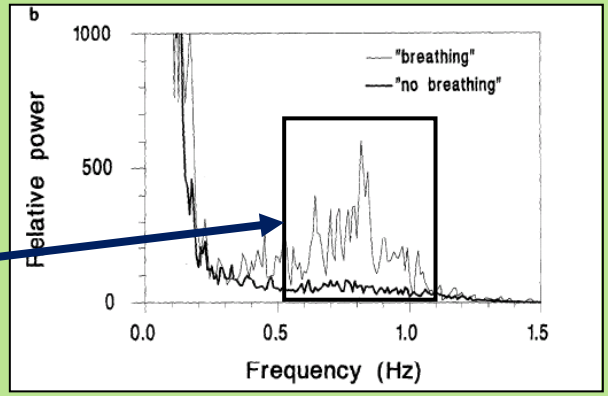
Schmidt A et al., Phys Meas, 2014

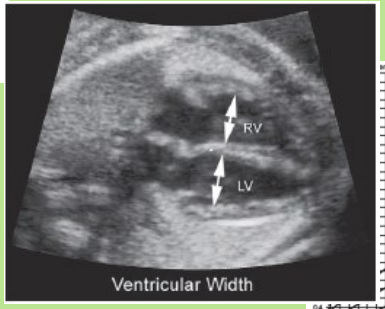
Synchronization of behavioral patterns

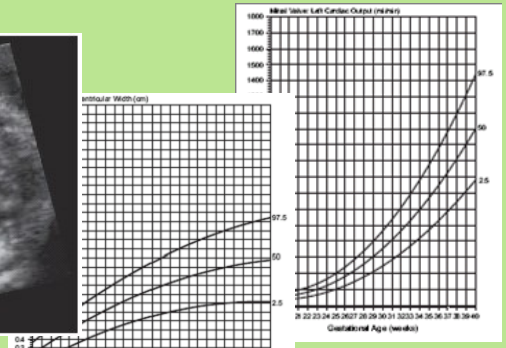
Wakai RT, EHD, 1993

Respiratory Sinus Arrhythmia (RSA)









deVore, Seminars Fet Neonat Medicine, 2005

Growth of the fetal heart,
Variation of stroke volume

Levels of autonomic regulation of fetal cardiac function

Temporal regulatory level	Physiologic correlate	Parameters of fHRV
long rhythms	sympathetic activation	SDNN, fLF, fVLF
short rhythms	vagal activity	RMSSD, fHF
long – term complexity	overlay of different regulatory circuits	KLE_fLF, AIF_125, AIF_long
Regularisation of fHR 0,4 – 1,7 Hz	Respiratory Sinus Arrhythmia	fHF, KLE_fHF, AIF_fHF
Intrinsic beat-to-beat variation	increasing beat-to-beat variation of stroke volume	KLE_NN, AIF_NN

Intraindividual longitudinal comparison

GA group	Mal a-b	Mal a-c	Mal b-c	Mal b-d	Mal c-d
a (23/1 – 28/0)					
b (28/1 – 31/0)	16				
c (31/1 – 35/0)		17	16		
d (> 35/0)				6	9

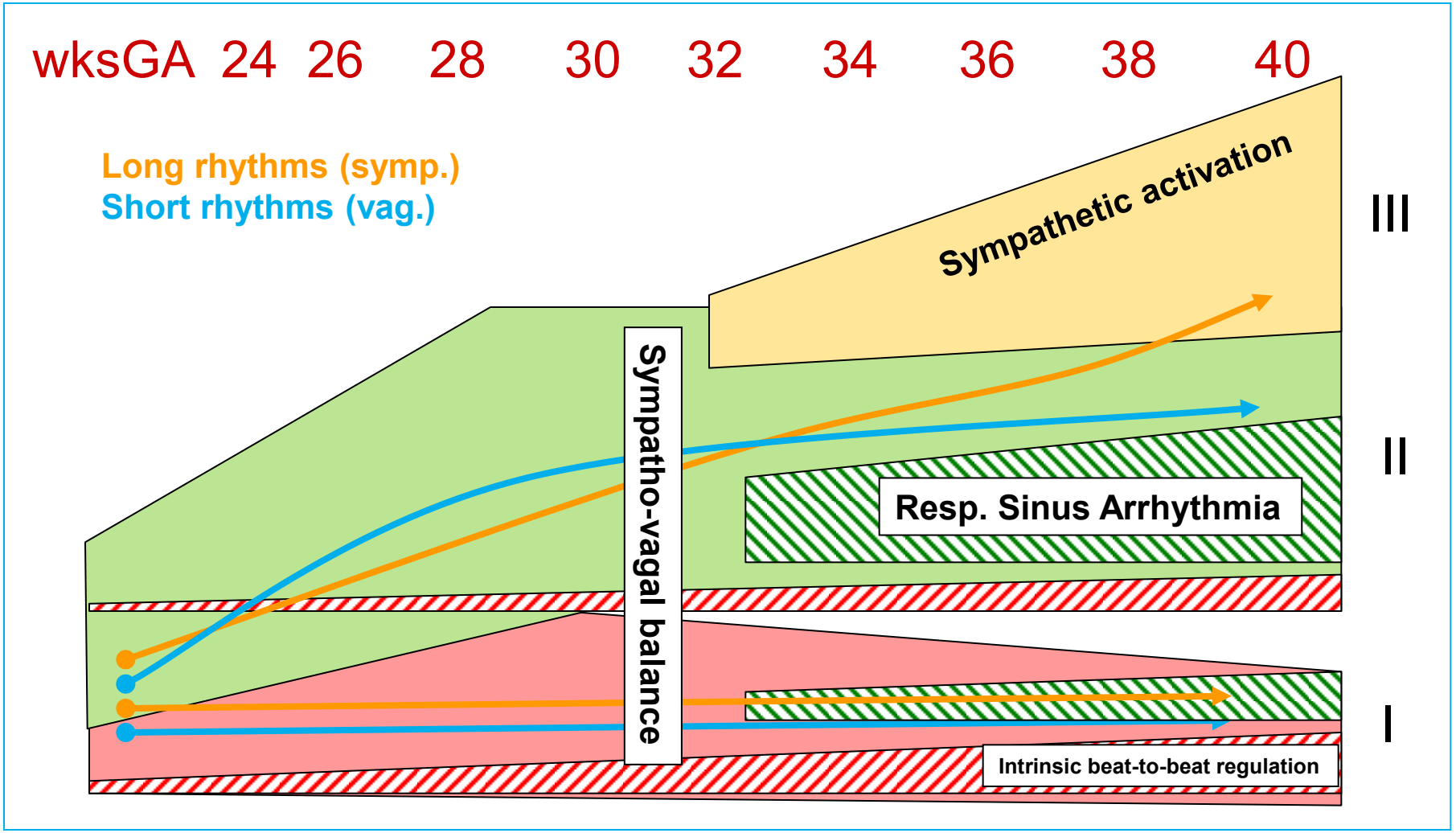
- unselected time series over 30 min
- Selected active fHR patterns 10 min
- GA group = gestational age range; MaI = maturational interval

Summary of the results (unselected / active)

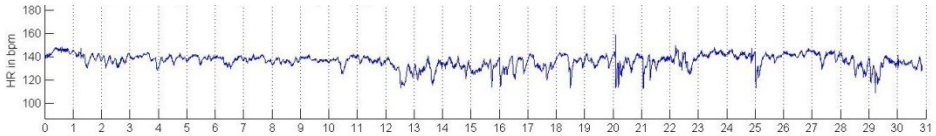
increase/decrease: ↗/ ↘ sgnf. ; (↗ / ↘) Trend

	SDNN	RMSSD	AIF_125	AIF_fHF	AIF_NN
Mal a-b		/ ↗	(↘) / ↘		
Mal a-c	↗/ ↗	/ (↗)	(↘) / ↘	(↗)/	
Mal b-c					
Mal b-d	(↗)/(↗)	(↗) / (↗)		(↗) / (↗)	
Mal c-d	/↗		(↘)	↗ / (↗)	↘ /

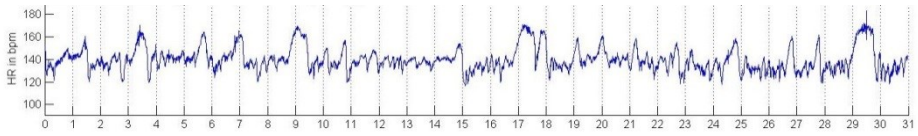
Intrauterine maturation of autonomic heart rate regulation (model)



Universal Principles of Maturation

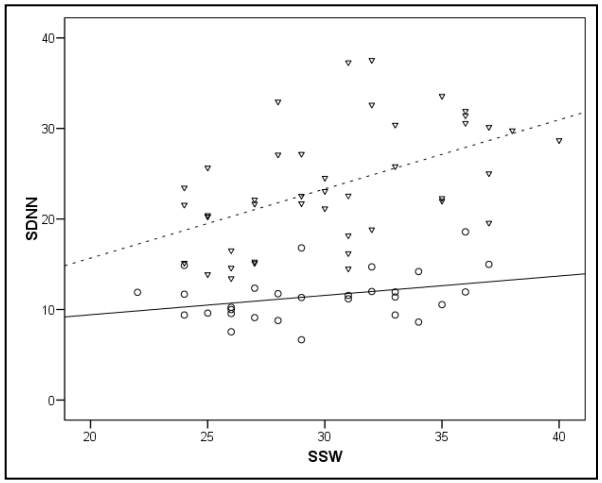


Heart rate pattern at 27+6 wks GA

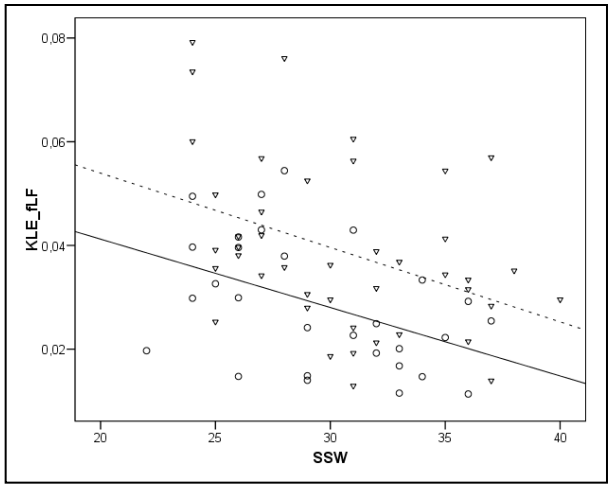


Heart rate pattern at 36+3 wks GA

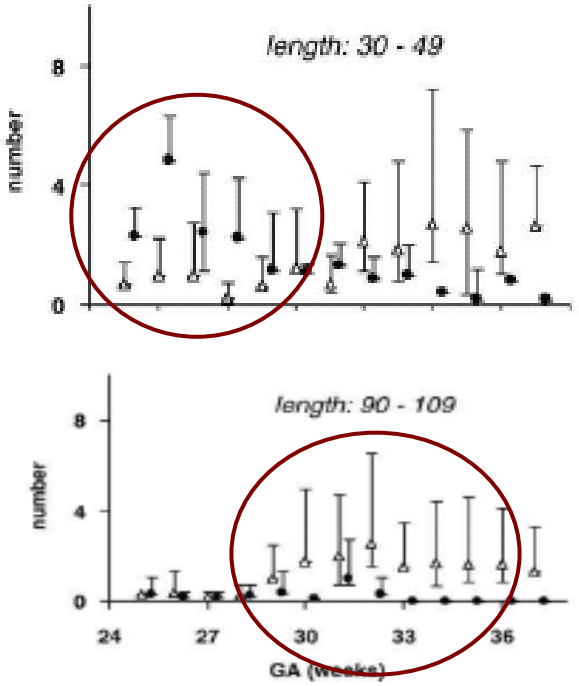
Increasing fluctuation amplitude

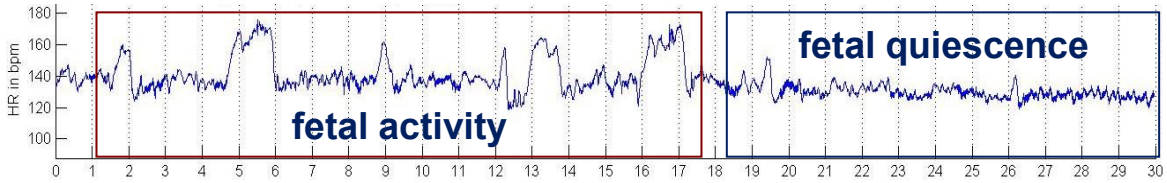


Increasing complexity



Formation of typical patterns





Representations of the universal principles of maturation in fHRV

Hoyer/Schneider, et al. PlosOne 2013

Parameter	Calculation	Interpretation
amplitude	Interquartile distance (20-95) of NN intervals	luctuation amplitude
gMSE(3)	Multiscale Entropy after ‚coarse gaining' 3 (Costa, 2005, 2008; Hoyer 2012, 2013)	Complexity of the heart rate pattern
skewness	asymmetry of the distribution of NN intervals (Hoyer, 2013)	decrease of decelerations, increase of accelerations
pNN5	Percentage of NN intervals > 5 ms (Task Force, 1997)	vagal rhythms, respiratoriy sinus arrhtyhmia
VLF/LF	Ratio of spectral band power of fVLF (0,02-0,08 Hz) and fLF (0,08-0,2 Hz) bands (David, 2007)	Baseline stability
STV	16 epochs/min, mean puls intervals, difference between adjecent epochs, mean	Short term variation of FHR (Dawes/Redman)

Coefficient of determination, R^2

30 min heart rate traces, unselected patterns

Parameter	linear	quadratic
STV	0.200	0.206
AMP	0.312	0.321
skewness	0.458	0.502
pNN5	0.347	0.367
VLF/LF	0.034	0.060
gMSE(3)	0.226	0.231
fABAS	0.648	0.656
fABAS+STV	0.649	0.657

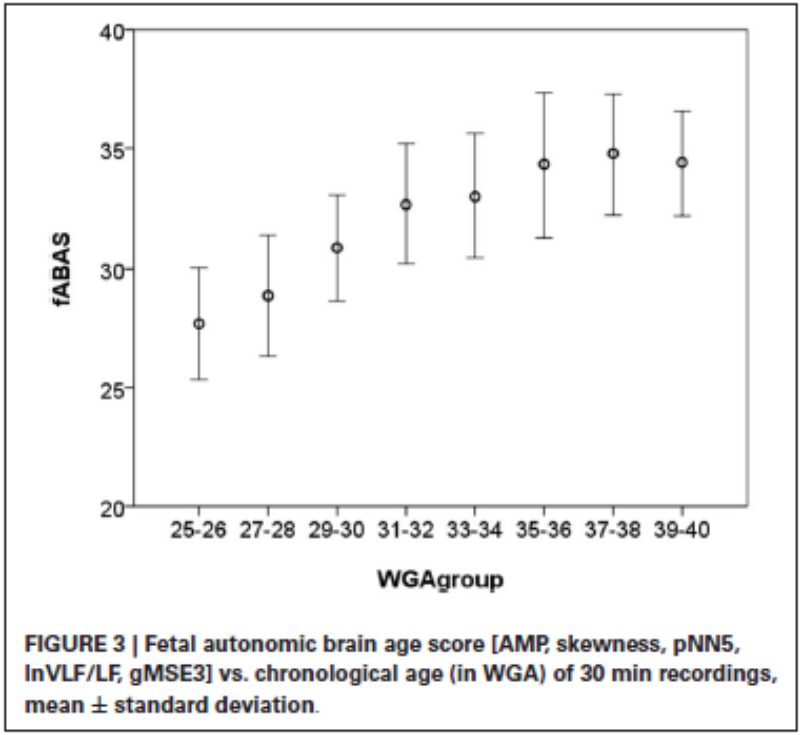


FIGURE 3 | Fetal autonomic brain age score [AMP, skewness, pNN5, lnVLF/LF, gMSE3] vs. chronological age (in WGA) of 30 min recordings, mean ± standard deviation.

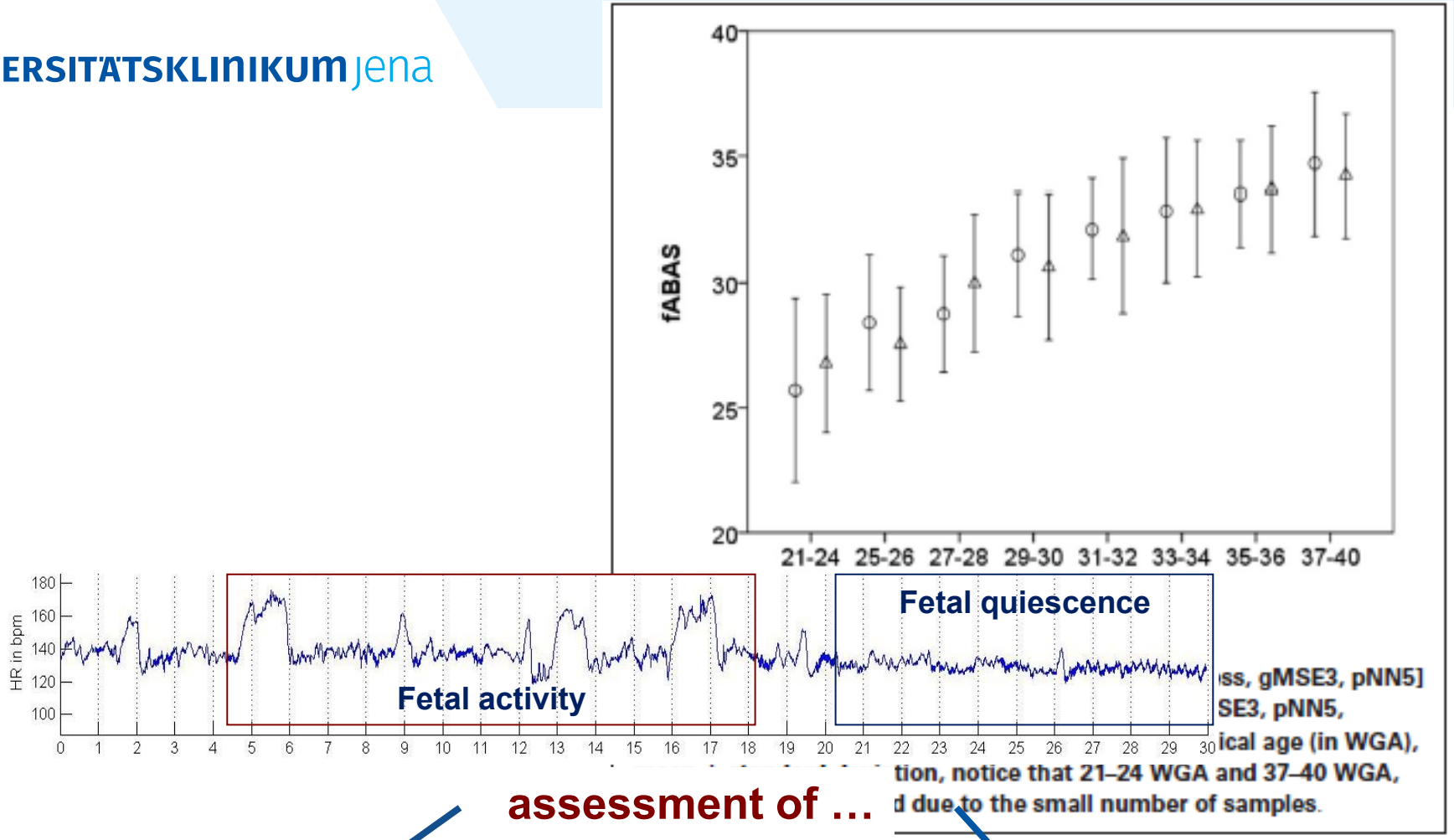
quadratic model
Saturation at ~ 32 wks GA

Pattern segmentation*, coefficient of determination, R^2

selected intervals of 10 min, quiet heart rate patterns

Parameter	linear			quadratic		
	reg	oDC	basic	reg	oDC	basic
skewness	0.316	0.123	0.032	0.320	0.127	0.038
pNN5	0.320	0.396	0.374	0.338	0.451	0.428
gMSE(3)	0.542	0.609	0.632	0.565	0.627	0.657
fABAS	0.626			0.641		
fABAS Schiefe, gMSE(3), gMSE(3) oDC, gMSE(3) basis	0.706			0.714		

*automatic stepwise elimination od DC and AC from pre-selected quiet fetal heart rate patterns



assessment of …

… fetal well-being

… fetal maturity (?)