Change of Spectral Analysis of Fetal Heart Rate During Clinical Hypnosis: a Prospective Randomised Trial from the 20th Week of Gestation Till Term

Spektralanalyse der fetalen Herzrate unter klinischer Hypnose: eine prospektiv randomisierte Studie von der 20. Schwangerschaftswoche bis zum Entbindungstermin

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Abstract
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Objective: To investigate the functional adaptive process of the fetal autonomic nervous system during hypnosis from the 20th week of gestation till term. Are there changes in the power spectrum analysis of fetal heart rate when the mother is having a clinical hypnosis or control period?

Study Design: Fourty-nine FHR recordings were analysed. Included recordings were from singletons and abdominal fetal ECG-monitored pregnancies. All women were randomised to receive clinical hypnosis followed by a period with no intervention or vice versa. Statistical analyses were performed with the Wilcoxon signed ranks and Spearman rho correlation tests.

Results: There was a significant difference found between fetal heart rate at baseline (144.3 ± 6.0) and hypnosis (142.1 ± 6.4). A difference was also detected between the standard deviation of the heart rate between baseline (6.7 ± 1.9) and hypnosis (6.8 ± 3.5). LFnu was smaller during baseline (80.2 ± 5.3) than during hypnosis (82.1 ± 5.7), whereas HFnu was significantly larger (19.8 ± 5.3 vs. 17.9 ± 5.7). There was no correlation between the gestation age and the change in LFnu, HFnu or ratio LF/HF due to the hypnosis intervention.

Conclusion: The functional adaptive process of the fetal autonomic system during hypnosis is reflected by a sympathovagal shift towards increased sympathetic modulation.

Zusammenfassung
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Fragestellung: In der vorliegenden Studie sollte überprüft werden, wie das autonome Nervensystem auf eine Hypnoseintervention zwischen der 20. Schwangerschaftswoche bis zum Entbindungstermin reagiert. Gibt es einen Unterschied der Spektralanalyse der fetalen Herzfrequenz, wenn die werdende Mutter eine Hypnoseintervention erhält im Vergleich mit der Kontrollperiode ohne Intervention?

Studiendesign: 49 Einlingsschwangerschaften mit abdominaler fetaler EKG-Ableitung wurden analysiert. Alle Schwangeren wurden randomisiert, um eine Hypnoseintervention und eine Kontrollperiode oder vice versa zu erhalten. Zur statistischen Analyse wurden der Wilcoxon-Signed-Rank-Test und der Spearman-Rho-Korrelationstest herangezogen.

Ergebnisse: Es ergab sich eine statistisch signifikante Differenz zwischen der fetalen Herzfrequenz zwischen Kontrollphase ($144,3 \pm 6,0$) und der Hypnoseintervention ($142,1 \pm 6,4$), sowie in der Standard-Deviation der Kontrollphase ($6,7 \pm 1,9$) und der Hypnoseintervention ($6,8 \pm 3,5$). LFnu war niedriger in der Kontrollphase ($80,2 \pm 5,3$) als während der Hypnoseintervention ($82,1 \pm 5,7$), wohingegen HFnu statistisch signifikant größer war ($19,8 \pm 5,3$ vs. $17,9 \pm 5,7$). Es gab keine Korrelation zwischen dem Gestationsalter und einer Änderung der LFnu, HFnu oder LF/HF während der Hypnoseintervention.

Schlussfolgerung: Das fetale autonome Nervensystem reagiert bei einer mütterlichen Hypnoseintervention durch einen sympathovagalen Shift in der Richtung eines erhöhten Sympathikotonus.

Introduction
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Hypnosis is a recognised psychological technique [1], which is characterised by deep relaxation, focused attention, vivid imagery and increased receptivity to suggestion [2]. Functional brain imaging [3,4] and EEG studies [5,6] showed that the hypnotic state is different from sleep, from alert awareness and relaxed rest. The hypnotisability varies from person to person, but is higher during pregnancy [7]. The ability to influence and access function beyond conscious control is increased during the hypnotic state [8,9], which might proof beneficial in preterm labour [10–12] and might be able to influence the blood flow of the A. umbilicalis [13].

The autonomic nervous system is altered during hypnosis which includes acute [14] and chronic [15,16] (after hypnotherapy) changes. Heart rate variability (HRV) provides a tool to evaluate acute cardiac autonomic alterations during hypnosis [17]. The changes of the autonomic nervous system (ANS) can be studied using spectral analysis of fetal heart rate (FHR) periods. In human adults frequency bands have been identified that can indicate the sympathetic and parasympathetic nervous system input [18,19]. The high frequency (HF) component is mainly indicating parasympathetic nervous system, whereas a combined sympathetic and parasympathetic nervous system is reflected by the low frequency (LF) components [19]. The sympathovagal balance can be evaluated using the ratio between LF and HF [19]. Due to maturation of the fetal autonomic nervous system the absolute LF and HF power increases as pregnancy progresses [20,21]. In the third trimester the increase in LF and HF power is not so high [21]. Furthermore typical reflex responses of the parasympathetic nervous system only begin at term and reach adult levels after birth [22]. Fetal LF and HF bands are influenced by the behavioural state [23], but results of our study group also showed an effect of fetal behavioural state depending on the state of the pregnant women [13,24].

Recently, a non-invasive abdominal fetal electrocardiogram (ECG), which provides true beat-to-beat evaluation with good signal quality [25–27], has been approved for clinical usage from the 20th week of gestation onwards.

To the best of our knowledge, no study has examined whether hypnosis influences fetal LF and HF bands during pregnancy.

Materials and Methods
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Study samples

All patients who had a single pregnancy were eligible to participate in this study. All (49/49) women who were informed about the study agreed to participate. None of the subjects had previous experience with hypnosis. None of the subjects had psychiatric or somatic symptoms and none had a history of cardiopulmonary, neurological, renal, psychiatric or other systemic disease. They were not using any drugs or medication. They were all non-smokers. Exclusion criteria in our study were fetal malformations, fetal growth retardation and maternal diabetes mellitus. The gestation age of the women participating in the study is shown in ❍ **Fig. 1**. All women have now delivered healthy newborns. The study protocols were approved by the local ethics committee. In addition, all women gave written informed consent.
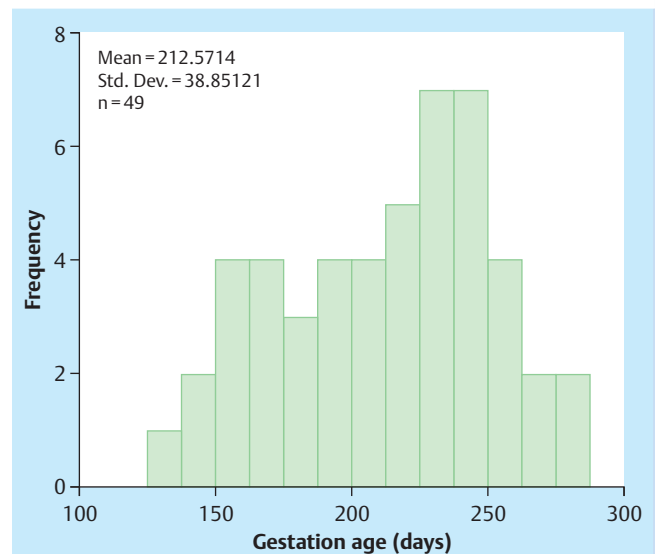

Fig. 1 Histogram of gestation age (days) (n = 49).

Study protocol

After ultrasound scan and preceded by a 10-minute rest period, five Ambu VLC-00-S electrodes were placed on the maternal abdomen: one electrode was placed on the midline within a range of 2 cm above the navel or during the vernix period; this electrode's position was 6 cm above the navel or during early gestation the electrode was placed 1 cm below the fundus of the uterus; one was placed 6 cm above the symphysis, two were placed at the right and left lateral abdominal wall; and finally one reference electrode was placed towards the back on the right lateral of the abdomen. This configuration allows 3 parallel abdominal fetal ECG detection channels around the maternal abdomen. The skin was prepared for low impedance by gentle excoriation of the surface skin cells as described by the Monica protocol (using 3M Skinprep 2236). The electrodes were connected to the Monica AN24 recorder (Monica Healthcare, Nottingham, UK), and the signal was sampled at a frequency of 900 Hz, thus giving a time resolution for the RR intervals of 0.9 ms. Data were analysed off-line after computer download. The Monica DK software was used to extract the beat-to-beat analysis, which uses a subtraction algorithm of the maternal ECG complex before detection of fetal ECG complexes (please see ❍ **Fig. 2**). The consecutive RR intervals were exported and missing beats and pauses were filtered and replaced by an interpolated value using Kubios HRV Version 2.0. All time periods with at least 360 beats in the 3-minute record period, which correspond to a heart rate of at least 120 beats per minute, were evaluated in this study. Additionally, the following results were excluded if the average fetal heart rated dropped below 130 beats/min, which could cause aliasing of the respiratory frequency [20].

All recordings were carried out at Marien-Hospital Witten (tertiary care teaching hospital) and were selected consecutively from November 2009 till February 2010. The recording session consisted of two periods: (a) a baseline recording, with the instruction to keep the eyes open and relax. The subjects remained awake, did not speak, and were not disturbed; (b) a standard hypnotic test (Creative Imagination Scale) and a standard hypnotic induction, intervention and wakening [28,29]. Each period was randomly allocated for each subject. The clinical hypnosis inter-
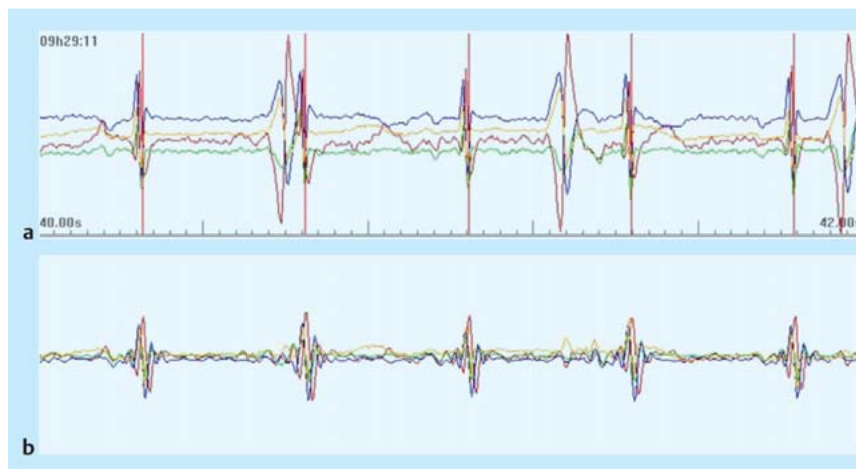
Fig. 2 a and **b**
a The Raw Monica AN24 Signal with fetal ECGs marked and
b the filtered signal with the only fetal ECGs.

vention was carried out by the same trained hypnotherapist (J. R.).

Data analysis
Power spectral density
The methods used in this study are mainly based on the guidelines given in [30]. For each 3-minute recording period, data sets consisting of 256 points, overlapping by 50%, were processed and power spectral density (ms2/Hz) was then computed using a fast Fourier transform algorithm [31] (Kubios HRV Version 2.0). Total power was computed for a low frequency (LF) band from 0.04 to 0.15 Hz and a high frequency (HF) band from 0.15 to 0.4 Hz [30, 32]. Since large variation existed within the subjects, LF and HF are expressed in normalised units (nu) [33]: $LFnu = [LF/(LF+HF) \times 100]$ and $HFnu = [HF/(LF+HF)] \times 100$ and as a low-to-high ratio: LF/HF.

Statistical methods
All results are shown as mean values ± standard deviation, median, quartiles and differences of the means. The Gaussian distribution of the differences between hypnosis and baseline measures was checked using the Q-Q-plots. If distributed normally, the paired t-test was used, otherwise the Wilcoxon signed rank test was applied. In order to test the hypothesis that the change in spectral frequency correlates with the gestational age of the fetus, the Spearman's rho correlation was calculated. The analyses were carried out using the SPSS Statistics 17.0 software (Scientific Packages for Social Sciences, Inc., Chicago, IL, USA). $P < 0.05$ for a two-tailed test was considered statistically significant.

Results
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Linear heart rate dynamics
Fetal mean values and standard deviation for HRV parameters are presented in ❍ **Table 1**. Q-Q-plot analysis showed that the fetal heart rate was distributed normally and a significant difference was found between baseline (144.3 ± 6.0) and hypnosis (142.1 ± 6.4). A difference was also detected between the standard deviation of the heart rate between baseline (6.7 ± 1.9) and hypnosis (6.8 ± 3.5). Fetal LFnu was smaller during baseline (80.2 ± 5.3) than during hypnosis (82.1 ± 5.7). Fetal HFnu was significantly larger (19.8 ± 5.3 vs. 17.9 ± 5.7) in control state compared to hypnosis (❍ **Table 1**). No statistically significant differ-

ence was found using the fetal LF/HF ratio. There was no correlation between gestation age and the change in fetal LFnu, HFnu or LF/HF ratio due to the hypnosis intervention.
A correlation was found between gestation age and fetal baseline heart rate ($r = -0.40$, $p = 0.005$), heart rate during hypnosis ($r = 0.45$, $p = 0.001$), baseline standard deviation of the heart rate ($r = 0.47$, $p = 0.001$) and standard deviation of the heart rate during hypnosis ($r = 0.41$, $p = 0.003$). Gestation age also correlated with baseline LFnu ($r = 0.38$, $p = 0.008$), HFnu ($r = 0.38$, $p = 0.008$) and the LF/HF ratio ($r = 0.35$, $p = 0.014$). No correlation was found between gestation age and fetal LFnu, HFnu and the LF/HF ratio during hypnosis.

Non-linear heart rate dynamics
No significant change was found for the fetal approximate entropy, Shannon entropy and sample entropy between baseline and hypnosis. Gestation age demonstrated a correlation with Shannon entropy ($r = 0.11$, $p < 0.001$), sample entropy ($r = 0.12$, $p < 0.001$) and approximate entropy ($r = 0.15$, $p < 0.001$). Fetal baseline LFnu and HFnu had a correlation with approximate entropy ($r = -0.60$, $p < 0.001$) and sample entropy ($r = -0.64$, $p < 0.001$), but not with Shannon entropy. Fetal baseline LF/HF ratio similarly showed a correlation with approximate entropy ($r = -0.68$, $p < 0.001$) and sample entropy ($r = -0.60$, $p < 0.001$), but not Shannon entropy. During hypnosis fetal LFnu, HFnu and LF/HF ratio demonstrated no correlation with non-linear heart rate dynamics at all.

Comments
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The main finding of this study is a fetal change of heart rate, standard deviation of heart rate and a shift towards sympathetic dominance during hypnosis compared to relaxed rest. This was apparent both from a decrease in HFnu power, an increase in LFnu power and from an increase of the LF/HF ratio. Our results add new arguments that fetuses can react to external stimulus with changes of HRV much earlier than previously thought [22, 23].

Heart rate
Heart rate results showed that the heart rate is slightly lower with increased standard deviation during hypnosis. These results support previous studies, which indicate that the fetus is more

Table 1 Fetal mean, standard deviation (SD), median, 1st and 3rd quartiles, p value and differences of the mean.

	Baseline				During hypnosis				P value	Differences of the mean			
	Mean ± SD	Median	1st Quartile	3rd Quartile	Mean ± SD	Median	1st Quartile	3rd Quartile		Mean ± SD	Median	1st Quartile	3rd Quartile
Heart rate, beats/min	144.3 ± 6.0	143.5	139.5	149.2	142.1 ± 6.4	141.8	137.3	147.7	0.002*	2.2 ± 4.7	1.4	0.2	4.4
Standard deviation of the heart rate, beats/min	6.7 ± 1.9	6.5	5.1	8.1	6.8 ± 3.5	6.2	5.0	7.8	0.041#	-0.1 ± 3.4	0.3	-0.2	1.0
LFnu	80.2 ± 5.3	80.6	76.4	83.2	82.1 ± 5.7	82.4	78.6	85.9	0.040*	-1.9 ± 6.4	-2.7	-4.9	0.4
HFnu	19.8 ± 5.3	19.4	16.8	23.6	17.9 ± 5.7	17.6	14.1	21.4	0.040*	1.9 ± 6.4	2.7	-0.4	4.9
LF/HF	6.9 ± 3.1	6.6	4.9	8.2	7.0 ± 2.7	6.7	4.8	8.2	0.964*	-0.03 ± 4.1	-0.3	-1.4	0.8
Shannon entropy	3.8 ± 0.2	3.8	3.6	4.0	3.8 ± 0.2	39	3.6	4.0	0.283*	-0.03 ± 0.2	-0.02	-0.2	0.1
Approximate entropy	0.8 ± 0.1	0.8	0.7	0.8	0.8 ± 0.2	0.8	0.7	0.9	0.175*	-0.02 ± 0.1	-0.03	-0.1	0.0
Sample Entropy	0.8 ± 0.2	0.8	0.7	0.9	0.8 ± 0.2	0.8	0.7	0.9	0.581*	-0.01 ± 0.1	-0.03	-0.1	0.1

* Paired t-test; # Wilcoxon signed rank test

active during hypnosis [13]. Similar to previous studies [21, 34], in our study fetal HRV changed with gestational age.

In adults, no conclusive results have been found whether hypnosis causes a decrease in heart rate [35–39].

HRV in the frequency domain

To our knowledge no study has focused on fetal autonomic cardiovascular control during hypnosis. Several studies have described the development of the frequency power spectrum in the course of pregnancy [40, 41] or respiratory sinus arrhythmia [42, 43].

In adults, only a few studies have focused on autonomic cardiovascular control during hypnosis using HRV indices. The results showed conflicting results with [36, 44, 45] and without [46, 47] change in parasympathetic activity. These discrepancies are most probably due to subtle differences in basal conditions, in HRV analysis, methodology in general (duration of different phases, free breathing or at a fixed frequency) and population selection (hypnotisability).

In our study increased fetal LFnu and decreased fetal HFnu can only be explained as secondary sympathetic reaction to the maternal hypnosis. In previous studies the increased fetal movements are consistent with this reaction to hypnosis [13, 24, 48], rather than the expected parasympathetic reaction of the fetus of deep relaxation like the mother [36, 44, 45].

Non-linear heart rate dynamics

Several studies demonstrated that non-linear dynamics also governs autonomic neural outflow [49–53]. In our collective only fetal approximate entropy was significant higher during hypnosis than the control period. Approximate entropy has also been used to demonstrate an increase of complexity in fetal heart rate during the course of pregnancy [54], which has also been shown in our study results.

Study limitations

Limitations of this study are that no evaluation for fetal respiration, which can influence the spectral analysis, has been done.

Conclusions
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Our results indicate that the functional adaptive process of the fetal autonomic system during hypnosis is reflected by a sympathovagal shift towards increased sympathetic modulation, with a decreased heart rate and higher standard deviation. With the newly available, CE-certified non-invasive fetal abdominal ECG fetal changes in autonomic system can be analysed with true beat to beat evaluation.

Contribution to Authorship
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All authors reviewed the results and wrote the article. The first author designed the study protocol, collected clinical data and carried out the hypnotic intervention. The first and second authors analysed the fetal heart rate data.

Funding
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Details of Ethics Approval
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We received ethics approval of the "Ethik-Kommission der Medizinischen Fakultät der Ruhr-Unversität Bochum, Germany", Reference No. 3358-08.

Conflict of Interest
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Prof. Dr. Hayes-Gill is employed by the University of Nottingham and is also a Director of Monica Healthcare Ltd.

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