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The diurnal rhythm in fetal heart rate in a twin pregnancy with discordant anencephaly: comparison with three normal twin pregnancies

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Abstract

In a discordant anencephalic twin the hypothesis was tested that the fetal brain is necessary for the expression of a diurnal rhythm in fetal heart rate. Fetal heart rate recordings were made over a 24 h period in a discordant anencephalic twin pregnancy and in three normal twin pregnancies. Cosinor analysis was used to assess rhythmicity in fetal heart rate and maternal heart rate or activity. Correlations between maternal and fetal rhythms were calculated. A significant diurnal rhythm was found for the fetuses of the control twins, but in neither of the fetuses of the discordant anencephalic twin pregnancy. The maternal rhythm was 1–2 h in advance of the heart rate rhythms in all fetuses except the anencephalic one, whose heart rate did not show any correlation with the maternal diurnal rhythm. We conclude that the fetal brain contributes to the generation of the diurnal rhythm in fetal heart rate and synchronization of maternal-fetal rhythms.

Keywords: Anencephaly; Twin pregnancy; Diurnal rhyhm; Fetal heart rate

1. Introduction

In the human adult, the presence of a diurnal rhythm in many physiological functions has been well established. The 'biological clock' in the brain, which

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Table 1
Clinical data of a discordant anencephalic twin and three 'normal' twins

Case	fetus 1/2	Gestational age at recording (weeks)	Gestational age at birth	Delivery mode	Sex	Zygosity	Weight	Apgar Score 5′	Neonatal problems
1	1 = anencephalic	35	37 5/7	Vaginal	Male	Bizygotic	1565	0	Died during delivery
	2 = normal				Female		2690	10	-
2	1	35	36 1/7	S.C.	Female	Bizygotic	2340	10	-
	2				Female		1570	9	-
3	1	36	36 6/7	Vaginal	Female	Bizygotic	1935	10	-
	2				Female		1990	10	-
4	1	35	35 4/7	S.C.	Male	Monozygotic	2155	10	
	2				Male		2410	10	Died of pneumonia at age of 2 months

regulates these rhythms, is located in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus. In the fetus a diurnal rhythm in mean heart rate and motility exists from mid-gestation onwards [10,11,17,19]. The fluctuations in fetal heart rate are strongly related to the maternal diurnal rhythm. Whether, or to what extent, the fetal brain contributes to the diurnal rhythm in fetal heart rate is not yet known [1,6,17].

A twin pregnancy with discordant anencephaly offered a unique opportunity to study the role of the fetal brain in the generation of prenatal diurnal rhythms. In this study we report our findings from a 24 h continuous fetal heart rate recording of a normal and an anencephalic fetus at 35 weeks of gestation. We compare the presence of a diurnal rhythm in heart rate in this discordant anencephalic twin pregnancy with the findings in three normal twin pregnancies.

2. Subjects and methods

In a 27-year-old primigravida, a twin pregnancy with discordant anencephaly was found by routine ultrasound at 14 weeks of gestation. The parents decided to continue the pregnancy. During pregnancy the anencephalic fetus developed hydramnios. The patient was admitted to hospital at 32 weeks because of mechanical discomfort. The normal fetus showed normal growth and cardiographic recordings were optimal. After informed consent, a continuous 24 h heart rate recording was made of both twins from 1400 to 1400 h at 35 weeks of gestation. A Hewlett Packard M1350A ultrasound heart rate monitor was used for the heart rate recording. Maternal rest-activity was simultaneously recorded, using a small ambulatory wrist monitor [7]. The anencephalic fetus died during delivery at 37 weeks of gestation. Postmortal examination showed a 'classic' case of anencephalia with an absent cerebrum including hypothalamus and cerebellum. Only rudiments of the pituitary gland were found, together with hypoplastic adrenal glands.

Three twin pregnancies of comparable gestational age served as controls. The clinical data of all patients are shown in Table 1. Patients 2 and 3 were admitted to hospital because of mild hypertension. In patient 4 discordant fetal growth was diagnosed by ultrasound. Continuous 24 h fetal heart rate monitoring was performed in the same way as described for the discordant anencephalic twin. The only methodological difference was that we recorded maternal heart rate instead of

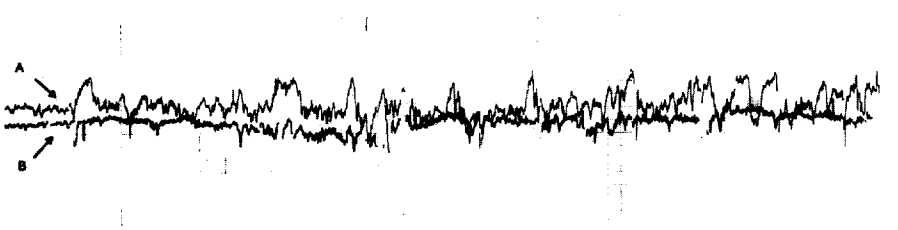

Fig. 1. Representative fetal heart rate (FHR) recording of the discordant anencephalic twin. Gestational age 35 weeks. Trace A: FHR of the normal twin. Trace B: FHR of the anencephalic twin.

maternal rest-activity simultaneously with the fetal heart rate in these control pregnancies. A Polar sporttester (Polar Electro OY, Finland) was used for measuring maternal heart rate every minute over 24 h.

Fetal heart rate data were analysed on-line and stored as mean heart rate per min and averaged per h. For statistical analysis of diurnal rhythm a cosinor analysis was performed on the fetal heart rate means. This method is based on fitting the data to a cosine function of a fixed period length (i.e. 24 h) by the method of least squares [2,9]. The following parameters of the fitted function were used for comparison among the subjects: mesor (24 h mean); amplitude (differences between the maximum and the mesor values) and acrophase (time of the peak of the rhythm). The statistical significance of the cosine fit is expressed as F-statistic. For each pair of twins the correlation between the heart rate rhythms of fetus 1 and fetus 2 were

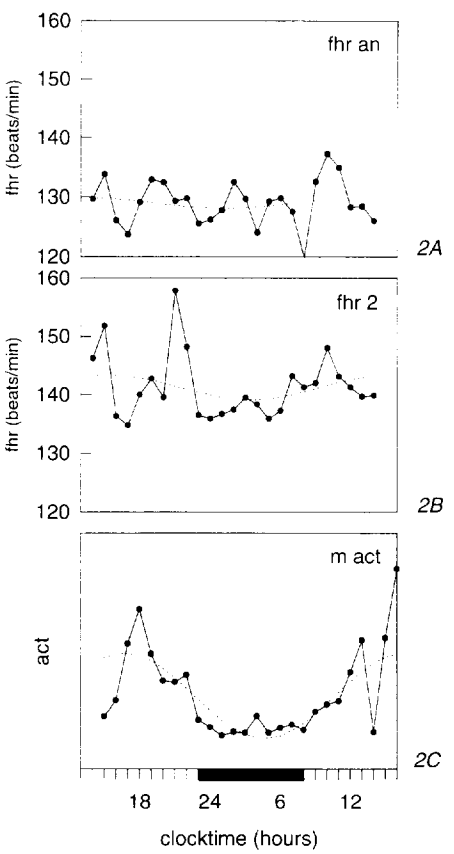

Fig. 2. Discordant anencephalic twin. (a and b) Mean fetal heart rate per h is plotted for both twins (solid line). Maternal activity is shown in (c) (solid line). A cosine fit with a period of 24 h is plotted as a dashed line. The night period of the mother is indicated by a black bar on the x-axis. fhr an = fetal heart rate in anencephalic twin; fhr2 = fetal heart rate in healthy twin; m act = maternal activity.

calculated. Similar tests were performed to examine the level of correlation between fetal and maternal rhythms.

3. Results

A representative part of the original fetal heart rate recording of the discordant anencephalic twin is shown in Fig. 1. Fig. 2 shows the mean fetal heart rate of the anencephalic fetus and its twin over 24 h, together with the day-night rhythm in maternal activity. The 24 h rhythm in fetal heart rate and maternal heart rate of the three control twins are shown in Figs. 3–5. In Fig. 6 the diurnal rhythms in fetal heart rate of all fetuses are presented in terms of amplitude, mesor, acrophase and F-statistic. The mean heart rate data of all control fetuses show a diurnal rhythm with

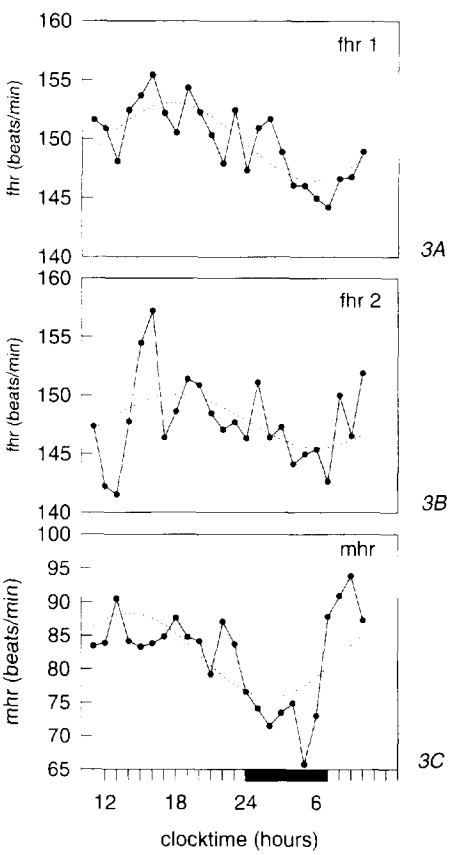

Fig. 3. Twin pregnancy 2. (a and b) Mean fetal heart rate per h is plotted for both twins (solid line). Maternal heart rate is shown in (c) (solid line). A cosine fit with a period of 24 h is plotted as a dashed line. The night period of the mother is indicated by the black bar on the x-axis. fhr = fetal heart rate; mhr = maternal heart rate.

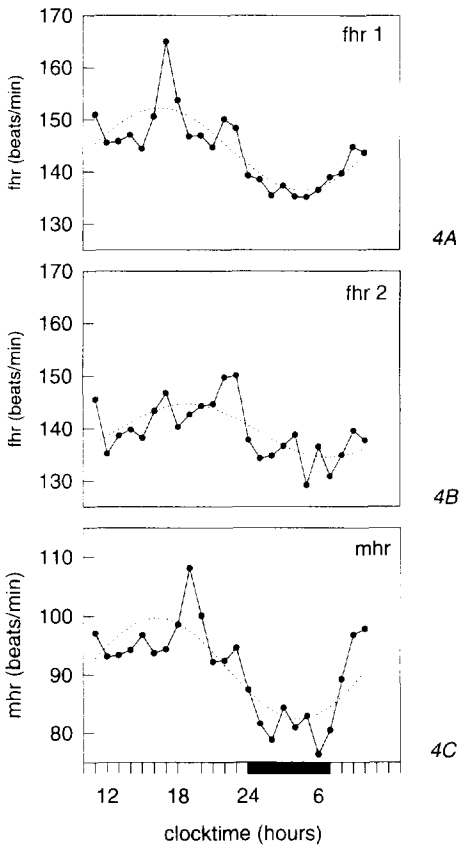

Fig. 4. Twin pregnancy 3. (a and b) Mean fetal heart rate per hour is plotted for both twins (solid line). Maternal heart rate is shown in (c) (solid line). A cosine fit with a period of 24 h is plotted as a dashed line. The night period of the mother is indicated by the black bar on the x-axis. fhr = fetal heart rate; mhr = maternal heart rate.

an amplitude between 2–8 beats per min; a mesor heart rate of 140–151 beats per min; and an acrophase between 1500 and 1930 h. Cosinor analysis demonstrated that the diurnal rhythm in fetal heart rate was significant at the 1 percent's level (F stat > 5.85, df $= (2, 21)$) in all control fetuses, except for one which showed a rhythm with a significance at the 10 percent's level (F stat $= 2.55$). No significant diurnal rhythm was found for the anencephalic fetus (F stat $= 0.29$) or for its normal twin (F stat $= 0.95$), despite a profound significant diurnal rhythm in maternal activity (F stat $= 12.3$). In Fig. 7a it is shown that the correlation between the individual fetal heart rate rhythms in all three control twins is clearly higher than the correlation between the anencephalic fetus and its twin. The correlations of the individual fetal heart rate rhythms and the maternal heart rhythms are significant for the three control twins, with the maternal acrophase being 1–2 h in advance of the fetal acrophase

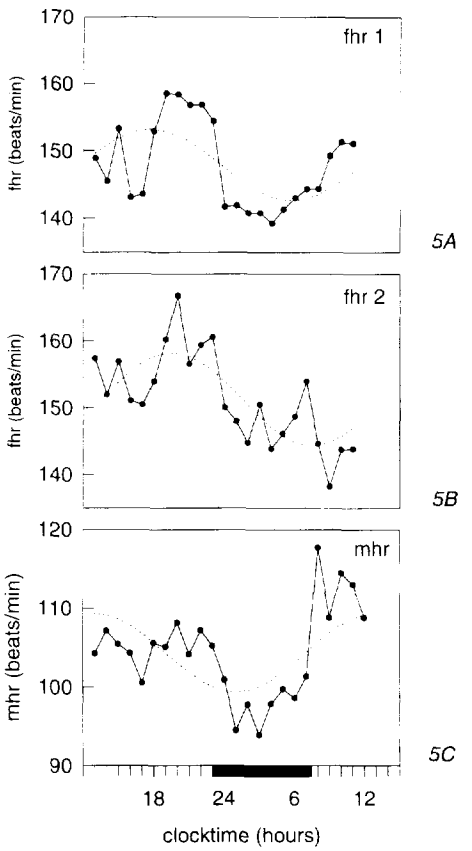

Fig. 5. Twin pregnancy 4. (a and b) Mean fetal heart rate per hour is plotted for both twins (solid line). Maternal heart rate is shown in (c) (solid line). A cosine fit with a period of 24 h is plotted as a dashed line. The night period of the mother is indicated by the black bar on the x-axis. fhr = fetal heart rate; mhr = maternal heart rate.

(Fig. 7b). Fig. 7c shows that there is no significant correlation between the anencephalic twin's heart rate rhythm and its mother's activity rhythm.

4. Comment

Diurnal rhythms in mean fetal heart rate are well established [10,11,17,19]. In the third trimester of pregnancy, the fetal heart rate rhythm is correlated with the maternal heart rate rhythm. However, the mechanism regulating this phenomenon is still unknown [1,10,17]. Animal studies indicate that the fetal brain plays an active role in the generation of diurnal rhythms before birth [12].

In accordance with the studies of Yoshizato [20], Terao [16], van der Moer [8] and Kurauchi [5], the fetal heart rate pattern of the anencephalic fetus in our study

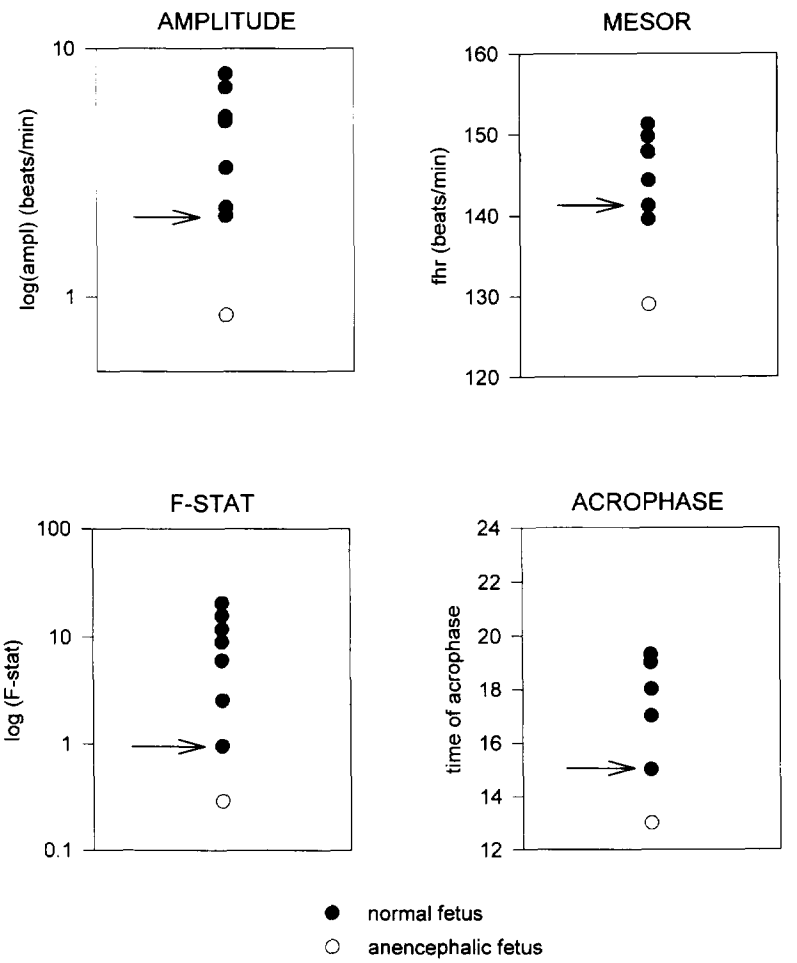

Fig. 6. Circadian analysis of fetal heart rate (fhr). Data from 4 twin-pregnancies (1 twin with discordant anencephaly). Each point represents one fetus. The circadian rhythm is described by four parameters: amplitude, mesor, F-statistic and acrophase (arrows indicate the normal twin of the anencephalic fetus).

corresponds with the absence of the central nervous system from the level of the medulla oblongata, which may be present in a rudimentary form. This was indeed confirmed by the findings from the autopsy material which showed that cerebrum including hypothalamus and cerebellum were absent.

This case offered a unique opportunity to explore whether the fetal brain is important for the expression of a diurnal rhythm in fetal heart rate in humans. Three control twin pregnancies were studied in the same way to compare the presence of diurnal rhythms in 'normal' twins with the findings in the discordant anencephalic twin. The presence of a clear diurnal rhythm in fetal heart rate in all normal twin pregnancies and the absence of these rhythms in the anencephalic fetus despite an

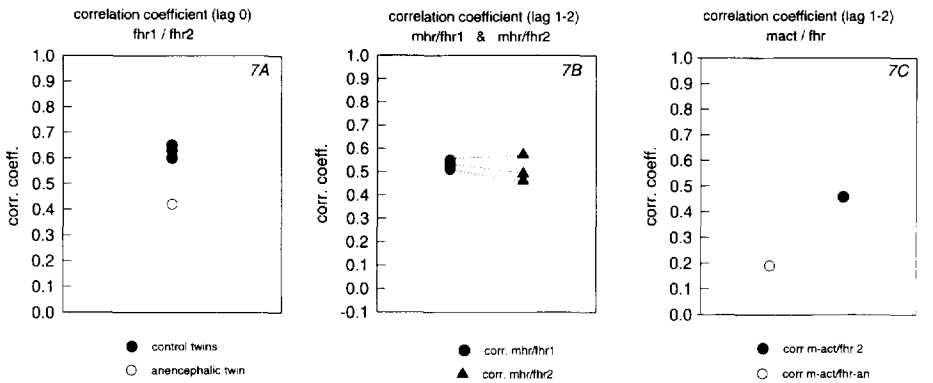

Fig. 7. (A) correlation between both fetuses in each pair of twins. (B) correlation between the individual fetal heart rate rhythms (fhr) and the maternal heart rate rhythm (mhr) in three control twins; the dashed lines connects the coefficients (corr.coeff.) of each pair of twins. (C) correlation (corr.) between both fetal heart rate rhythms and the maternal activity (mact) in the discordant anencephalic twin pregnancy.

intact maternal diurnal rhythm supports our hypothesis that the fetal brain is indeed crucial for the generation of a fetal diurnal rhythm.

The question arises why the normal fetus in this discordant anencephalic twin did not show a diurnal rhythm. The mechanism of 'tactile communication between twins in utero' [14] could partly explain this phenomenon: several studies [3,4,13–15] have demonstrated a remarkable synchronicity of fetal heart rate, movements and behavior patterns between both fetuses in normal twins. It is hypothesized that the movements of one fetus may provoke movements in the other fetus, and that this 'tactile communication' accounts for simultaneous fetal heart rate patterns in both fetuses. The importance of twin-twin interactions for similar heart rate patterns in twins is confirmed by the high correlation coefficients between the heart rate rhythms of the normal twins (Fig. 7a). This high correlation can not be explained by monozygosity, as two control twins were bizygotic (Table 1). The correlation coefficient of the discordant anencephalic twin is markedly lower, but still just reaches significance (Fig. 7a). Anencephalic fetuses with a defect hindbrain show qualitatively and quantitatively abnormal motor behavior, characterized by forceful, jerky general movements, which are of large amplitude and occur in burst-pause patterns [18]. It is plausible that such forceful movements of the anencephalic fetus in our study influenced the behaviour and heart rate of its twin and were responsible for the disturbance of the diurnal rhythm of the normal fetus.

From this study of a discordant anencephalic twin pregnancy in which we explored the role of the fetal brain for the generation of diurnal rhythms in fetal heart rate, the following conclusions can be drawn:

1. The fetal brain might indeed contribute to the generation of a diurnal rhythm in fetal heart rate.
2. The diurnal fetal heart rate rhythm 'follows' the maternal heart rate in normal

pregnancy by 1–2 h. Although the exact mechanism still remains unknown, the absence of such a correlation in the anencephalic fetus suggests that the 'fetal brain' is the intermediatory factor between maternal input signals and the expression of overt fetal diurnal rhythms.

3. The demonstrated influence of the anencephalic twin on its normal twin, as well as the high correlation between co-twins strenghtens the hypothesis of 'tactile communication' between twins.

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