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A Hypothesis on the Abnormal Seasonality of Schizophrenic Births

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Summary. The hypothesis is proposed that the abnormal seasonality of schizophrenic births is partly a consequence of seasonal variation of conception and of an associated seasonal variation of risk of premature delivery.

Key words: Seasonal variation – Pregnancy duration – Excess risk of schizophrenic births

Introduction

Abnormal seasonality of schizophrenic births has been observed by many authors (see Häfner et al. [9] for an overview) and seems to be well-established. Several hypotheses to explain this phenomenon have been put forward, but none of them is very convincing [2]. We propose a new hypothesis which is based on statistical consequences of seasonal variation of conception. Briefly, it is demonstrated by means of a statistical model that seasonal variation of conception in human populations and a corresponding variation of the resulting deliveries leads to seasonal variation of the risk of preterm birth, given the birthday, for purely statistical reasons. It is implied by recent research (e.g. [8, 12, 13, 15, 16] that preterm birth and pregnancy complications are associated with increased risk of psychic disorder, thus, as was pointed out by Lewis [11], reviving an old idea that Kraepelin introduced in the 1913 edition of his textbook, about "internal" causes of dementia praecox in early childhood. This association was also found in longitudinal studies [3]. Preterm babies were found to have an increased risk for schizophrenia [4]. Excess obstetric complications among schizophrenics in particular have been described [3, 9]. The relative risk of schizophrenia in patients with obstetric complications has been estimated to be 2.5:1 [8]. Some authors refer to these assumed connections as a "neurodevelopmental" approach to schizophrenia [11, 14].

In a subsample of 8.794 births taken from a perinatal study conducted in the Federal Republic of Germany, the hypothesis that there is no seasonality in the risk of premature delivery was tested and rejected. The observed as well as theoretically predicted seasonality in preterm births could provide a possible explanation for the abnormal seasonality of schizophrenic births. This hypothesis is supported by a similarity in the pattern of excess schizophrenic births as established previously [9] and the pattern of excess premature deliveries observed here.

Our contribution is organized as follows. In the next section, a statistical model for the relation between conceptions, deliveries and preterm births is given, and it is shown how seasonality of conceptions entails seasonality of preterm births. Then, the seasonality of conceptions over the year and the resulting seasonality of excess preterm births for the sample of births is investigated and compared with the predictions of the model. A discussion follows.

A Model for Conception Times, Birthdays and Seasonality in Preterm Births

We assume here that time of conception U, pregnancy duration S and time of birth T are related by the following equation:

$$T = U + S,$$

where U and S are assumed to be independent and the variables U, S and T are measured discretely in units of "$\frac{1}{48}$ year", i.e. each unit consists of $365 \div 48 = 7.604$ days and equals approximately 1 week (units different from 1 week have to be considered in order to be able to divide the year into an integer number of such units), counted modulo 48, e.g. unit 49 is equivalent to unit 1. Denoting by p_U, p_S, and p_T the discrete frequency distributions associated with U, S, and T, this implies (see Feller [5], p. 266)

$$p_T(t) = \sum_{i=1}^{48} p_U(t-i)\, p_S(i).$$

Seasonality in conceptions U therefore results in (shifted) seasonality of birthdays T. We are interested in the conditional distribution of pregnancy duration given birthday:

$$p_{S\mid T}(s \mid t) = \frac{p_U(t-s)\, p_S(s)}{\sum_{i=1}^{48} p_U(t-i)\, p_S(i)}$$

Corresponding estimates of these probabilities are obtained by replacing the true frequencies per unit

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Table 1. Illustration of effect of seasonal changes in conceptions on frequency of premature deliveries

Rate of conceptions	Units (months)				Number of expected births at T9	Premature births	
	T0	T1	T2	T3		Number	Proportion
Constant	1000	1000	1000	1000	1000	140	14.0%
Expected births at T9 from these conceptions	860	80	40	20			
Increasing	1000	1100	1200	1300	1022	162	15.9%
Expected births at T9 from these conceptions	860	88	48	26			
Decreasing	1000	900	800	700	978	118	12.1%
Expected births at T9 from these conceptions	860	72	32	14			

("month") by estimated frequencies per unit, i.e. observed number of events during the respective unit divided by all observed events (compare Armitage [1], p. 111 and Koller [10], p. 73). The estimated rate of preterm births is then obtained as an estimate of the conditional probability of a preterm birth given the time unit when the birth occurred. We follow Koller [10] in defining a preterm birth as one with less than 37 weeks or 259 days of pregnancy duration, which in terms of the above units is approximately the same as less than 34 units or $\frac{34}{48} = 258.54$ days:

$$\hat{p}(S \leq 34 \mid T = t) = \sum_{s=0}^{34} \hat{p}_{S\mid T}(s \mid t),$$

where

$$\hat{p}_{S\mid T}(s \mid t) = \frac{\hat{p}_U(t-s)\,\hat{p}_S(s)}{\sum_{i=1}^{48} \hat{p}_U(t-i)\,\hat{p}_S(i)}$$

and $\hat{p}_S$, $\hat{p}_U$ denote the respective relative frequency estimates of p_S, p_U (see [1]). From this we obtain the expected numbers of premature deliveries for each unit. It follows from this model that moderate seasonality of conceptions will lead to sizeable effects on the seasonality of preterm births (compare also [6], [7]). This is illustrated by the following example, which was suggested by a referee.

We assume here that the distribution of pregnancy durations is measured in units of 1/12 year (approximate months) and is such that 1000 conceptions at a time lead to 860 births on time after 9 months, to 80 premature births after 8 units (months), 40 premature births after 7 units (months), and 20 premature births after 6 units (months). Then we compare three possible cases for the number of conceptions occurring in four consecutive units (months): constant, increasing and decreasing rates of conceptions. We see from Table 1 that in the first case we expect 14.0%, in the second 15.9%, and in the third 12.1% premature deliveries. The changes in rates of premature deliveries found in this example are smaller than the actual amplitude of seasonality found in a birth sample which is analysed in the following section. This is a hint that this model explains only a part of the observed seasonality.

Analysis of conceptions and deliveries in a birth sample

Data on a sample of 11984 births were collected in a perinatal study conducted by Koller and collaborators in the Federal Republic of Germany [10]. The sample is described in detail [10] and consists of births between 1964 and 1974. It is not completely representative insofar as only births delivered in 21 large women's hospitals from all parts of the Federal Republic of Germany were considered, and only those births can be analysed here where reliable information on the time of conception was available; this leads to a sample of mothers with higher than average socio-economic status, higher than average age and a higher than average likelihood of living in a big city as compared with the general population.

We selected a subsample of 8794 births which occurred during the core years of the study (all births in the years 1967–1971) in order to avoid biases due to end effects (during starting and termination phase of the study); the study did not begin on 1 January and end on 31 December. All computations involving the model described above as well as chi-square goodness-of-fit tests were done in terms of $\frac{1}{48}$ year as time unit. Statistical tests were applied to find out whether the distribution of conceptions and of births is uniform or not, whether the number of premature births per time unit could be explained by multiplying the number of births in each time unit with a fixed constant, and whether the number of premature births can be explained by the above model. More precisely, we obtained the following chi-square values with 47 *df* for the null hypotheses: distribution of births is uniform (relative frequency of births per unit is 8794 ÷ 48), $\chi^2 = 93.91$, $P < 0.001$; distribution of conceptions is uniform, $\chi^2 = 142.08$, $P < 0.001$; distribution of premature deliveries is determined by distribution of births, i.e. relative number of premature deliveries is constant, viz, number of premature births in a given time unit is equal to: (number of births in time unit) × (number of premature births per year)/(number of all births per year), $\chi^2 = 60.6$, $P < 0.1$; number of premature births is given by the model, $\chi^2 = 51.9$, $P > 0.1$.

The conclusion is that uniformity of conceptions as well as births is rejected significantly, from which it follows that there must exist a seasonality in the premature births different from that in all births. The last two chi-square values show that although the hypothesis of constant relative risk of premature delivery cannot be rejected at the 5% level (only at the 10% level), the predictions made by the model on the number of premature births in each month are better: the corresponding chi-square value (at 47 *df*) drops by more than 8 from 60.6 to 51.9 and the corresponding *P* value exceeds 0.1.

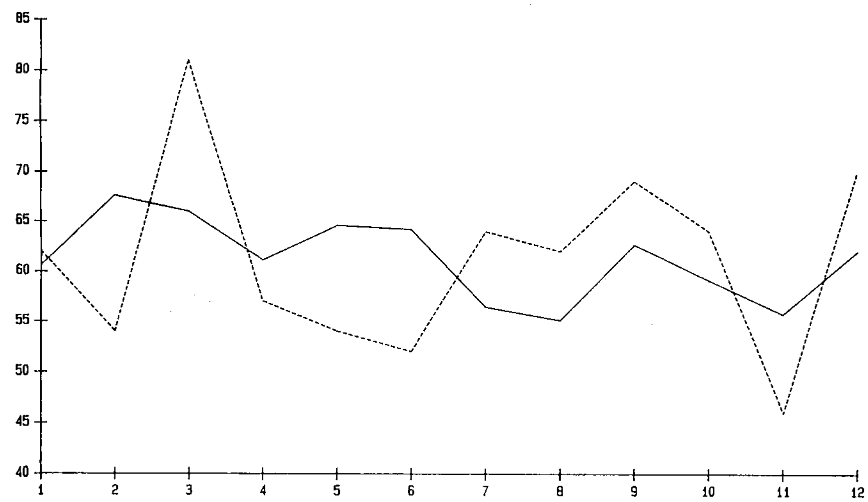

Fig. 1. Comparison of observed premature deliveries and those predicted by the model. Time unit on x-axis is 1/12 year; on y-axis unit is number of cases. *Dashed line* shows observed premature deliveries, *solid line* predicted premature deliveries

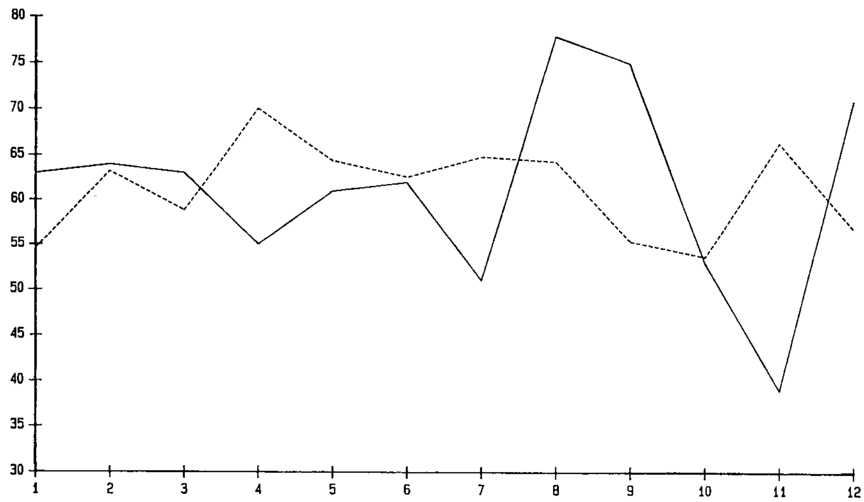

Fig. 2. Distributions of premature and non-premature deliveries in dependency on time of conception (x-axis, unit 1/12 year). Non-premature deliveries multiplied by [total number of premature deliveries ($n = 735$)]/[total number of non-premature deliveries ($n = 8059$)]. Unit of y-axis is number of cases. *Dashed line* shows non-premature deliveries, *solid line* premature deliveries

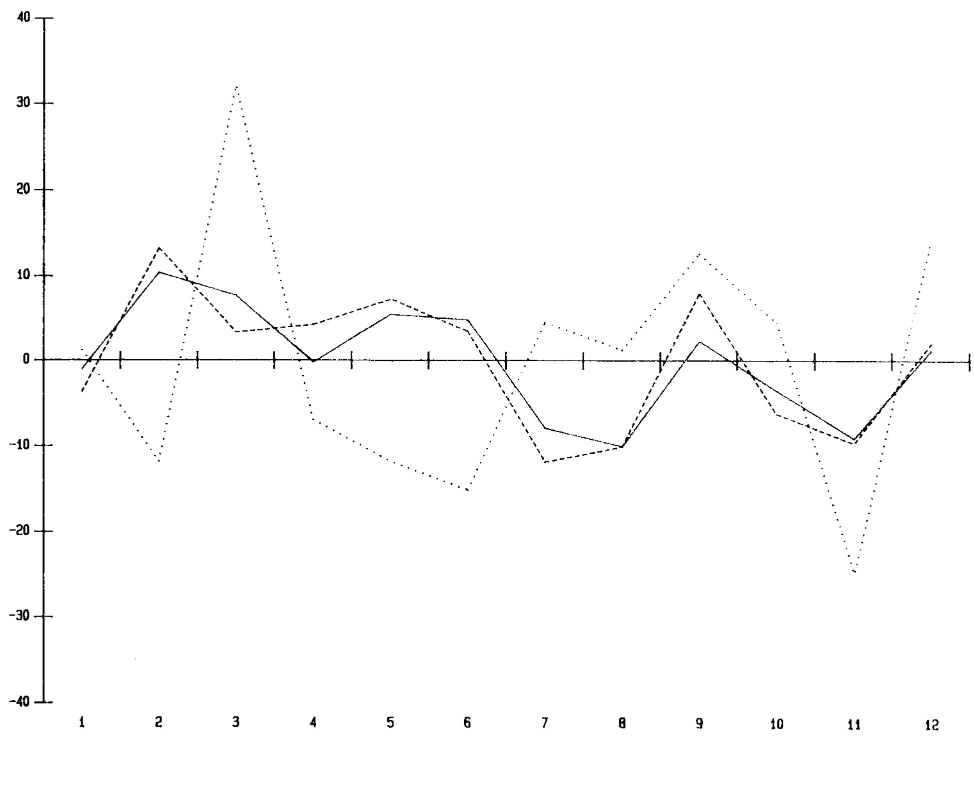

Fig. 3. Observed relative deviations from uniform distribution for births, conceptions and premature deliveries in sample of 8794 births between 1967 and 1971 (pooled together) containing 735 premature deliveries. Time unit on x-axis is 1/12 year; on y-axis unit is percent deviation. *Solid line* shows deliveries; *dashed line* conceptions, shifted backwards by 3/12 years; *dotted line* premature deliveries. For further explanation see text

The fit of the model is visualized in Fig. 1, which shows some discrepancies between predicted and observed numbers of premature deliveries per time unit. It seems that these discrepancies are due to some extent to a dependency of the probability of a premature delivery on the time of conception. In spite of the fact that the correlation between time of conception and duration of pregnancy is only 0.02 ($n = 8794$), as well as of a P value of 0.27 for a Kruskal-Wallis test examining the homogeneity of pregnancy durations over $\frac{1}{12}$ year ranges, plotting the distributions of premature and normal deliveries separately reveals some characteristic discrepancies (Fig. 2). Premature deliveries are more often conceived at $\frac{8.5}{12}$ years and less often at $\frac{11}{12}$ years. This leads to increased numbers of premature deliveries at $\frac{3}{12}$ years and reduced numbers at $\frac{6}{12}$ years, as indicated in Fig. 1.

The relative values of various quantities (as compared with their values under the uniform distribution) in the birth sample are displayed in Fig. 3. The time unit here is $\frac{1}{12}$ year $= \frac{365}{12}$ days, or approximately a month. For example, the expected number of conceptions per time unit would be $E = 8794 \div 12$. Displayed is $(O - E) \div E$ (in percent). The conceptions are displayed 3 months earlier than their actual timing in order to facilitate the comparison with the deliveries. All conceptions and deliveries are pooled together.

Discussion

We have introduced a simple and natural model which predicts that any oscillation of conceptions will lead to an oscillation of risk of premature delivery, and the analysis of a birth sample shows that there occur indeeed such oscillations. Further it was shown that the model explains the observed oscillation of premature births better than the assumption that the fraction of premature births among all births is uniform over the year. However, the model does not account for all premature births. These unaccounted premature births are due to some extent to a non-uniformity in the probability of a premature delivery given the time of conception, which might be due to climatic or other seasonal influences. This could be adjusted for by a more refined statistical model, where p_S depends also on $u = t - s$, the time of conception. However, such a model would be unduly complicated and would not strengthen our point. Other reasons for discrepancies are the categorisation of data as well as random fluctuations and inaccuracies in calculating times of conception. For instance, for the 30% increase of premature deliveries observed in March, the 95% confidence interval is approximately $(30 \pm 7)\%$, indicating that the observed relative changes are not very accurate under the given number of cases.

From the literature, it seems plausible that premature delivery via minimal brain damage is connected with psychic disorders, so that we might expect a seasonal component of schizophrenic births in particular, being caused by this seasonal variation of risk of premature delivery. We presented some evidence in favour of such a purely biological hypothesis, which might apply more generally to other psychic disorders besides schizophrenia, like mental retardation, depressive syndromes and neurosis, where Häfner et al. [9] found evidence of similar seasonal variations as for schizophrenic births.

Our aim is modest. We suggest here that the seasonality of premature deliveries yields a possible, maybe only partial, explanation of the seasonality of schizophrenic births. One unsettled point, for example, is that the seasonality in the risk of premature deliveries might be similar to, but could still be quite different from the seasonality found for psychic disorder births, although a comparison of the excess risk for premature deliveries as shown in Fig. 3 and the illustration of excess risk for schizophrenic births in Häfner et al. [9] reveal some similarity. It would be of interest to see whether the present hypothesis could be substantiated by a case-control or even cohort study, obtaining information on the pregnancy duration and possible pregnancy complications in controls as well as in a sample of schizophrenic patients, or more generally, of patients with psychic disorders.

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