Hospitalization in the first years of life and development of psychiatric disorders at age 6 and 11: a birth cohort study in Brazil

Hospitalização nos primeiros anos de vida e desenvolvimento de transtornos psiquiátricos com 6 e 11 anos de idade: um estudo de coorte de nascimentos no Brasil

Hospitalización durante los primeros años de vida y desarrollo de trastornos psiquiátricos a edades comprendidas entre los 6 y 11 años: un estudio de cohorte de nacimientos en Brasil

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Abstract

This study aimed to evaluate the medium-term effects that hospitalization in the first 48 months of life has on the development of psychiatric disorders at 6 and 11 years of age among individuals in a birth cohort in a middle-income country. We analyzed data from a 2004 birth cohort (N = 4,231) in the city of Pelotas, Rio Grande do Sul State, Brazil. The frequency of hospitalization was investigated at 12, 24 and 48 months of life. When the children were 6 and 11 years old, psychiatric disorders were investigated with the Development and Well-Being Assessment. *We used logistic regression to adjust for potential confounders. The overall frequency of hospitalization during the first 48 months of life was 33.1% (95%CI: 31.4; 34.7). Among the hospitalized children 25.6% (95%CI: 24.1; 27.1), 4.7% (95%CI: 4.0; 5.5) and 2.8% (95%CI: 2.3; 3.5) were hospitalized 1, 2 or ≥ 3 times during this period, respectively. After adjustment for potential confounders, the chance of presenting any psychiatric disorder at 6 and 11 years of age was higher for the children who had been hospitalized during the first 48 months of life than for those who had not, with OR of 1.50 (95%CI: 1.19; 1.88) and 1.63 (95%CI: 1.28; 2.07), respectively. Our results support the hypothesis that hospitalization in the early stages of life has an effect on the subsequent mental health of children. Preventive measures are needed in order to minimize the negative experiences of children who are hospitalized during infancy.*

Mental Disorders; Hospitalization; Cohort Studies

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Introduction

Hospitalization is defined as being admitted to a hospital (for medical care or observation) and remaining there for at least 24 hours [1]. It can be considered a stressful, traumatic event in the life of an individual, because it implies a rupture in family and social relations [2,3,4,5,6,7,8]. This process is even more intense and marked in childhood, given that children have limited mechanisms to cope with stressful experiences. In children, the main sources of stress during hospitalization are maternal separation, the use of invasive procedures and routine changes [2,3,4,5,6,7,8].

The first years of life are simultaneously a time of great opportunity and a time of great vulnerability for brain development. Crucial aspects of brain architecture begin to be formed before and immediately after birth, and many fundamental aspects of that architecture are established in the first years of life [9,10]. Stress in childhood can affect the structural and functional systems of the developing brain, making an individual more vulnerable to psychological problems [11,12]. There is evidence that long-term exposure to stress in general, as well as to specific environmental stresses during sensitive periods of development, produces structural and functional disturbances, leading to a wide variety of physical and mental deficits in the short, medium and long term [13,14,15].

The mental health of individuals is influenced by individual, behavioral, socioeconomic and environmental characteristics [16]. In childhood and adolescence, mental disorders are associated with factors such as gender, age, skin color, birth weight, gestational age, parental education, family income, smoking and alcohol consumption during pregnancy, maternal mental health, chronic diseases, stressful and traumatic events, mother-child interaction, etc. [17,18].

Globally, about 20% of children and adolescents suffer from some disabling mental illness; suicide is the third leading cause of death among adolescents and approximately half of all adult mental illnesses begin in adolescence [19].

Between 1970 and 1999 various studies were conducted in high-income countries. Despite certain methodological limitations, such as insufficient sample sizes, high losses to follow-up and failure (in some studies) to adjust for confounding variables, they reported a greater likelihood of having behavioural problems or emotional problems during childhood and adolescence for children who had been hospitalized for prolonged periods (or on more than one occasion) in the first years of life than for those who had not, those in the former group also being found to perform more poorly in school [20,21,22,23,24,25,26]. Those studies also showed that hospitalized infants were typically separated from their families; remained bedridden and inactive; rarely received analgesia or anaesthesia; and had prolonged hospital stays. Such studies prompted changes in the practices related to the hospitalization of infants, the most important change being that mothers are now allowed to keep their babies with them day and night (a practice known as "rooming-in") during the immediate post-partum period, as well as being allowed to be present throughout the hospitalization of the infant [27].

In an extensive review of the literature, we identified no studies evaluating the medium- and long-term effects that hospitalization in the first years of life has on mental health now that practices related to the hospitalization of infants have been changed. Therefore, the objective of this study was to evaluate a birth cohort in terms of the medium-term effects that hospitalization during the first 48 months of life has on the development of psychiatric disorders by the ages of 6 and 11 years.

Methods

Participants

We studied a birth cohort comprising all live births occurring between January 1 and December 31, 2004, among mothers living in the urban area of Pelotas, Rio Grande do Sul State, Brazil. Live births were identified during daily visits to the maternity wards of the five municipal hospitals. Of a total of 4,287 births, 4,231 were live births and were included in the cohort. The mothers were interviewed within the first 24h after delivery (refusal rate of less than 1%). A structured questionnaire designed to collect information related to the family, mother and child, as well as to the pregnancy and the use of health care services, was administered by trained interviewers. The children in the cohort were

evaluated in their homes at 3, 12, 24 and 48 months of age, with follow-up rates > 90%. The children, together with their mothers or legal guardians, were invited to the Federal University of Pelotas School of Medicine, where a dedicated clinic had been constructed, for additional follow-up assessments at 6 and 11 years of age, the attendance rates for which were 90.2% and 86.6%, respectively. Details of the study methodology can be found in previous publications [28,29].

Study outcome

Psychiatric disorders at 6 and 11 years of age were identified with the *Development and Well-Being Assessment* (DAWBA) [30]. Designed for use in individuals 5-17 years of age, the DAWBA allows psychiatric diagnoses to be made in accordance with the criteria established in the DSM-IV [31] and the 10th revision of the International Classification of Diseases (ICD-10) [32] the latter being used in this study. Trained psychologists that administered the DAWBA assessment to the mothers or legal guardians of the evaluated children were blind to the exposures of interest.

The following DAWBA sections were applied: separation anxiety disorder; specific phobia; social phobia; generalized anxiety disorder; post-traumatic stress disorder; panic disorder and agoraphobia; obsessive compulsive disorder; attention deficit hyperactivity disorder; oppositional defiant disorder; conduct disorder; eating disorders; and tic disorders. We analyzed three types of psychiatric outcome measures: any psychiatric disorder; externalizing disorders (including oppositional defiant disorder, conduct disorder and attention deficit hyperactivity disorder); and internalizing disorders (including anxiety and depression).

Main exposure

Hospitalization in the cohort was investigated at 3, 12, 24 and 48 months. The questions posed were as follows: (at 3 and 12 months) "Has (the child) been admitted to the hospital from birth until now?"; (at 24 months) "Has (the child) been admitted to the hospital since (his/her) first birthday?"; and (at 48 months) "Has (the child) been admitted to the hospital since (his/her) second birthday?". By aggregating the information from each of those follow-up assessments, we constructed a dichotomous (yes/no) variable characterizing the occurrence of hospitalization at any point during the first 48 months of life. The hospitalizations that occurred after hospital discharge at birth were considered. We also analyzed frequency of hospitalizations during the first 48 months of life (0, 1, 2, and ≥ 3 times). The term hospitalization is used as a synonym for "hospitalizations during the first 48 months of life".

Potential confounding factors

Information related to the characteristics of the mother and the children were collected in the perinatal period. Family income in the month prior to the interview was a variable that was collected continuously and analyzed in quintiles (the first quintile representing the poorest 20% of the population). Maternal level of education at the time of delivery was categorized as 0-4, 5-8, 9-11 or ≥ 12 years of schooling. Maternal age at the time of delivery was categorized as < 20, 20-34 or > 34 years. The mothers were also categorized, by parity, as nulliparous, primiparous or multiparous. Maternal marital status was analyzed as a dichotomous variable, as having a partner or not (single, widowed or divorced). The skin color of the mother was categorized as white or as black/brown, as observed by the interviewer. Mothers who responded in the affirmative to the question "During the pregnancy, did you feel depressed or nervous?" were classified as having had depression during the pregnancy. Maternal smoking and alcohol consumption during pregnancy were evaluated retrospectively at the time of delivery. Women who had smoked at least one cigarette a day in any trimester of the pregnancy were classified as having smoked regularly during the pregnancy. Alcohol consumption during pregnancy was defined as ingestion of any dose of alcohol during any trimester of the pregnancy. Planned pregnancy was analyzed as a dichotomous (yes/no) variable. The type of delivery was classified as vaginal or caesarean. Neonatal birth weight was measured by hospital staff using a scale (with a precision of 10g) that was calibrated regularly by the research team. Neonates weighing less than 2,500g were classified as low-birth-weight infants. Gestational age was based on the date of the last

menstrual period whenever that was consistent with the body weight, body length and head circumference at birth, according to the normal curves of those parameters for sex and gestational age [33]. If the date of the last menstrual period was inconsistent with those parameters or was unknown, we adopted the estimated clinical maturity of the newborn in accordance with the method described by Dubowitz et al. [34]. Neonates born before 37 weeks of gestational age were considered preterm infants. Admission of the infant to the neonatal intensive care unit was analyzed as a dichotomous (yes/no) variable.

Statistical analysis

The χ^2 test was used in order to compare the occurrence of hospitalization with the distribution of the characteristics of the mothers and infants. When appropriate, we performed the χ^2 test for linear trend. To evaluate the association between hospitalization and psychiatric disorders at 6 and 11 years of age, we used logistic regression analysis, calculating odds ratios (OR) and 95% confidence intervals (95%CI). Using multiple logistic regression, we assessed the association between any hospitalization and frequency of hospitalizations and psychiatric disorders (any, internalizing or externalizing disorders), adjusting for the characteristics of the mothers and infants. For each outcome measure, we constructed three models: the crude analysis (Model 1); the crude analysis adjusted for the characteristics of the mothers (Model 2); and the crude analysis adjusted for the characteristics of the mothers and for the characteristics of infants (Model 3). If the significance level was below 0.20, the variable remained in the model as a potential confounder for the next level.

Ethical aspects

At each follow-up assessment, the mother or legal guardian of each child gave written informed consent. The respondents were assured that the data would remain confidential, that their participation was voluntary and that they could leave the study at any time, without consequences for the child or family. Based on the child psychiatrist's evaluation children who needed further assessment and advice were referred to local care services available in the city. The study was approved by the Ethics Research Committee of the Federal University of Pelotas School of Medicine.

Results

Of the 4,231 individuals who comprised the original cohort, information related to hospitalization and to the development of a psychiatric disorder at 6 or 11 years of age was available for 3,132 (74%). That lack of information was found to be associated with lower family income (p < 0.001), lower maternal levels of education (p = 0.028), prematurity (p < 0.001) and low birth weight (p = 0.024).

The frequency of hospitalization was 33.1% (95%CI: 31.4; 34.7). Among the hospitalized children 25.6% (95%CI: 24.1; 27.1), 4.7% (95%CI: 4.0; 5.5) and 2.8% (95%CI95: 2.3; 3.5) were hospitalized 1, 2 or ≥ 3 times during this period, respectively.

We found that a higher frequency of hospitalization was associated with lower family income, a lower level of maternal education and lower maternal age (χ^2 test for linear trend p < 0.001 for all) (Table 1). Hospitalization was higher among the children of mothers who had no partner, who had black or brown skin colour or who reported being depressed or smoked during pregnancy, as well as being higher among the children of mothers who were multiparous than among those of mothers who were primiparous or nulliparous. Neither planned pregnancy nor consumption of alcohol during pregnancy was associated with hospitalization.

Table 2 shows hospitalization in relation to the characteristics of the infant. The frequency of hospitalization was higher among the infants who were male, as well as among those who had low birth weight, those who had been preterm infants and those who had been admitted to the neonatal intensive care unit after birth.

Psychiatric disorders, whether externalizing or internalizing, were more common among the children who had been hospitalized than among those who had not (Figure 1). At six years of age,

Table 1

Hospitalization during the first 48 months of life, in relation to the characteristics of the mothers, in the 2004 Pelotas (Brazil) birth cohort (N = 3,132).

Characteristics of the mothers	n (%)	Hospitalization during the first 48 months of life	
		n (%)	p-value *
Family income (quintiles)			< 0.001 **
1st (poorest)	592 (18.9)	240 (40.5)	
2nd	637 (20.3)	232 (36.4)	
3rd	633 (20.2)	210 (33.2)	
4th	669 (21.4)	187 (28.0)	
5th (wealthiest)	601 (19.2)	166 (27.6)	
Education, in years of schooling			< 0.001 **
0-4	461 (14.9)	199 (43.2)	
5-8	1,286 (41.5)	445 (34.6)	
9-11	366 (11.8)	116 (31.7)	
≥ 12	985 (31.8)	263 (26.7)	
Age (years)			< 0.001 **
< 20	570 (18.2)	226 (39.7)	
20-34	2,110 (67.4)	689 (32.7)	
> 34	451 (14.40)	120 (26.6)	
Marital status			0.025
With a partner	2,643 (84.4)	852 (32.2)	
No partner	489 (15.6)	183 (37.4)	
Skin color			0.011
White	2,287 (73.0)	726 (31.7)	
Black/Brown	845 (27.0)	309 (36.6)	
Parity			0.005
Nulliparous	1,224 (39.1)	395 (32.3)	
Primiparous	843 (26.9)	250 (29.7)	
Multiparous	1,064 (34.0)	389 (36.6)	
Depression during pregnancy			0.003
No	2,377 (75.9)	752 (31.6)	
Yes	754 (24.1)	282 (37.4)	
Planned pregnancy			0.167
No	1,090 (34.8)	692 (33.9)	
Yes	2,041 (65.2)	373 (31.5)	
Smoking during pregnancy			< 0.001
No	2,299 (73.4)	715 (31.1)	
Yes	833 (26.6)	320 (38.4)	
Alcohol consumption during pregnancy			0.503
No	3,035 (96.9)	1,006 (33.2)	
Yes	97 (3.1)	29 (29.9)	

* χ2 test;

** χ2 test for linear trend.

a greater frequency of any psychiatric disorder was observed in hospitalized children than among those classed as non-hospitalized, 15.9% (95%CI: 13.8; 18.3) and 10.8% (95%CI: 9.5; 12.2), respectively. With regard to internalization and externalization disorders, the frequency was higher among children hospitalized compared to non-hospitalized children, but this difference was not statistically significant. At 11 years, both the frequency of any psychiatric disorder (15.4%, 95%CI: 13.2; 17.7, p < 0.001) and of externalizing disorders (6.6%, 95%CI: 5.1; 8.2%, p < 0.001) and internalization (7.5%,

Table 2

Hospitalization during the first 48 months of life, in relation to the characteristics of the infants, in the 2004 Pelotas (Brazil) birth cohort (N = 3,132).

Characteristics of the infants	n (%)	Hospitalization during the first 48 months of life	
		n (%)	p-value *
Type of delivery			0.749
Vaginal	1,694 (54.1)	564 (33.3)	
Caesarean	1,438 (45.9)	471 (32.8)	
Gender			0.023
Male	1,610 (51.4)	562 (34.9)	
Female	1,522 (48.6)	473 (31.1)	
Low birth weight			< 0.001
No	2,846 (90.9)	879 (30.9)	
Yes	285 (9.1)	156 (54.7)	
Pre-term birth			< 0.001
No	2,691 (86.0)	805 (29.9)	
Yes	437 (14.0)	227 (52.0)	
NICU admission at birth			< 0.001
No	2,955 (94.6)	910 (30.8)	
Yes	169 (5.4)	120 (71.0)	

NICU: neonatal intensive care unit.

* χ^2 test.

95%CI: 6.0; 9.3, p < 0.001) was higher in the children who had been hospitalized compared to the non-hospitalized children.

Table 3 shows the crude and adjusted analyses of the association between hospitalization (yes/no) and the development of a psychiatric disorder by 6 and 11 years of age. In the crude analysis, the chance of having any psychiatric disorder at 6 and 11 years of age was higher among children who had been hospitalized than for those who had not. After adjustment for potential confounding factors, the effect size of the association was reduced but remained statistically significant. For the association between hospitalization and the development of an internalizing disorder by 6 or 11 years of age, adjusting for the characteristics of the mothers and infants did not substantially alter the effect size observed in the crude analysis. In the crude analysis, the chance of presenting an externalizing disorder at 6 and 11 years of age was 64% and 93% higher, respectively, for the children who had been hospitalized than for those who had not. After having been adjusted for the characteristics of the mothers and infants, the association between hospitalization and the development of an externalizing disorder at 6 years of age lost its significance, although the association with the development of an externalizing disorder at 11 years of age remained significant.

Table 4 shows the crude and adjusted analyses of the association between the frequency of hospitalization (0, 1, 2, ≥ 3 times) and the development of a psychiatric disorder at age 6 and 11. In the crude analysis was observed a dose-response relationship between the frequency of hospitalizations and the chance of having any psychiatric, internalizing or externalizing disorder at age 6, but not at age 11. At age 6, after adjustment for potential confounding factors, the odds of having any psychiatric disorder and internalizing disorder for children with ≥ 3 hospitalizations were two times higher than among those who never hospitalized. At age 11, children that hospitalized ≥ 3 times had higher odds of having any psychiatric disorder, internalizing and externalizing disorders than those that never hospitalized.

Figure 1

Frequency of psychiatric disorders at 6 and 11 years of age among children in the 2004 Pelotas (Brazil) birth cohort: comparison between those who had been hospitalized during the first 48 months of life and those who had not.
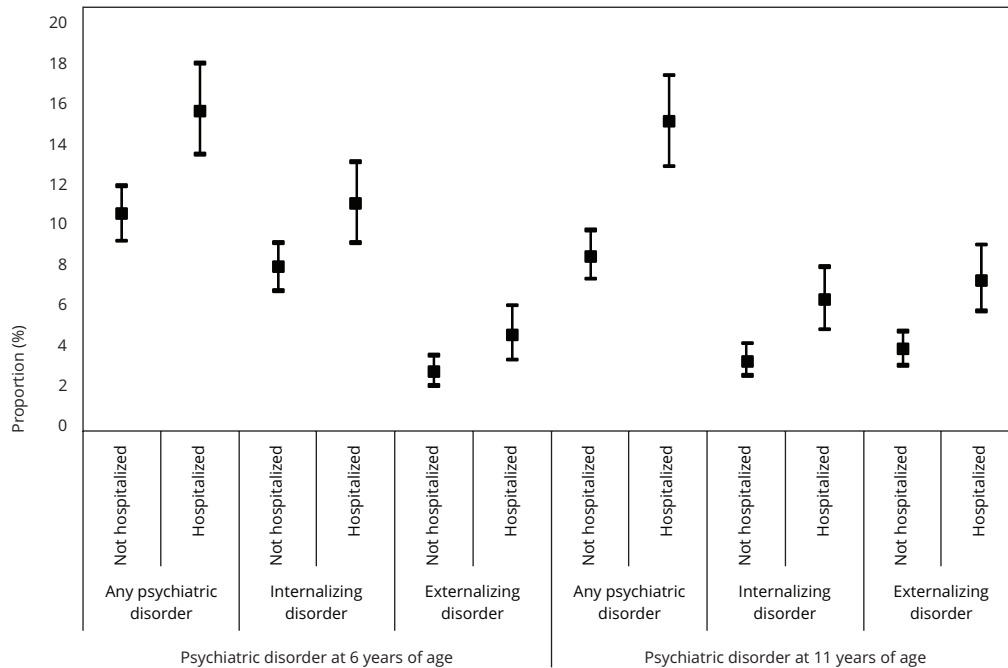
Discussion

The results of the present study suggest that children hospitalized in the first 48 months of life are more likely to develop any psychiatric disorder, internalizing and externalizing disorders at 6 and 11 years of age than are children who were not, even after the analyses have been adjusted for a variety of characteristics related to the mothers and infants. The chance of presenting any psychiatric disorder at age 6 and 11 among children with ≥ 3 hospitalizations was almost two-times higher than among those who never hospitalized.

Some of the main determinants associated with childhood hospitalization found in the literature such as males, prematurity, low birth weight, low family income, low maternal schooling, and smoking exposure were also observed in this study [35,36,37,38]. Birth weight and gestational age have a great influence on the child's health status in the first years of life and are inversely associated with the risk of infectious diseases and hospitalization [35,36,37,38]. The study by Macedo et al. [38] evaluated the risk factors for hospitalization due to acute respiratory disease in children up to one year of age in the four hospitals in the city of Pelotas, found that the absence or low maternal schooling, previous history of wheezing and shortness of breath, use of beak, maternal smoke, age under six months and male sex were associated with the risk of hospitalization for acute respiratory disease.

Corroborating with the findings of this study Douglas et al. [20] reported that the incidence of troublesome behavior at 13-15 years of age was significantly higher among children who had been hospitalized (≥ 7 days or on multiple occasions) before 5 years of age than among those who had not (20.6% vs. 14.7%; p < 0.01). Quinton et al. [21] found that the occurrence of behavioral problems was found to be significantly more common among children who had previously been hospitalized for ≥ 4 days than among children who had not and emotional disorders were five times more

Table 3

Crude and adjusted analyses of the association between hospitalization during the first 48 months of life and development of a psychiatric disorder by 6 and 11 years of age in the 2004 Pelotas (Brazil) birth cohort.

Analyses of children hospitalized in the first 48 months of life *	At 6 years of age		At 11 years of age	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Any psychiatric disorder				
Model 1 = crude analysis	1.56 (1.26; 1.93)	< 0.001	1.90 (1.51; 2.38)	< 0.001
Model 2 = Model 1 + characteristics of the mother **	1.48 (1.18; 1.84)	0.001	1.69 (1.34; 2.14)	< 0.001
Model 3 = Model 2 + characteristics of the child ***	1.50 (1.19; 1.88)	< 0.001	1.63 (1.28; 2.07)	< 0.001
Internalizing disorders				
Model 1 = crude analysis	1.44 (1.12; 1.84)	0.004	1.92 (1.37; 2.70)	< 0.001
Model 2 = Model 1 + characteristics of the mother **	1.40 (1.09; 1.80)	0.010	1.80 (1.27; 2.54)	0.001
Model 3 = Model 2 + characteristics of the child ***	1.46 (1.11; 1.88)	0.006	1.92 (1.35; 2.74)	< 0.001
Externalizing disorders				
Model 1 = crude analysis	1.64 (1.12; 2.39)	0.011	1.93 (1.41; 2.65)	< 0.001
Model 2 = Model 1 + characteristics of the mother **	1.35 (0.91; 1.99)	0.135	1.67 (1.29; 2.30)	0.003
Model 3 = Model 2 + characteristics of the child ***	1.30 (0.87; 1.95)	0.195	1.56 (1.11; 2.18)	0.010

95%CI: 95% confidence interval; OR: odds ratio.

* Reference category = never hospitalized;

** Family income, level of education, marital status, skin color, depression during pregnancy, smoking during pregnancy and alcohol consumption during pregnancy;

*** Gender, type of delivery, birth weight, pre-term birth and admission to the neonatal intensive care unit at birth.

common among the children who had experienced ≥ 2 hospitalizations in the first years of life than among those who had not. Haslum [22] reported that hospitalization before 5 years of age was associated with inattentive/hyperactive behavior, as evaluated by teachers, and with antisocial, inattentive/hyperactive behavior, as evaluated by the parents (p < 0.001 for both). The children who had been hospitalized on multiple occasions had significantly worse *Rutter Children's Behaviour Questionnaire* (RCBQ) scores for antisocial behaviour than those who had been hospitalized only once (β = 0.13, p < 0.02), and that the association remained significant even after adjustment for social factors, family characteristics and the length of the hospital stay(s). Youngblut et al. [24] evaluated the effects that age at admission and length of hospital stay had in children 3-5 years of age. The authors found that the length of hospital stay correlated only weakly with the scores on the various *Child Behaviour Checklist* (CBCL) subscales (anxious/depressed, somatic, withdrawn, aggressive and delinquent), whereas age at hospitalization correlated positively with aggressive behavior.

Our findings support the hypothesis that exposure to risk factors during critical periods of growth and development increases the susceptibility to developing mental disorders in later life [13]. Psychiatric disorders are multifactorial conditions, the development of which is influenced by biological, genetic, social and environmental factors. Therefore, stressful situations in early life have the potential to cause physiological and metabolic changes that increase the risk of developing psychiatric disorders in later life [9,10,11]. Brain circuits and hormonal systems are formed and activated in early life. When a child experiences a stressor, their body attempts to regulate stress by releasing hormones, which can be a useful compensatory mechanism, although prolonged or frequent responses to stress can increase the risk of physical and mental health problems [10,11]. In addition, a dose-response pattern was observed in the association between number of hospitalizations and a child's internalizing disorders after adjustment for potential confounding factors. A plausible explanation for this association would be based in the classical conditional theory, where a reflexive or automatic type of stimulus could acquire the capacity to evoke a response that was originally evoked by another stimulus. According to this theory, the child could associate the neutral stimulus (hospital) with an unconditioned stimulus (physical disease – which causes unpleasant feelings) increasing negative emotional responses (fear, anxiety,

Table 4

Crude and adjusted analyses of the association between frequency of hospitalization during the first 48 months of life (0, 1, 2, ≥ 3 times) and development of a psychiatric disorder by 6 and 11 years of age in the 2004 Pelotas (Brazil) birth cohort.

Number of hospitalizations in the first 48 months of life (0 = reference) *	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
At 6 years of age			
Any psychiatric disorder	p < 0.001	p = 0.001	p < 0.001
1	1.44 (1.14; 1.83)	1.38 (1.08; 1.76)	1.40 (1.09; 1.79)
2	1.85 (1.19; 2.86)	1.69 (1.07; 2.65)	1.74 (1.10; 2.76)
≥ 3	2.43 (1.45; 4.08)	2.24 (1.32; 3.81)	2.34 (1.37; 4.02)
Internalizing disorder	p = 0.013	p = 0.029	p = 0.015
1	1.36 (1.04; 1.79)	1.33 (1.01; 1.76)	1.37 (1.03; 1.82)
2	1.67 (1.01; 2.77)	1.63 (0.97; 2.74)	1.71 (1.01; 2.89)
≥ 3	1.96 (1.07; 3.61)	1.90 (1.02; 3.55)	2.05 (1.09; 3.85)
Externalizing disorder	p = 0.037	p = 0.385	p = 0.434
1	1.47 (0.97; 2.25)	1.26 (0.82; 1.94)	1.21 (0.77; 1.88)
2	2.09 (1.02; 4.29)	1.46 (0.70; 3.06)	1.44 (0.68; 3.06)
≥ 3	2.36 (0.99; 5.61)	1.86 (0.76; 4.55)	1.90 (0.76; 4.73)
At 11 years of age			
Any psychiatric disorder	p < 0.001	p = 0.001	p < 0.001
1	1.97 (1.54; 2.51)	1.78 (1.39; 2.29)	1.71 (1.32; 2.21)
2	1.09 (0.62; 1.93)	0.93 (0.52; 1.66)	0.90 (0.50; 1.62)
≥ 3	2.69 (1.57; 4.61)	2.29 (1.32; 3.99)	2.22 (1.27; 3.88)
Internalizing disorder	p < 0.001	p = 0.002	p < 0.001
1	2.05 (1.44; 2.93)	1.92 (1.33; 2.77)	2.05 (1.41; 2.97)
2	0.95 (0.38; 2.40)	0.88 (0.35; 2.23)	0.94 (0.37; 2.38)
≥ 3	2.36 (1.05; 5.29)	2.18 (0.96; 4.96)	2.49 (1.09; 5.70)
Externalizing disorder	p < 0.001	p = 0.006	p = 0.024
1	2.05 (1.47; 2.87)	1.81 (1.28; 2.55)	1.70 (1.19; 2.42)
2	1.17 (0.53; 2.59)	0.93 (0.42; 2.08)	0.90 (0.40; 2.02)
≥ 3	2.04 (0.92; 4.56)	1.60 (0.70; 3.62)	1.50 (0.65; 3.46)

95%CI: 95% confidence interval; OR: odds ratio.

Note: Model 1 = crude analysis; Model 2 = Model 1 + characteristics of the mother (family income, level of education, marital status, skin color, depression during pregnancy, smoking during pregnancy and alcohol consumption during pregnancy); Model 3 = Model 2 + characteristics of the child (gender, type of delivery, birth weight, pre-term birth and admission to the neonatal intensive care unit at birth).

* Reference category = never hospitalized;

sadness) during and after hospitalization. The presence of a biological gradient (dose-response relationship), one of Hill's criteria, may suggests a causal association. However, length of hospital stay, an important variable, was not available in the present study. Some investigations have shown that the longer the hospitalization, the greater the risk for behavioral/emotional problems among children [20,21,22,23,24,25,26]. Future studies should address not only hospitalization/number of hospitalizations during childhood but also length of hospital stay, trying to discriminate whether the greatest risk is found only among those individuals who had prolonged hospitalizations.

Among the positive aspects of this study is its prospective longitudinal design, which involved population-based monitoring with high follow-up rates. Because this was a longitudinal study, the temporality of the association between exposure and outcome was preserved. In addition, the possibility of a recall bias was reduced because the occurrence of the exposure was investigated at various time points (at 3, 12, 24 and 48 months). Another positive aspect is that psychiatric disorders were identified through the use of a validated instrument applied by psychologists who were trained and supervised, thus ensuring the quality of the data.

Our study has certain limitations. The information about the psychiatric problems of the children was obtained solely from the mothers or legal guardians. Follow-up losses (associated with low family income, lower maternal schooling, prematurity and low birth weight) may indicate the presence of selection bias on the study, probably underestimating the effect of the association found, since the frequency of hospitalization in families with these characteristics was higher. The information regarding maternal psychological distress and maternal habits such as alcohol intake and smoking during pregnancy was collected by means of a questionnaire without a more detailed investigation or use of validated and standardized instruments. This fact could have jeopardized the correct identification of exposed mothers and the impact of these exposures on the outcome. Finally, our data pertain to a single medium-sized city and therefore might not be representative of the population of Brazil as a whole.

In conclusion, our results support the hypothesis that hospitalization in the early stages of life has a subsequent effect on the mental health of children and adolescents. This is quite relevant, given that half of all mental health problems in adulthood begin in childhood or adolescence [39,40,41]. Despite the improvements in hospital practices seen in the last decade, hospitals are far from being safe and appropriate environments for children. Preventive measures such as the practice of humanized care and the qualification of health services are needed in order to minimize the negative experiences of hospitalized children. Further studies, conducted in different socioeconomic contexts, are warranted in order to confirm the consistency of the association detected here.

Contributors

V. L. S. Silva, G. V. A. França, T. N. Munhoz and A. Matijasevich participated in the data design, analysis, interpretation of the results and article writing. I. S. Santos, A. J. D. Barros and F. C. Barros collaborated with the interpretation/writing of the findings. All authors read and approved the final version of the manuscript.

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Resumo

O estudo teve como objetivo avaliar os efeitos no médio prazo da hospitalização nos primeiros 48 meses sobre o desenvolvimento de transtornos psiquiátricos aos 6 e 11 anos de idade entre membros de uma coorte de nascimentos em um país de renda média. Analisamos os dados de uma coorte de nascimentos de 2004 (N = 4.231) na cidade de Pelotas, Rio Grande do Sul, Brasil. Foi investigada a frequência da hospitalização aos 12, 24 e 48 meses de vida. Quando as crianças tinham 6 e 11 anos de idade, os transtornos psiquiátricos foram investigados com o Development and Well-Being Assessment. *Usamos a regressão logística para ajustar os potenciais fatores de confusão. A frequência global de hospitalização durante os primeiros 48 meses de vida foi 33,1% (IC95%: 31,4; 34,7). Entre as crianças que tinham sido hospitalizadas, 25,6% (IC95%: 24,1; 27,1), 4,7% (IC95%: 4,0; 5,5) e 2,8% (IC95%: 2,3; 3,5) foram internadas 1, 2 ou ≥ 3 vezes durante o período, respectivamente. Depois de ajustar para os potencias fatores de confusão, as chances de apresentar qualquer transtorno psiquiátrico aos 6 e 11 anos de idade foram mais altas em crianças que haviam sido hospitalizadas nos primeiros 48 meses de vida, com OR de 1,50 (IC95%: 1,19; 1,88) e 1,63 (IC95%: 1,28; 2,07), respectivamente. Nossos resultados corroboram a hipótese de que a hospitalização na primeira infância tem efeito sobre a saúde mental posterior. São necessárias medidas preventivas para minimizar as experiências negativas de crianças com história de hospitalização na infância.*

Transtornos Mentais; Hospitalização; Estudos de Coortes

Resumen

A Este estudio tuvo como meta evaluar los efectos a medio plazo que tiene una hospitalización durante los primeros 48 meses de vida en el desarrollo de trastornos psiquiátricos entre los 6 y 11 años de edad, con individuos en una cohorte de nacimientos en un país de renta media. Analizamos los datos de una cohorte de nacimientos de 2004 (N = 4.231) en la ciudad de Pelotas, Rio Grande do Sul, Brasil. Se investigó una frecuencia de hospitalización a los 12, 24 y 48 meses de vida. Cuando los niños tenían entre 6 y 11 años de edad, se investigaron los trastornos psiquiátricos con una evaluación sobre desarrollo y bienestar. Se usó regresión logística para ajustar potenciales factores de confusión. La frecuencia general de hospitalización durante los primeros 48 meses de vida fue de un 33,1% (95%CI: 31,4; 34,7). Entre los niños hospitalizados un 25,6% (95%CI: 24,1; 27,1), 4,7% (95%CI: 4,0; 5,5) y 2,8% (95%CI: 2,3; 3,5) estuvieron hospitalizados 1, 2 o ≥ 3 veces durante este período, respectivamente. Tras ajustar los factores de confusión, la oportunidad de presentar cualquier trastorno psiquiátrico entre los 6 y 11 años de edad fue mayor para los niños que habían sido hospitalizados durante los primeros 48 meses de vida, respecto a quienes no lo habían estado, con un OR de 1,50 (95%CI: 1,19; 1,88) y 1,63 (95%CI: 1,28; 2,07), respectivamente. Nuestros resultados avalan la hipótesis de que la hospitalización en estadios tempranos de la vida tuvo un efecto en la futura salud mental de los niños. Son necesarias medidas preventivas, con el fin de minimizar las experiencias negativas de los niños que habían sido hospitalizados durante la infancia.

Trastornos Mentales; Hospitalización; Estudios de Cohortes