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Present and previous psychopathology of juvenile onset migraine: a pilot investigation by Child Behavior Checklist

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Abstract The objective was to describe the premorbid state of migraine with juvenile onset. Thirty subjects with migraine and 30 healthy subjects were enrolled in a case-control study. A structured questionnaire (Child Behavior Checklist, CBCL) was administered to the mothers and ratings were obtained for the past two age periods (0–3 and 4–6 years) and for the present state. CBCL scores of the migraine group (MG) were compared to those of the control group (CG) during the three periods. A longitudinal study was performed to evaluate the evolution of psychopathology comparing CBCL scores of MG in the three age periods. During the premorbid period MG showed significantly higher mean scores on total, internalising, anxious-depressive scales. In the longitudinal perspective, internalising traits were present in the premorbid period in MG. Children later diagnosed as having migraine differ from CG in several scales during different age periods. Migraine could be considered as the expression of a previous vulnerability.

Keywords Migraine • Child Behavior Checklist • Premorbid state

Introduction

Population-based studies reported that the prevalence of migraine in childhood and adolescence ranges from 3% to 14% [1–6]. From the time of Wolff's early portrait of the childhood personality characteristics of migraine patients, the research began to explore the association of headache first with broad personality traits and then with distinct psychiatric symptoms [7, 8]. Maratos and Wilkinson underlined that an "emotional upset" is the most frequently reported (86%) precipitating factor [9]. The Authors did not suggest a different personality of migrainous children but that there might be some association between the physiological process that underlies the migrainous attack and the emotional disturbance in these children.

Population-based studies about the relationship between migraine and psychopathology during development and in adults have provided consistent evidence for a positive association between migraine, anxiety disorder and depression [10–15]. Population-based studies of young adults outlined the association of migraine with anxiety disorders (generalised anxiety and panic disorder) and depression by using standardised Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnosis [16–18]. The association between anxiety and depression, however, is strong also in the absence of migraine [19].

Pine et al. [20] and Cooper et al. [21] concluded that headaches were twice as common in depressed adolescents than in non-depressed, but they did not find an association with anxiety.

Guidetti et al. investigated the relationship between migraine and psychiatric factors in an 8-year follow-up: 16% of children with migraine had anxiety disorder, compared with 3% of children with tension-type headache. The longer chronicity of migraine was moreover related to the presence of anxiety at the beginning of the attack in 75% of children [22].

In order to investigate premorbid behavioural patterns we used the Child Behavior Checklist (CBCL, Italian version by Frigerio, 1998), an empirically based assessment instrument, one of the most frequently used to obtain standardised reports of children's behavioural problems and competencies, as observed by the parents; its validity and reliability are described in the literature [23].

The CBCL rates child behavioural and emotional problems both globally and along the two dimensions of "Internalising" symptoms composed of "Withdrawn", Somatic Complaints" and "Anxious/Depressed" subscales, and "Externalising" symptoms, such as "Aggressive" and "Delinquent" behaviour. The validity of Internalising and Externalising profile patterns is well documented in the literature [24, 25]. Behavioural and emotional disturbances in childhood tend to outline three groups: the frightened, inhibited one, the aggressive, antisocial one and the mixed one [26].

Anttila et al. found that children with migraine had significantly higher levels of total, internalising and somatic symptoms in the CBCL questionnaire, as well as social and family problems, than those without migraine and had higher levels of somatic symptoms than children with tension-type headache [23, 27]. However this study also showed that many children with migraine did not report high levels of psychiatric symptoms. Mazzone et al. assessed tension-type headache, migraine patients and controls using the CBCL (and other tests). Although most headache patients had scores within the normative non-pathological range, both tension-type headache and migraine patients had higher CBCL total, internalising and externalising scores than controls [28].

To our knowledge no previous studies have addressed the premorbid state of migraine by means of retrospectively used CBCL.

The aims of the present study were twofold: to investigate the features of the premorbid state in migraine of juvenile onset by means of comparison with a group of healthy children and to analyse developmental pathways of migraine patients in order to highlight the onset of psychiatric symptoms.

Methods

Sample

Thirty consecutive migraine-affected children referred to our Division of Child and Adolescent Neuropsychiatry, a suburban public academic hospital providing care to patients of all socioeconomic levels, between January and December 2005 were enrolled. The sample included 24 females and 6 males, aged from 7 to 16. All subjects were at their first specialist assessment for migraine and were referred to our centre after an initial evaluation by the paediatrician. The assessment included a full medical, neurological and psychiatric history and a general physical, neurological and psychiatric examination of the child. This assessment was performed by senior neuropsychiatrists. Blood examinations, urine analysis, wake and sleep EEG recordings, cardiology and otolaryngology examinations, ophthalmic tests, magnetic resonance or computed tomography scan were required in the presence of specific indications to exclude secondary headaches [29]. All the participants of the clinical sample had undergone a routine psychological assessment (clinical interview and psychometric test) and none of them had a history of referral or had received treatment for a psychiatric disorder or general medical condition. The psychometric test was represented by the Wechsler Intelligence Scale for Children (WISC-III-R) [30]. All the participants had an IQ in the normal range.

Diagnosis of migraine was done according to the International Classification of Headache Disorders (ICHD-II) criteria for migraine and their widely accepted modifications for paediatric age were fulfilled by the subjects. Twenty-six (87%) patients had migraine without aura, and four (13%) had migraine with aura [31, 32]. The mean age of the participants was 10.9±2.6 years and the mean age at the first episode of migraine was 8.3±2.7 years.

The mother was asked to complete 3 forms of CBCL, referring to the present and to the past in two premorbid periods: 0–3 years and 4–6 years.

Table 1 Demographic and clinical features of the two groups

	Migraine group (MG)	Control group (CG)
Age upon entry into study (mean±SD)	10.9±2.6	11.1±2.5
Age of onset (years, mean±SD)	8.4±2.7	
Female (%)	80	80
Full scale IQ (WISC-R-III) (mean±SD)	103.1±6.9	
Family status (%)		
Intact	90	93.3
One parent	10	6.7
Out of home	0	
Socioeconomic status (%)		
Upper/middle	86.7	90
Lower	13.3	10

*$p<0.05$; **$p<0.01$

This migraine group (MG) was compared with a control group (CG) of 30 subjects: 24 girls and 6 boys, aged from 7 to 16 (mean 11.1±2.5 years).

The CG was randomly recruited from a population of school students attending local primary and secondary schools. None of them had a history of referral or had received treatment for migraine or psychiatric disorder.

Both groups were comparable for sex and age. Socioeconomic condition was evaluated following Hollingshead and Redlich's criteria [33]. The economic condition (mean 69.57; SD=21.8) corresponds to the third class, which indicates a medium socioeconomic level. Demographic and clinical characteristics of the two groups are reported in Table 1.

If inclusion criteria were satisfied, parents of eligible participants and youths were informed about the research project and signed informed consent was obtained. The local Ethics Committee approved the research project, which was conducted according to the principles established in the Declaration of Helsinki.

Measures and procedure

In order to investigate premorbid behavioural patterns we used the CBCL (Italian version by Frigerio, 1998), which is a parent-form questionnaire composed of questions about social competencies and behavioural problems. From the row scores, three summary scores (Total Problems, Internalising, Externalising), eight scales of behavioural problems defined as syndromes (Withdrawn, Somatic, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Destructive/Delinquent Behaviour, Aggressive Behaviour), a total score for social competencies and three partial scores (Activity, Social, School) are obtained. For every score the cut-off between normal, borderline and clinical range has been detected through the study of a huge normative sample [23, 24].

We adopted the cut-off score that distinguishes clinical cases and borderline ones from normal (values higher than 63 for summary scales, higher than 67 for syndrome scales and lower than 30 for competency scale).

The retrospective use of CBCL has already been applied by other authors [34–37]. For this study the CBCL items were changed to the past tense as proposed by Baum and Walker [34].

We administered three forms of the CBCL: the first one concerning the present time, another one the first three years of life and the last one concerning child problems within the 4–6 age period. In this way we captured social and behavioural problems on the CBCL from three time frames: at the time of visit, during the first three years of life and at 4–6 years. All the interviews were filled out by the mother. To exclude any possible overlap of the prodromal phase with the premorbid symptoms, we invited the parents to fill the 4–6 CBCL referring to the childhood period ending 1 year before evidence of full-blown migraine symptomatology.

Statistical analysis

To perform case control comparison between MG and CG at the three age periods, the mean scores at each CBCL subscale were submitted to statistical analysis using Student's *t*-test.

Repeated measures ANOVA was performed using the age as the independent factor and CBCL scores as the dependent variables to check for possible differences between the three age periods (0–3, 4–6 and 7–16) of the MG and CG. Paired Student's *t*-test was also used to compare mean scores at different CBCL subscales of MG between 0–3 and 4–6 age periods and between 4–6 and 7–16 age periods.

The data were analysed with SPSS 9.0 for Windows.

Results

The mean values of all CBCL scores were in the normal range both for MG and CG. However we evaluated differences in absolute values of mean scores, considering the vicinity to the cut off-point.

In the 7–16 years group, children of MG have significantly higher mean CBCL scores than those of CG in several scales: total problems, internalising, somatic, anxious/depressive, thoughts and attention problems. At the same time they have lower scores in the school competence scale (Table 2). The MG have symptom scores above the cut-off point of normal functioning significantly more

Table 2 Comparison between MG and CG at the three age periods

Age period	0–3			4–6			7–16		
	MG	CG	*p*	MG	CG	*p*	MG	CG	*p*
CBCL competence scale									
Total				38.7 (6.5)	39.6 (5.7)	n.s.	39.7(4.8)	42.3 (5.5)	n.s.
Activities				34.6 (7.0)	35.7 (5.5)	n.s.	36.0 (5.7)	36.8 (5.9)	n. s.
Social				43.8 (6.4)	44.7 (6.4)	n.s.	44.9 (5.2)	44.8 (6.2)	n.s.
School				49.7 (4.7)	50.5 (4.1)	n.s.	50.2 (5.9)	52.7 (3.0)	*

Cont. →

Cont. Table 2

Age period	0–3			4–6			7–16		
	MG	CG	*p*	MG	CG	*p*	MG	CG	*p*
CBCL syndrome scale									
Withdrawn	53.7 (4.1)	50.4 (1.2)	n.s.	54.2 (6.5)	51.2 (2.9)	*	54.2 (6.0)	52.3 (4.6)	n.s.
Somatic C	55.9 (6.4)	51.2 (3.7)	***	61.7 (7.4)	52.0 (3.3)	***	64.2 (8.0)	52.9 (3.8)	***
Sleep P	53.2 (6.8)	50.8 (2.0)	n.s.						
Anxious/Depr	53.9 (6.4)	50.5 (2.4)	**	56.5 (6.3)	50.5 (1.7)	***	56.2 (7.1)	51.2 (2.8)	**
Social P				55.03 (6.3)	50.4 (1.2)	**	53.6 (5.5)	51.4 (2.8)	n.s.
Thought P				51.4 (4.4)	50.2 (1.3)	n.s.	52.9 (5.0)	50.5 (2.6)	*
Attention P				54.9 (7.2)	50.7 (1.7)	**	55.9 (7.1)	52.0 (3.2)	**
Destructive/Delinquent P	50.6 (1.9)	50.6 (2.0)	n.s.	52.3 (4.6)	51.3 (2.9)	n.s.	51.5 (3.1)	52.0 (3.2)	n.s.
Aggressive B	50.1 (0.2)	50.3 (1.3)	n.s.	52.3 (4.5)	50.9 (3.0)	n.s.	52.3 (3.9)	51.4 (3.1)	n.s.
CBCL summary scale									
Internalizing	45.8 (10.1)	41.3 (6.2)	*	56.1 (8.6)	41.8 (7.2)	***	55.8 (11.0)	44.1 (9.0)	***
Externalizing	39.5 (6.4)	37.3 (6.6)	n.s.	45.0 (9.8)	40.1 (9.0)	n.s.	46.7 (9.5)	45.9 (7.3)	n.s.
Total P	43.4 (8.8)	37.7 (7.7)	**	50.8 (11)	37.6 (7.8)	***	51.6 (11.9)	45.0 (7.2)	**

*$p<0.05$; **$p<0.01$; ***$p<0.001$

often than the CG considering total problems (16.6%–0%) as well as internalising (30% compared to 3.3%) and somatic scale (26.6%–0%).

In the retrospective evaluation of age 4–6 (symptom free), significant higher scores between MG and CG were found in the total problems scale, internalising, somatic, anxious/depressive, attention, social problems and withdrawn (Table 2). The percentage of clinical subjects in MG were the following: total problems scale 13.3%, internalising problems 20%, somatic problems 20%, total competencies 43.3% and activities 13.3%.

In the retrospective evaluation of age 0–3, significantly higher scores between MG and CG were found in the total problems scale, internalising, somatic and anxious/depressive (Table 2). The percentage of clinical subjects at this age period was negligible.

Therefore we found four scales with a significant difference between MG and CG in all the age periods: total problems, internalising, somatic complaints and anxious/depressed problems.

In a longitudinal perspective of the clinical group, ANOVA analyses showed statistically significant differences between the three age periods in the following scales: total problems ($p<0.01$), internalising ($p<0.001$), externalising ($p<0.01$) and aggressive syndrome scale ($p<0.05$).

At the *t*-test analysis, we did not find statistically significant differences between the 7–16 and 4–6 age periods. Comparing the age periods of 4–6 and 0–3, significant differences were found in total problems ($p<0.01$), internalising ($p<0.001$), somatic ($p<0.01$) and also in externalising ($p<0.01$) and aggressive syndrome scale ($p<0.01$). No differences were found in the scale anxious/depressive.

Figures 1–4 show the comparison between the clinical group and CG in the most significant CBCL scales (total

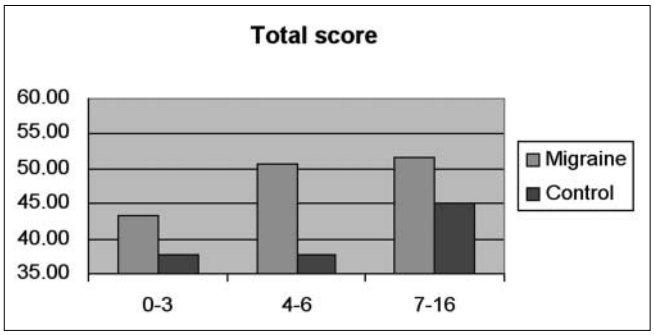

Fig. 1 Total score: Comparison between MG and CG in the three age periods

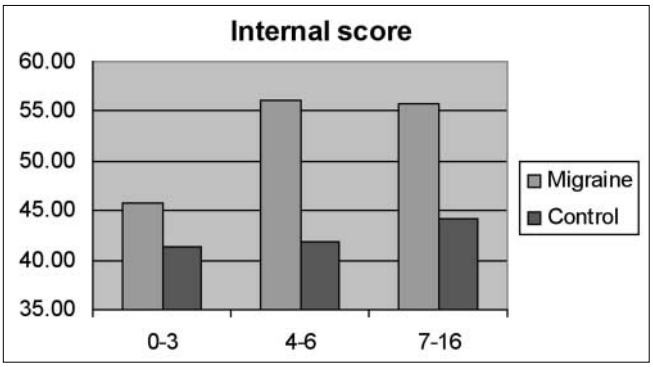

Fig. 2 Internalising score: comparison between MG and CG

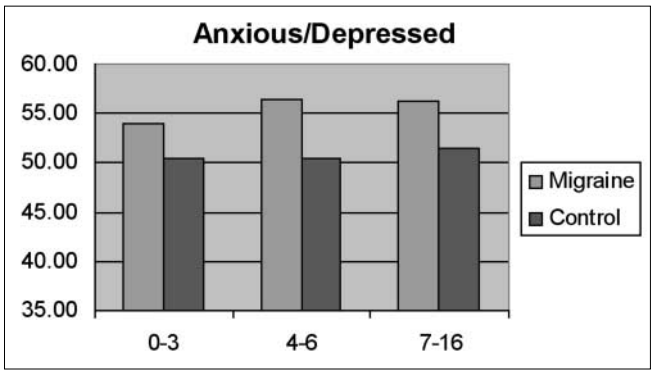

Fig. 3 Anxious/depressed score: comparison between MG and CG

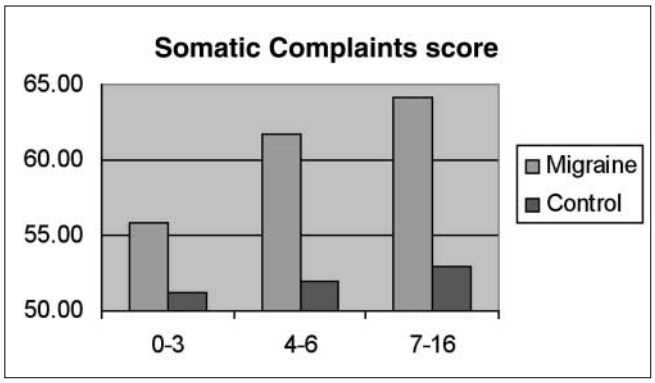

Fig. 4 Somatic complaints score: comparison between MG and CG

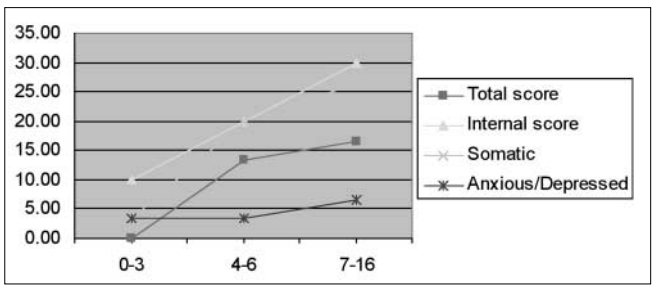

Fig. 5 Percentages of MG patients with clinical score at CBCL in a longitudinal perspective

problems, internalising, somatic and anxious/depressed) at the three age periods while the trend of the clinical percentage in MG over the years is illustrated in Figure 5.

The ANOVA analyses were performed also for the control group but no statistically significant differences were demonstrated.

Discussion

In our study children with migraine had significantly higher total, internalising, anxious-depressive CBCL scores than those without migraine. Similar results were reported by Anttila et al., who found that children with migraine had significantly higher scores of total, internalising and somatic symptoms than those without migraine [27]. The strong associations between migraine, depression and anxiety in children and adults demonstrated in some studies is partially confirmed by our findings of higher – but below threshold – scores in the anxious-depressed scale [9, 10, 12, 16, 38]. Egger et al. studied a large population of children aged 9–15 years: girls who met DSM-III-R criteria for a depressive disorder had a four times higher prevalence of headaches than girls who were not depressed; girls with anxiety disorders had a three times higher prevalence of headaches than girls who were not anxious [39]. Mazzone et al. found that a higher proportion of tension-type headache patients had pathological CBCL total and internalising scores than controls while children with migraine had a pathological score only for the internalising scale [28].

Similarly to Anttila et al., in our study somatic complaints were connected with migraine [22]. The association between multiple somatic complaints and symptoms of anxiety and depression has already been reported [16, 40]. Kowacs et al. evaluated symptoms of depression, anxiety and general psychiatric symptoms among migraine patients, compared with a group of patients suffering from another chronic medical illness without neurological or psychiatric impairment and with a group of healthy volunteers. Statistical differences in the score of depression, anxiety and general psychiatric symptoms scale were observed between migraine sufferers and other groups. The inclusion of the psoriasis group was an attempt to refute the argument that, in case of a significant association of the addressed symptoms with migraine, this association would have occurred simply because of the presence of a chronic disorder [41].

The present study also shows a higher prevalence of "school problems" at CBCL in the school-aged migraine sufferers. Previous studies have shown that children with migraine do not have problems in school performance but do have problems in their relationships with other children [42]. We also found that, during the pre-scholar period, children of the MG had a significantly higher rate of social problems when compared with the CG.

In our MG the prevalence of "attention problems" at CBCL is higher than in the CG. Anttila et al. found that girls with migraine had higher levels of attention problems (without school problems) compared to those without migraine but this association was not confirmed for boys [27].

In the longitudinal perspective, internalising traits are also definitely present in the premorbid period; in particular the difference was statistically significant during the 0–3 years and 4–6 years age periods, when children who would go on to develop migraine had higher internalising scores.

Maratos and Wilkinson underlined that a significantly higher proportion of migrainous children than controls

showed signs of a neurotic disorder (mainly anxiety or depression) and had a higher prevalence of neurotic disorder in the previous year [9]. A 26-year longitudinal study found that study members diagnosed with migraine in young adulthood were largely defined by a history of headache, "neurotic" behaviour and anxiety disorders [43].

Therefore we also agree with Egger et al.'s hypothesis of a spectrum of association among headaches, depression and anxiety [39]. On the other hand, our study does not support Merikangas et al.'s hypothesis that childhood anxiety disorders precede the advent of migraines and that depressive disorders are developed as later sequelae of headaches [16].

Internalising symptoms could possibly represent a premorbid state that precedes migraine onset. It could be hypothesised that migraine might be considered as the expression of a previous vulnerability.

In the past, psychiatric comorbidity has often been underestimated. Considering and treating migraine only as a symptom introduces the risk of sustaining and feeding the underlying mechanisms, determining progressive chronicity particularly during infancy and adolescence. In young patients, migraine and tension-type headache change their characteristics over time, with high levels of spontaneous remission and improvement [44, 45]. Guidetti et al. [22] underlined the psychopathological consequences due to persistence of headaches over time. The presence of psychiatric comorbidity (comorbidity with anxiety disorders and depression) in their population is related to a worsening or persisting situation after an 8-year follow-up. Psychopathological evaluation and early diagnosis of emotional problems are therefore of the utmost importance in order to prevent chronicity of migraine. The definition of premorbid characteristics of migraine could potentially help to identify the population at risk for migraine, and would allow treatment interventions to begin before the frank onset of symptoms.

The internalising component may represent a feeding and persistent factor for migraine [46]. The demonstration of an internalising score in a cephalalgic patient, by means of CBCL, could be of the utmost importance in order to prevent the chronicity of migraine.

We have to consider that pathologic cut-off is often not reached in diseases with a minor psychiatric component, like migraine. In such cases, scores in the normal range, but near borderline cut-off, could be considered as significant and, possibly, a specific cut-off for migraine patients could be proposed. It has to be taken into account, however, that parents have been found to be poorer reporters of internalising symptoms compared to the child [47]. For this reason CBCL parents' reports may underestimate anxiety symptoms in children.

Our study has some limitations. First, a questionnaire method was used to investigate internalising symptoms. Future longitudinal studies should include a clinical assessment of psychiatric disorders and child impairment, using DSM criteria for psychopathology.

The group of patients included in this study presented with a homogenous symptomatology, migrainous pain, defined by literature as having the strongest association with internalising disorders. So the present study does not contribute to the definition of differences between migraine and tensive headache and between male and female. Moreover the study sample included a small number of patients. In the future, prospective trials with increased sample size aimed at investigating the pattern of developmental course in the different subtypes of headache should be designed.

Another important limitation is the possible influence of cognitive and emotional biases in the procedure of compiling the test, being based on mothers' retrospective memory task. We considered that the examined age periods were relatively recent in time, differently from adult studies, therefore we supposed that mothers' memories were more able to differentiate the premorbid behaviour of their child from the morbid one. In our study mothers have filled out the questionnaires at the early stage of the illness of their child so that the recall bias due to the duration of illness was extremely reduced. Furthermore, the retrospective use of CBCL has already been applied by other Authors [32–35].

Only retrospective parent reports were used. Some studies of this kind have used ratings of premorbid functioning performed only by clinicians [48]. We need studies using different informants (parents, teachers, clinicians), which together may shed light on the premorbid period of migraine. Prospective trials with the CBCL questionnaire submitted to more than one informant could be useful for obtaining more objective information.

In conclusion, our study suggests that migraine can be interpreted as a disease that has its roots in previous behavioural problems, and can therefore represent a symptom that follows an early constitutional fragility. The appearance of internalising and externalising difficulties in the period 4–6 years is due to the fact that in the pre-school period psychopathology becomes less fluctuating and its organisation is more stable. Even though they rarely reach the clinical threshold at CBCL questionnaire, children who develop migraine are different from healthy children because of the higher rate of behavioural problems.

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