

Original article

## Psychological assessment in children and adolescents with Benign Paroxysmal Vertigo

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### Abstract

Migraine in childhood and adolescence has been associated with the presence of behavioural and emotional difficulties, but only few data are available with respect to unusual types of headache syndromes such as Benign Paroxysmal Vertigo of Childhood (BPVC). Aim of the present study was to evaluate the behavioural and emotional profiles of clinically referred children and adolescents suffering from BPVC and migraine, as compared to normal controls. According to the revised International Classification of Headache Disorders (ICHD-2) the BPVC belongs to the category of “primary headache”, as a migraine equivalent, in a subset that is called “periodic syndromes of childhood”. A total of 60 clinically referred children and adolescents (4–15 years) 21 suffering from BPVC and 20 from migraine, according to the diagnostic criteria of the ICHD-2, and 19 normal control (NC) were recruited in this study. Psychological assessment were performed using the Child Behaviour Checklist (CBCL), the Children’s Depression Inventory (CDI) and the Multidimensional Anxiety Scale for Children (MASC). Although most of the patients suffering from headache had scores within the normative non-pathological range, both BPVC and migraine patients had significantly higher CBCL total, internalizing, and externalizing scores, as compared to NC. Furthermore, both BPVC and migraine groups displayed significantly higher CDI and MASC scores than NC group. No differences were found between the two types of headache. In conclusion, clinically referred children and adolescents with BPVC and migraine showed higher indices of behavioural and emotional symptoms, both internalizing and externalizing, as compared to normal peers.

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### 1. Introduction

Vertigo and migraine (M) represent two of the most common reasons why children and adolescents are referred to the paediatric neurological practice.

Benign Paroxysmal Vertigo of Childhood (BPVC), described for the first time by Basser [1], is a paroxysmal, non-epileptic, recurrent event characterized by subjective or objective vertigo occurring in children that not show any additional neurological problems. BPVC is considered a fairly common cause of vertigo in children, with a prevalence rate of 2.6% [2].

In 2004, the International Headache Society published the revised International Classification of Headache Disorders (ICHD-2), which includes the BPVC under the category of “primary headache”, in the subset called “periodic syndromes of childhood” [3]. These syn-

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dromes, quite peculiar to children, are characterized by a wide variety of episodic symptoms, including movement disorders, vomiting, ataxia, and vertigo, and may not include migraine at all. However, a high proportion of children with vertigo subsequently develop migraine [4]. Moreover, there is a family history of migraine in at least 50% of cases, and anti-migraine drugs may bring relief to the vertigo episodes. For these reasons, BPVC is considered as a migraine equivalent by most authors [5].

In childhood, migraine could be one of the somatic manifestations of psychiatric conditions, such as anxiety and depression [6], or conversely, migraine itself could be considered as a source of stress, which can cause in turns anxiety symptoms [7]. Thus, the relationship between vertigo, migraine and psychiatric disorders seems very intricate. Psychological problems have been extensively investigated in migraine patients [8]; however, children and adolescents suffering from BPVC have received less attention.

In adult samples, several studies have reported an association between vestibular disorders and psychiatric conditions, showing higher levels of anxiety, depression and somatization in patients with vertigo as compared to healthy controls [9–11]. By contrast, to date only a few studies have investigated the same association in children and adolescents.

The purpose of our study was to evaluate the presence of behavioural and emotional symptoms among clinically referred children suffering from BPVC and migraine. More in details, our aims were:

- to evaluate the relationship between BPVC or migraine and the indices of behavioural and emotional difficulties, as compared to controls;
- to investigate if BPVC and M patients showed similar behavioural and emotional profiles, as compared to controls.

## 2. Methods

### 2.1. Patients and controls

Children and adolescents, aged 4–15 years, referred to the clinic of Child and Adolescent Neuropsychiatry of the Paediatric Department at the University of Catania, Italy, during the year 2008, and meeting diagnostic criteria for Benign Paroxysmal Vertigo of Childhood or Migraine, according to the revised International Classification of Headache Disorders (ICHD-2) [3], were enrolled in this study. Normal Controls (NC) were randomly selected from a database of healthy children attending a well-being paediatric clinic for routine checks.

The ethics committee of the University Hospital of Catania approved the study design. The participants'

parents who accepted to take part in the research signed a consent form, and children and adolescents assented to participation.

### 2.2. Assessment

Physical and neurological assessment, including EEG and ophthalmological examination were performed for each subject. All patients and controls received a complete battery of audiological and vestibular tests. In particular, the investigation of vestibular system included tests to explore vestibulospinal reflex (Romberg's Test, Unterberger's Stepping Test and Positional Tests), spontaneous and gaze nystagmus (Hallpike Manoeuvre), and vestibulo-ocular reflex (Rotational and Caloric Tests). The vestibular examination was completed by cerebral Magnetic Resonance Imaging (MRI) in a few cases. Finally, all patients and controls underwent a psychological evaluation, which included the following instruments:

- The Child Behaviour Checklist (CBCL), which is a 113-item questionnaire completed by the parents. The CBCL rates child behaviour and emotional problems both globally and along the two dimensions of internalizing symptoms, such as anxiety and depression, and externalizing symptoms, such as aggression and hyperactivity. Raw scores for each clinical factors were transformed to T-scores based on published norms, and scores >70 were considered indicative of clinical impairment [12,13].
- The Children's Depression Inventory (CDI), which was completed by the child, was used to rate symptoms of depression. The CDI is a self-rating scale that consists of 27 items scored on a three-point scale (0, absent; 1, moderate; 2, severe) reflecting growing severity of symptoms. A 19-point cut-off indicates the ideal threshold discriminating children at risk of depression from healthy children [14].
- The Multidimensional Anxiety Scale for Children (MASC), which was also completed by the children, was used to score symptoms of anxiety. The MASC is a 39-item self-report scale, which is used to investigate the following main areas: physical symptoms, harm avoidance, social anxiety and separation anxiety. The raw scores were converted into standard T-scores, and scores >50 indicate the presence of anxiety's symptoms [15].

### 2.3. Statistical analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS 11.0 for Mac OS-X). Both descriptive and inferential analyses were undertaken.  $\chi^2$  analyses for dichotomous variables,

and one-way ANOVAs with post hoc Bonferroni multiple comparison test were conducted for continuous variables. Test results with  $P < 0.05$  were regarded as statistically significant.

### 3. Results

#### 3.1. Clinical characteristics

The patients sample included 41 children and adolescents. Among them, 21 (9 males and 12 females; age range 4–15; mean age  $\pm$  SD  $10.52 \pm 3.14$ ) had BPVC and 20 (10 males and 10 females; age range 8–14; mean age  $\pm$  SD  $10.70 \pm 2.00$ ) had migraine. Nineteen subjects were included in the NC group. Demographic and clinical characteristics of the 60 children participating in the study are summarized in Table 1. No age and gender significant differences were reported between the BPVC ( $N = 21$ ), M ( $N = 20$ ), and NC children ( $N = 19$ ). The socioeconomic status of the families was similar between the groups.

All the subjects had normal neurological, vestibular and ophthalmological examinations, as well as brain MRI or EEG exams, which did not reveal any clinically significant abnormalities.

#### 3.2. Psychological profiles

Compared with NC, both BPVC and M had significantly higher scores on all the administered rating scales (CBCL, CDI, and MASC) (Table 2).

CBCL analysis showed higher scores for the externalizing symptoms in both BPVC ( $60.78 \pm 10.15$ ) and M groups ( $60.47 \pm 7.40$ ), as compared to NC group ( $52.60 \pm 10.32$ ,  $P < 0.05$ ), with no statistically significant differences between BPVC and M groups. Similarly, CBCL internalizing scores were significantly higher in the BPVC ( $70.33 \pm 8.77$ ) and in the M group ( $66.47 \pm 6.33$ ) than NC ( $58.27 \pm 7.94$ ), with  $P < 0.001$  for the comparison with BPVC and  $P < 0.01$  for the comparison with M group. The M group revealed higher but not statistically significant MASC ( $60.05 \pm 7.28$ ) and CDI ( $13.74 \pm 7.85$ ) scores than the BPVC group ( $53.44 \pm 6.54$  and  $9.56 \pm 5.45$ , respectively). The CDI scale showed higher T-scores in BPVC group ( $9.56 \pm 5.45$ ) and in M group ( $13.74 \pm 7.85$ ) than in the NC group ( $7.00 \pm 4.96$ , with  $P < 0.05$  vs BPVC and  $P < 0.01$  vs M). Likewise, the NC group ( $46.57 \pm 6.74$ ) had lower MASC scores than both BPVC ( $53.44 \pm 6.54$ ,  $P < 0.05$ ) and M groups ( $60.05 \pm 7.28$ ,  $P < 0.001$ ).

Most of the patients, however, had scores within the non-pathological range, according to the established norms (Table 3). A higher proportion of both BPVC (86%) and M (60%) patients had pathological CBCL internalizing scores than NC (21%), with  $P < 0.01$  vs BPVC and  $P < 0.05$  vs M. On the MASC scale, both BPVC and M groups displayed a higher rate of children in the pathological range, compared to the NC. Indeed, the 33% and the 65% of children, in the BPVC and M groups respectively, showed pathological scores on the MASC and these rates were significantly higher

Table 1  
Subjects demographics and clinical characteristics.

Groups	BPVC ( $N = 21$ )	Migraine ( $N = 20$ )	Normal controls ( $N = 19$ )	$P^a$
Males/females	9/12	10/10	7/12	0.708
Age (mean $\pm$ SD)	$10.52 \pm 3.14$	$10.70 \pm 2.00$	$10.50 \pm 2.28$	0.287
Age at onset (mean $\pm$ SD)	$8.34 \pm 3.67$	$9.02 \pm 2.65$	–	

<sup>a</sup>  $\chi^2$  test for categorical variables and ANOVA for continuous variables.

Table 2  
Psychological and behavioural ratings.

	BPVC ( $N = 21$ )	Migraine ( $N = 20$ )	Normal controls ( $N = 19$ )	$P$	Pairwise contrasts <sup>f</sup>
CBCL Total <sup>a</sup>	$62.11 \pm 11.21$	$60.82 \pm 7.40$	$52.80 \pm 9.96$	0.026	BPVC > *NC; M > *NC
CBCL Intern. <sup>b</sup>	$70.33 \pm 8.77$	$66.47 \pm 6.33$	$58.27 \pm 7.94$	0.001	BPVC > ***NC; M > **NC
CBCL Extern. <sup>c</sup>	$60.78 \pm 10.15$	$60.47 \pm 7.40$	$52.60 \pm 10.32$	0.037	BPVC > *NC; M > *NC
CDI <sup>d</sup>	$9.56 \pm 5.45$	$13.74 \pm 7.85$	$7.00 \pm 4.96$	0.004	BPVC > *NC; M > **NC
MASC <sup>e</sup>	$53.44 \pm 6.54$	$60.05 \pm 7.28$	$46.57 \pm 6.74$	0.001	BPVC > *NC; M > ***NC

<sup>a</sup> Parent Child Behaviour Checklist Total Score (T-scores).

<sup>b</sup> Parent Child Behaviour Checklist Internalizing Score (T-scores).

<sup>c</sup> Parent Child Behaviour Checklist Externalizing Score (T-scores).

<sup>d</sup> Children's Depression Inventory (raw scores).

<sup>e</sup> Multidimensional Anxiety Scale for Children (T-scores).

<sup>f</sup> Pairwise contrasts were conducted only if the overall  $P$  was statistically significant (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ).

Table 3  
Number of subjects with scores in the pathological range.

	BPVC ( <i>N</i> = 21) N(%)	Migraine ( <i>N</i> = 20) N(%)	Normal controls ( <i>N</i> = 19) N(%)	$\chi^2$ <sup>a</sup>	<i>P</i> <sup>b</sup>	Pairwise contrasts <sup>c</sup>
CBCL Total	9 (43)	8 (40)	3 (16)	3.88	NS	
CBCL Intern.	18 (86)	12 (60)	4 (21)	17.12	<0.001	BPVC > **NC; M > *NC
CBCL Extern.	11 (52)	8 (40)	3 (16)	5.89	NS	
CDI	0 (0)	4 (20)	0 (0)	–	–	–
MASC	7 (33)	13 (65)	0 (0)	18.52	<0.001	BPVC > ***NC; M > ***NC

<sup>a</sup>  $\chi^2$  test with Yates' adjustment or Fisher's exact test as applicable.

<sup>b</sup> *P* for the three CBCL tests was Bonferroni corrected for multiple comparisons; NS, not statistically significant.

<sup>c</sup> Pairwise contrasts were conducted only if the overall *P* was statistically significant (\**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001).

(*P* < 0.001) than control children, none of which exhibited scores in the pathological range. Finally, the number of patients with pathological scores on the CBCL total, externalizing and CDI scales was too small for the rates to reach statistical significance (Table 3).

#### 4. Discussion

We found that indices of behavioural and emotional difficulties, anxiety, depressive and hyperactivity symptoms were elevated among clinically referred children suffering from BPVC or M compared with normal peers. Most patients, however, had behavioural and psychological scores within the normative, non-pathological range.

The association between psychiatric disorders, migraine and vertigo is difficult to clarify [16]. There are bidirectional associations of migraine with both major depression and panic disorders, with migraine being a risk factor for first-onset major depression and panic disorder and vice versa [17,18]. Dizziness is the second most common symptom of panic attacks after palpitations [19] and it can be a symptom of major depression as well. Indeed, patients with panic attack and anxiety have an increased rate of vestibular abnormalities [20], which may reflect an elevated risk of patients with vestibular disorders to develop an anxiety disorder [21].

Our results confirm a significant association between childhood migraine and the presence of symptoms of emotional and behavioural challenges, and are consistent with previous reports [22–24]. These symptoms have also been reported in other subtypes of headache, such as the Chronic Daily Headache Syndrome (CDH). A recent study investigating psychiatric comorbidity and suicide risk in 121 adolescents with chronic daily headache showed high comorbidity of psychiatric disorders (47%), mainly major depression (21%) and panic disorder (19%), and a high suicidal risk (21%) was also assessed [25]. The presence of anxiety and depression symptoms in different subtypes of migraine could be attributable to a common mechanism, so far still unknown, underlying the two conditions. Moreover, several neurotransmitters involved in the patho-

genesis of migraine (calcitonin-gene related peptide, serotonin, noradrenaline, dopamine), are also known to modulate the activity of vestibular neurones and could contribute to the pathogenesis of both migraine and BPVC [26,27].

Several studies have investigated the interaction between vestibular and psychiatric disorders, including potential links between the stress-related hormones and the inner ear fluid balance. Specifically, the inner ear fluid composition is the result of delicate homeostatic mechanisms that include the epithelial ion transport system, blood labyrinth barriers and a constant blood supply [28], it is likely that the increase of stress-related hormones, as a result of the abnormal activation of the hypothalamus–pituitary–adrenal axis that has been shown to occur in psychiatric disorders such as mood disorders and anxiety [29], might interfere with the inner ear blood flow and modify the inner ear fluid balance [30]. Besides, genetic defects of ion channels have been identified as the cause of various paroxysmal neurologic disorders. The findings of an abnormal voltage-gated calcium-channel gene in familial hemiplegic migraine and episodic ataxia type 2 [31] – both of which can have migraine and vertigo as prominent symptoms – have prompted the search for a susceptibility gene in the same region. So far, no such genetic defect could be identified [32].

We also found that indices for internalizing symptoms were higher among BPVC children than M children, while global and externalizing scores did not differ between the two groups.

It was hypothesized that a recurrent vestibular dysfunction causes the development of anxiety disorders. Various studies show that children and adolescents with chronic illness with recurrent episodes have an increased risk of emotional and behavioural problems. Indeed, a study assessing differences in psychological profile across children with different chronic illnesses showed that children with neurological chronic disorders had higher rate of emotional and behavioural problems than children with asthma and other chronic illnesses [33]. More representative research studies, conducted on children suffering from various types of neurological and non-neurological chronic conditions,

are needed to determine a pattern of behavioural and psychological symptoms that might be typical for each disease.

Another study showed that patients with Menière's disease and vestibular migraine, but not vestibular deficits, had the highest psychiatric comorbidity [34]. Thus the course of vertigo syndromes and the possibility of a pre-existing psychopathological personality should be considered as risk factors to develop a psychiatric disorder [34].

A high degree of psychiatric disorders has repeatedly been described among patients with vertigo syndromes and attributed to vestibular dysfunction. As a consequence, a structured psychological and psychometric testing and an interdisciplinary therapy should be provided in cases with vertigo [35]. Therefore, additional studies are needed to understand whether vertigo are an expression of psychological difficulties, such anxiety and depression, or, conversely, vertigo itself are a source of stress, which can cause the anxiety. The interface between BPVC and psychological symptoms remains unclear and the design of this study does not allow us to distinguish vertigo-induced psychological difficulties from pre-existing symptoms.

Taken together, these data suggest that children clinically referred for BPVC may have, as the group children referred for M, behavioural, emotional and temperamental difficulties. Although only a relatively small proportion of BPVC and M patients had scores that were actually in the psychopathological range based on normative references, the higher scores indicate the presence of significantly more subclinical behavioural and emotional difficulties than in normal controls. Moreover, higher ratings of behavioural and emotional symptoms, even if in most cases subclinical, are indicative of some kind of difficulties and increase the risk for developing psychopathology in the future [36]. Thus, the association between BPVC and indices of behavioural and psychological difficulties that were elevated compared with normal controls, but on average still in the normative range, suggests that vertigo and psychological symptoms may be related, thus underscoring the need for a broad and comprehensive approach to children referred for vertigo.

This study has a number of important limitations that must be taken into account in interpreting the data. Most notably, the sample size is relatively small and more appropriate for exploratory analyses than for definitive hypothesis testing. Furthermore, the sample was entirely derived from a single university clinic and may not reflect other academic and non-academic settings. As already pointed out, this was a clinically referred sample and not intended to be representative of children with BPVC in the general population. Finally, symptom scores were entirely derived from assessment scales filled out by the parents and self-

report questionnaires completed by the children themselves. While these rating scales have been shown to be valid instruments for screening children with psychiatric disorders, formal diagnoses of psychiatric disorders cannot be inferred. Since higher scores were found for BPVC children and their parents, based on parental report, it cannot be excluded that the informant's emotionality affected the ratings of the child, resulting in over-reporting of emotional and behavioural symptoms. Future studies should include data from informants other than the parents or the child, such as, for instance, teacher and clinician ratings.

In conclusion, future prospective research is needed to determine if behavioural and psychological problems anticipate the onset of BPVC and migraine, emerge concurrently with BPVC and migraine symptoms, or follow the manifestation of BPVC and migraine.

## References

- [1] Basser LS. Benign paroxysmal vertigo of childhood (a variety of vestibular neuronitis). *Brain* 1964;87:141–52.
- [2] Abu-Arafeh I, Russel G. Paroxysmal vertigo as a migraine equivalent in children: a population-based study. *Cephalalgia* 1995;15:22–5.
- [3] Headache classification subcommittee of the international headache society. International classification of headache disorders, vol. 24(Suppl. 1), 2nd ed. ICHD-II, *Cephalalgia*; 2004. p. 9–160.
- [4] Lanzi G, Balottin U, Fazzi E, Tagliasacchi M, Manfrin M, Mira M. Benign paroxysmal vertigo of childhood: a long-term follow-up. *Cephalalgia* 1994;14:458–60.
- [5] Brandt T. Vertigo in childhood. In: Brandt T, editor. *Vertigo: its multisensory syndromes*. London: Springer; 2003. p. 375–81.
- [6] Venable VL, Carlson CR, Wilson J. The role of anger and depression in recurrent headache. *Headache* 2001;41:21–30.
- [7] Holmes WF, MacGregor A. Migraine related disability. *Neurology* 2001;56:S13–9.
- [8] Mazzone L, Vitiello B, Incorpora G, Mazzone D. Behavioural and temperamental characteristics of children and adolescents suffering from primary headache. *Cephalalgia* 2006;26:194–201.
- [9] Monzani D, Casolari L, Guidetti G, Rigatelli M. Psychological distress and disability in patients with vertigo. *J Psychosom Res* 2001;50:319–23.
- [10] Jacob RG, Furman J, Durrant JD, Turner SM. Panic, agoraphobia, and vestibular dysfunction. *Am J Psychiatry* 1996;153:503–12.
- [11] Eager S, Luxon LM, Davies RA, Cohelho A, Ron MA. Psychiatric morbidity in patients with peripheral vestibular disorder: a clinical and neuro-otological study. *J Neurol Neurosurg Psychiatry* 1992;55:383–7.
- [12] Achenbach TM, Eofbrock C. Manual for the child behaviour checklist and revised child behavior profile. Burlington (VA): University of Vermont; 1983.
- [13] Achenbach TM. Manual for the CBCL/4–18 and profile. Burlington (VA): Department of Psychiatry, University of Vermont; 1991.
- [14] Kovacs M. The children's depression inventory: a self-rated depression scale of school-aged youngsters. Pittsburgh: University of Pittsburgh School of Medicine; 1982.
- [15] March JS. Multidimensional anxiety scale for children. Tonawanda (NY): Multi-Health System Inc.; 1997.
- [16] Neuhauser H, Lempert T. Vertigo and dizziness related to migraine: a diagnostic challenge. *Cephalalgia* 2004;24:83–91.

- [17] Breslau N, Schultz LR, Stewart WF, Lipton RB, Lucia VC, Welch KM. Headache and major depression: is the association specific to migraine? *Neurology* 2000;54:308–13.
- [18] Breslau N, Schultz LR, Stewart WF, Lipton R, Welch KMA. Headache types and panic disorder. Directionality and specificity. *Neurology* 2001;56:350–4.
- [19] Margraf J, Taylor B, Ehlers A, Roth WT, Agras WS. Panic attacks in the natural environment. *J Nerv Ment Dis* 1987;175:558–65.
- [20] Jacob RG, Furman JM, Durrant JD, Turner SM. Panic, agoraphobia, and vestibular dysfunction. *Am J Psychiatry* 1996;153:503–12.
- [21] Eagger S, Luxon LM, Davies RA, Coelho A, Ron MA. Psychiatric morbidity in patients with peripheral vestibular disorder. A clinical and neuro-otological study. *J Neurol Neurosurg Psychiatry* 1992;55:383–7.
- [22] Anttila P, Sourander A, Metsähonkala L, Aromaa M, Helenius H, Silanpää M. Psychiatric symptoms in children with primary headache. *J Am Acad Adolesc Psychiatry* 2004;43:412–9.
- [23] Andrasik F, Kabella E, Qinn S, Attanasio V, Blanchard EB, Rosenblum EL. Psychological functioning of children who have recurrent migraine. *Pain* 1988;34:43–52.
- [24] Cunningham SJ, McGrath PJ, Ferguson HB, Humphreys P, D'Astons J, Latter J, et al. Personality and behavioural characteristics in paediatric migraine. *Headache* 1987;27:16–20.
- [25] Wang SJ, Juang KD, Fuh JL, Lu SR. Psychiatric comorbidity and suicide risk in adolescents with chronic daily headache. *Neurology* 2007;68:1468–73.
- [26] Cass SP, Furman JM, Ankerstjerne K, Balaban C, Yetiser S, Furman J, et al. Migraine-related vestibulopathy. *Ann Otol Rhinol Laryngol* 1997;106:182–9.
- [27] De Waele C, Muhlethaler M, Vidal PP. Neurochemistry of the central vestibular pathways. *Brain Res Rev* 1995;20:24–46.
- [28] Sánchez-Fernández JM, Rivera-Pomar JM. A scanning electron microscopy study on human otoconia genesis. *Acta Otorhinolaryngol (Stockh)* 1984; 97:479–88.
- [29] Pariante CM, Lightman SL. The HPA axis in major depression: classical theories and new developments. *Trends Neurosci* 2008;31:464–8.
- [30] Fuchs E, Flugge G. Chronic social stress: effects on limbic brain structures. *Physiol Behav* 2003;79:417–27.
- [31] Ophoff RA, Terwindt GM, Vergouwe MN, van Eijk R, Oefner PJ, Hoffman SM, et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the CA2<sup>+</sup> channel gene CACNL1A4. *Cell* 1996;87:543–52.
- [32] Oh AK, Lee H, Jen JC, Corona S, Jacobson KM, Baloh RW. Familial benign recurrent vertigo. *Am J Med Genet* 2001;100:287–91.
- [33] Hysing M, Elgen I, Gillberg C, Lundervold AJ. Emotional and behavioural problems in subgroups of children with chronic illness: results from a large-scale population study. *Child Care Health Dev* 2009;35:527–33.
- [34] Best C, Eckhardt-Henn A, Diener G, Bense S, Breuer P, Dieterich M. Interaction of somatoform and vestibular disorders. *J Neurol Neurosurg Psychiatry* 2006;77:658–64.
- [35] Eckhardt-Henn A, Best C, Bense S, Breuer P, Diener G, Tschan R, et al. Psychiatric comorbidity in different organic vertigo syndromes. *J Neurol* 2008;255:420–8.
- [36] Roza SJ, Hofstra MB, van der Ende J, Verhulst FC. Stable prediction of mood and anxiety disorders based on behavioral and emotional problems in childhood: a 14-year follow-up during childhood, adolescence, and young adulthood. *Am J Psychiatry* 2003;160:2116–21.