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Are Neurodevelopmental Problems more Frequent in Children with Delayed Visual Maturation?

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Keywords: Delayed visual maturation; Poor visual contact; Temporary visual inattention; Neurodevelopmental problems.

Abbreviations: ADD: Attention Deficit Disorder; ADHD: Attention Deficit Hyperactivity Disorder; ASD: Autism Spectrum Disorder; CVI: Cortical Visual Impairment; DVM: Delayed Visual Maturation; HELLP: Hemolysis, Elevated Liver enzymes, Low Platelet; IUGR: Intrauterine Growth Retardation.

Abstract

Objective: The diagnosis of 'delayed visual maturation' (DVM) is the terminology preferably used in a normal developing baby with a transient visual deficit and normal ophthalmological findings. With longer follow-up more neurological problems emerge in this group of patients at follow-up.

Methods: We report a combined retrospective and prospective study of the ophthalmological and neurodevelopmental outcome in 65 babies with the initial diagnosis of DVM, who presented at the department of ophthalmology, University Hospitals Leuven between 2000 and 2015.

Results: Fourty-nine of the 65 patients (75%) showed a normal psychomotor development at follow-up. In 16/65 patients (25%) however, neurodevelopmental problems became evident. Two patients (3%) had learning problems, 3 patients (5%) were diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), 1 patient (2%) with Attention Deficit Disorder (ADD) and 10 patients (15%) with Autism Spectrum Disorder (ASD); 7 of them have severe psychomotor retardation.

Conclusion: Babies and children with the initial diagnosis of 'isolated DVM' should be carefully monitored by the pediatrician for neurodevelopmental problems.

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Introduction

Normally, a full-term baby shows visual fixation at birth or shortly thereafter. Visual contact is an important milestone in the normal development of a newborn, as it is the main sensory input for further cognitive and social development [1]. Absent, poor or delayed visual contact is a common problem in pediatric and pediatric ophthalmology clinics, and it can be caused by a structural eye problem or by a neurological problem. It is a challenge to make the right diagnosis and a thorough perinatal, family, ophthalmological and neurological history and a complete ophthalmological examination should be performed in every child presenting with this problem. An electrophysiological assessment with flash electroretinogram will rule out a retinal problem in a child with poor visual contact with or without nystagmus and with no obvious structural eye problem. Delayed Visual Maturation (DVM) is the terminology preferably used in a normal baby with normal ophthalmological findings with a transient visual deficit. This phenomenon has been described since many years [2,3]. A normal perinatal history does not exclude a neurological deficit at follow-up; so the diagnosis of DVM cannot be made solely on this basis and only after a long enough follow-up. With longer follow-up more neurological problems emerge in babies who initially presented with poor visual contact [4]. We here want to report the long term visual and neurological outcome in a large cohort of patients with the initial diagnosis of delayed visual maturation.

Methods

Between 2000 and 2015, three hundred and ten babies were referred to the department of ophthalmology, University Hospitals Leuven because of absent visual contact. A full family, pregnancy and delivery history and history for general disease including neurological problems was taken. All babies underwent a complete ophthalmological examination. Special attention was paid to the external aspect of the eyes, eye position, eye movements, pupils and pupillary reactions. All babies underwent a slitlamp examination before and after dilation with cyclopentolate 0.5% or tropicamide 0,5%; and an indirect fundoscopy and retinoscopy. Electrophysiological testing with flash electroretinogram and neurological assessment with brain imaging (ultrasonography or Magnetic Resonance Imaging (MRI)) were performed in a selected group of patients with respectively presumed retinal or neurological disease. Babies diagnosed with neurological disease including epilepsy and those with structural ophthalmic abnormalities and nystagmus explaining the poor visual contact, were excluded from this study.

After investigation, sixty-eight babies were withheld with the diagnosis of 'delayed visual maturation'. Ophthalmological and pediatric follow-up was planned in all of them. This study includes a retrospective and prospective analysis; and was approved by the Ethics Committee Research University Hospitals Leuven and is registered on ClinicalTrials.gov identifier NCT04251338. The retrospective study consisted of data extraction of ophthalmological and pediatric files. In addition, a prospective analysis was carried out in order to assess long term visual and neurological outcome in this patient population. Questionnaires were sent to the 65 patients and their parents after informed consent had been obtained (Table 1).

Table 1: List of questionnaires sent to patients and their parents.

1.	Does your child attend regular education? If not, which type of special school does he /she attend?
2.	Was there any need for physio- or speech therapy at any point and for what reason?
3.	Does your child wear (wore) glasses with/without patching? What is the refractive correction? Are there any other visual problems?
4.	Does (did) your child have problems with writing, reading and/or calculating?
5.	Are there any other health problems? Is your child on any medication?
6.	Are you aware of genetic diagnoses in your child?
7.	Does your child have a follow-up appointment scheduled and by whom?

Results

Between 2000 and 2015, 310 babies were examined because of absent visual contact at the department of ophthalmology, University Hospitals Leuven, between the corrected age of 3 and 6 months. Sixty-eight babies were withheld with the diagnosis of 'delayed visual maturation'. Sixty-seven of the 68 babies were referred: 44 of them were referred by the pediatrician, 21 patients by the ophthalmologist and 2 children by the general practitioner. For 1 patient the parents attended the clinic without referral. Fifty of the 68 patients were boys and 18 were girls. Perinatal history revealed preterm birth in two babies (at 30 and 36 weeks of gestation); they both presented at the corrected age of 3 months. All other babies were born at term. Pregnancy and delivery history revealed problems in 17 babies (Table 2). The first ophthalmological examination, apart from the visual problem, was perfectly normal in all sixty-eight patients; no ocular or neurological disease was diagnosed.

All patients showed visual improvement and normalisation of visual contact after 2 to 6 months of follow-up. Follow-up time in this patient population was between 3 months and 13 years with a mean follow-up of 35 months. In 37 babies the last ophthalmological follow-up was between the age of 3 and 6 months, in 9 patients between 7 and 12 months, in 9 patients between 1 and 6 years, and in 13 patients between 7 and 13 years.

Follow-up data of 65/68 patients were obtained based on the questionnaires sent to the parents (Table 1); 3 patients were lost for follow-up. Fourty-nine of the 65 patients showed a normal psychomotor development at follow-up; all of them follow regular education. Within this 'normal developing' group feeding problems during the first year of life were seen in two patients, severe gastro-oesophageal reflux in six babies and two of them were crybabies. One patient needed physiotherapy for writing problems which normalized at the age of 7 and one patient had poor hand-eye coordination during primary school. Also, within those 49 developmentally normal patients, four patients needed a hypermetropic correction, two were treated for amblyopia and three patients were diagnosed with oculomotor apraxia.

In 16/65 patients however, neurodevelopmental problems became evident at follow-up (Table 3). They were born between 35 and 41 weeks of gestational age, with a birthweight between 2365 gram and 3450 gram. Two patients developed learning problems, of whom one was diagnosed with dyslexia and the other with writing and calculating problems in association with low average intelligence. They both attend special education. Three patients were diagnosed with Attention Deficit Hyperactivity Disorder (ADHD), two of them having severe behavioral problems with need for medication. In one of them, there was a history of familial intellectual disability. One patient was diagnosed with Attention Deficit Disorder (ADD) and needed special education. In 10 patients the diagnosis of Autism Spectrum Disorder (ASD) was put forward with only one of them attending a regular school, however with special support. Nine of the ten patients needed special education; 7 of them have severe psychomotor retardation.

Three of those sixteen patients have a refractive correction, one with hypermetropic correction and amblyopia and two with astigmatic correction.

Table 2: Pregnancy and delivery complications in mother and child (N= mother or baby). IUGR: Intrauterine Growth Retardation, HELLP: Hemolysis, Elevated Liver enzymes, Low Platelet.

Pregnancy and delivery problems	N
Pregnancy diabetes	2
Preclampsia	1
HELPP syndrome	1
Prolonged labour	1
Caesarean section	8
- Breech or face location	3
- IUGR	1
- Poor labour	1
- Umbilical cord strangulation	1
- Dystocia	1
- Bradycardia	1
Bradycardia during labour	1
Hypoxia with quick recovery	1
Umbilical cord strangulation	1
Meconial aspiration	1

Table 3: Neurodevelopmental problems in children with DVM at follow-up. (N= children with initial diagnosis of DVM).

Associated neurological problems	N
ADHD	3
ADD	1
ASD	10
Learning problems	2

16/65 patients were diagnosed with associated neurological problems at follow-up: ADHD, Attention Deficit Hyperactivity Disorder, ADD, Attention Deficit Disorder, ASD, and Autism Spectrum Disorder

Discussion

The term 'Delayed Visual Maturation' (DVM) can be applied in children who initially appear to be blind and to those who show poor vision, have a normal ocular and systemic examination, and who subsequently develop a normal visual acuity at follow-up [5]. Beauvieux was the first author to describe DVM as a 'temporary visual inattention' in babies with an anomalous optic disc (la pseudoatrophie des nouveau-nés). Based on the presence or absence of associated abnormalities he considered two types of DVM, the first as an isolated entity, with full visual recovery by the age of 4 months and the second group with associated problems as strabismus, refractive errors and intellectual disability and with slow visual recovery [2]. Later, the combination of DVM with other ocular and systemic disorders were described and a wide variation of classifications was published with no consensus as to the etiology of this phenomenon [6-9].

The term 'Delayed visual maturation' suggests that the cause for visual inattention is rather a delay in the normal process in visual development, with perfect normalisation at follow-up. However, children with 'delayed visual maturation' have been found to develop other neurodevelopmental problems more often. True isolated DVM is rare, but the prevalence is unknown and the cause is not well understood. Coady et al discussed the diagnosis and the differential diagnosis of DVM and conclude that if an infant has a normal ophthalmological examination with no nystagmus and no eye motility disorders, DVM and CVI (cortical visual impairment) are the main differential diagnoses [10]. MRI (magnetic resonance imaging) and a thorough perinatal history can help to differentiate between both. In his Costenbader lecture, Hoyt states that the term 'delayed visual maturation' is misleading because there is no evidence that any primary visual system is delayed and also because it implies that these children only have a temporary visual problem, with no suffering other adverse consequences [11]. He suggests to return to the term 'temporary visual inattention' as this terminology does not preclude 'a perfect normal outcome'. Hoyt reported a retrospective study group of 98 patients with the diagnosis of delayed visual maturation from 1981 to 2001. Ophthalmological findings in this group were within the expected range. Strabismus was present in seven patients; five of them with amblyopia. One patient had keratoconus and four were highly myopic. In sharp contrast, there was a high prevalence of neurodevelopmental and educational problems in 57% of patients. Twenty-two (22%) patients had learning disabilities, 11 (11%) had attention deficit disorder, 9 (9%) patients developed seizures, 5 (5, 5%) had cerebral palsy with normal MRI findings, four (4%) had a diagnosis of autism and 5 (5%) patients had an an other psychiatric disorder. In our patient group of babies with 'delayed visual maturation', the great majority (75 %) of patients developed normally. Diagnosis of associated problems with DVM at follow-up in our study was based on a combination of analysis of retrospective patient file data together with the prospectively obtained data from questionnaires completed by the parents. In ten patients (15%) autism (ASD) was diagnosed, in 3 patients ADHD (5%), in 1 patient ADD (2%), and in 2 patients learning problems (3%). Remarkably in our study, 50 of the 68 patients were boys, 18 were girls. Neurodevelopmental problems were encountered in 25% at follow-up, which is less frequent than reported by Hoyt et al in his patient group but more frequent than described in other smaller samples [5]. Autism has been frequently mentioned in follow- up studies of children with DVM, however, no large samples have been described. So,

it is hard to report on the prevalence of autism within those 'DVM' patients [5]. Compared to the prevalence of ASD in a typical population, which amounts to about one in 120 children, the frequency of ASD in children with DVM seems much larger [12]. In our study group of children, the prevalence of autism was found to be significantly higher compared to the prevalence of autism in a typical population (chi-square test: (p=6, 46. 10^{-5}) [13]. On the other hand, in a systematic review, Canu et al described early behavioural indicators of autism spectrum disorder of which visual inattentiveness was found to be an important one. Deficient visual tracking, search and attention were all typically seen in siblings of children with ASD who later were diagnosed with the condition [14]. Similarly, in a recent overview of early markers, visual orienting was found to be a potential biomarker in children at high risk of ASD [13]. These atypical gaze patterns could be a sign of deficient processing of information mandatory for adequate social interaction.

Previous research has shown that new borns already have a good level of perceptual functioning. As such, any disturbance in this development might be a sign of an underlying brain disorder. Indeed, children with brain damage can be identified at an early stage just by examining their visual function [15]. Also, in children with an intellectual disability due to a genetic disorder, severe DVM has been described [16]. Therefore, one could argue to perform a brain MRI (Magnetic Resonance Imaging) in every baby with DVM who at follow-up develops neurodevelopmental problems.

Similar to Hoyt's findings, AD (H) D was also frequent in our sample (7%), compared to the general reported numbers [7,17]. As in ASD, studies in ADHD, performed mainly in young adults reveal significantly more problems with visual search [18]. There is converging evidence that ASD and ADHD have shared genetic underpinnings with common patterns of deficient sustained visual attention in infants.

Finally, in our sample, 3% of the children presented with learning disorders on follow-up. Among developmental problems, learning disorders are the most frequently reported with figures ranging between 3 and 9% depending on the type of learning disorders. Among children with DVM, learning disorders are probably not more frequent, but they could be an early sign for later developmental problems. In a previous paper, we reported our clinical observation that with a longer follow up, more neurological problems emerged in all sub classifications of babies presenting with poor visual contact. We concluded that a follow up till school age in a child presenting with "isolated delayed visual maturation" is advisable before considering the DVM as a "transient phenomenon in a normal baby" [4].

Limitations of the study include a small sample size and the retrospective recruitment of patients within a tertiary centre. Some patients presenting at a local community hospital could have been missed; although generally we experience a quick referral of babies with this problem by general practitioner and pediatrician because of the awareness of a variation of underlying problems.

In conclusion, our results show that the approach to the child with a so called DVM should be interdisciplinary. Children with an 'isolated DVM' should be carefully monitored by pediatricians; because neurodevelopmental problems are more frequent [10]. Even when, after a short follow up, visual function seems to recover, a continuous follow up by a pediatrician seems warranted.

This combined retrospective and prospective study on the long term follow-up of children with the initial diagnose of delayed visual maturation confirms the observation by Hoyt and is of value in determining the true incidence and pathogenesis of neurodevelopmental problems in children with DVM [5].

References

1. Wattam-Bell J, Birtles D, Nyström P, von Hofsten C, Rosander K, et al. Reorganization of Global Form and Motion Processing During Human Visual Development. Curr Biol. 2010; 20: 411-415.
2. Beauvieux J. La cécite apparente chez le nouveau-né: la pseudo-atrophie grise du nerf optique. Arch Ophthalmol. 1947; 7: 241-249.
3. Illingworth RS. Delayed visual maturation. Arch Dis Child. 1961; 36: 407- 409.
4. Casteels I, Spileers W, Missotten L, Casaer P. The baby with poor visual contact. Br J Ophthalmol. 1998; 82: 1228-1229.
5. Russell-Eggitt I, Harris CM, Kriss A. Delayed visual maturation: an update. Dev Med Child Neurol. 1998; 40: 130- 136.
6. Uemura Y, Oguschi Y, Katsumi O. Visual developmental delay. Ophthalmic Pediatr Genet. 1981; 1: 49-58.
7. Hoyt CS, Jastrzebski G, Marg E. Delayed visual maturation in infancy. Br J Ophthalmol. 1983; 67: 127-130.
8. Cole GF, Hungerford J, Jones RB. Delayed visual maturation. Arch Dis Child. 1984; 59: 107-110.
9. Fielder AR, Russell-Eggitt IR, Dodd, KL, Mellor DH. Delayed visual maturation. Trans Ophthalmol Soc UK. 1985; 104: 653-661.
10. Coady PA, Good WV. Delayed visual maturation: a visual inattention problem. Expert Rev Ophthalmol. 2011; 6: 421-430.
11. Hoyt CS. Costenbader lecture. Delayed visual maturation: the apparently blind infant. J AAPOS. 2004; 8: 215-219.
12. Lai MC, Lombardo MV, Baron-Cohen S. Autism. Lancet. 2014; 383: 896-910.
13. Zwaigenbaum L, Penner M. Autism spectrum disorder: advances in diagnosis and evaluation. BMJ. 2018; 361: k1674.
14. Canu D, Van der Paelt S, Canal-Bedia R, Posada M, Vanvuchelen M et al . Early non-social behavioural indicators of Autism Spectrum Disorder (ASD) in siblings at elevated likelihood for ASD: a systematic review. Eur Child Adolesc Psychiatry. 2020.
15. Rossi A, Gnesi M, Montomoli C, Chirico G, Malerba L et al. Neonatal Assessment Visual European Grid (NAVEG): Unveiling neurological risk. Infant Behav Dev. 2017; 49: 21-30.
16. Knight-Jones E, Knight S, Heussler H, Regan R, Flint J et al. Neurodevelopmental profile of a new dysmorphic syndrome associated with submicroscopic partial deletion of 1p36.3. Dev Med Child Neurol. 2000; 42: 201-206.
17. Sayal K, Prasad V, Daley D, Ford T, Coghill D. ADHD in children and young people: prevalence, care pathways, and service provision. Lancet Psychiatry. 2018; 5: 175-186.
18. Kim S, Chen S, Tannock R. Visual function and color vision in adults with Attention-Deficit/Hyperactivity Disorder. J Optom. 2014; 7: 22-36.